中山醫學大學公共衛生學系博士班

博士論文

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從家庭、生活習慣、工作相關因素、肌肉骨骼疼痛探討職業倦怠的原因及其與工作相關傷害的關係

To explore the causes of burnout and association with work-related injuries from family, living habits, work-related factors, and musculoskeletal pain

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中文摘要

引言

倦怠(Burnout) 於 1974 年由臨床心理學家 Herbert Freudenberger 首次描述。倦怠(burnout) 是一種身體的、情緒的及心理的耗竭狀態，它是由於長期參與對情緒有要求的工作環境所導致。Maslach Burnout Inventory (MBI)以及 Copenhagen Burnout Inventory (CBI)是最常被使用去評估倦怠的工具。倦怠在美國每年至少造成了近 46 億美元的損失並且影響了將近一半的醫生、護士及其他的醫療人員。此外，倦怠也會影響與病人相關的照護品質。過去的研究已經表明了倦怠與工作相關傷害(work-related injuries, WRIs)有關而且也會增加受傷的風險。本研究將建立職業倦怠的模型，以識別職業倦怠的危險因素，並探討職業倦怠與醫務人員的 WRI/銳器傷 (SI) 之間的關係。

方法與材料

本研究是在 2021 年以台灣台中一所醫學大學員工為調查基礎所做的一個觀察型及橫斷面研究，總共有 1633 人完成了包含北歐肌肉骨骼問卷(Nordic MS Questionnaire, NMQ)及哥本哈根倦怠問卷(Copenhagen burnout inventory, CBI)在內的調查，CBI 包含了個人倦怠(PB)、工作相關倦怠(WB)及客戶倦怠(CB)等三個尺度。在排除了資料漏失的問卷後共有 1250 份為有效問卷。統計分析採用了 t 檢定、 卡方(chi-square test)或費雪精確檢定、因子分析(factor analysis)、線性回歸及索博中介分析(Sobel test)。統計分析軟體是使用 SAS Enterprise Guide 6.1，統計顯著水準訂為 $P < 0.05$。

結果

研究表明了工作經驗(WE)、教育程度、已婚、為人父母、在假日積極與朋友及家人參與休閒活動(LAFF)、每週定期運動習慣(REW)、慢性病(CD)、一個月內

飲酒(AU)、每天睡眠時間短於 6 小時(SSLD)、加班(OT)、不定期輪班 (IRS)、不同的專業職域、常常頸部與肩膀疼痛(NBSP)、常常腳踝疼痛(BAP)以及常常雙膝疼痛(BKP)都與倦怠顯著相關。職業倦怠的性別差異與性別主導職業有關，女醫師的 WB 明顯高於男醫師。PB、WB、CB 與工作相關傷害(WRIs)及尖銳物扎傷(SIs)密切正相關。SSLD、OT、IRS、護士職業、NBSP 等也都與 WRIs/SIs 相關，其中 PB、WB 及 CB 也是這些關係的中介因子。CD、BKP 也與 WRIs/SIs 有顯著關係，PB 及 WB 是這些關係的中介因子。BAP 與 WRIs 緊密相關但與 SI 沒有顯著相關，PB 及 WB 為 BAP 與 WRIs 的中介因子。

結論

本研究通過三種職業倦怠量表和統計方法確定了職業倦怠發展的原因。 此外我們還確定很少與家人和朋友進行休閒活動，睡眠不足、AU、OT 和輪班、CD 和 MS 疼痛會增加倦怠程度，這將進一步增加 WRIs/SIs 的發生率。 因此，WRI 的預防計劃應包括職業倦怠的高危識別機制，及早發現工傷高危員工，進一步緩解職業倦怠症狀，有效避免工傷的發生。

關鍵字: 個人倦怠、工作相關倦怠、顧客倦怠、中介效應、工作相關傷害、尖銳物扎傷

Abstract

Introduction

Burnout was first described in 1974 by the clinical psychologist Herbert Freudenberger. Burnout is a state of physical, emotional, and mental exhaustion that results from long-term involvement in work situations that are emotionally demanding. Maslach Burnout Inventory (MBI) and Copenhagen Burnout Inventory (CBI) were most used instruments to assess burnout.

Burnout cause total losses of US$4.6 billion in the United States each year and affects approximately half of all nurses, physicians, and other clinicians. In addition, burnout also affects patient-related quality of care. The previous studies demonstrated burnout is related to work-related injuries (WRIs) and increase in the risk of injury. The present study would establish the relationship models of burnout to identify risk factors of burnout and explore the relationship between burnout and WRIs/sharps injuries (SIs) for medical worker.

Methods and materials

This is an observational and cross-sectional study which was based on members at a hospital affiliated with a medical university in Taichung, Taiwan, in 2021. 1633 individuals completed the questionnaires including Nordic Musculoskeletal Questionnaire (NMQ) and the Copenhagen burnout inventory (CBI). CBI included three burnout scales that are personal burnout (PB), work-related burnout (WB) and client burnout (CB), respectively. Among them, 1250 questionnaires were determined to be valid after exclusion for missing data. Statistical methods included t test, chi-square test or fisher exact test, factor analysis, linear regression, and Sobel test. Analysis was conducted using SAS Enterprise Guide 6.1 software, and significance was set at P

< 0.05.

Results

The present study demonstrated participants with master's degree or above or married or parenthood significantly reported low level for WB and CB than others and those with regular exercise every week (REW) reported low level for PB, WB and CB than others. Participants with chronic diseases (CD) or ever alcohol use (AU) or sleep duration per day less than 6 h (SSLD) or work overtime (OT) or shift work including irregular shift (IRS) and regular shift (RS) work or physicians/nurses reported high level for PB, WB and CB than others. Work experience (WE) and engaging in leisure activities with family or friends (LAFF) in vacation were negatively related to PB, WB and CB. Neck and both shoulders pain (NBSP) was positively related to PB, WB and CB. Both ankles pain (BAP) and both knees pain (BKP) was positively related to PB and WB. Sex difference of burnout was associated with sex--dominated occupations. Under low proportion of women than men in physician field, women physicians significantly reported high WB than man physicians. PB/WB/CB was closely relevant to WRIs/SIs and was mediation factors between WRIs/SIs and SSLD, or work OT, or IRS work, or Nurse, or NBSP. PB/WB mediated the relationship between WRIs/SIs and CD or BKP, too. However, PB/WB only mediated the relationship between WRIs and BAP.

Conclusion

The present study has determined the reasons of burnout development by three burnout scales and statistical methods. In addition, we also determined seldom engaging in leisure activity with family and friends, lack of sleep, AU, OT and shift, CD, and MS pain will increase burnout degree, which will further raise incidence of WRIs/SIs. Therefore, the prevention plans of WRIs should include the high-risk identification mechanism of burnout and early find the high-risk employee of work injuries to further relieve burnout symptoms and effectively avoid occurrence for injuries.

Keywords: Personnel Burnout, Work-Related Burnout, Client-related Burnout, Mediation Effect, Work-Related Injuries, Sharps Injuries.

Contents

Abbreviation

ADS, **AD**ministration Staff
AU, **A**lcohol **U**se
BAP: Both **A**nkles **P**ain
BKP: Both **K**nees **P**ain
CB: Client-related **B**urnout
CBI: **C**openhagen **B**urnout **I**nventory
CD: **C**hronic **D**iseases
DS: **D**ay **S**hift
IRS: **I**r**R**egular **S**hift
LAFF: **L**eisure **A**ctivities with **F**amily or **F**riends
MLR: **M**ultiple **L**inear **R**egression
MS: **M**usculo**S**keletal
NBSP: **N**eck and **B**oth **S**houlders **P**ain
NMQ: **N**ordic **M**usculoskeletal **Q**uestionnaire
OT: **O**ver**T**ime
PB: **P**ersonal **B**urnout
PTs: **P**rofessional and **T**echnical personnel
REW: **R**egular **E**xercise per **W**eek
RS: **R**egular **S**hift
SIs: **S**harps **I**njuries
SLD: **SL**eeping **D**uration
SSLD: **S**hort (less 6 hours per day) **SLD**
ULR: **U**nary **L**inear **R**egression
WB: **W**ork-related **B**urnout
WE: **W**ork **E**xperience
WRIs: **W**ork-**R**elated **I**njuries.

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1.Introduction

1.1 History, Measured Methods and Definition of Burnout

Burnout was first described in 1974 by the clinical psychologist Herbert Freudenberger, who found emotional depletion and accompanying psychosomatic symptoms among the clinic's volunteer staff. He called the phenomenon "burnout" which borrowed the term from drug-addict slang. In addition, he defined burnout as exhaustion resulting from "excessive demands on energy, strength, or resources" in the workplace, characterizing it by a set of symptoms including malaise, fatigue, frustration, cynicism, and inefficacy[1]. The social psychologist Christina Maslach and her colleagues came across the same term "burnout" in California when interviewing a variety of human services workers and developed a model of burnout consisting of three dimensions: emotional exhaustion, depersonalization, and a diminished sense of personal accomplishment[2]. In 1981, she proposed the Maslach Burnout Inventory (MBI), which consists of three subscales including emotional exhaustion, depersonalization, and a diminished sense of personal accomplishment to measure the extent of an individual's symptoms along each dimension[2]. The MBI remains the one of most used instruments to assess burnout to this day. However. MBI has been cast doubted on its temporal and sequential consistency[3] and has been pointed to difficulties when it is used outside of a human service setting[4]. In addition, the depersonalization and exhaustion subscale items are all negatively keyed, the personal accomplishment subscale items are all positively keyed. This structure has been criticized as leading to artificial factor solutions[5], and inflated intrascale correlations[6].

Considering exhaustion as the core of the burnout concept, researchers from

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Denmark developed the Copenhagen Burnout Inventory (CBI) [7] which is a new burnout questionnaire and allows measuring burnout in different settings (not just the service professions) and higher accuracy than MBI. In addition, CBI also overcomes the limitations of MBI and satisfies the need to measure burnout suitably[7]. CBI has extremely high internal reliability and low nonresponse rate, a questionnaire with three sub-dimensions. The three separate parts of the questionnaire including personal burnout (PB), work-related burnout (WB) and client burnout (WB) were designed to be applied in different domains. PB dimension is defined in the following way: "PB is the degree of physical and psychological fatigue and exhaustion experienced by the person", whose questionnaire were formulated in a way so that all human beings can answer them[7]. WB dimension was defined as "The degree of physical and psychological fatigue and exhaustion that is perceived by the person as related to his/her work", which assume that the respondent has paid work of some kind[7]. CB dimension was defined as "The degree of physical and psychological fatigue and exhaustion that is perceived by the person as related to his/her work with clients", whose questionnaire includes the term client (or a similar term such as patient, student, inmate, etc.)[7]. CBI possesses excellent psychometric properties and seems to be an more appropriate measure of burnout in populations of health professionals compared with Maslach Burnout Inventory[8]. Except to English version, CBI has been translated several language versions such as Malay[9], Greek[10], Chinese[11] [12], Portuguese[13], Korean[14], and Spanish[15] etc.

In May 2018, burnout was recognized as an "occupational phenomenon" in the *International Classification of Diseases, 11th Revision* (*ICD-11*) of the World Health Organization. Burnout is a state of physical, emotional, and mental exhaustion that results from long-term involvement in work situations that are emotionally

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demanding.[16] The specific definition of burnout in the *ICD-11* is "a syndrome conceptualized as resulting from chronic workplace stress that has not been successfully managed." A harmonized definition of occupational burnout approved by experts from 29 countries within the Network on the Coordination and Harmonization of European Occupational Cohorts, which demonstrated "In a worker, occupational burnout or occupational physical and emotional exhaustion state is an exhaustion due to prolonged exposure to work-related problems"[17].

1.2 Background

Burnout is responsible for high physician turnover and reduced clinical hours, which cause total losses of approximately US$4.6 billion in the United States each year[18]. Moreover, burnout affects approximately half of all nurses, physicians, and other clinicians[19]. A study about burnout and self-reported quality of health care in a nationwide sample of 1311 clinicians in surgery in Germany illustrated about 48.7% of the clinicians meet the criteria for burnout[20]. A systematic review and meta-analysis for 45,539 nurses across 49 countries suggested one-tenth of the nurses worldwide suffered high burnout symptoms[21]. Studies on resident physicians and nurses have indicated that most cases of burnout are personal or work related. Studies have noted that WB and PB occur in 30% and 50% of individuals with burnout, respectively[22]. Notably, burnout also affects patient-related quality of care[20].

1.3 Literature Review

According to numerous literatures, the influence ranges were very widely for burnout which included sex, family, living habits, workplace, and physical health etc. The present study will review literatures about burnout following above order step by step and further determined research objective.

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Sex difference for burnout

There were numerous reasons for the development of burnout according to previous studies. An early study suggested the sex of the employee is not a major factor in burnout [23]. However, studies in human service professionals have demonstrated higher burnout in women than in men [24], and that the burnout level is significantly higher among female resident physicians [22]. A previous study reported that women in male-dominated occupations experience higher psychological distress than women in female-dominated occupations [25].

Burnout and family factors

Marital state and parenthood also impact developing burnout and 57.26% health workers reported that they could minimize burnout by getting support from family[26]. Aimed women nurses study found family members and friend play a vital role for developing burnout which could predict 29% of the variance of burnout[27]. A cross-sectional study of 563 working doctors suggested disturbance of home and family life by work is related to high burnout.[28]

Burnout and living habits

Short sleep duration (SSLD) impacts several domains of psychological health such as stress and burnout. A study in USA for 32,749 people aged 18 years or older found association between sleep duration per day less than 6 hours and high self-reported stress[29]. A study for 2268 full-time nurses in 39 hospitals demonstrated nurses who slept less than 6 h per working day experienced higher risk for PB (odds ratio= 3.0, $P < 0.05$), WB (odds ratio= 3.4, $P < 0.05$), and CB (odds ratio= 2.0, $P < 0.05$) than those who slept more than 7 h per working day[30].

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Although some study think alcohol use (AU) is helpless to improve stress[31], many people adopted AU to alleviate stress which caused by working overtime,[32, 33] even drinking for pain-coping.[34] A multinational study of 2623 doctors, nurses and residents for exploring the associations between burnout and alcohol consumption, which suggested burnout is significantly positively associated with higher alcohol consumption[35].

Burnout and work-related factors

Work experience (WE) was also related to burnout. Some previous studies demonstrated lack of WE therapists faced with increasingly complex work conditions and demands, they may develop a sense of hopelessness in relation to their inability to reach their own idealistic expectations and standards, ultimately leading to disillusionment and burnout[36, 37].

In Taiwan, 97% and 83% of doctors in medical centers and regional hospitals, respectively, work overtime (OT)[38]. In addition, an OT work's study for 1560 full-time employees found less than 40 , between 40 and 60 , and more than 60 weekly work hours were significantly correlated with burnout in a dose-dependent manner (odds ratios for upper against lower tertile were 1.58 and 2.29, $P < 0.01$) [39].

Shift work is a common work schedule for hospital worker to support 24 hours service. In total, 684 nurses study demonstrated irregular shift (IRS) working schedule was also related to a significantly higher burnout syndrome[40]. The positive relationship between burnout and shift work was also observed in policemen. A burnout's study about 3140 police officers found irregular schedules and long shifts were associated with increased risk of overall burnout[41].

Burnout and physical health

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Physical health is also related to burnout, including musculoskeletal (MS) pain and chronic diseases (CD). Lower back (26.9%), shoulders (20.9%) and neck (20.6%) were most reported one of pain sites based on the point prevalence[42]. A study aimed to 4507 lawyers, physicians, nurses, teachers, church ministers, bus drivers, and information technology workers in Norway suggested burnout is related to MS pain[43]. In addition, a prospective study for 650 employed men and women found burnout symptoms were associated with a 1.67-fold increased risk of MS pain which illustrated burnout is a risk factor for the development of MS pain in seemingly healthy individuals[44].

A Finland's survey for 3368 employees aged 30–64 years suggested the prevalence of diseases was related to the severity of burnout; about half (54%) of those with no burnout had at least one physical illness compared to 63% of those with mild burnout and 71% of those with severe burnout[45]. In specific chronic diseases, burnout is an independent risk factor for future incidence of coronary heart disease[46] and type 2 diabetes[47], too.

Burnout and work-related injuries

There was evidence shown burnout is related to work-related injuries. In USA, 682 employees in cross-units of the administrative services completed survey of burnout found that workload and exhaustion was related to the incidence of injuries during the subsequent year[48]. A prospective cohort study for a total of 10,062 forest industry employees in Finnish demonstrated each one-unit increase in the burnout score was related to a 9% increase in the risk of injury[49] which shown burnout could be closely relevant to WRIs.

Sharps injuries (SIs), which frequently occur among health care workers, constitute a critical problem. SI occurrence has been reported to be associated with

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occupational factors such as WE[50], work hours[51], and shift work schedules[52] as well as demographic characteristics such as sex[53] and age[54]. Moreover, one article asserted that the experience of SIs was related to the mental health of health care workers[55].

1.4 Research Objectives

A systematic review and meta-analysis for physician demonstrated organizational and individual interventions are effective at reducing burnout[56]. Based on this, the study would model the relationship of burnout to explore the cause of burnout and affect the work-related injuries for medical worker. We believe these findings could suggest effective strategies for hospital to improve burnout and work-related injuries for medical worker in further.

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2. Materials and Methods

2.1 Source and Valid Samples for Participants

This manuscript is an observational and cross-sectional study, which was based on members at a hospital affiliated with a medical university in Taichung, Taiwan, in 2021 and had been approved with the expedited review by Institutional Review Board of the Chung Shan Medical University Hospital on Aug 25, 2021 (No: CS1-21108). Of the 2531 individuals to whom the questionnaires including Copenhagen Burnout Inventory (CBI) and Nordic Musculoskeletal Questionnaire (NMQ) were sent, 1633 (64.52%) completed the questionnaires. After exclusion for missing data, 1250 questionnaires (49.39%) were determined to be valid.

2.2 Questionnaires Design

The questionnaire separated several sections including the general basic demographic variables, family variables, living habits variables, work-related variables, physical health variables, variables for NMQ, CBI, and work-related injuries.

Demographic and family factors

The general basic demographic and living/work-related variables questionnaire included the participants' work experience, occupational category, height (cm), and body weight (kg). The education degree was also included in questionnaire that the response options are “Below high school”, “Bachelor”, “Master”, and “PhD”. Participants were asked whether he/she has married? The responses' options were "married" and “others”. In addition, participants also were asked whether he/she raises the children? The responses' options were “without child”, “one child”, “two children”, “three children”, and “over three children”. The questionnaire also surveys whether

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participants engage in **leisure activities with family or friends (LAFF)** in vacation time? The responses' options were "always", "often", "sometimes", "seldom", and "never" -are scored as 100, 75, 50, 25, and 0 points, respectively. Regarding **exercise frequency** in questionnaire, the responses' options were "at least once a day", "at least once a week", "at least once a month", "less than once a month", and "never", respectively.

Variables for living habits

The participants were also asked whether they drunk coffee frequently? The responses' options to the question were "never", "sometimes", "one cup a day", "two cups a day", "at least two cups a day" -are scored as 0, 25, 50, 75, and 100 points. In response to the question on smoking habit, option was "smoking in past month", "never" or "have quit smoking". Alcohol Use (AU) habit in past month also was included, the responses' options were "everyday", "occasionally", and "never". In response to the question on sleep duration (SLD) per day for participants, options were classified to "less 5 hours", "between 5 and 6 hours", "between 6 and 7 hours", "between 7 and 8 hours", and "above 8 hours".

Variables for work-related factors

Possible responses to the question on **overtime (OT)** work was the following: seldom, fewer than 45 h per month, 45–80 h per month, and more than 80 h per month. As for **work schedule**, the options given were **day shift (DS)** work, **night shift** work, **irregular shift (IRS)** work, and **regular shift (RS)** work.

Variables for physical health

On the questionnaire, the participants were asked whether they had a listed

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chronic disease (CD), with the selection of one or more diseases classified as a "yes" response.

Nordic MS Questionnaire (NMQ)

This study adopted the NMQ modified and translated by the Taiwan Institute of Occupational Safety and Health[57]. The NMQ, which is used in the investigation of the site and frequency of MS pain, was developed in a project funded by the Nordic Council of Ministers. The NMQ has acceptable reliability[57] and has been applied in a wide range of occupational groups, including nurses[58].

Items on the NMQ include questions on the presence of pain attributable to work-related factors in the preceding year and on the pain sites, the options for which were the:

neck (N1), left shoulder (N2), right shoulder (N3),
upper back (N4), waist or lower back (N5),
left elbow (N6), right elbow (N7), left wrist (N8), right wrist (N9),
left hip/thigh/buttock (N10), right hip/thigh/buttock (N11),
left knee (N12), right knee (N13),
left ankle (N14), and right ankle (N15).

If a participant answered "yes" to the question on the experience of work-related pain over the past year, they were instructed to indicate its frequency: every day, once a week, once a month, or once every half year, or at least once every half year -are scored as 100, 80, 60, 40, and 20 points, respectively.

In the present study, factor analysis was conducted on the NMQ results to

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determine the underlying variables that explained most of the questionnaire. According to the principle proposed by Hair *et al.*[59] factors that should be retained have feature vector values exceeding 1. Through varimax rotation, the standardized scoring coefficients constituted new factor loadings and were defined as new factors according to the corresponding significance of the factor loadings.

Variables for work-related and sharps injuries

The participants were also asked whether they had experienced **work-related injuries (WRIs)** or **sharps injuries (SIs)** in the past year. The response options to the two questions were "always", "often", "sometimes", "seldom", and "never"-are scored as 100, 75, 50, 25, and 0 points, respectively.

Variables for three burnout scales

Copenhagen burnout inventory (CBI) questionnaire

The present study used the Chinese version of CBI, which has proven to be a reliable and valid tool for assessment of burnout problems; [11, 12] thus, it was used to evaluate burnout in the present study. Regarding CB, client was defined as patient and had been denoted on questionnaire.

The first six items, which concern PB, are as follows:

C1: "How often do you feel tired?"

C2: "How often are you physically exhausted?"

C3: "How often are you emotionally exhausted?"

C4: "How often do you think 'I can't take it anymore'?"

C5: "How often do you feel worn out?"

C6: "How often do you feel weak and susceptible to illness?"

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Items 7–13, which concern WB, are as follows:

C7: "Is your work emotionally exhausting?"

C8: "Do you feel burnt out because of your work?"

C9: "Does your work frustrate you?"

C10: "Do you feel worn out at the end of the working day?"

C11: "Are you exhausted in the morning at the thought of another day at work?"

C12: "Do you feel that every working hour is tiring for you?"

C13: "Do you have enough energy for family and friends during leisure time?"

Items 14–19, which concern CB, are as follows:

C14:" Do you find it hard to work with clients?"

C15:" Does it drain your energy to work with clients?"

C16:" Do you find it frustrating to work with clients?"

C17:" Do you feel that you give more than you get back when you work with clients?"

C18:" Are you tired of working with clients?"

C19:" Do you sometimes wonder how long you will be able to continue working with clients?"

Regarding the calculated method for three burnout scales

The response options—"always", "often", "sometimes", "seldom", and "never/almost never"—are scored as 100, 75, 50, 25, and 0 points, respectively, except for item C13, which is inverse scored (ie, the responses are scored as 0, 25, 50, 75, and 100 points, respectively). Levels of PB, WB, and CB are represented by the mean of the total PB, WB, and CB scores (the sum of scores on items C1–C6, items C7–C13, and items C14-C19), respectively.

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2.3 Statistical Methods

The categorical variables were subjected to the chi-square test or Fisher exact test. Significance in the differences among the means of continuous variables was determined using the *t* test or one-way ANOVA. Multiple linear or logistic regression was conducted to control the interference of potential risk factors in the association between the independent variable (IV) and the dependent variable (DV)-specifically, to determine whether adjustments to variables significantly affected IV–DV associations.

Mediation analysis

Mediation effects were analyzed on the basis of the strategy proposed by Baron and Kenny [60], in which:

(1) the IV significantly affects the mediator (first-stage effect)

(2) the IV significantly affects the DV in the absence of the mediator

(3) the mediator has a significant unique effect on the DV (second-stage effect)

(4) the effect of the IV on the DV weakens upon addition of a mediator to the model (direct effect).

A mediation model suitable for the combination of categorical and continuous variables was developed by Iacobucci (2012) [61]; the formulas are as follows:

$$\hat{Y} = b_{01} + cX$$

$$\hat{M} = b_{02} + aX$$

$$\hat{Y} = b_{03} + c'X + bM$$

$$Z_a = \hat{a}/\widehat{S_a}$$

$$Z_b = \hat{b}/\widehat{S_b}$$

where X is an independent variable; $\hat{Y}$ is a dependent variable; $\hat{M}$ is the adjusted variable (i.e., the mediating factor); a is a logistic or linear regression coefficient of X against $\hat{M}$ when $\hat{M}$ and X are a DV and an IV, respectively; b is the logistic or linear regression coefficient of $\hat{M}$ against $\hat{Y}$; c is the logistic or linear regression coefficient of X against $\hat{Y}$; and c' is the logistic or linear regression coefficient of X against $\hat{Y}$ with $\hat{M}$ as the adjusting variable. The standard errors of a and b are represented by s_a and s_b, respectively.

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If $\hat{M}$ and $\hat{Y}$ are all continuous variables, the original formula of the Sobel test is applicable:

$$Z = \frac{a \times b}{\sqrt{b^2 {s_a}^2 + a^2 {s_b}^2}}$$

If $\hat{M}$ and $\hat{Y}$ are categorical variables or a combination of categorical and continuous variables, the original formula of the Sobel test is rederived into a new formula:

$$Z_{mediation}\,(Z_m) = \frac{\frac{a}{s_a} \times \frac{b}{s_b}}{\sqrt{{Z_a}^2 + {Z_b}^2 + 1}}$$

The results exceeding |1.96|, |2.57|, and |3.90| (for a two-tailed test) are significant at $\alpha = 0.05$, 0.01, and 0.0001, respectively.

Suppression effect

The traditional mediation effect is generally recognized as a, b, c, and c' in the same direction. However, a suppression effect would be present when the direct and mediated effects of an IV on a DV have opposite signs [62, 63], and the suppression variable would increase the predictive validity of another variable (or a set of variables) by its inclusion in a regression equation [62]. For clearly judging the suppression effect, a study examining statistical similarities among mediating, confounding, and suppression variables indicated that when $a \times b$ has the opposite sign to that of c', $a \times b$ is an estimate of the suppressor effect [63], whose statistical significance could be verified using the Sobel test.

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Analysis was performed using SAS Enterprise Guide 6.1 software (SAS Institute Inc., Cary, NC, USA), and significance was set at $P < 0.05$.

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3. Results and Discussion

3.1 Basic Variables Descriptions

Sex and family factors

As shown in Table 1, Women was much higher proportion (81.28%) than men for participants. The proportion of married was 48.96% for all participants. Participants without child reached 55.76%. The proportion of raising two children (24.56%) was highest among participants with raising the child. There were 84.24% participants for sometimes, or often, or always engaging in leisure activities with family or friends (LAFF) in vacation.

Living habits

The proportion of exercise frequency at least once a week was highest and was 46.80%, next to at less than once a month was 19.52%. The proportion was 17.84% for participants who never have drunk coffee in a month and was 40.56% for those who have drunk coffee at least one cup a day. The mean of drink coffee frequency score was 32.26±21.15. The proportion was 62.08% for participants who never reported alcohol use (AU) in a month and was 37.92% for those who reported AU occasionally or every day in a month. The proportion was highest for participants with sleep duration (SLD) per day between 6 and 7 h and reached 44.64%, next to those with SLD per day between 5 and 6 h and reached 34.80%. The proportion was only 3.68% for participants with SLD per day less 5 h.

Work-related factors

The mean of work experience (WE) is 10.88±9.51 years for all participants. The highest proportion of WE were in 1-5 years, which reaches 28.48%. The proportion was

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12.96% for WE less than 1 year and was over 40% for WE less than 5 years. For education degree, 78.80% participants had bachelor's degree. The proportion was 16.80% for above master's degree. The participants who seldom work overtime (OT) per month were 63.28% for all participants. The participants who work OT per month was less 45h, or between 45 and 80h, or more than 80h were 36.72% for all participants. The participants with day shift (DS) work were 63.12% for all participants, which is highest proportion, next to was regular shift (RS) work, irregular shift (IRS) work, and night shift work, which were 13.20%, 12.32%, and 11.36%, respectively.

Professional fields

The professional fields were classified to 13 fields, respectively. Among them, Nurses were largest group and were 40.96% for all participants, next to Administration (ADS) staff and others and were 31.84% for all participants. Physician including attending and resident were third big group and were 8.96% for all participants. The other professional fields were reclassified to professional and technical personnel (PTs) and were 18.24% for all participants.

Healthy factors

The proportion was 39.28% for participants with at least one listed chronic disease (CD).

Work-related and sharps injuries

The proportion was 48.24% for participants who never have experienced work-related injuries (WRIs) in past year. The proportion for participants who always/often/sometimes/ seldom experienced WRIs was 51.76%. The mean of WRIs score was 16.48±18.65. In past year, the proportion was 73.36% for participants who never experienced sharps injuries (SIs) and was 26.24% for those who ever have experience SIs. The mean of SIs score was 7.60±13.54.

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3.2 Factor Analysis for NMQ

Table 3 demonstrated Musculoskeletal (MS) pain's incidence in a year for both shoulders, neck, waist or lower back, upper back was 42.24%, 35.60%, 29.12%, and 16.72%, respectively. The mean score of frequency for neck, waist or lower back, right shoulders, left shoulder, and upper back was 26.21±37.41, 20.90±35.01, 16.96±33.42, 15.15±31.87, and 12.86±29.81, respectively. Because the eigenvalues of factors 1 and 2 exceeded 1, these factors were retained. Although the eigenvalue of factor 3 was lower than 1, it was retained for maximum explaining questionnaire. The factor loadings were converted into standardized scoring coefficients through varimax rotation. The relatively large factor loading values in bold for factors 1, 2, and 3 correspond to frequency score for neck and both shoulders pain (NBSP), both ankles pain (BAP), and both knees pain (BKP), respectively. The explained variation in FNBS pain, FBA pain, and FBK pain was 73.86%, 23.11%, and 8.67%, respectively.

3.3 Association Between Burnout and Surveyed Variables

Synthesized Table 2 and Table 4 that AU (c= 4.35, P < 0.001), SSLD (c= 8.11, P < 0.0001), work OT (c= 10.53, P < 0.0001), IRS work (c= 7.66, P < 0.0001), CD (c= 5.39, P < 0.0001), physician (c= 10.17, P < 0.0001), and NBSP (c= 8.27, P < 0.0001), BAP (c= 1.59, P < 0.01), and BKP (c= 2.29, P < 0.01) are risk factors of PB. The risk factors of WB included AU (c= 3.47, P < 0.01), SSLD (c= 6.52, P < 0.0001), work OT (c= 9.50, P < 0.0001), CD (c= 4.01, P < 0.0001), physician (c= 9.94, P < 0.0001), NBSP (c= 6.49, P < 0.0001), BAP (c= 1.49, P < 0.01), and BKP (c= 1.57, P < 0.01). AU (c= 3.68, P < 0.01), SSLD (c= 3.84, P < 0.01), work OT (c= 6.51, P < 0.0001), RS work (c=

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6.36, P < 0.0001), nurses (c= 7.74, P < 0.0001), and NBSP (c= 3.79, P < 0.0001) were risk factors of CB. It is worth mentioning that WE (c= -0.11, P < 0.05), LAFF (c= -0.13, P < 0.0001), and REW (c= -6.04, P < 0.0001) were protective factors of PB. WE (c= -0.19, P < 0.01), Master's degree or above (c= -2.56, P < 0.05), married (c= -3.70, P < 0.0001), parenthood (c= -4.19, P < 0.0001), LAFF (c= -0.16, P < 0.0001), and REW (c= -5.88, P < 0.0001) were protective factors of WB. WE (c=-0.14, P < 0.01), Master's degree or above (c= -3.45, P < 0.01), married (c= -3.63, P < 0.01), parenthood (c= -5.12, P < 0.0001), LAFF (c= -0.14, P < 0.0001), and REW (c= -5.43, P < 0.0001) were protective factors of CB. No matter PB, WB and CB were risk factors of WRIs and SIs. Therefore, these risk and protective factors would be added to models of MLR and mediation/suppression for burnout to further explore the reasons for developing or relieving burnout and whether burnout play a key role for WRIs and SIs.

3.4 Models of Burnout Established

3.4.1 Linear regression models

Table 5 showed the independent risk factor of PB/WB/CB in ULR and multiple linear regression (MLR) models. In MLR model, WE, parenthood, LAFF, SSLD, working OT, IRS work, RS work, Physician, Nurse, PTs, NBSP, BAP, and BKP were independent risk/protective factors for PB. WE, LAFF, SSLD, working OT, IRS work, RS work, Physician, Nurse, PTs, NBSP, BAP, and BKP were independent risk/protective factors for WB. Parenthood, LAFF, working OT, RS work, Physician, Nurse, PTs, and NBSP were independent risk/protective factors for CB.

3.4.2 First-stage effect of mediation and suppression model

Mediated/suppressed models would be established to explore possible causes for agent variables affect burnout. Table 6 shown WE was statistically associated with

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parenthood, LAFF, REW, suffering CD, ever AU, IRS work, DS work, and BKP, that met so-call "the first-stage effect". (1) Parenthood was statistically associated with LAFF, suffering CD, EAU, SSLD, working OT, IRS work, DS work, and NBSP, that met so-call "the first-stage effect", too; (2) Working OT was statistically associated with parenthood, LAFF, REW, ever AU, SSLD, IRS work, and NBSP, that met so-call "the first-stage effect", too; (3) IRS work was statistically associated with parenthood, REW, SSLD, working OT, and NBSP, that met so-call "the first-stage effect", too; (4) DS work was statistically associated with parenthood, LAFF, REW, ever AU, and SSLD, that met so-call "the first-stage effect", too; (5) Physician was statistically associated with REW, ever AU, SSLD, working OT, that met so-call "the first-stage effect", too; (6) Nurse was statistically associated with parenthood, LAFF, REW, working OT, IRS work, DS work, and NBSP, that met so-call "the first-stage effect", too. All variables satisfied the first-stage effect would be selected to as possible mediated factors to further test.

3.4.3 Direct / second-stage effect of mediation and suppression effect

Table 6-1, Table 6-2, and Table 6-3 shown the direct effect and the second-stage effect for PB/WB/CB. According to a, s_a, b, and s_b values in Table 6-1~6-3, P value was calculated by Z or $Z_{mediation}$ [61] formulates to test the statistic significant of mediated/suppressed effect. If b is a logistic regression coefficient, Z is a value calculated by $Z_{mediation}$ [61]. If b is a linear regression coefficient, Z is value calculated by the original formula of the Sobel test.

3.4.4 Simple mediated and suppressed models for burnout

Table 7 showed all models of mediation and suppression effect for PB/WB/CB. The sign in "()" represents the positive or negative relationship between independent

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variable (IV) and mediated factor. "m" represents mediated effect is exist in IV and dependent variable (DV) and "S" represents suppressed effect is exist in IV and DV. "NS" represents mediated or suppressed effect is not statistically significant in IV and DV. The presentation of Table 7 is advantage to descript full picture for mediation and suppression effect. Follow chapters will through these models to explore the relationship between risk factors and burnout.

Followed Sections will further explore the association between burnout and women/men, family, living habits, personal health, and workplace. In addition, study also will assess whether burnout will impact work-related injuries and will try by statistical methods to identify whether there are existed significant relationship between mental health and work-related injuries.

3.5 Sex Difference for Burnout

3.5.1 Association between sex and burnout

As shown in Table 2, there was not statistically significant sex difference for PB (c= 2.30, P > 0.05), WB (c= 1.88, P > 0.05) and CB (c= 1.53, P > 0.05) despite women reported high PB, WB, and CB level than men. As shown in Table 2-1, compared with man physicians, woman physicians were significantly relevant to WB (c= 8.42, P < 0.05). Table 2-2 presented there were not significant differences of PB (c= -3.06, P > 0.05), WB (c= -3.90, P > 0.05), and CB (c= -7.53, P > 0.05) between man's nurses and woman's nurses.

3.5.2 Discussion for sex difference of burnout

Was there different level for burnout between women and men? An early study suggested the sex of the employee is not a major factor in burnout [23]. Despite women

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reported high PB/WB/CB than men in Table 2, there was not significant difference in statistic. However, studies in human service professionals have demonstrated higher burnout in women than in men [24]. The studies seemed different results. However, another study reported that women in male-dominated occupations experience higher psychological distress than women in female-dominated occupations [25]. Table 2-1 presented that the proportion of women physician was only 34.82% which is a few groups. In addition, despite woman physicians common reported high level for PB (c= 7.69, P > 0.05), WB (c= 8.42, P < 0.05), and CB (c= 7.09, P > 0.05) than man physicians, only WB was statistically significant. Regarding nurses, the proportion of woman nurses was 96.48%, which instead is a very majority. As shown in Table 2, despite there were not statistically significant, woman nurses common reported low level of PB (c= -3.06, P > 0.05), WB (c= -3.99, P > 0.05) and CB (c= -7.53, P > 0.05) than man nurses. That could result from the samples of men were only 18 persons which were much less than women. Therefore, nurse occupation to be in female-dominated occupation.

Table 5-2 presented the effect of woman physicians for WB could be fully explained by WE (c= -0.18, P < 0.05), RS work (c= 15.86, P < 0.01), and NBSP (c= 6.50, P < 0.0001). Woman physicians had less WE, more RS work, and reported high NBSP than man physicians. According to a prospective cohort study of workers from industrial and service companies in Denmark illustrated a high level of distress predicted subsequent neck/shoulder pain[64] that might imply woman physicians could bear more distress than men physicians in present study. In addition, WE was low for woman physicians than man physicians (6.53±7.03 vs 10.28±11.06, P < 0.05) and woman physicians had more RS work compared with man physicians (odds ratio= 3.35, P <0.05, not in the Table). The difference for work experience and stress between women and men imply physician professional field could be a male-dominated

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occupation. The previous study also demonstrated even when women constitute a high proportion of the physician workforce, they may continue to be underrepresented in positions of leadership and prestige[65]. Based on this, we suggested sex difference of burnout was associated with sex--dominated occupations.

3.6 Family-Related Factors and Burnout

3.6.1-1 Association between burnout, marriage state, and parenthood

As shown in Table 2, participants who have married reported low WB (32.32±15.41 vs 36.02±16.96, $P < 0.0001$) and CB (28.00±16.28 vs 31.64±17.90, $P < 0.01$) than those who have not married. Compared to unmarried, married was a protective factor for WB ($c = -3.70$, $P < 0.0001$) and CB ($c = -3.63$, $P < 0.01$).

The raising one child, two children, three children, and over three children were reclassified to a new variable "**parenthood**" due to less sample number for every group. Table 2 shown participants who are parenthood sustained lower WB (31.87±15.74 vs 36.06±16.54, $P < 0.0001$) and CB (27.00±16.48 vs 32.12±17.46, $P < 0.0001$), respectively. Therefore, parenthood was a protective factor for WB and CB ($c = -4.19$, -5.12; both for $P < 0.0001$).

As shown in Table 5, the regression coefficient c for parenthood was -0.30 ($P > 0.05$) in ULR model for PB, however, which was 2.41 ($P < 0.05$) in MLR model for PB. That demonstrated that parenthood was an independent risk factor for PB instead of protective factor after adjusting other risk factors.

As shown in Table 5-1, after respectively adjusting LAFF, SSLD, OT, three shift work dummy variables, and three professional field dummy variables, the regression coefficient c (original value was -0.30) of "parenthood" were to 0.66, 0.17, 0.42, 1.08, and 0.97, their c symbol is all opposite before and after. Despite not statistical signification, these adjusting variables could interference the positive or negative

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relationship between parenthood itself and PB.

ULR and MLR models (Table 5) of parenthood to WB/CB shown that parenthood effect to WB/CB could be explained by other risk factors due to the c absolute value was reduced. The mediated/suppressed models in Table 7 could further explore relationship among WB/CB, parenthood and explain variable. As shown in Table 7, under mediation effect, the reasons of parenthood sustaining low level for WB/CB were positively engaging in LAFF (impacting WB and CB), less AU (impacting WB), less reporting SSLD (impacting WB), less work OT (impacting WB and CB), less IRS work (impacting WB), and more DS work (impacting WB and CB). However, under suppression effect, participants who were parenthood would easily suffer CD (impacting WB) and sustain high NBSP (impacting WB and CB) which would further increase level of WB or CB.

Parenthood was an important stage to life. However, the present study found that the process seems to impact differently development for PB/WB/CB, respectively. These results seem to imply the complex and different relationship among burnout, work, family, and children.

3.6.1-2 Discussion for the relationship between burnout and parenthood

A multidimensional conception of burnout implies a work-restricted scope is deconstructed. In addition, the burnout is a chronic, unresolvable stress according to the putative cause of burnout, which is not limited to work[66]. Personal burnout is the degree of physical and psychological fatigue and exhaustion experienced by the person[7]. In addition, parenthood is a both complex and stressful activity, which causes parents enduring exposure to chronic parenting stress and form so-call "parental burnout" and there was statistically significant and positive correlations between parental burnout and professional burnout in emotion exhaustion dimension [67]. These

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results imply parental burnout and personal burnout could have impacted each other or have common outcomes or damages for parents.

The present study also found parenthood was an independent risk factor for PB which obviously be related to worsen PB. This important find is echo each other with previous study's' results regarding parent burnout. In addition, parenthood was instead favorable to relieve CB. We reviewed the definition about CB, the definition follow: "The degree of physical and psychological fatigue and exhaustion that is perceived by the person as related to his/her work with clients". The source for fatigue and exhaustion come from client and do not come from child. Participants played two roles – parent and service provider. According to a theory of work-family enrichment[68] illustrated that participation in one role may enrich the quality of life in the other role. Therefore, the role for parent would enrich the role for service provider, that was consistent with our find in present study.

3.6.2-1 Association between leisure activities and burnout

The frequency for engaging in leisure activities with family or friends was scored by 100, 75, 50, 25, and 0 points and was defined as a new continuous variable – leisure activities with family or friends (LAFF). The result in Table 2 presented LAFF was negative relevant to PB ($c = -0.13$, $P < 0.0001$), WB ($c = -0.16$, $P < 0.0001$), and CB ($c = -0.14$, $P < 0.0001$). It was a protective factor for PB/WB/CB.

As shown in Table 5, LAFF was an independent protective factor for PB ($c = -0.06$, $P < 0.01$), WB ($c = -0.09$, $P < 0.0001$), and CB ($c = -0.08$, $P < 0.01$). This result represented that LAFF itself could play an important role for relieving burnout. The mediation/suppression models (Table 7) could help us to further understand the possible reasons for LAFF relieving burnout. As shown in Table 7, under mediation effect, negatively engaging in LAFF is one of causes for work OT worsening PB/WB/CB.

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Positively engaging in LAFF is one of causes for married/parenthood relieving WB/CB. According to mediation effect in Table 7, participants with DS work could positively engage in LAFF which could help participants to further relieve WB/CB. However, nurse reported highest CB level which could result from nurses negatively engaged in LAFF (Table 7, mediation effect).

3.6.2-2 Discussion for the relationship between burnout and leisure activities

The present study found positively engaging in LAFF had important function for relieving burnout from personal, work-related, and client. According to questionnaire's content, LAFF included two element, leisure activities and interaction/support with friends and family. Greater friend-based and colleague-based social support were both indirectly associated with lower personal and work-related burnout scores[69]. People feel more stress, participating in leisure activities will relieve the stress and cope with emotion, and moderately maintain physical and mental health [70, 71]. By providing leisure benefits, organizations can facilitate employees to better manage work pressure, boost employee morale, help to reduce role conflict, and enhance employee's satisfaction with life[72]. A study for flight attendants in Taiwan demonstrated leisure coping strategies can regulate job demands—burnout—health problems and when flight attendants suffer from burnout, they can adopt leisure coping strategies to improve their negative emotions.[73]. Therefore, the present study's evidence supported the opinion that leisure activities combined friendly interaction with friends and family would be an effective strategy for relieving burnout.

The previous study[74] also illustrated that assume a fixed amount of time and human energy, people participate in multiple roles inevitably will experience conflict and stress that detract from their quality of life. Based on this view, people would have not enough energy to engage in leisure activities with family or friends due to heavy

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work or overtime work. Table 6 shown working OT was negative related to LAFF (c= -4.26, P < 0.01). The present study's results support previous studies opinion that participants who work OT really reduce opportunity for engaging in LAFF.

Despite married individuals spent significantly less time for leisure activities than did single individuals[75], the various aspects of positive parental functioning were related to increases in overall leisure time and leisure time spent with spouse for both mothers and fathers[76]. In addition, the cohesion, adaptability, family functioning, and satisfaction with family life were positive related to family leisure[77]. Therefore, common leisure activity with family is key for positive parenthood role and satisfaction with family life. The mediated models in present study demonstrated participants who married or were parenthood would positive engage LAFF which is advantageous for relieving WB and CB. We revisit the questionnaire content about LAFF. The content was "Whether participants engage in leisure activities with family or friends in vacation time?". The premise of leisure activities is to spend the holiday with family or friends and not alone. Therefore, the LAFF should be as a family leisure instead of pure personal leisure activities. The successful family role (husband, or wife, or parents) for participants enhanced by family leisure activity that will further enhance the role of service provider that would relieve WB and CB at the same time. Above result was consistent with theory of work-family enrichment. [68].

The previous study illustrated the shift workers and dayworkers showed significant differences (p<0.0001) on almost leisure activity[78]. The present study also found participants who were DS work would positively engage in LAFF than others. Table 7 determined LAFF mediated the relationship between DS work and relieved WB/CB which represented positive family role also will enhance staff or service-provider roles.

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3.7 Living Habits and Burnout

3.7.1-1 Association between regular exercise and burnout

As shown in Table 1, the participants who exercise at least once a day or a week was 56.88% for all participants, therefore, both were reclassified as a new variable "regular exercise every week" (REW) and other frequency class was classified as a reference variable – "No weekly regular exercise". As shown in Table 2, REW was negative relevant to PB, WB, and CB (c =-6.04, -5.88 -5.43, respectively; for all P < 0.0001) and participants with REW sustained low PB (33.40±17.30 vs 39.44±18.59, P < 0.0001), WB (31.67±16.15, P < 0.0001), and CB (27.51±17.21 vs 32.95±16.74, P < 0.0001) than others. According to Table 7, REW was effectively protective factors. REW was a mediation factor which could effectively against the unfavorable effect of OT and IRS work for PB and WB according to mediation effect in Table 7. In addition, under mediation effect for REW, Participants who had day shift work easily kept REW which could effectively sustain low level for PB/WB/CB. Although physicians common reported high PB and WB, REW seemed to effectively relieve PB and WB due to suppression effect. However, the same effect was not observed on nurses.

3.7.1-2 Discussion for the relationship between burnout and regular exercise

Physiological changes by physical activity could reduce the persons' physiological sensitivity to chronic stress[79], that could lead to faster physical recovery after a stressful experienced situation and therefore to a reduction of the risk of burnout[80]. There is a positive dose-response relationship between physical activity and emotional well-being[81]. A systematic review study demonstrated physical activity seems to be effective in reducing burnout[82]. Healthy exercise habits are associated with lower risk of burnout[83].

The present study demonstrated participants who report REW experienced low

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PB, WB and CB. It is consistent with the previous studies regarding REW and burnout.

3.7.2-1 Association between coffee assumption / alcohol use and burnout

As shown in Table 2, participants also reported the habits for coffee consumption and alcohol use. The frequency for coffee consumption was not significantly related to PB ($c = 0.02$, $P > 0.05$), WB ($c = -0.02$, $P > 0.05$), and CB ($c = -0.02$, $P > 0.05$). Alcohol use (AU) every day or occasionally were combined to a new dummy variable – "ever AU". "Never AU" is as a reference variable. Participants who have reported ever AU experienced high PB (38.70±17.84 vs 34.35±18.08, $P < 0.0001$), WB (36.36±15.53 vs 32.89±16.65, $P < 0.01$), and CB (32.15±17.11 vs 28.46±17.14, $P < 0.01$) than others. Therefore, AU was a risk factor for PB ($c = 4.35$, $P < 0.0001$), WB ($c = 3.47$, $P < 0.01$), and CB ($c = 3.68$, $P < 0.01$). According to mediation effect of AU in Table 7, AU was one of reasons that physicians and participants who work OT sustained high level of PB/WB.

3.7.2-2 Discussion for the relationship between burnout and alcohol use

Whether alcohol actually reduces stress is debatable[31]. One study illustrated AU should increase stress and would be ineffective for negative reinforcement[84]. The burnout were strongly associated with alcohol abuse or dependence among American surgeons[85]. Burnout was significantly positively associated with higher AU among doctors, nurses and residents[35]. The present study found same results with the past studies that participants who report AU sustained higher level for PB, WB and CB.

3.7.3-1 Association between sleep duration per day and burnout

Because of subjects for sleep duration (SLD) less 5 hours per day being less, the ranks of SLD per day were reclassified to two ranks – SLD less 6 hours per day (SSLD)

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and SLD over 6 hours per day. SSLD was as a dummy variable and SLD over 6 hours was as a reference variable. SSLD was significantly associated with PB ($c = 8.11$, $P < 0.0001$), WB ($c = 6.52$, $P < 0.0001$), and CB ($c = 3.84$, $P < 0.01$) and participants who have reported SSLD experienced high PB (40.99±19.00 vs 32.88±16.80, $P < 0.0001$), WB (38.22±17.03 vs 31.70±15.34, $P < 0.0001$), and CB (32.22±17.80 vs 28.38±16.68, $P < 0.01$) than others.

As shown in Table 5, SSLD was associated with PB ($c = 8.11$, $P < 0.0001$), WB ($c = 6.52$, $P < 0.0001$), and CB ($c = 3.84$, $P < 0.01$). In MLR model, SSLD was an independent risk factor for PB ($c = 4.25$, $P < 0.0001$) and WB ($c = 2.78$, $P < 0.01$). However, the effect of SSLD impacting CB could been explained by other risk factors due to absolute value of c for SSLD reduced after adjusting variables.

The mediation/suppression models (Table 7) noted that sleep problem plays the important role between OT/IRS work and burnout. Specifically, SSLD mediated the relationship between OT and PB/WB/CB and the relationship between IRS work and PB/WB. In addition, Table 7 further illustrated that physicians often reported SSLD which was the one of reasons for physicians sustained high level for PB/WB. Parenthood reported low level for WB which was partially resulted from SSLD.

3.7.3-2 Discussion for the relationship between burnout and sleep duration

The past many studies had demonstrated the relationship for sleep, burnout, and OT work. Such as too little sleep (< 6 h) was as the main risk factor for burnout development[86] and burnout is also associated with disturbed sleep[87] . Some studies also illustrated the working OT is related to short or disturbed sleep, too[88, 89]. The present study has observed the same result that SSLD was significantly relevant to burnout. It is worth mentioning that the present study successfully through mediation/suppression models established in Table 7 to link the relationship for OT

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work, sleeping duration, and burnout that hint the lack of sleep could be a bridge for shift work and burnout. The past studies demonstrated that burnout was associated with shift or irregular shift work[40] [90]. In addition, the prevalence of insomnia, sleep deprivation depended significantly on the shift system[91]. The reason that shift work impacts sleep could be explained by "shift work sleep disorder". Shift work sleep disorder is a common yet under-recognized and undertreated sleep disorder caused by a sleep/wake pattern that is misaligned with the endogenous circadian rhythm[92]. A study for full-time nurses in 39 hospitals found compared with those slept longer than 7 h, nurse who slept less than 6 h per working day had higher risk for personal burnout, work-related burnout, and client-related burnout[30]. Despite our participants do not just include nurses and included doctors and other medical staff and adjusting variables were not exactly same, however, we found SSLD worsen PB, WB, and CB for participants still was obviously. Synthesize past literature and present research results, we could determine SSLD is a key that IRS work sustained high level for burnout.

3.8 Work-Related Factors and Burnout

3.8.1-1 Association between work experience / education degree and burnout

As shown in Table 2, work experience (WE) was as a continuous variable according to questionnaire. The present study demonstrated WE was significantly relevant to PB ($c = -0.11, P < 0.05$), WB ($c = -0.19, P < 0.01$), and CB ($c = -0.14, P < 0.01$). The education degrees were reclassified to "master's degree or above" and "university or below university degree" due to the participants with PhD or below high school were seldom (39 and 55 samples). Participants with university or below university degree reported high WB (34.64±16.28 vs 32.08±16.36, P < 0.05) and CB (30.44±17.44 vs 26.98±15.77, P < 0.01) than those with master's degree or above. Compared with University or below university degree, Master's degree or above was a

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protective factor for WB (c =-2.56, P < 0.05) and CB (c =-3.45, P < 0.01).

As shown in Table 5, WE (c= -0.14, P < 0.01; c= -0.11, P < 0.05) was an independent protective factor for PB/WB. The regression coefficient c for WE was -0.14 (P < 0.01) in ULR model for CB, but which was -0.01 (P > 0.05) in MLR model for CB. That represented WE effect to CB was explained by other risk factors. Table 7 further illustrated the relationships of burnout, risk factors, and WE by mediated/suppressed models. Burnout (including PB/WB/CB) would gradually be relieved followed increasing work experience, under mediation effect, these causes of relieving burnout included married (impacting WB/ CB), parenting (impacting WB/CB), REW (impacting PB/WB/CB), seldom AU (impacting PB/WB/CB), not often IRS work (impacting PB/WB/CB), often DS work (impacting PB/WB/CB). However, under suppression effect, CD and BKP would offset the advantage that WE relieve PB/WB. In addition, BKP also offset the advantage that WE relieve CB.

3.8.1-2 Discussion for the relationship between work experience and burnout

A study for a systematic review of the literature for burnout among psychotherapists make a description for the relationship in work experience and burnout. The original description follows "it is possible that as inexperienced psychotherapists are faced with increasingly complex work conditions and demands, they may develop a sense of hopelessness in relation to their inability to reach their own idealistic expectations and standards, ultimately leading to disillusionment, depersonalization, and burnout."[37] As shown in Table 5, increased WE was closely related to relieved PB (= -0.11, P < 0.05)/WB (c= -0.19, P < 0.01)/CB (c= -0.14, P < 0.01) and was independent protective factors for PB (c= -0.14, P < 0.01) and WB (c= -0.11, P < 0.05), respectively. The present research result for medical employee was consistent with above study for psychotherapists. According to Table 7, REW, seldom AU, not often

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IRS work, and often DS work were mediation factors of relationship between increased work experience and reduced level for burnout. Therefore, the present study could determine that burnout level could be improved for junior or young medical employee by effectively work-related interventions including avoided AU, often IRS work, and increased proportion of DS work. Due to BKP was suppression factor between WE and burnout, junior or young medical employee should specially note the problem for BKP.

3.8.2-1 Association between overtime / shift work and burnout

As shown in Table 1, the subjects who work overtime (OT) more than 80h and work OT between 45 and 80h per month were only 5 and 43 persons, respectively, therefore, which and subjects who work OT < 45h per month were combined to a new dummy variable – "work OT ", and the subjects who seldom work OT was as a reference variable. Table 2 demonstrated work OT was significantly relevant to PB (c = 10.53, P < 0.0001), WB (c = 9.50, P < 0.0001), and CB (c = 6.51, P < 0.0001). Participants who work OT reported high PB (42.67±18.25 vs 32.14±16.87, P < 0.0001), WB (40.22±15.69 vs 30.72±15.65, P < 0.0001), and CB (33.98±17.83 vs 27.47±16.39, P < 0.0001) than those who seldom work OT. There was significant difference of PB, WB, and CB level (for all P < 0.0001) among shift work schedules. Participants with irregular shift (IRS) work reported highest PB (41.78±18.08; c = 7.76, P < 0.0001) and WB (40.33±15.82; c = 8.48, P < 0.0001), however, participants with regular shift (RS) work report high CB (34.04±16.53; c = 6.37, P < 0.0001) than others. Participants with day shift (DS) work reported lowest PB, WB, and CB, therefore, the present study found DS work was a protective factor for burnout.

In MLR model (Table 5), work OT was independent risk factors of PB (c= 6.91, P < 0.0001), WB (c= 6.18, P < 0.0001), and CB (c= 3.95, P < 0.0001). According to mediation models in Table 7, the causes that participants who work OT sustained high

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level for burnout were negatively engaging in LAFF (impacting PB/WB/CB), without keeping REW (impacting PB/WB/CB), reporting AU (impacting PB/WB/CB), experiencing SSLD (impacting PB/WB/CB), IRS work (impacting PB/WB), and sustaining high NBSP (impacting PB/WB/CB).

In MLR model (Table 5), IRS work (c= 3.32, P < 0.05; c= 3.97, P < 0.01) and RS work (c=4.00, P < 0.01; c= 3.88, P < 0.01) were independent risk factors for PB and WB. However, RS work (c= 3.93, P < 0.01) was an independent risk factor of CB. The mediation/suppression models in Table 7 demonstrated reduced REW, SSLD, work OT, and high level for NBSP were one of causes that participant with IRS work sustained high level for PB and WB. Participants who were DS worker seem to report low burnout than others. According to mediation/suppression models in Table 7, positively engaging LAFF, keeping REW, and seldom experienced SSLD were one of causes that participants whose work's schedule were DS sustained low level for WB/CB than others.

3.8.2-2 Discussion for the relationship between overtime work and burnout

Many studies had determined work OT or long work hours were closely to burnout development. Nurses and clinicians working OT are more likely to experience burnout[93]. A study for 182 clinicians demonstrated participants working overtime reported significantly increased burnout.[94] A cross-sectional survey for 1560 full-time employees in Taiwan found long working hours (working over 40 hours per week) are correlated with burnout.[39] Furthermore, nurses working shifts of ten hours or longer were up to two and a half times more likely than nurses working shorter shifts to experience burnout[93]. The present study found participants who work OT sustained significantly high level of PB/WB/CB than those who seldom work OT. Our another a study (shown in Table 1, doi: 10.12998/wjcc.v9.i25.7391) at a hospital affiliated with a medical university in Taichung, Taiwan, in 2020, that also

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demonstrated participants who work OT more than 45 h per month reported highest level for PB and WB. There was a significant dose-response between OT work and PB or WB.

The past study demonstrated participants who experienced overtime and decreased interaction with family or friends were easily the deterioration of mental well-being[95]. In addition, participants whose working hours exceed standard recommendations are more likely to increase their alcohol use[96] for alleviating stress [32, 33]. From the view for medicine, the long working hours aggravates risk factors of atherosclerosis to cause circulatory system diseases, probably through its harmful effects to worsen workers' lifestyle, to cause lack of sleep[97]. The previous study also observed short sleep duration and overtime degree were in dose- response[98]. A survey of 2,617 registered nurses demonstrated extended work schedules were associated with musculoskeletal injury/disorders[99]. The shortening of regular workdays from over 7 hours to 6 hours may considerably reduce the prevalence of neck-shoulder pain[100]. The mediation models in Table 7 further found participants who work OT would negatively engage in LAFF, and often experienced SSLD, and didn't keep REW, and often reported short sleep duration, and measured high NBSP. That could cause burnout to worse for participants who work OT. These models were consistent with the previous research studies.

3.8.2-3 Discussion for the relationship between shift work and burnout

Shift work especially IRS work has been approved unfavorable to burnout by many studies. A cross-sectional study of health care workers demonstrated burnout was found more frequently among shift workers than those who did not work shifts[90]. Nurses who have irregular shift work schedule had high level of burnout syndrome than those have RS work schedule[40]. Other occupation also observed similar trend such

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as irregular schedules and increased night shifts were related to higher burnout risk in police[41]. Our another a study in 2020 (shown in Table 1, doi: 10.12998/wjcc.v9.i25.7391) also demonstrated participants with irregular shift work reported high level PB and WB than others. In addition, we found SSLD and NBSP play mediated role between IRS work and PB/WB. The previous Section has determined sleep problem is an important that IRS work impacts burnout. Another study for nurses also demonstrated adverse schedules are significantly related to MS disorders [99]. Above results represented IRS really impacts physical health for medical staff which could further damage mental health including burnout

3.8.3-1 Burnout difference among different professional fields

Table 2 illustrated there was significant difference of burnout among professional fields. Among them, the physician reported high PB (41.03±20.89; c = 10.17; both for $P < 0.0001$) and WB (39.38±18.45; c = 9.94; both for $P < 0.0001$) than others. Nurse reported high CB (33.48±17.62; c = 7.74; both for $P < 0.0001$) than others.

Table 7 demonstrated AU, SSLD, and OT were one of the causes of worsen PB/WB for physician. In addition, keep REW could against worsen PB/WB in physicians. As shown in Table 7, the causes that nurse's professional field easily worsen CB were that nurses didn't positive engage in LAFF, didn't keep REW, work OT, work IRS, and increased NBSP.

3.8.3-2 Discussion for the relationship between professional field and burnout

The present study found physicians' professional field itself still impacted burnout after adjusting the problems for LAFF, alcohol use, lack of sleep, work OT, shift work, MS pain. The past study also demonstrated the burnout is markedly higher amongst practicing physicians than individuals in other careers after adjusting for work

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hours and other factors[101, 102]. Attributed to reasons, work-related stressors[103, 104], excessive workloads[105], and work–home conflicts[106] were associated with burnout amongst physicians. Another, the present study had extra found different from past that physician's PB/WB sustained high level that also could be caused by AU, SSLD, and work OT. It is worth mentioning, according to mediation or suppression effect in Table 7, physicians common reported regular exercise weekly which also was often helpful to relieve PB/WB. Alcohol abuse and dependence is a significant problem in US surgeons, that were strongly associated with burnout [85]. According to the mediation model for burnout/AU/physicians in Table 7, physicians always adopted AU to face burnout, however, that is in vain.

One of the reasons for the high rate of insufficient sleep for physicians is the medical training culture. Trained physicians are instilled in the idea that sleep is optional, because they continue to work long shifts even when working hours are limited[107]. Table 7 demonstrated SSLD was mediation factor between physicians and PB/WB that also confirmed the medical training culture about physicians ignored sleep problem. It's this culture to cause high burnout for physicians than others.

Nurse professional field seem to bear high CB than other professional fields that would be explained by so-call "medical model"[108], whose statement is "people are not held responsible for either the origin of their problems or the solution to their problems". Patients are seen as ill or incapacitated, they are expected to accept their state as well as the diagnosis and the advice and treatment of an expert. It is clear that the expectation of investments of the patients are quite low, even lower than those of the professional. Therefore, nurses had a low level of burnout when interacting with a low investor patient and a high level of burnout when interacting with a high investor patient[109]. Corresponds to the practice of clinic, physicians have powerful professional authority to patient than nurses in ordinary people's minds, therefore, that

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could be the possible cause that nurses experienced high CB than physicians.

Generally speaking, the physical activity level of nurses is generally insufficient[110] and over 50% of nurses were insufficiently active[111] . A recent study of nurses found that many nurses did not participate in leisure-time physical activity[112]. Physical activity at work may not have the same positive impact on health as leisure activities[113]. Table 6 also demonstrated nurse is negative related to LAFF ($c = -4.51$, $P < 0.01$) and REW ($c = -0.82$, $P < 0.0001$) that is consistent with past studies. Table 7 further linked nurses, LAFF/REW, and burnout from client and determined LAFF/REW could improve burnout level for nurses.

Stressors had significant effect on increasing musculoskeletal discomforts of organs such as neck, shoulders and back for nurses [114]. Burnout impacting MS pain was similar, Mediation/suppression models in Table 7 found nurses often report high NBSP (neck or shoulders pain degree) which would cause burnout caused by client to sustain high level. Therefore, the strategy and resource of relieved MS pain for nurses is important for improvement of burnout.

3.9 Physical Health and Burnout

3.9.1-1 Association between chronic diseases / musculoskeletal pain and burnout

As shown in Table 2, participants who suffered chronic diseases (CD) sustained high level for PB (39.27±18.59 vs 33.89±17.48, $P < 0.0001$) and WB (36.64±16.84 vs 32.63±15.78, $P < 0.0001$). CD was a risk factor for PB and WB ($c = 5.39$ and 4.01; both for $P < 0.0001$).

As shown in Table 4, NBSP was positive relevant to PB ($c = 8.27$, $P < 0.0001$), WB ($c = 6.49$, $P < 0.0001$), and CB ($c = 3.79$, $P < 0.0001$). In addition, BAP was positive relevant to PB ($c = 1.59$, $P < 0.01$) and WB ($c = 1.49$, $P < 0.01$). There was positive relationship between BKP and PB ($c = 2.29$, $P < 0.01$) or WB ($c = 1.57$, $P < 0.01$).

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As shown in Table 5, NBSP (c= 6.86; c= 5.51, for both P < 0.0001), BAP (c= 1.38; c= 1.33, for both P < 0.01), and BKP (c= 1.68, P < 0.01; c= 1.16, P < 0.05) were independent risk factor for PB and WB. However, only NBSP (c= 3.23, P < 0.0001) was independent factor risk for CB. Apparently, NBSP obviously and directly sustained high burnout.

In addition, MS pain also played a bridge role (mediation effect) between risk factors and burnout. According to mediation effect in Table 7, NBSP was one of the reasons work OT sustained PB/WB/CB, IRS work sustained PB/WB, and nurses' professional field sustained CB. We had determined married/parenthood were closely relevant to WB and CB, however, married/parenthood also caused sustained high NBSP that will offset the relieved effect of married/parenthood for WB/CB. Increased WE was negative relevant to PB/WB/CB, however, BKP increased accompanied by work experience increased that also partially offset the protective effect of WE for burnout. Therefore, improvement plan of burnout should more note knee health problem for older senior staff.

3.9.1-2 Discussion for chronic diseases / musculoskeletal pain and burnout

The past study had demonstrated there are positive association between burnout and MS pain, too[43]. We also determined NBSP, BAP, and BKP were related to sustained PB and WB, too. It is worth mentioning that MS pain often play mediation factor for sustaining high burnout. According to MLR models in Table 5, NBSP was an independent risk factor for PB/WB/CB. In addition, we also determined the relationship of OT, NBSP and burnout by mediation models in Table 7 those participants who work OT often suffered pains from neck or both shoulders which would further worse burnout degree caused by overtime work. A prospective study in apparently healthy individuals demonstrated baseline levels of burnout predict the onset of regional

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neck/shoulder and/or low back pain and burnout symptoms were associated with a 1.67-fold increased risk of MS pain[115]. Another prospective study demonstrated nurses who reported low mood or stress at baseline were more likely to develop neck/shoulder pain later[116]. Despite the present study is a cross-sectional study, which through MLR and mediation models to confirm direct impacting and the mediation effect of neck and both shoulders pain for burnout. These results are highly consistent with the past study and determined the importance role for MS pain on burnout development.

The previous studies also found the shortening of regular workdays from over 7 hours to 6 hours may considerably reduce the prevalence of neck-shoulder pain[100]. Compared with fixed shift work, the irregular shift workers for male were associated with shoulders and neck pain and those for female were associated with neck pain[117]. The present study had further linked OT/IRS, burnout and MS pain by mediation models in Table 7 those participants who work OT or work IRS easily suffered neck or both shoulders pain which would cause burnout degree to further worse. Therefore, the relieve neck and both shoulders pain also should be included in improvement plan of burnout for medical employee.

The previous study demonstrated work experience significantly increases the morbidity of pain [118]. However, the present study determined WE was only relevant to BKP. Moreover, BKP suppressed the protective effect WE to PB/WB/CB.

Participants who were parenthood (c= 0.12, P < 0.05) and married (c= 0.15, P < 0.01) would increase NBSP. The relationship was similar to past study that domestic work and stress from overload further exacerbate musculoskeletal disorders because they interfere with the recovery process[119]. The present study has illustrated parenthood was closely related to worsen PB and NBSP that could imply closely relationship among both. According to Table 7, We determined NBSP will cause WB/CB for people married or parented to worsen by suppressed effect. This finds

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coincidentally with the previous study that poor psychological status may predict neck and shoulders pain [120, 121].

The three highest prevalence rates of MS pain for nurses were found for the neck, shoulders and back[122]. Compared with other professional fields, nurses' professional field was closely related to NBSP (Table 6, c= 0.15, P < 0.01).

3.10 Burnout and Work-Related / Sharps Injuries

3.10.1 Statistical test for association

Table 2 demonstrated work-related injuries (WRIs) was significantly relevant to PB (c = 0.38, P < 0.0001), WB (c = 0.33, P < 0.0001), and CB (c = 0.23, P < 0.0001). Similarly, Sharps injuries (SIs) was closely relevant to PB (c = 0.25, P < 0.0001), WB (c = 0.22, P < 0.0001), and CB (c = 0.20, P < 0.0001), too.

The past studies for administrative services[48] and forest industry employees[49] demonstrated burnout was relevant to risk of injuries. The present study demonstrated linear regression coefficients of 3 sub-burnout dimension to WRIs were between 0.23-0.38. Regarding forest industry employees, each one-unit increase in the burnout score was related to a 9% increase in the risk of injury[49] which is obviously lower than medical employee compared with the present study. In line with reports for nurses and the healthcare employees that there was association between burnout and SIs[123, 124].

The present research confirmed that there were positive dose-response between burnout and WRIs/SIs for medical employee.

3.10.2 Risk factors of work-related and sharps injuries

As shown in Table 8, CD (c= 4.64, P < 0.0001), AU (c= 3.10, P < 0.01), SSLD (c= 3.71, P < 0.01), work OT (c= 6.58, P < 0.0001), IRS work (c= 5.08, P < 0.0001),

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Nurse (c= 5.64, P < 0.0001), NBSP (c= 5.89, P < 0.0001), BAP (c= 1.78, P < 0.01), and BKP (c= 3.10, P < 0.0001) were risk factors of WRIs. In addition, As shown in Table 8, CD (c= 1.74, P < 0.05), AU (c= 3.22, P < 0.0001), SSLD (c= 2.52, P < 0.01), work OT (c= 4.43, P < 0.0001), IRS work (c= 4.03, P < 0.01), NBSP (c= 1.78, P < 0.01), and BKP (c= 1.02, P < 0.05) were risk factors for SIs. However, women (c= -2.22, P < 0.05) was a protective factor of SIs compared to men.

Followed Sections will further explore association between risk factors and burnout and model risk factors, burnout, and WRIs/SIs to assess.

3.10.3 Sex difference of WRIs and SIs

As shown in Table 8, there was not difference of WRIs between men and women (c= 0.69, P > 0.05). However, the sex difference was found in SIs. Women sustained low correlation for SIs than men (c= -2.22, P < 0.05).

A study indicated that male health workers were 10 times more likely to sustain an SI than were female health workers[125] that is consistent with the present study.

3.10.4 Role of burnout between chronic diseases and work-related / sharps injuries

The index for ability of explanation was "d", which is defined the reduced proportion for regression coefficient of risk factor to WRIs before and after adjusting variable. If the regression coefficient before adjusting variable was statistically significant and which was not statistically significant after adjusting variable, that was call "fully explanation the effect " and "d" value would not be calculated. If the regression coefficient before adjusting variable was not statistically significant, the ability of explanation did not be estimated. If the regression coefficient before adjusting variable was statistically significant and which was also statistically significant after

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adjusting variable, that was call "partial explanation the effect" and "d" value would be calculated. "d" value is higher, the ability of explanation is stronger.

As shown in Table 8-1, CD was significant related to WRIs (c= 4.64, P < 0.0001) that could be explained by PB, WB, and CB effect and ability of explanation is 45.69% (d=45.69), 36.42% (d=36.42), and 6.68% (d=6.68), respectively. Table 8-2 presented the mediation effect that PB (Z= 4.81, P < 0.0001) and WB (Z= 4.08, P < 0.0001) mediated the relationship between WRIs and CD.

As shown in Table 8-3, PB and WB effect could fully explain the relationship between CD and SIs. CB effect only could explain 8.62% (d= 8.62) the relationship between CD and SIs. Table 8-4 demonstrated PB (Z= 4.05, P < 0.0001) and WB (Z= 3.64, P < 0.01) were mediation factors for the relationship between CD and SIs.

Persons with chronic health conditions, such as chronic heart disease, diabetes, arthritis, blindness, or difficulty seeing, and asthma and depression confer an increased risk work-related injury[126, 127]. In addition, burnout is related to CD, such as coronary heart disease[46], cardiovascular disease[128], and type 2 diabetes[47]. The present study linked CD, burnout, and WRIs by mediated model (Table 7) which determined PB/WB is one of causes that CD sustained high WRIs. Therefore, physical diseases could impact people psychology which caused work-related injuries occurrence. The mental health promoting for medical worker suffering CD is demand immediate attention in preventing of work-related injuries.

As shown in Table 8 and Table 8-4, participants who suffer CD sustain high level for SIs (c= 1.74, P < 0.05) and PB/WB (c= 5.39/4.01, P < 0.0001). The mediated models further demonstrated PB/WB (Z= 4.05, P < 0.0001; Z= 3.64, P < 0.01) is a mediated factor. Therefore, this is an important find that mental health could play a positive and helpful role of SIs caused by physical disease.

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3.10.5 Role of burnout between alcohol use and work-related / sharps injuries

Table 8-1 demonstrated AU was significantly related to WRIs (c= 3.10, P < 0.01). The relationship could be fully explained by PB/WB effect and could be explained 31.29% proportion by CB effect. Table 8-2 presented PB (Z= 3.96, P < 0.0001), WB (Z= 3.54, P < 0.01), and CB (Z= 3.41, P < 0.01) mediated the relationship between WRIs and AU.

As shown in Table 8-3, PB, WB and CB could explain 17.39% (d= 17.39), 14.91% (d= 14.91), and 13.35% (d= 13.35) the relationship between SIs and AU, respectively. Table 8-4 demonstrated PB (Z= 3.49, P < 0.01), WB (Z= 3.24, P < 0.01), and CB (Z= 3.14, P < 0.01) mediated the relationship between AU and SIs.

There were a significant association between alcohol consumption and work-related injuries among farmers.[129, 130] The odds of injury also significantly increased with increased frequency of drinking per week[130]. However, for young U.S. workers in early research, common occupational injuries (excluding sprains and strains) may not be strongly associated with alcohol dependence[131]. Despite there were different results about the association for alcohol use and WRIs in past studies, the difference in the formal reported injuries and self-report injuries could be the one of main reasons. The present study adopted self-report questionnaire of WRIs that demonstrated AU were closely relevant to WRIs. The mediation models further determined the relationship among AU, burnout, and WRIs that burnout (PB/WB/CB) was one of causes that AU sustained high WRIs that seldom be mentioned in past studies.

As shown in Table 8-4, the mediation models further demonstrated burnout (PB/WB/CB) mediated the relationship between AU and SIs which determined AU is also through burnout to impact SIs. This is new evidence which is seldom mentioned in past studies. The find could extend new vision for SIs prevention of medical worker

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and highlight the importance for quitting alcohol use.

3.10.6 Role of burnout between short sleep duration and work-related / sharps injuries

Table 8-1 demonstrated, the relationship between short sleeping duration (SSLD) and WRIs (c= 3.71, P < 0.01) could be fully explained by PB/WB effect, and CB effect could only explain 27.22% (d=27.22). Table 2 showed PB (Z= 6.78, P < 0.0001), WB (Z= 6.30, P < 0.0001), and CB (Z= 3.51, P < 0.01) mediated the relationship between SSLD and WRIs.

As shown in Table 8-3, The relationship between SSLD and SIs could be fully explained by PB effect, however, WB and CB only explained 36.11% (d= 36.11) and 18.25% (d= 18.25). Table 8-4 demonstrated PB (Z= 5.01, P < 0.0001), WB (Z= 4.95, P < 0.0001), and CB (Z= 3.23, P < 0.01) mediated the relationship between SSLD and SIs.

People with sleep insufficiency often reported frequent physical distress, frequent mental distress, activity limitations, depressive symptoms, anxiety, and pain[132]. The determined relationship for burnout and SSLD in previous section has been fully discussion. The National Health Interview Survey for USA suggested the work-related injury risk significant increases with decreasing usual daily self-reported sleep hours[133]. In addition, A systematic literature search demonstrated workers with sleep problems had a 1.62 times higher risk of being injured than workers without sleep problems[134]. Therefore, the association between sleep and work injuries was confirmed. According to mediation model, we further determine burnout (PB/WB/CB) was one of reasons for SSLD sustained high WRIs, too.

Despite reduction in SLD increase the risk of occupational injury[135], the present study also confirmed SIs is same as occupational injury that sleep duration less

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than 6 h easier sustained high SIs (Table 8, c= 2.52, P < 0.01). Table 8-4 determined PB/WB/CB mediated the relationship between SSLD and SIs which represented burnout play an important role between SSLD and SIs. Among them, only PB fully mediated the relationship between SSLD and SIs that represented participants who experienced SIs that caused by SSLD commonly sustained higher PB level. This could be proofed by Table 8-4 that SSLD impacting PB (a= 8.11, P < 0.0001) was strong than WB (a= 6.52, P < 0.0001) and CB (a= 3.84, P < 0.01). The previous study also found same trend that PB were significantly associated with impaired sleep quality[136].

3.10.7 Role of burnout between overtime work and work-related / sharps injuries

Table 8-1 demonstrated the relationship between work OT and WRIs (c= 6.58, P < 0.0001) could be partially explained by PB, or WB, or CB and the ability of explanation were 61.55% (d=61.55), 59.12% (d=59.12), and 24.32% (d=24.32), respectively. Table 8-2 illustrated PB (Z= 8.08, P < 0.0001), WB (Z= 8.24, P < 0.0001), CB (Z= 5.16, P < 0.0001) mediated the relationship between WRIs and OT.

As shown in Table 8-3, PB, WB and CB could partially explain 27.09% (d= 27.09), 25.96% (d= 25.96) and 15.08% (d= 15.08) the relationship between work OT and SIs, respectively. Table 8-4 demonstrated PB (Z= 4.85, P < 0.0001), WB (Z= 5.19, P < 0.0001), and CB (Z= 4.22, P < 0.0001) mediated the relationship between work OT and SIs.

The working in jobs with OT schedules was associated with a 61% higher injury hazard rate compared to jobs without overtime[137]. The present study confirmed the adverse relations of working OT with WRIs (Table 8, c= 6.58, P < 0.0001), too. Further study in mediated models (Table 9) found participants who work OT sustained high WRIs due to worsen PB/WB/CB. It represented work OT could through mental factor such as burnout to impact WRIs. This is an important find and view to preventing WRIs

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in future.

In one study, an increase in weekly work hours increased the occurrence of SIs among nurses[138]. The present study further also confirmed work OT was significant relevant to SIs (Table 8, c= 4.43, P < 0.0001) for participants including physician, nurse, and other professional fields. It represented OT impacting WRIs could be a widely problem among different medical professional fields. PB/WB/CB only explained 15%~28% the relationship between work OT and SIs (Table 8-3) and partially mediated the relationship between work OT and SIs (Table 8-4, Z= 4.85, P < 0.0001; Z= 5.19, P < 0.0001; Z= 4.22, P < 0.0001). These results suggested that work OT affected SIs directly or indirectly (through an unknown path). Studies have noted that increased OT was significantly associated with impairments in attention, executive function[139], and stress response[140]. Whether OT work affects SI incidence through these factors remains to be determined. However, the present study confirmed burnout was one of causes that working OT sustained high SIs.

3.10.8 Role of burnout between irregular shift work and work-related / sharps injuries

Table 8-1 demonstrated the relationship between irregular shift (IRS) work and WRIs (c=4.35, P < 0.01) could be fully explained by PB and WB effect. CB could partially explain 26.90% (d=26.90). Table 8-2 demonstrated PB (Z= 4.05, P < 0.0001), WB (Z= 4.74, P < 0.0001), and CB (Z= 2.82, P < 0.01) mediated the relationship between WRIs and IRS work.

As shown in Table 8-3, The relationship between IRS work and SIs could be explained through PB, WB, and CB effect, their explained proportion were 23.26% (d= 23.26), 26.20% (d= 26.20%), and 14.17% (d= 14.17), respectively. Table 8-4 illustrated PB (Z= 3.55, P < 0.01), WB (Z= 4.08, P < 0.0001), and CB (Z= 2.66, P < 0.01) mediated

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the relationship between IRS work and SIs.

The working shifts repeated disruption of the circadian system[141], in addition, the misalignment of circadian rhythms of body functions is responsible of the so-called "jet lag" syndrome, which could cause feelings of fatigue, sleepiness, insomnia, digestive troubles, irritability, poorer mental agility, and reduced performance efficiency[142]. Above these damages from "jet lag" syndrome could be related to burnout such as feelings of fatigue and insomnia. Shift work had a statistically difference with work-related injuries compared to non-shift work[143, 144]. Therefore, there could be a connection among shift work, burnout, and WRIs. The present study found only IRS work was significantly relevant to WRIs among people who work shift work. RS work was not statistical significantly relevant to WRIs. Burnout including PB, WB, and CB paly mediation factors between IRS work and WRIs that demonstrated burnout obviously sustains high WRIs for participants who have IRS work. The present study confirmed mental health also impacts WRIs occurrence for people with IRS work.

In the same vein, studies have observed that working regular shifts exerted protective effects against SIs compared with irregular shift work [51, 54]. Consistent with results from other studies, Table 8 demonstrated irregular shift work was significantly associated with SIs (c= 4.03, P < 0.01), but regular shift work was not significant (c= 1.79, P > 0.05). Table 8-4 shown PB (Z= 3.55, P < 0.01), WB (Z= 4.08, P < 0.0001), and CB (Z= 2.66, P < 0.05) partially mediated the relationship between IRS work and SIs, indicating that burnout was also one of causes that IRS work sustains SIs; in others, irregular shifts may have exerted effects on SIs through other routes.

3.10.9 Role of burnout between nurses and work-related / sharps injuries

Table 8-1 shown the relationship between nurse and WRIs (c=4.84, P < 0.0001)

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that could be partially explained by PB, WB, and CB effect could partially explain 53.31% (d= 53.31), 53.10% (d= 53.10), and 32.23% (d= 32.23). Table 8-2 showed PB (Z= 5.72, P < 0.0001), WB (Z= 6.01, P < 0.0001), and CB (Z= 5.08, P < 0.0001) mediated the relationship between WRIs and nurses.

Table 8-3 demonstrated the relationship between nurse and SIs (c= 2.43, P < 0.01) that could be partially explained by PB, WB, and CB effect could partially explain 35.39% (d= 35.39), 34.98% (d= 34.98), and 29.63% (d= 29.63). Table 8-4 presented PB (Z= 4.55, P < 0.0001), WB (Z= 4.82, P < 0.0001), and CB (Z= 4.33, P < 0.0001) mediated the relationship between nurses and SIs.

Nurses' inclination to report injuries was higher in organizations with onsite health programs[145]. The Occupational Health Safety Network (OHSN) to collect detailed injury data included falls, patient handling, and workplace violence demonstrated nurse assistants and nurses had the highest injury rates of all occupations examined according to injuries occurring from January 1, 2012–September 30, 2014[146]. Our study found that nurses were significantly relevant to WRIs compared with other professional fields (Table 7, c= 5.64, P < 0.0001). The further analysis in Table 8-1 found the relationship between nurses and WRIs could be fully explained by PB and WB effect and be partially explained by CB effect (d= 34.93%). The mediation analysis (Table 8-2) also determined nurses' burnout really play a pivotal role in WRIs.

The reasons of SIs occurrence were complex and multiple such as younger than 25 years of age, irregular shift work, significant fatigue after work, and suboptimal staffing levels[147]. In addition, there were significant differences of SIs among departments[54]. The present study demonstrated nurses through burnout (PB/WB/CB) to increase SI occurrence that suggests that mental health factors also could cause SIs occurrence for nurses. Therefore, a full prevention plan of SIs should include improvement plans for mental health.

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3.10.10 Role of burnout between MS pain and work-related / sharps injuries

Table 8-1 demonstrated the relationship between NBSP and WRIs (c= 5.89, P < 0.0001) that could be explained by PB effect, WB effect, and CB effect, respectively. Among them, the ability of explanation for PB, WB, and CB was 47.54% (d= 47.54), 39.57% (d= 39.57), and 13.92% (d= 13.92), respectively. The relationship between BAP and WRIs (c= 1.78, P < 0.01) that could be explained by PB effect (35.96%), WB effect (35.96%), and CB effect (14.04%). The relationship between BKP and WRIs (c= 3.10, P < 0.0001) that could be explained by PB effect (29.03%), or WB effect (21.29%), or CB effect (10.00%). As shown in Table 8-2, PB (Z= 9.29, P < 0.0001), WB (Z= 9.06, P < 0.0001), and CB (Z= 5.17, P < 0.0001) mediated the relationship between WRIs and NBSP. PB (Z= 2.64, P < 0.01), WB (Z= 2.76, P < 0.01) mediated the relationship between WRIs and BAP. PB (Z= 3.36, P < 0.01) and WB (Z= 2.57, P < 0.01) mediated the relationship between WRIs and BKP.

Table 8-3 demonstrated PB could fully explain the relationship between FNBS pain and SIs. However, WB and CB could partially explain 46.63% (d= 46.63), and 23.60% (d= 23.60) the relationship between FNBS pain and SIs, respectively. In addition, PB, WB, and CB could fully explain the relationship between BKP and SIs. Table 8-4 presented PB (Z= 5.63, P < 0.0001), WB (Z= 4.13, P < 0.0001), and CB (Z= 4.39, P < 0.0001) mediated the relationship between FNBS and SIs. Among them, PB and WB fully mediated the relationship between SIs and NBSP. PB (Z= 3.11, P < 0.01) and WB (Z= 2.47, P < 0.05) fully mediated the relationship between BKP and SIs.

The previous Section had illustrated MS pain was associated with burnout. Table 8 demonstrated FNBS and FBK pain were significantly relevant to SIs (c= 1.78, P < 0.0001; c= 1.02, P < 0.05). Based on these results, we further explored the relationships among SIs, burnout, and MS pain. As shown in Table 8-4, PB fully mediated the

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relationship between SIs and NBSP or BKP ($Z= 5.63$, $P < 0.0001$; $Z= 3.11$, $P < 0.01$). WB partially mediated the relationship between SIs and NBSP or BKP ($Z= 4.13$, $P < 0.0001$; $Z= 2.47$, $P < 0.01$). In addition, CB partially mediated the relationship between SIs and NBSP ($Z= 4.39$, $P < 0.0001$). NBSP and BKP seem to be closely related to PB, WB, and CB when exploring the causes of SIs occurrence.

The past study also really found severity of pain in the neck / shoulder area were associated with an increased risk of burnout[148] and psychosocial elements of work were more involved in the persistence of the symptoms in the knee[149]. Our study confirms previous studies that neck/shoulders/knee pain sites seem to be associated with mental health and linked the relationship between SIs and neck/shoulders/knee pain through mediation effect of burnout. These results more extend views for preventing of SIs that SIs is not only an education and safety culture problem which also could be an outcome of complex influence process for physiology and psychology.

3.10.11 Difference of burnout effect for WRIs and SIs

SIs was one of WRIs, too. Is there difference for burnout impacting them? Table 9 showed that there was not obvious difference in both except to BAP. SIs for nurse was not significantly different compared with other professional fields. However, nurses reported high WRIs incidence than other professional fields. The regression coefficient for nurse to SIs was 1.75, but which is not statistically significant. It represented there could be obviously difference for SIs occurrence among different nurses' departments. In addition, the cause could come from education or train. The previous study also illustrated a continuous educational effort leads to a reduction of sharps injuries[150]. Despite pain site difference, MS pain did not only impact WRIs and impacted SIs, too. Therefore, burnout's mediated effect had consistent effect on occurrence for WRIs and SIs.

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4. Conclusion

4.1 Summary

The present study has determined the reasons of burnout development by three burnout scales and statistical methods. In addition, we also determined increased work-related (WRIs) and sharps injuries (SIs) will result from high burnout level caused by sex-dominated occupations, negative family role, lack of sleep and increased alcohol use (AU), overtime (OT) and shift, chronic diseases (CD), and musculoskeletal (MS) pain.

Sex difference for burnout

The proportion of man is high than women in physician's field, women physicians significantly experience high burnout from work than man physicians. The proportion of woman is markedly high than man in nurse's field. Despite of not statistically significant, men nurse common reported high burnout level than women nurses. The present study suggest sex difference of burnout was associated with sex-dominated occupations.

Family factors and burnout

People married or parenthood is relevant to lower work-related burnout (WB) and client burnout (CB). Parent's role itself instead be unfavorable factor to personal burnout (PB) after adjusting other risk factors. Positively engaging in leisure activity with family and friends (LAFF) is helpful for a successful role of parents which can further enhance the role quality of staff or service provider which could sustain lower level of WB and CB.

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Living habits and burnout

People who experience short sleep duration (SSLD) common reported high level for PB and WB than others. OT and irregular shift (IRS) work could lead to SSLD which will further sustain high level of PB and WB. The one of reasons for physicians reporting high PB and WB than others is lack of sleep. Sufficient sleep duration is one of causes that day shift (DS) staffs sustain low PB and WB level than others.

AU can't alleviate burnout which is instead an unfavorable factor of burnout. People who work OT adopt AU, which is unhelpful to relieve burnout and instead sustain high level for PB, WB and CB. In addition, AU is one of reasons for physicians reporting high PB and WB than others, too.

Work-related factors and burnout

Young or junior employee reported lower burnout level in three burnout scales. Increased work experience was negatively relevant to burnout. Compared with seldom OT, medical employee who work OT sustained high level of PB, WB, and CB. People who work shift sustain high PB, WB, and CB than others, but people who work IRS experienced higher PB and WB than those who work regular shift work. People who work OT or IRS could experience shorter sleep duration or often report neck or both shoulders pain that could further worse PB and WB.

DS was a protective factor of PB, WB, and CB whose protective effect resulted from people who have DS work could often engaged in leisure activity with family and friends or had habit of regular exercise weekly (REW), or sufficient sleep duration per day (> 6 h). There was difference of burnout among professional fields. Among them, the main reasons for physicians reporting high PB and WB than others were AU, OT, and lack of sleep. Physicians and nurses reported high CB than others. Physicians have powerful professional authority to patient than nurses that cause markedly high-level

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CB for nurses compared with physicians.

Physical health and burnout

Compared with people without CD, people who reported suffered at least one CD sustained significantly high burnout level in personal and work-related burnout scales. There was dose-response between MS pain (neck and both shoulders pain (NBSP), both ankle pain (BAP), and both knee pain (BKP)) and PB or WB, however, CB was only relevant to NBSP. The one of reasons for nurses sustained high CB was NBSP.

Work-related injuries and burnout

CD, AU, SSLD, work OT, IRS work, Nurses, MS pain including NBSP, BAP, and BKP are unfavorable factors for WRIs. Burnout is also closely relevant to these unfavorable factors and mediated bridges in these risk factors and WRIs, too. SIs is one of WRIs for medical staff common and there are almost same risk factors with WRIs except to Nurse professional field and BAP. In addition, burnout plays mediated roles in risk factors and SIs, too.

Finally, summarized present study's results with two Figures which is presented in Figure 1 and Figure 2 that are very valuable to preventing burnout and work-related injuries.

Suggestions

Burnout impacts every medical employee and causes hugely hidden loss for personal, family, and institutions. More important, it could harm patient safety. Regarding preventing burnout, medical institutions should encourage employees to increase parent-child interaction and positively engage in LAFF and keep regularly

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exercise after getting off work is necessary. The courses of quit alcohol use should be arranged to staff and avoid long workhours, OT, and irregular shift. In addition, the problem for physician on alcohol use, sleep, and overtime work should be paid attention much more. Based on the markedly relationship between burnout and MS pain, employee relief plans (including resource or education courses) of neck and both shoulders pain should be supplied.

Poor personal health, bad living habits damage mental health and further causes injuries in workplace. It represents the prevention plans for WRIs and SIs should include the work plan for the high-risk identification of burnout to early find the high-risk employee for work injuries and relieve burnout symptoms, and effectively reduce the incidence for WRIs/SIs.

4.2 Evaluation

The present study is 3rd research plan for SIs and burnout, which was approved by the Institutional Review Board of Chung Shan Medical University Hospital on Aug 25, 2021 (CSMUH NO: CS1-21108) whose license was on Appendix A. The first research was approved by the Institutional Review Board of Chung Shan Medical University Hospital on December 2, 2019 (CSMUH No: CS19137) whose license and published manuscript by journal were on Appendix B and doi: 10.12998/wjcc.v9.i35.10937. That was focus on the relationship among SIs, OT work and healthy body weight. The result indicated heavy overtime work (> 80 h/month) was associated with needle and SIs risk. Compared with the present study that work OT sustained high SIs, both results were consistent. However, we must indicate there is difference in SIs definition and sample collected come from different years. The definition of NSI in CS19137 was at least one NSI notified hospital by employee in past one year (yes/no), but the present study was SIs occurrence frequency (always

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/often / sometimes / seldom /never) in past year for employee's self-reported questionnaire. The self-reported advantage is the sample size could be extended, which could reduce the problem for employee not notifying hospital for sharps injuries. Therefore, we changed the method of collected data to self-report of participants.

The second research was approved by the Institutional Review Board of Chung Shan Medical University Hospital on July 22, 2020 (CSMUH No: CS19150) whose license and published manuscript by journal were on Appendix C and doi: 10.12998/wjcc.v9.i25.7391. The study had added new theme for burnout and more new variables. It demonstrated burnout was determined to contribute to SIs occurrence; specifically, burnout mediated the relationships of SIs with frequent MS pain, work OT, and IRS work. Despite second study's SIs is categorical variables and the present study's SIs is continuous variable which is occurrence frequency of SIs, both conclusions are still consistency. In addition, a new variable CB measured by client burnout scale was added to present study and could sufficiently illustrate the profile of burnout than previous studies. Same to PB and WB, CB mediated the relationships of SIs with frequent MS pain, work OT, and IRS work, too. The present study also found burnout was a mediated factor in SIs and CD, or AU, or SSLD. The second research CS19150 illustrated there was significant difference of burnout among WE rank, occupation groups, drinking in past month, sleep duration ranks, exercise per day, chronic disease, overtime work ranks, and work schedule classes that were consistent with the present study. Our study has special, interesting, and important new finds compared with research CS19150 that people who married or parenting or people engage in leisure activities with family or friends in vacation time sustained low level for work-related burnout.

The present study adopted mediation analysis could further find the reasons for burnout that different from other studies that only explored the association between risk

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factors and burnout by multiple linear regression method. Burnout is closely relevant to WRIs and SIs which is seldom mentioned in other studies. In addition, married and parenting was associated with burnout were interesting discoveries. Despite parenthood itself worsens PB, it instead relieves WB and CB. This leads to an interesting point that successful family live and successful career is not necessarily conflict in mental health that is a new find that is seldom mentioned in past studies, too. A find seldom mentioned in other studies that leisure activity with family and friends is favorable for relieved burnout and even reduces occurrence for WRIs/SIs.

Except to the association between neck/shoulders pain and burnout have been determined in present study, we also determined burnout is a key that workplace factors such as work OT and IRS work cause specific body pain.

4.3 Limitation

Despite we have got excellent and significantly results for the relationship between burnout and married or parenting, the duration of marriage and the child's age are lack. We don't determine whether long marriage relationship will cause burnout to sustain? Whether will parent's burnout gradually relieve by adulthood of children? These could cause interference to study's results. LAFF was as an index for successful family role seem to be insufficient which should seek more rigorous questionnaire to strengthen measured index. Although sex-dominated occupations could affect burnout development for men or women in our study and other studies, The proportion of men or women is as a basis of determined sex-dominated occupations is not sufficient in present study. Therefore, we should collect more variables (such as supervisor position or pressure of sexism) to determine this result. The types of occupational injuries are multiple which could have different occurrence reasons. The present study only adopted "work-related" to include these injuries. Therefore, we cannot know the relationship

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between other different injuries and burnout. Despite we have determined a specific injuries SIs are closely relevant to burnout, we cannot determine other injuries (such as falling, slipping and cutting) are relevant to burnout, too. The present study's data collected didn't include department information for participants, that could cause results to be interfered by work style or type. In addition, workload for participants and frequency of contact with patients or visitors are not be included in the present study which could not truly reflect busy condition for employee despite work OT had be included.

4.4 Future Work

This study was performed in the context of the coronavirus disease 2021 pandemic, which may have been more demanding on medical personnel than the non-pandemic period. Therefore, a similar study that assesses the regular work conditions and exposure of health care workers during the non-pandemic period should be replicated and compared with the result of the pandemic period. In addition, this study is a cross-section study that unable to capture the progress and changes of participants or environment. We have planned to conduct a series questionnaire about burnout for same group in the next few years which will be favorable for prospective cohort study. New questionnaires for social support, family relationship and parent burnout will be adopted by reviewing literatures and workplace bullying survey also will be added which will be contributed for further exploring new reasons for burnout. In Taiwan, care of elderly parents is a common problem that adult children must face. Therefore, raising elderly parents' options should be added in questionnaire to future explore the relationship between burnout and raising elderly parents.

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6. Tables

Table 1 The basic variables descriptions for all 1250 participants

Basic variables	subjects	proportion %
Sex		
Women	1016	81.28
Men	234	18.72
Married state		
Married	612	48.96
others	638	51.04
Raising the child		
without child	697	55.76
one child	185	14.80
two children	307	24.56
three children	57	4.56
over three children	4	0.32
Leisure activities with family or friends		
always	78	6.24
often	383	30.64
sometimes	592	47.36
seldom	186	14.88
never	11	0.88
Exercise frequency		
At least once a day	126	10.08
At least once a week	585	46.80
At least once a month	226	18.08
Less than once a month	244	19.52
Never	69	5.52
Frequency for drink coffee		
at least two cups a day (100 points)	16	1.28
two cups a day (75 points)	47	3.76
one cup a day (50 points)	444	35.52
sometimes (25 points)	520	41.60
never (0 points)	223	17.84
Alcohol use in a month		
everyday	4	0.32
occasionally	470	37.60
never	776	62.08
Sleep duration per day		
less 5 hours	46	3.68
between 5 and 6 hours	435	34.80
between 6 and 7 hours	558	44.64
between 7 and 8 hours	180	14.40
above 8 hours	31	2.48
Work experience (10.88±9.51)		
less 1 years	162	12.96
1-5 years	356	28.48
5-10 years	169	13.52
10-15 years	199	15.92
15-20 years	125	10.00
20-25 years	142	11.36
25-30 years	41	3.28
over 30 years	56	4.48
Education degree		
Below high school	55	4.40
Bachelor	985	78.80
Master	171	13.68
PhD	39	3.12
Work OT per month		
> 80 h	5	0.40
45-80 h	43	3.44
< 45 h	411	32.88
seldom	791	63.28
Shift work schedule		
Irregular shift work	154	12.32
regular shift work	165	13.20
Night shift work	142	11.36
Day shift work	789	63.12
Professional field		
Attending physician	57	4.56
Resident physician	55	4.40
Nurses	512	40.96
Respiratory therapist	12	0.96

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Physical therapist	35	2.8
Social worker	10	0.8
Nurse Practitioner	50	4.00
Nutritionist	12	0.96
Occupational Therapist	30	2.40
Medical Radiation Technologist	39	3.12
Medical technologist	37	2.96
Psychologist	3	0.24
Administration Staff and others	398	31.84
With chronic disease		
Yes	491	39.28
No	759	60.72
Experienced work-related injuries in a year		
always (100 points)	4	0.32
often (75 points)	18	1.44
sometimes (50 points)	129	10.32
seldom (25 points)	496	39.68
never (0 points)	603	48.24
Experienced sharps injuries in a year		
always (100 points)	0	0.00
often (75 points)	4	0.32
sometimes (50 points)	39	3.12
seldom (25 points)	290	23.20
never (0 points)	917	73.36

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Table 2 The association between burnout and surveyed variables

		PB		WB		CB	
Surveyed variables	subjects	mean ±SD	c	mean ±SD	c	mean ±SD	c
Sex							
Women	1016	36.43±17.84	2.30	34.56±16.33	1.88	30.14±16.96	1.53
Men	234	34.14±19.16	1.00	32.68±16.22	1.00	28.62±18.28	1.00
Marriage state				***		**	
Married	612	35.80±17.64	-0.40	32.32±15.41	-3.70***	28.00±16.28	-3.63**
Unmarried	638	36.20±18.56	1.00	36.02±16.96	1.00	31.64±17.90	1.00
Raising the child				***		***	
Parenthood	552	35.84±18.42	-0.30	31.87±15.74	-4.19***	27.00±16.48	-5.12***
Not parenthood	697	36.14±17.87	1.00	36.06±16.54	1.00	32.12±17.46	1.00
Leisure activities with family or friends							
LAFF	1250	-	-0.13***	-	-0.16***	-	-0.14***
Exercise frequency		***		***		***	
Regular exercise every week	711	33.40±17.30	-6.04***	31.67±16.15	-5.88***	27.51±17.21	-5.43***
No weekly regular exercise[7]	539	39.44±18.59	1.00	37.55±15.95	1.00	32.95±16.74	1.00
The frequency for coffee consumption							
Coffee consumption score	1250		0.02		-0.02		-0.02

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Alcohol use habit in a month		***		**		**	
Ever AU	474	38.70±17.84	4.35***	36.36±15.53	3.47**	32.15±17.11	3.68**
Never alcohol use	776	34.35±18.08	1.00	32.89±16.65	1.00	28.46±17.14	1.00
Sleeping duration per day		***		***		**	
SLD < 6h (SSLD)	481	40.99±19.00	8.11***	38.22±17.03	6.52***	32.22±17.80	3.84**
SLD > 6h	769	32.88±16.80	1.00	31.70±15.34	1.00	28.38±16.68	1.00
Work experience							
WE (years)	1250	-	-0.11*	-	-0.19**	-	-0.14**
Education degree				*		**	
Master's degree or above	210	36.09±18.36	0.11	32.08±16.36	-2.56*	26.98±15.77	-3.45**
University or below university degree	1040	35.99±18.07	1.00	34.64±16.28	1.00	30.44±17.44	1.00
Experiencing overtime work per month		***		***		***	
Work OT	459	42.67±18.25	10.53***	40.22±15.69	9.50***	33.98±17.83	6.51***
seldom work OT	791	32.14±16.87	1.00	30.72±15.65	1.00	27.47±16.39	1.00
Work schedule		***		***		***	
IRS work	154	41.78±18.08	7.76***	40.33±15.82	8.48***	33.71±18.50	6.05***
RS work	165	39.22±19.55	5.20**	38.01±17.26	6.16***	34.04±16.53	6.37***
Night shift	142	37.06±18.85	3.05	36.22±16.21	4.36**	32.98±19.12	5.31**
DS work	789	34.02±17.33	1.00	31.85±15.74	1.00	27.67±16.36	1.00
Professional field		***		***		***	
physician	112	41.03±20.89	10.17***	39.38±18.45	9.94***	31.81±18.91	6.07**
Nurses	512	39.88±17.85	9.01***	37.82±16.05	8.38***	33.48±17.62	7.74***
PTs	228	33.81±17.11	2.95*	31.86±15.41	2.42	27.94±16.30	2.20
Ads	398	30.86±16.63	1.00	29.44±15.00	1.00	25.74±15.61	1.00
Suffering CD		***		***			
Yes	491	39.27±18.59	5.39***	36.64±16.84	4.01***	30.57±18.30	1.17
No	759	33.89±17.48	1.00	32.63±15.78	1.00	29.40±16.47	1.00
Experienced work-related injuries							
WRIs score	1250	-	0.38***	-	0.33***	-	0.23***
Experienced sharps injuries							
SIs score	1250	-	0.25***	-	0.22***	-	0.20***

*, P < 0.05; **, P < 0.01; ***, P < 0.0001; PB, personal burnout; WB, work-related; CB, client burnout; c, the linear regression coefficient of independent variable; AU, alcohol use; OT, overtime; IRS, irregular shift work; RS, regular shift; DS, day shift; c, the linear regression coefficient of surveyed variable against burnout.

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Table 2-1 Sex difference of burnout for physicians

Character	subjects	PB		WB		CB	
		mean ±SD	c	mean ±SD	c	mean ±SD	c
Sex							
Women	39	46.05±23.67	7.69	44.87±20.46	8.42*	36.43±17.25	7.09
Men	73	38.36±18.88	-	36.45±16.69	-	29.35±19.40	

*, P < 0.05; **, P < 0.01; ***, P < 0.0001; PB, personal burnout; WB, work-related; CB, client burnout; c, the linear regression coefficient of surveyed variable against burnout.

Table 2-2 Sex difference of burnout for nurses

Character	subjects	PB		WB		CB	
		mean ±SD	c	mean ±SD	c	mean ±SD	c
Sex							
Women	494	39.77±17.62	-3.06	37.68±16.08	-3.90	33.22±17.31	-7.53
Men	18	42.82±23.82	-	41.67±15.00	-	40.74±24.19	-

*, P < 0.05; **, P < 0.01; ***, P < 0.0001; PB, personal burnout; WB, work-related; CB, client burnout; c, the linear regression coefficient of surveyed variable against burnout.

Table 3 MS pain sites and factor analysis of the Nordic musculoskeletal questionnaire

MS pain site	MS pain subjects	Prevalence %	frequency score	Factor loading		
			mean ±SD	Factor 1	Factor 2	Factor 3
Neck	445	35.60	26.21±37.41	***0.33***	-0.02	-0.03
left shoulder	251	20.08	15.15±31.87	***0.33***	0.01	-0.02
right shoulder	277	22.16	16.96±33.42	***0.33***	0.02	-0.07
upper back	209	16.72	12.86±29.81	0.17	-0.01	-0.00
waist or lower back	364	29.12	20.90±35.01	0.08	-0.03	0.01
left elbow	56	4.48	3.44±16.67	-0.05	-0.04	-0.05
right elbow	84	6.72	5.22±20.33	-0.03	-0.05	-0.00
left wrist	65	5.20	4.08±18.21	-0.05	-0.02	-0.02
right wrist	129	10.32	7.65±23.88	-0.05	-0.06	-0.02
left hip/thigh/buttock	56	4.48	3.36±16.25	-0.05	-0.09	-0.00
right hip/thigh/buttock	56	4.48	3.34±16.19	-0.02	-0.07	-0.06
left knee	69	5.52	3.94±17.14	-0.05	-0.08	***0.51***
right knee	74	5.92	4.51±18.69	-0.02	-0.07	***0.47***
left ankle	27	2.16	1.52±11.12	-0.01	***0.51***	-0.01
right ankle	22	1.76	1.28±10.39	-0.04	***0.58***	-0.03
		eigenvalues		5.18	1.60	0.66
		explained variation %		59.03	18.17	7.51

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Table 4 The association between burnout and MS pain

MS pain	The unary linear regression coefficient c		
	PB	WB	CB
NBSP	8.27***	6.49***	3.79***
BAP	1.59**	1.49**	0.92
BKP	2.29**	1.57**	1.19

*, P < 0.05; **, P < 0.01; ***, P < 0.0001; c, the linear regression coefficient of MS pain against burnout.

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Table 5 The linear regression models of three burnout scales

Main effect/DV	The linear regression coefficients (c)					
	PB		WB		CB	
	ULR	MLR[1]	ULR	MLR[1]	ULR	MLR[1]
WE	-0.11*	-0.14**	-0.19**	-0.11*	-0.14**	-0.01
Parenthood	-0.30	2.41*	-4.19***	-1.38	-5.12***	-3.00**
Not parenting	1.00	1.00	1.00	1.00	1.00	1.00
LAFF	-0.13***	-0.06**	-0.16***	-0.09***	-0.14***	-0.08**
SSLD	8.11***	4.25***	6.52***	2.78**	3.84**	1.17
SLD > 6h	1.00	1.00	1.00	1.00	1.00	1.00
Working OT	10.53***	6.91***	9.50***	6.18***	6.51***	3.95***
Seldom working OT	1.00	1.00	1.00	1.00	1.00	1.00
IRS work	7.76***	3.32*	8.48***	3.97**	6.05***	2.19
RS work	5.20**	4.00**	6.16***	3.88**	6.37***	3.93**
NS work	3.05	1.17	4.36**	1.27	5.31***	1.43
DS work	1.00	1.00	1.00	1.00	1.00	1.00
Physician	10.17***	7.75***	9.94***	7.69***	6.07**	4.01*
Nurse	9.01***	5.29***	8.38***	4.44***	7.74***	4.65***
PTs	2.95*	3.43**	2.42	3.52**	2.20	3.06*
ADs	1.00	1.00	1.00	1.00	1.00	1.00
NBSP	8.27***	6.86***	6.49***	5.51***	3.79***	3.23***
BAP	1.59**	1.38**	1.49**	1.33**	0.92	0.81
BKP	2.29**	1.68**	1.57**	1.16*	1.19	1.01

*, P < 0.05; **, P < 0.01; ***, P < 0.0001; DV, dependent variable; URL, unary linear regression; MRL, multiple linear regression; [1], MRL models adjusted sex, education degree, REW, CD, ever AU and all main effects.

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Table 5-1 The effect of parenthood against PB after adjusting single risk factor

AV	the linear regression coefficient parenthood effect (AV)
-	-0.30
LAFF	0.66 (-0.13***)
SSLD	0.17 (8.12***)
working OT	0.42 (10.56***)
IRS work	1.08 (7.99***)
RS work	1.08 (5.51**)
NS work	1.08 (3.43*)
Physician	0.97 (10.29***)
Nurse	0.97 (9.14***)
PTs	0.97 (2.85)
NBSP	-1.28 (8.32***)
BAP	-0.31 (1.59**)
BKP	-0.45 (2.31**)

*, P < 0.05; **, P < 0.01; ***, P < 0.0001; AV, adjusted variable.

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Table 5-2 The effect of sex against WB after adjusting single risk factor

AV	the linear regression coefficient c of women for WB women vs men	AV
Not adjusted	8.42*	-
WE	-0.11	-0.18*
Parenthood	6.37	-5.05
LAFF	8.71*	-0.20*
SSLD	8.35*	9.72**
working OT	8.95*	8.83**
IRS work	5.04	8.52
RS work	5.04	15.86**
NS work	5.04	17.66
NBSP	-1.85	6.50***
BAP	-1.85	0.47
BKP	-1.85	1.88*

*, P < 0.05; **, P < 0.01; ***, P < 0.0001; AV, adjusted variable.

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Table 6 The first-stage effect in the mediation model for

IV/DV		first-stage effect (a)							
		mar.[1]	pare.[1]	LAFF[2]	REW[1]	CD[1]	AU[1]	SSLD[1]	OT[1]
WE	a	0.10***	0.11***	0.12*	0.03***	0.03***	-0.03***	-0.00	-0.01
	s_a	0.01	0.01	0.06	0.01	0.01	0.01	0.01	0.01
mar.	a	-	4.43***	7.28***	0.26*	0.36**	-0.23*	-0.35**	-0.36**
	s_a	-	0.20	1.14	0.12	0.12	0.12	0.12	0.12
pare.	a	4.43***	-	7.42***	0.22	0.39**	-0.30*	-0.25*	-0.30*
	s_a		-	1.15	0.12	0.12	0.12	0.12	0.12
OT	a	-0.36**	-0.30*	-4.26**	-0.37**	0.18	0.46**	0.52***	-
	s_a	0.12	0.12	1.20	0.12	0.12	0.12	0.12	-
IRS	a	-0.53**	-0.54**	-0.70	-0.68**	-0.21	0.17	0.60**	0.42*
	s_a	0.18	0.18	1.76	0.17	0.18	0.18	0.17	0.17
DS	a	1.26***	1.22***	3.70**	0.78***	0.16	-0.25*	-0.27*	-0.20
	s_a	0.13	0.13	1.20	0.12	0.12	0.12	0.12	0.12
Phy.	a	-0.23	-0.35	1.56	0.65**	-0.04	0.90***	0.44*	0.60**
	s_a	0.20	0.21	2.03	0.22	0.20	0.20	0.20	0.20
Nurse	a	-0.52***	-0.59***	-4.51**	-0.82***	-0.09	-0.10	0.21	0.55***
	s_a	0.12	0.12	1.17	0.12	0.12	0.12	0.12	0.12

*, $P < 0.05$; **, $P < 0.01$; ***, $P < 0.0001$; a, logistic/linear regression coefficient, s_a, standard error of
parenting; [1], the corresponding field value is logistic regression coefficient; [2], the corresponding fie

Table 6-1 The tested results of mediation effect for PB

IV/M		direct effect and second-stage effect												
		mar.[1]	pare.[1]	LAFF[2]	REW[1]	CD[1]	AU[1]	SSLD[1]	OT[1]	IRS[1]	DS[1]	NBSP[2]	BAP[2]	BKP[2]
WE	c'	-0.12*	-0.13*	-0.09	-0.08	-0.15**	-0.09	NCF	NCF	-0.10	-0.05	NCF	NCF	-0.14*
	b	0.52	0.73	-0.12***	-5.88***	5.83***	4.16***	-	-	6.32***	-5.17***	-	-	2.51**
	S_b	1.12	1.14	0.03	1.03	1.05	1.06	-	-	1.56	1.08	-	-	0.67
	Z	0.31	0.64	1.79	**-2.62****	**2.61****	**-2.33***	-	-	**-2.80****	**-3.42****	-	-	**3.75****
OT	c'	NA	NA	10.09***	10.06***	NCF	10.17***	9.66***	-	10.27***	NCF	8.88***	NCF	NCF
	b	-	-	-0.10***	-5.19***		3.25**	6.92***	-	5.56**	-	7.75***	-	-
	S_b	-	-	0.02	0.99		1.02	1.00	-	1.49	-	0.49	-	-
	Z	-	-	**2.89****	**2.62****		**2.40***	**3.65****	-	**2.01***	-	**4.06*****	-	-
IRS	c'	NA	NA	NCF	5.64**	NCF	NCF	5.45**	5.56**	-	NA	4.99**	NCF	NCF
	b	-	-	-	-5.63***	-	-	7.74***	10.27***	-	-	8.15***	-	-
	S_b	-	-	-	1.02	-	-	1.03	1.02	-	-	0.51	-	-
	Z	-	-	-	**3.20****	-	-	**3.17****	**2.39***	-	-	**2.47***	-	-
DS	c'	NA	NA	-4.96***	-4.40***	NCF	-5.15***	-4.89***	NCF	NA	-	NCF	NCF	NCF
	b	-	-	-0.12***	-5.25***	-	4.05**	7.80***	-	-	-	-	-	-
	S_b	-	-	0.03	1.03	-	1.04	1.02	-	-	-	-	-	-
	Z	-	-	**-2.44***	**-3.98*****	-	-1.79	**-2.14***	-	-	-		-	-
Phy.	c'	NCF	NCF	NCF	6.48**	NCF	4.64**	4.68**	4.02*	NCF	NCF	NCF	NCF	NCF
	b	-	-	-	-6.37***	-	4.00**	7.94***	10.32***	-	-	-	-	-

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	S_b	-	-	-	1.02	-	1.06	1.03	1.02	-	-	-	-	-
	Z	-	-	-	**-2.64****	-	**2.85****	**2.10***	**2.86****	-	-	-	-	-

*, P < 0.05; **, P < 0.01; ***, P < 0.0001; c', linear regression coefficient of IV to PB in the exist of mediated factor. M, mediated factor; [1], b is a logistic regression coefficient and Z is a value calculated by $Z_{mediation}$ [61]; 2, b is a linear regression coefficient and Z is value calculated by the original formula of the Sobel test; NCF, Non-compliance with the first-stage effect; NA, not applicable

Table 6-2 The tested results of mediation effect for WB

IV/M		direct effect and the second-stage effect												
		mar.[1]	pare.[1]	LAFF[2]	REW[1]	CD[1]	AU[1]	SSLD[1]	OT[1]	IRS[1]	DS[1]	NBSP[2]	BAP[2]	BKP[2]
WE	c'	-0.13*	-0.11*	-0.17**	-0.15**	-0.22***	-0.17**	NCF	NCF	-0.16**	-0.12*	NCF	NCF	-0.21***
	b	-2.71**	-3.25**	-0.15***	-5.54***	4.65***	3.09**	-	-	6.49***	-5.86***	-	-	1.89**
	S_b	1.00	1.02	0.02	0.92	0.94	0.95	-	-	1.39	0.96	-	-	0.60
	Z	**-2.60****	**-3.05****	-1.93	**-2.65****	**2.53***	**-2.15***	-	-	**-3.00****	**-3.84****	-	-	**3.15****
Mar.	c'	-	-1.12	-2.65**	-3.34**	-4.07***	-3.52**	-3.19**	-2.94**	-3.33**	-2.08*	-4.67***	NCF	NCF
	b	-	-3.30*	-0.15***	-5.66***	4.37***	3.27**	6.25***	9.24***	6.56***	-5.75***	6.69***	-	-
	S_b	-	1.50	0.02	0.92	0.94	0.94	0.93	0.92	1.39	0.98	0.47	-	-
	Z	-	**-2.19***	**-4.86*****	**-2.02***	**2.48***	-1.63	**-2.65****	**-2.86****	**-2.46****	**-5.00*****	**2.94****	-	-
Par.	c'	NA	-	-3.13**	NCF	-4.60***	-3.96***	-3.82***	-3.56***	-3.85***	-2.66**	-4.67***	NCF	NCF
	b	-	-	-0.14***	-	4.45***	3.18***	6.29***	9.25***	6.50***	-5.62***	6.66***	-	-
	S_b	-	-	0.02	-	0.93	0.94	0.93	0.92	1.39	0.98	0.46	-	-
	Z	-	-	**-4.74*****	-	**2.65****	**-1.96***	**-1.97***	**-2.42***	**-2.49***	**-4.87*****	**2.37***	-	-
OT	c'	NA	NA	8.93***	9.05***	NCF	9.23***	8.82***	-	9.22***	NCF	8.22***	NCF	NCF
	b	-	-	-0.14***	-5.11***	-	2.47**	5.44***	-	6.07***	-	6.01***	-	-
	S_b	-	-	0.02	0.89	-	0.92	0.91	-	1.34	-	0.46	-	-
	Z	-	-	**3.17****	**2.69****	-	**2.15***	**3.48****	-	**2.13***	-	**4.00*****	-	-
IRS	c'	NA	NA	NCF	6.08***	NCF	NCF	6.09***	6.07***	-	NA	5.75***	NCF	NCF
	b	-	-	-	-5.43***	-	-	6.11***	9.22***	-	-	6.35***	-	-
	S_b	-	-	-	0.92	-	-	0.93	0.91	-	-	0.47	-	-

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	Z	-	-	-	**3.28****	-	-	**3.08****	**2.39***	-	-	**2.46***	-	-
DS	c'	NA	NA	5.85***	-5.45***	NCF	-6.20***	-5.99***	NCF	NA	-	NCF	NCF	NCF
	b	-	-	-0.14***	-4.90***	-	3.11**	6.14***	-	-	-	-	-	-
	S_b	-	-	0.02	0.92	-	0.93	0.92	-	-	-	-	-	-
	Z	-	-	**-2.82****	**-4.09*****	-	-1.71	**-2.11***	-	-	-	-	-	-
Phy.	c'	NCF	NCF	NCF	6.62***	NCF	5.00**	5.01**	4.33**	NCF	NCF	NCF	NCF	NCF
	b	-	-	-	-6.21***	-	3.09**	6.34***	9.28***	-	-	-	-	-
	S_b	-	-	-	0.92	-	0.95	0.93	0.92	-	-	-	-	-
	Z	-	-	-	**-2.68****	-	**2.59****	**2.07***	**2.86****	-	-	-	-	-

*, P < 0.05; **, P < 0.01; ***, P < 0.0001; c', linear regression coefficient of IV to PB in the exist of mediated factor. M, mediated factor; [1], b is a logistic regression coefficient and Z is a value calculated by $Z_{mediation}$ [61]; 2, b is a linear regression coefficient and Z is value calculated by the original formula of the Sobel test; NCF, Non-compliance with the first-stage effect; NA, not applicable

Table 6-3 The tested results of mediation effect for CB

		direct effect and the second-stage effect												
IV/M		mar.[1]	pare.[1]	LAFF[2]	REW[1]	CD[1]	AU[1]	SSLD[1]	OT[1]	IRS[1]	DS[1]	NBSP[2]	BAP[2]	BKP[2]
WE	c'	-0.08*	-0.04	-0.13*	-0.11*	-0.16**	-0.12*	NCF	NCF	-0.13*	-0.08	NCF	NCF	-0.16**
	b	-3.03**	-4.83***	-0.14***	-5.19***	1.62	3.40**	-	-	4.00**	-5.59***	-	-	1.44*
	S_b	1.06	1.07	0.02	0.98	1.01	1.00	-	-	1.48	1.02	-	-	0.64
	Z	**-2.74****	**-4.16*****	-1.92	**-2.58****	1.36	**-2.20***	-	-	**-2.19***	**-3.66****	-	-	**2.25***
Mar.	c'	-	0.97	-2.67**	-3.30**	-3.76**	-3.44**	-3.34**	-3.12**	-3.41**	-2.15*	-4.21***	NCF	NCF
	b	-	-5.88**	-0.13***	-5.22***	1.51	3.48**	3.55**	6.24***	3.96**	-5.29***	3.97***	-	-
	S_b	-	1.57	0.02	0.97	1.00	1.00	0.99	0.99	1.48	1.04	0.52	-	-
	Z	-	**-3.69****	**-4.56*****	**-1.98***	1.29	-1.63	**-2.21***	**-2.68****	-1.92	**-4.49*****	**2.79****	-	-
Par.	c'	NA	-	-4.18***	NCF	-5.27***	-4.88***	-4.91***	-4.69***	-4.91***	-3.81**	-5.58***	NCF	NCF
	b	-	-	-0.13***	-	1.68	3.32**	3.54**	6.17***	3.78*	-4.85***	3.98***	-	-
	S_b	-	-	0.02	-	0.99	0.99	0.99	0.99	1.47	1.03	0.51	-	-
	Z	-	-	**-4.58*****	-	1.45	-1.95	-1.75	**-2.30***	-1.89	**-4.19*****	**2.29***	-	-
OT	c'	NA	NA	5.96***	6.07***	NCF	6.18***	6.13***	-	6.34***	NA	5.78***	NCF	NCF
	b	-	-	-0.13***	-4.92***	-	3.00**	3.08**	-	3.77**	-	3.45***	-	-
	S_b	-	-	0.02	0.96	-	0.99	0.99	-	1.46	-	0.52	-	-
	Z	-	-	**3.12****	**2.61****	-	**2.32***	**2.50***	-	1.72	-	**3.55***	-	-
DS	c'	NA	NA	-5.45***	-5.08***	NCF	-5.74***	-5.72***	NCF	NA	-	NCF	NCF	NCF
	b	-	-	-0.13***	-4.52***		3.34**	3.48**	-	-	-	-	-	-
	S_b	-	-	0.02	0.98		0.99	0.99	-	-	-	-	-	-

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	Z	-	-	**-2.79****	**-3.73****		-1.72	1.84	-	-	-	-	-	-
Nur.	c'	NA	NA	5.55***	5.26***	NCF	NCF	NCF	5.39***	5.83***	4.72***	5.62***	NCF	NCF
	b	-	-	-0.13***	-4.40***	-	-	-	5.79***	3.11*	-4.33***	3.55***	-	-
	S_b	-	-	0.02	0.98	-	-	-	0.99	1.47	1.05	0.52	-	-
	Z	-	-	**3.32****	**3.73****	-	-	-	**3.58****	1.92	3.89**	2.75**	-	-

*, $P < 0.05$; **, $P < 0.01$; ***, $P < 0.0001$; c', linear regression coefficient of IV to PB in the exist of mediated factor. M, mediated factor; [1], b is a logistic regression coefficient and Z is a value calculated by $Z_{mediation}$ [61]; 2, b is a linear regression coefficient and Z is value calculated by the original formula of the Sobel test; NCF, Non-compliance with the first-stage effect; NA, not applicable

Table 7 Mediation and suppression models of burnout

			Mediation or suppression effect												
IV	DV	c'	1.mar.	2.pare.	3.LAFF	4.REW	5.CD	6.AU	7.SSLD	8.OT	9.IRS	10.DS	11. NBSP	12.BAP	13.BKP
1.WE	PB	-	NS	NS	NS	(+) **m****	(+) S**	(-) **m***	NCF	NCF	(-) **m****	(+) **m****	NCF	NCF	(+) S**
2.OT	PB	+	NA	NA	(-) m**	(-) m**	N	(+) m*	(+) m**	X	(+) m*	NCF	(+) m***	NCF	NCF
3.IRS	PB	+	NA	NA	NCF	(-) m**	NCF	NCF	(+) m**	(+) m*	X	NA	(+) m*	NCF	NCF
DS	PB	-	NCF	NCF	(+) m*	(+) m***	NCF	NS	(-) m*	NCF	NCF	-	NCF	NCF	NCF
4.Phy.	PB	+	NCF	NCF	NCF	(+) S**	N	(+) m**	(+) m*	(+) m**	NCF	NCF	NCF	NCF	NCF
5.WE	WB	-	(+) m**	(+) m**	NS	(+) m**	(+) S*	(-) m*	NCF	NCF	(-) m**	(+) m**	NCF	NCF	(+) S**
6.mar.	WB	-	X	(+) ***m****	(+) m***	(+) m*	(+) S*	NS	(-) m**	(-) m**	(-) m**	(+) m***	(+) S**	NCF	NCF
7.pare.	WB	-	NA	X	(+) m***	NCF	(+) S**	(-) m*	(-) m*	(-) m*	(-) m*	(+) m***	(+) S*	NCF	NCF
8.OT	WB	+	NA	NA	(-) m**	(-) m**	NCF	(+) m*	(+) m**	X	(+) m*	NCF	(+) m***	NCF	NCF
9.IRS	WB	+	NA	NA	NCF	(-) m**	NCF	NCF	(+) m**	(+) m*	X	NA	(+) m*	NCF	NCF
10.DS	WB	-	NA	NA	(+) m**	(+) m***	NCF	NS	(-) m*	NCF	NA	X	NCF	NCF	NCF
11.Phy.	WB	+	NCF	NCF	NCF	(+) S**	NCF	(+) m**	(+) m*	(+) m**	NCF	NCF	NCF	NCF	NCF
12.WE	CB	-	(+) m**	(+) ***m******	NS	(+) m**	NS	(-) m*	NCF	NCF	(-) m*	(+) **m****	N	N	(+) S*
13.mar.	CB	-	X	(+) **m****	(+) m***	(+) m*	NS	NS	(-) m*	(-) m**	NS	(+) m***	(+) S**	N	N
14.pare.	CB	-	NA	X	(+) m***	NCF	NS	NS	NS	(-) m*	NS	(+) m***	(+) S*	N	N
15.OT	CB	+	NA	NA	(-) m**	(-) m**	NCF	(+) m*	(+) m*	X	NS	NA	(+) m*	N	N
16.DS	CB		NA	NA	(+)m**	(+)m**	NCF	NS	NS	N	NA	X	NCF	NCF	NCF

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17.Nur.	CB	NA	NA	(-) m**	(-) m**	NCF	NCF	NCF	(+) m**	NS	(-) m**	(+) m**	NCF	NCF

*, P < 0.05; **, P < 0.01; ***, P < 0.0001; phy., physician, mar., married, pare., parenting; +/-, positive/negative relationship for IV and DV; (+/-), positive/negative relationship for IV and mediated factor; m, mediated effect; s, suppressed effect; NA, not applicable; NS, not statistically significant; NCF, Non-compliance with the first-stage effect

Table 8 Identification of risk factors for WRIs and SIs

IV/DV	subjects	WRIs mean ± SD	WRIs c	SIs mean ± SD	SIs c
Sex					
Women	1016	16.61±18.97	0.69	7.19±13.18	-2.22*
Men	234	15.92±17.19	1.00	9.40±14.91	1.00
Work experience[1]					
WE	1250	-	0.07	-	-0.05
Education degree					
Master's degree or above[1]	210	15.83±17.01	-0.78	6.67±12.36	-1.12
University or below university degree[2]	1040	16.61±18.97	1.00	7.79±13.77	1.00
Marriage state					
Married	612	16.95±18.91	0.93	7.19±13.39	-0.80
others	638	16.03±18.39	1.00	7.99±13.68	1.00
Raising the child					
Parenting[3]	553	17.04±18.80	1.01	7.41±13.68	-0.33
Not Parenting	697	16.03±18.53	1.00	7.75±13.44	1.00
Engaging in LAFF[1]					
LAFF	1250	-	-0.04	-	-0.22
Exercise frequency					
REW	711	16.10±18.41	-0.87	7.60±13.74	-0.01
Not REW	539	16.98±18.96	1.00	7.61±13.29	1.00
With CD					
Yes	491	19.30±19.45	4.64***	8.66±14.60	1.74*
No	759	14.66±17.89	1.00	6.92±12.77	1.00
The frequency for drink coffee[1]					
Coffee intake score	1250	-	-0.00		0.01
Alcohol use habit in a month					
Ever AU	474	18.41±19.37	3.10**	9.60±14.73	3.22***
Never AU	776	15.30±18.10	1.00	6.38±12.62	1.00
Sleeping duration					

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per day					
SSLD	481	18.76±19.23	3.71**	9.15±14.59	2.52**
Not SSLD	769	15.05±18.09	1.00	6.63±12.75	1.00
Experiencing OT work per month					
Work OT	459	20.64±20.50	6.58***	10.40±15.91	4.43***
seldom work OT	791	14.07±17.03	1.00	5.97±11.66	1.00
Shift work schedule[2]					
irregular shift	154	20.29±19.76	5.08**	10.88±15.11	4.03**
regular shift	165	18.18±22.49	2.97	8.64±14.78	1.79
Night shift	142	17.43±18.83	2.22	7.04±12.76	0.20
day shift	789	15.21±17.36	1.00	6.84±12.99	1.00
Professional field[2]					
physicians	112	14.96±18.21	1.26	6.92±11.24	-0.37
Nurses	512	19.34±19.59	5.64***	9.03±14.34	1.75
PTs	228	15.68±17.51	1.99	5.26±10.48	-2.02
ADs	398	13.69±17.68	1.00	7.29±14.43	1.00
MS pain[1]					
NBSP	1250	-	5.89***	-	1.78***
BAP	1250	-	1.78**	-	0.39
BKP	1250	-	3.10***	-	1.02*

*, P < 0.05; **, P < 0.01; ***, P < 0.0001; [1], They are all continuous variables and are added to model individually; [2], All dummy variables were added to model at the same time.

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Table 8-1 The impact of burnout against WRIs

risk factor		the adjusting variable for WRIs					
		PB		WB		CB	
	c	c'	d (%)	c'	d (%)	c'	d (%)
CD	4.64***	2.52*	45.69	2.95**	36.42	4.33***	6.68
AU	3.10**	1.37	NC	1.62	NC	2.13*	31.29
SSLD	3.71**	0.46	NC	0.93	NC	2.70*	27.22
Work OT	6.58***	2.53*	61.55	2.69*	59.12	4.98***	24.32
IRS work[1]	4.35**	1.72	NC	1.36	NC	3.18*	26.90
Nurses[2]	4.84***	2.26*	53.31	2.27	53.10	3.28**	32.23
NBSP	5.89***	3.09***	47.54	3.56***	39.56	5.07***	13.92
BAP	1.78**	1.14*	35.96	1.14*	35.96	1.53**	14.04
BKP	3.10***	2.20**	29.03	2.44**	21.29	2.79***	10.00

*, P < 0.05; **, P < 0.01; ***, P < 0.0001; c, the linear regression coefficient for risk factor without adjusting burnout.; c', the linear regression coefficient for risk factor after adjusting burnout; $d(\%) = c - c'/c \times 100$; NC, not calculated; [1], reference variable is other participants except to subjects who work irregular shift; [2], reference variable is other participants except to nurses.

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Table 8-2 The mediation effect of burnout against WRIs

IV/M	PB					WB					CB				
	a	s_a	b	s_b	Z	a	s_a	b	s_b	Z	a	s_a	b	s_b	Z
CD	5.39***	1.04	0.39***	0.03	***4.81*****	4.01***	0.94	0.42***	0.03	4.08***	1.17	1.00	0.27***	0.03	1.16
AU	4.35***	1.05	0.40***	0.03	3.96***	3.47**	0.95	0.43***	0.03	***3.54****	3.68**	1.00	0.27***	0.03	3.41**
SSLD	8.11***	1.03	0.40***	0.03	***6.78*****	6.52***	0.93	0.43***	0.03	***6.30*****	3.84**	1.00	0.26***	0.03	3.51**
OT	10.53***	1.02	0.39***	0.03	8.08***	9.50***	0.92	0.41***	0.03	8.24***	6.51***	0.99	0.25***	0.03	5.16***
IRS[1]	6.58***	1.55	0.40***	0.03	***4.05*****	6.98***	1.39	0.43***	0.03	4.74***	4.40**	1.48	0.27***	0.03	2.82**
Nurses[2]	6.56***	1.03	0.39***	0.03	5.72***	6.12***	0.92	0.42***	0.03	6.01***	6.14***	0.98	0.26***	0.03	5.08***
NBSP	8.27***	0.51	0.34***	0.03	9.29***	6.49***	0.47	0.36***	0.03	9.06***	3.79***	0.52	0.22***	0.03	5.17***
BAP	1.59**	0.59	0.40***	0.03	2.64**	1.49**	0.53	0.43***	0.03	2.76**	0.92	0.56	0.27***	0.03	1.62
BKP	2.29**	0.66	0.40***	0.03	3.36**	1.57**	0.60	0.42***	0.03	2.57**	1.19	0.63	0.26	0.03	1.85

*, P < 0.05; **, P < 0.01; ***, P < 0.0001; M, mediated factor; a, the linear regression coefficient of IV against M; s_a, the standard error for a; b, the linear regression coefficient of M against PB/WB/CB; s_b, the standard error for b; Italic bold font represented fully mediated effect; ; [1], reference variable is other participants except to subjects who work irregular shift; [2], reference variable is other participants except to nurses.

Table 8-3 The impact of burnout against SIs

risk factor	the adjusting variable for SIs							
		PB		WB		CB		
	c	c'	d (%)	c'	d (%)	c'	d (%)
Women	-2.22*	-2.54**	NE	-2.50**	NE	-2.41*	NE
CD	1.74*	1.02	NC	1.16	NC	1.59*	8.62
AU	3.22***	2.66**	17.39	2.74**	14.91	2.79**	13.35
SSLD	2.52**	1.47	NC	1.61*	36.11	2.06**	18.25
Work OT	4.43***	3.23***	27.09	3.28***	25.96	3.73***	15.80
IRS work[1]	3.74**	2.87*	23.26	2.76*	26.20	3.21**	14.17
Nurses[2]	2.43**	1.57*	35.39	1.58*	34.98	1.71*	29.63
NBSP	1.78***	0.78	NC	0.95*	46.63	1.36**	23.60
BKP	1.02*	0.71	NC	0.79	NC	0.87	NC

*, P < 0.05; **, P < 0.01; ***, P < 0.0001; c, the linear regression coefficient for risk factor without adjusting burnout; c', the linear regression coefficient for risk factor after adjusting burnout; $d(\%) = c - c'/c \times 100$; NE, not estimate; NC, not calculated; [1], reference variable is other participants except to subjects who work irregular shift; [2], reference variable is other participants except to nurses.

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Table 8-4 The mediation effect of burnout against SIs

	PB					WB					CB				
IV/M	a	s_a	b	s_b	Z	a	s_a	b	s_b	Z	a	s_a	b	s_b	Z
CD	5.39***	1.04	0.13** •	0.02	***4.05**** •	4.01** •	0.94	0.14** •	0.02	***3.64****	1.17	1.00	0.12***	0.02	1.15
AU	4.35***	1.05	0.13** •	0.02	3.49**	3.47**	0.95	0.14** •	0.02	3.24**	3.68**	1.00	0.12***	0.02	3.14**
SSLD	8.11***	1.03	0.13** •	0.02	***5.01**** •	6.52** •	0.93	0.14** •	0.02	4.95***	3.84**	1.00	0.12***	0.02	3.23**
OT	10.53***	1.02	0.11** •	0.02	4.85** •	9.50** •	0.92	0.12** •	0.02	5.19***	6.51***	0.99	0.11***	0.02	4.22***
IRS[1]	6.58***	1.55	0.13** •	0.02	3.55**	6.98** •	1.39	0.14** •	0.02	4.08***	4.40**	1.48	0.12***	0.02	2.66**
Nurses[2]	6.56***	1.03	0.13** •	0.02	4.55** •	6.12** •	0.92	0.14** •	0.02	4.82***	6.14***	0.98	0.12***	0.02	4.33***
NBSP	8.27***	0.51	0.12** •	0.02	***5.63**** •	6.49** •	0.47	0.13** •	0.03	4.13***	3.79***	0.52	0.11***	0.02	4.39***
BKP	2.29**	0.66	0.14** •	0.02	***3.11****	1.57**	0.60	0.15** •	0.02	***2.47****	1.19	0.63	0.12***	0.02	1.80

•, $P < 0.05$; **, $P < 0.01$; ***, $P < 0.0001$; Italic bold font represented fully mediated effect; [1], reference variable is other participants except to subjects who work irregular shift. [2], reference variable is other participants except to nurses.

Table 9 The mediation models of burnout, risk factors and WRIs/SIs

		DV							
		WRIs			SIs				
		mediation factor			mediation factor				
IV	c	PB	WB	CB	c	PB	WB	CB	
CD	+	(+) m^{***}	(+) m^{*}	NA	+	(+) m^{***}	(+) m^{**}	NA	
AU	+	(+) m^{***}	(+) m^{**}	(+) m^{**}	+	(+) m^{**}	(+) m^{**}	(+) m^{**}	
SSLD	+	(+) ***m^{***}***	(+) m^{***}	(+) m^{**}	+	(+) m^{**}	(+) m^{***}	(+) m^{**}	
OT	+	(+) m^{***}	(+) m^{***}	(+) m^{**}	+	(+) m^{***}	(+) m^{***}	(+) m^{***}	
IRS	+	(+) m^{***}	(+) m^{***}	(+) m^{**}	+	(+) m^{***}	(+) m^{***}	(+) m^{**}	
Nurse	+	(+) m^{***}	(+) m^{***}	(+) m^{***}	+	(+) m^{***}	(+) m^{***}	(+) m^{***}	
NBSP	+	(+) m^{***}	(+) m^{***}	(+) m^{***}	+	(+) m^{***}	(+) m^{***}	(+) m^{***}	
BAP	+	(+) m^{**}	(+) m^{**}	NA	NS	NA	NA	NA	
BKP	+	(+) m^{**}	(+) m^{**}	NA	+	(+) m^{**}	(+) m^{*}	NA	

•, $P < 0.05$; **, $P < 0.01$; ***, $P < 0.0001$; +/-, positive/negative relationship c: (+/-), positive/negative relationship between IV and mediated factor; m, mediation effect; s, suppression effect; NA, not applicable; NS, not statistically significant.

doi:10.6834/csmu202200004

7. Figures

Figure 1 Development and impacting factors of Burnout

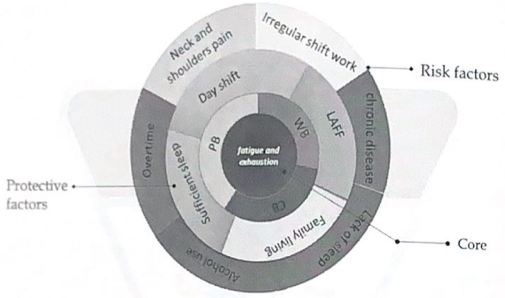
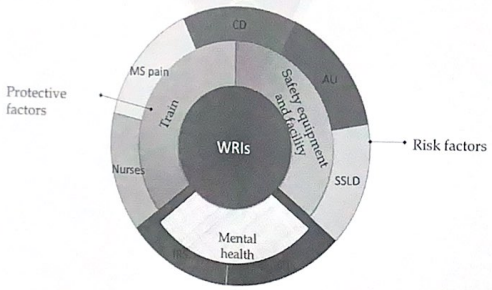


Figure 2 Development and impacting factors of Work-related injuries



doi:10.6834/csmu202200004

8. Appendix

Appendix A. Permission of Research Proposal for CS1-21108

中山醫學大學附設醫院第一人體研究倫理審查委員會

The Institutional Review Board
Chung Shan Medical University Hospital
No.110, Sec.1, Chien-Kuo N. Road, Taichung, Taiwan 402
Phone: 04-24739595 Fax: 04-35073516

研究計畫許可書

CSMUH No: CS1-21108

計畫名稱： 醫療工作場所職業傷害發展的探索
計畫主持人及服務機構： 陳詠昕／中山醫學大學附設醫院
經費來源： 主持人自行支付
會議日期： NA
版　　本：【計畫書：Version 1.0，日期：2021/06/23；Waiver 1：V1.0，日期：2021年6月23日】
許可審查效期間： 自民國 110 年 08 月 25 日至民國 113 年 08 月 24 日
期中報告繳交頻率：每年(12 個月)繳交一次，若需申請延長試驗，請於效期屆滿前申請。
上述計畫已於 110 年 08 月 25 日經本院人體研究倫理審查委員會依據簡易審查作業基準同意執行，有關計畫主持人的職責、義務、及注意事項均詳列於背面，請參閱並遵守。

主任委員 曹堯

中華民國一一〇年八月二十五日

Permission of Research Proposal
Chung Shan Medical University Hospital

Date: Aug 25, 2021

Protocol Title: Exploration on the Development of Burnout in Medical Workplace
Principle Investigator & Affiliated Institution: Yong-Hun Chen／Chung Shan Medical University Hospital
Date of meeting: NA
Version: 【see above】
Effective duration approved: 2021/08/25 to 2024/08/24
Frequency of Interim Report: every 12 months Please file an extension before the expiry date, if you need.
Above study has been approved with the expedited review by Institutional Review Board of the Chung Shan Medical University Hospital on Aug 25, 2021. About the essential duties, obligations and responsibilities of the principal investigator please refer to the back page.

Thomas Chang-Yao TSAO

Thomas Chang-Yao TSAO, MD/PhD.
Chairman
The Institutional Review Board

本委員會組織與執行皆符合 ICH-GCP 規範及赫爾辛基宣言之精神
This Committee has been organized and operated in conformance with ICH-GCP requirements and the essence of Declaration of Helsinki.

doi:10.6834/csmu202200004

Appendix B. Permission of Research Proposal for CS19137

中山醫學大學附設醫院第一人體研究倫理審查委員會

The Institutional Review Board
Chung Shan Medical University Hospital
No.110, Sec.1, Chien-Kuo N. Road, Taichung, Taiwan 402
Phone: 04-24739595 Fax: 04-35073516

研究計畫許可書

CSMUH No:CS19137

計畫名稱：超時工作與肥胖問題對醫學人員尖銳物扎傷的影響
計畫主持人及服務機構：陳詠心／中山醫學大學附設醫院
會議日期：108/11/28
版　本：【計畫書：V001，日期：2019/11/21；Waiver1：V001，日期：2019/11/21】
許可書有效期間：自民國 108 年 12 月 2 日至民國 109 年 12 月 1 日
期中報告繳交頻率：每年 12 個月繳交一次，並需申請延長試驗，請於效期屆滿前申請。
上述計畫已於 108 年 12 月 2 日經本院人體研究倫理審查委員會依據一般(全會)審查作業程序執行，有關計畫主持人的職責、義務、及注意事項均詳列於背面，請參閱並遵守。

主任委員 韓志平

中　華　民　國　一　〇　八　年　十　二　月　五　日

Permission of Research Proposal
Chung Shan Medical University Hospital

Date: Dec.5, 2019

Protocol Title: The effect of overtime work and obesity to medical staff sharps injury
Principle Investigator & Affiliated Institution: YongHsin Chen／Chung Shan Medical University Hospital

Date of meeting：2019/11/28
Version:【see above】
Effective duration approved: 2019/12/2 to 2020/12/1
Frequency of Interim Report: every 12 months. Please file an extension before the expiry date, if you need.
Above study has been approved with the full-board review by Institutional Review Board of the Chung Shan Medical University Hospital on Dec.2, 2019. About the essential duties, obligations and responsibilities of the principal investigator, please refer to the back page.

Chib-Ping Han, MD/PhD.
Chairman
The Institutional Review Board

本委員會組織與執行皆符合 ICH-GCP 規範及赫爾辛基宣言之精神
This Committee has been organized and operated in conformance with ICH-GCP requirements and the essence of Declaration of Helsinki.

doi:10.6834/csmu202200004

Appendix C. Permission of Research Proposal for CS19150

中山醫學大學附設醫院第一人體研究倫理審查委員會　複本

The Institutional Review Board
Chung Shan Medical University Hospital
No.110, Sec.1, Chien-Kuo N. Road, Taichung 40201, Taiwan
Phone: 04-24739595 Fax: 04-35073516

研究計劃免除審查證明書

計畫名稱：　過度疲勞是否是尖銳物扎傷的危險因素?　CSMUH No: CS19150
計畫主持人及服務機構：陳詠心／中山醫學大學附設醫院
經費來源：主持人自行支付
版　本：【計畫書：V0617，日期：2020/06/17；Waiver 1：V0722，日期：2020 年 7 月 22 日】
許可書有效期間：自民國 109 年 08 月 19 日至民國 112 年 08 月 18 日
效期屆滿，自動失效；若計畫仍未執行完畢，主持人須重新提出申請。

上述計畫已於 109 年 08 月 19 日經本院人體研究倫理審查委員會依據免除審查程序同意執行。有關計畫主持人的職責，義務及注意事項均詳列於背面，請參閱並遵守。

主任委員　曹昌堯

中　華　民　國　一　〇　九　年　八　月　十　九　日

Certification of Exempt Review
Chung Shan Medical University Hospital

Date: Aug. 19, 2020

Protocol Title: Whether is overfatigue the risk factor of sharps injury?
Principle Investigator & Affiliated Institution: Yong-Hsin Chen／Chang Shan Medical University Hospital
Version:【see above】
Effective duration approved: 2020/08/19 to 2023 /08/18
This certificate will be automatically void after the validity period. The principal investigator should resubmit a new application, if the research is not yet completed.

Above study has been approved with the exempt review by Institutional Review Board of the Chung Shan Medical University Hospital on Aug 19, 2020. About the essential duties, obligations and responsibilities of the principal investigator, please refer to the back page.

Thomas Chang-Yao TSAO, MD/PhD.
Chairman
The Institutional Review Board

本委員會組織與執行皆符合 ICH-GCP 規範及赫爾辛基宣言之精神
This Committee has been organized and operated in conformance with ICH-GCP requirements and the essence of Declaration of Helsinki.

doi:10.6834/csmu202200004

Journal of *Personalized Medicine*

MDPI

Article

The Effects of Frequent Coffee Drinking on Female-Dominated Healthcare Workers Experiencing Musculoskeletal Pain and a Lack of Sleep

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Abstract: Previous research has demonstrated that chronic diseases can occur due to musculoskeletal (MS) pain and poor sleep. It is also worth noting that the caffeine in coffee can reduce overall sleep duration, efficiency, and quality. Thus, the present study examines the effects of frequent coffee drinking (two cups per day) on individuals experiencing MS pain and a lack of sleep during the COVID-19 period. This observational and cross-sectional study recruited 1615 individuals who completed the self-reported (Nordic musculoskeletal) questionnaire. Long-term, frequent coffee drinking and a sleep duration of less than 6 h per day were significantly associated with neck and shoulder pain among healthy individuals. The mediation model demonstrated that the shorter sleep duration and drinking multiple cups of coffee per day had a two-way relationship that worsened such pain over the long term. Specifically, individuals who experienced such pain frequently drank multiple cups of coffee per day, which, in turn, shortened their sleep durations. In summary, long-term coffee drinking creates a vicious cycle between MS pain and sleep duration. Therefore, the amount of coffee should be fewer than two cups per day for individuals who sleep less than 6 h per day or suffer from MS pain, especially neck and shoulder pain.

Keywords: coffee; musculoskeletal pain; sleep; Nordic musculoskeletal questionnaire; neck and shoulder pain

Citation: Chen, Y.-H.; Chou, Y.-H.; Yang, T.-Y.; Jong, G.-P. The Effects of Frequent Coffee Drinking on Female-Dominated Healthcare Workers Experiencing Musculoskeletal Pain and a Lack of Sleep. *J. Pers. Med.* **2023**, *13*, 25. https://doi.org/10.3390/jpm13010025

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1. Introduction

Coffee is one of the most popular beverages for people of many ages. It is a complex chemical mixture that contains caffeine, which is a purine alkaloid that is naturally found in coffee beans [1] and contributes to its bitterness [2]. Caffeine stimulates the central nervous system, which can increase alertness, blood circulation, and respiration [3]. However, caffeine has biphasic effects, i.e., lower doses can provide some behavioral stimulation, whereas higher doses can lead to anxiety, aversion, irritability, and discomfort [4]. Despite clinical studies demonstrating the adjuvant analgesic effects of caffeine [5], long-term coffee drinking can negatively affect health and musculoskeletal (MS) pain. In health, individuals drinking more than five cups of coffee per day can have an increased risk of myocardial infarction or unstable angina [6]. In MS pain, related research showed that drinking more than seven cups of coffee per day was associated with a higher risk of knee osteoarthritis among Korean men [7]. Interestingly, patients with chronic back pain tend to drink two times as much caffeine as those without such pain [8], whereas individuals with

chronic daily headaches were generally high caffeine consumers before the onset of such headaches [9].

MS pain is common in many occupations, and it is one of the main reasons for long-term sick leave [10]. In the United States, 13% of the total workforce experienced a loss caused by body pains, with lost productive time costs estimated at USD 61.2 billion annually [11]. Although different occupations can affect MS pain at various anatomical sites and have diverse risk factors [12], a recent study in the Netherlands showed that the top three self-reported MS pains include lower-back pain, shoulder pain, and neck pain [13]. In addition, previous studies have demonstrated that work hours [14,15], occupational stress [16,17], alcohol consumption [18–21], sleep duration [22–24], exercise habits [25], and chronic diseases [26,27] contribute to MS pain.

Poor sleep quality is a common health problem among medical staff [28,29]. Reduced sleep duration and poor sleep quality have become more common during the past decades [30], leading to poor health outcomes [31] and even increased mortality [32]. Despite the recommended minimum sleep duration of 7 h per night for healthy adults, only 25% of adults achieve this amount [33]. Notably, lack of sleep can lead to impaired daytime function [34], increased occupational injury [35], and reduced productivity [36].

Overall, a close relationship was found between sleep and MS pain. For instance, because sleep problems can significantly reduce pain tolerance [37], individuals with chronic pain are more likely to experience insomnia [38]. Caffeine in coffee can also reduce total sleep duration, efficiency, and quality [39]. In addition, frequent consumption of caffeinated drinks can negatively affect habitual sleep duration [40].

From a micro and physiological perspective, adenosine is a purine nucleoside and a ubiquitous endogenous neurotransmitter that signals through four receptors (A1R, A2AR, A2BR, and A3R) in the brain to inhibit arousal and increase drowsiness [41]. Among these four receptors, A1R may be related to pain-sensing neurons [42]. Some evidence has demonstrated that A1R activation can produce antinociception of postoperative [43], neuropathic [44], and inflammatory [45] pain. In this regard, one study of mice found that acupuncture causes the release of nucleotides and adenosine to relieve pain [46]. However, these antinociceptive effects can be blocked by caffeine [47]. Notably, individuals with chronic insomnia were found to have reduced adenosine [48]. Moreover, impaired sleep significantly increases the risk of reduced pain tolerance [39]. These results suggest that the effects of caffeine on adenosine could play a pivotal role in pain development. Based on previous research, we propose the following hypotheses:

Hypothesis 1: *Coffee intake is significantly associated with increased risk of MS pain.*

Hypothesis 2: *Individuals with shorter sleep durations are more susceptible to MS pain.*

Hypothesis 3: *Coffee intake could lead to a vicious circle between lack of sleep and MS pain.*

2. Materials and Methods

This observational and cross-sectional study was initially conducted from a hospital affiliated with a medical university in Taichung, Taiwan, from March to April 2021. All 2531 healthcare workers who had served for one year in the hospital were distributed a QR code for a Google Forms-linked questionnaire by email. Among them, 1633 (64.52%) individuals completed the self-reported questionnaire, after which 1615 (63.81%) were deemed valid after those with missing data were excluded. Specifically, we used questionnaires, including the Nordic musculoskeletal questionnaire (NMQ), to obtain the participants' basic demographic variables, family factors, living habits, work, physical health, and MS pain. The study protocol was approved by the Institutional Review Board of Chung Shan Medical University Hospital on 25 August 2021 (No: CS1-21108).

This study adopted the NMQ, modified and translated by the Taiwan Institute of Occupational Safety and Health [49], to survey the presence of pain attributable to work-

related factors in the preceding year. The pain sites on the NMQ were classified as the neck, left or right shoulder, upper back, waist or lower back, left or right elbow, left or right wrist, left hip/thigh/buttock, right hip/thigh/buttock, left or right knee, and left or right ankle. The options for the frequency of each pain site were every day, once a week, once a month, once every half a year, and at least once every half a year, scored as 100, 80, 60, 40, and 20 points, respectively. Factor analysis was also adopted in the NMQ to determine the underlying variables that could effectively explain most of the questionnaire items. Through varimax rotation, the standardized scoring coefficients constituted new factor loadings and were defined according to their corresponding significance. The new factors that featured vector values exceeding 1 were retained according to the principle proposed by Hair et al. [50].

In the questionnaire, the basic response options included male or female for gender; age; "married" or "other" for marriage; and "without child," "one child," "two children," "three children," and "more than three children" for having children. The survey also asked if the participants engaged in leisure activities with family/friends during vacation time. The response options included "always," "often," "sometimes," "seldom," and "never." Regarding their education, the response options were "master's degree or above" and "university degree or below," while the response options for self-reported sleep duration per day included "less than 5 h," "between 5 and 6 h," "between 6 and 7 h," "between 7 and 8 h," and "more than 8 h." As for their coffee intake per day, the response options were "more than 2 cups per day," "2 cups per day," "1 cup per day," "occasionally," and "never." Regarding their alcohol use, the response options included "alcohol use in a month" and "no alcohol use in a month," while the response options were "yes" and "no" for exercising at least once a week. As for their overtime work, the response options were "seldom," "fewer than 45 h per month," "45 to 80 h per month," and "more than 80 h per month," while "irregular," "regular," "night," and "day" were the response options for shift schedules. Finally, the participants were classified as physicians, nurses, professional and technical personnel, and administrative staff. They were also asked about the presence of chronic diseases. In this regard, the presence of one or more diseases was classified as a "yes" response.

Regarding the statistical methods, factor analysis [50] was adopted for the NMQ to determine new underlying variables, while a *t*-test or one-way ANOVA was adopted to examine the differences between the continuous variables. Additionally, a chi-square test or Fisher's exact test was conducted to determine the significant differences in the categorical variables, while simple/multiple linear or logistic regression was used to examine the correlation between the dependent variable (DV) and the independent variable (IV), in the absence (or presence) of the controlled variables. The mediation effects among the IV, DV, and mediator were based on the following strategy proposed by Baron and Kenny [51]: 1) in the presence of the first-stage effect, the IV significantly affects the mediation factor; 2) in the absence of the mediation factor, the IV significantly affects the DV; 3) in the presence of the second-stage effect, the mediation factor has a significant effect on the DV; and 4) the effect of the IV on the DV weakens upon the addition of a mediation factor in the model.

A mediation model suitable for combining the categorical and continuous variables was developed by Iacobucci (2012) [52]. The formulas are as follows:

If the mediation factor and dependent variables are continuous variables, then the original formula of the Sobel test is applicable:

$$Z = \frac{a \times b}{\sqrt{b^2 {s_a}^2 + a^2 {s_b}^2}}$$

If the mediation factor or dependent variables are categorical variables, then the original formula of the Sobel test is rederived into a new formula:

$$Z_{mediation}\ (Z_m) = \frac{\frac{a}{s_a} \times \frac{b}{s_b}}{\sqrt{\left(\frac{a}{s_a}\right)^2 + \left(\frac{b}{s_b}\right)^2 + 1}}$$

Among them, a is the simple linear or logistic regression coefficient for the independent variable against the mediation factor, while b is the regression coefficient for the mediation factor against the dependent variable in the binary linear or logistic regression model. Additionally, s_a and s_b represent the standard deviations of a and b, respectively, while the results exceeding $|1.96|$, $|2.57|$, and $|3.90|$ (for the two-tailed test) are significant at $\alpha = 0.05$, 0.01, and 0.0001, respectively. In this study, the analyses were performed using SAS Enterprise Guide 7.1 software (SAS Institute Inc., Cary, NC, USA), and the significance was set at $p < 0.05$.

3. Results

Regarding the detailed description, the description of the basic demographics, sleep duration per day, and coffee intake of 1615 participants are shown in the Supplementary Information Tables S1–S3. The results demonstrated that marriage ($p = 0.016$), engaging in leisure activities with family/friends ($p < 0.0001$), coffee intake per day ($p < 0.0001$), exercise at least once a week ($p = 0.008$), overtime work in a month ($p < 0.0001$), shift schedules ($p < 0.0001$), and profession ($p = 0.005$) were associated with sleep duration per day. In addition, gender ($p = 0.024$), age ($p < 0.0001$), marriage ($p < 0.0001$), having children ($p < 0.0001$), education ($p < 0.0001$), alcohol use ($p < 0.0001$), exercise at least once a week ($p = 0.002$), and profession ($p = 0.001$) were related to coffee intake.

Table 1 illustrates that the common pain sites included both shoulders (43.09%), neck (36.22%), waist or lower back (27.93%), and upper back (16.90%). According to the principle proposed by Hair and Anderson (1995) [50], Factors 1 and 2 were retained because their vector values exceeded 1. In addition, the factor loadings were converted into standardized scoring coefficients through varimax rotation. The relatively large factor loading values for Factors 1 and 2 corresponded to the neck and both shoulder pain and both ankle pain sites, respectively. Thus, Factors 1 and 2 were redefined into two new variables: the neck and both shoulder pain (NBSP) score and the both ankle pain (BAP) score.

Table 1. MS pain sites and factor analysis of the NMQ.

MS Pain Sites	N	%	Score	Factor Loading	
			Mean ± SD	Factor 1	Factor 2
Neck	585	36.22	26.76 ± 37.64	0.33	−0.02
Left shoulder	325	20.12	15.07 ± 31.62	0.33	−0.01
Right shoulder	371	22.97	17.64 ± 33.89	0.33	0.02
Upper back	273	16.90	12.90 ± 29.77	0.17	0.00
Waist or lower back	451	27.93	20.20 ± 34.72	0.08	−0.04
Left elbow	70	4.33	3.29 ± 16.26	−0.05	−0.04
Right elbow	113	7.00	5.33 ± 20.43	−0.04	−0.04
Left wrist	77	4.77	3.72 ± 17.38	−0.05	0.00
Right wrist	162	10.03	7.51 ± 23.66	−0.03	−0.03
Left hip/thigh/buttock	67	4.15	3.12 ± 15.64	−0.05	−0.07
Right hip/thigh/buttock	68	4.21	3.17 ± 15.83	−0.02	−0.04
Left knee	80	4.95	3.78 ± 16.98	−0.05	−0.07
Right knee	88	5.45	4.17 ± 18.05	−0.02	−0.04
Left ankle	29	1.80	1.26 ± 10.10	−0.02	0.49
Right ankle	25	1.55	1.10 ± 9.58	−0.02	0.54
			Eigenvalues	4.93	1.55
			Explained variation %	57.59	18.12

N, individuals; %, the proportion of individuals suffering from MS pain.

According to Table 2, there were significant differences in the NBSP scores for gender ($p < 0.001$), age ($p = 0.003$), marriage ($p = 0.003$), having children ($p = 0.006$), education ($p = 0.034$), sleep duration per day ($p < 0.001$), coffee intake per day ($p = < 0.001$), alcohol use ($p = 0.001$), exercise at least once a week ($p = 0.001$), overtime work per month ($p < 0.0001$), profession ($p = 0.036$), and suffering from chronic diseases ($p < 0.0001$). There were no significant differences in the BAP scores among the survey variables, except for education ($p < 0.0001$). Regarding the other survey variables, the females obtained higher NBSP scores than the males (0.04 ± 0.93 vs. −0.17 ± 0.84). Moreover, individuals who were 38–45 years of age (0.15 ± 0.96), were married (0.07 ± 0.96), were parents (0.07 ± 0.96), had a master's degree or above (0.11 ± 0.99), had a sleep duration of less than 5 h (0.26 ± 1.04), drank more than two cups of coffee per day (0.61 ± 1.25), used alcohol in a month (0.10 ± 0.97), had no weekly exercise (0.09 ± 0.97), worked overtime more than 45 h per month (0.54 ± 1.35/ 0.44 ± 1.14), were nurses (0.08 ± 0.94), or suffered from chronic diseases (0.20 ± 1.03) achieved higher NBSP scores than the others. Simple multiple linear or logistic regression was also used to examine the correlation between the dependent and independent variables in the absence (or presence) of the controlled variables.

Table 2. Differences in the frequency of pain among the survey variables.

		Score on the Frequency of Musculoskeletal Pain			
		Mean ± SD			
Survey Variables	**Individuals**	**NBSP Score**	***p*-Value**	**BAP Score**	***p*-Value**
Gender					
Female	1314	0.04 ± 0.93	<0.001 [a]	−0.01 ± 0.85	0.643 [a]
Male	301	−0.17 ± 0.84		0.02 ± 0.90	
Age					
Less than or equal to 29	412	−0.11 ± 0.86	0.003 [b]	−0.00 ± 0.81	0.420 [b]
Between 29 and 38	433	0.01 ± 0.90		−0.06 ± 0.41	
Between 38 and 45	302	0.15 ± 0.96		0.04 ± 1.01	
More than or equal to 45	468	−0.01 ± 0.95		0.03 ± 1.06	
Marriage					
Married	779	0.07 ± 0.96	0.003 [a]	−0.02 ± 0.79	0.330 [a]
Other	836	−0.07 ± 0.87		0.02 ± 0.91	
Having children					
Parents	703	0.07 ± 0.96	0.006 [a]	−0.00 ± 0.88	0.914 [a]
Not parents	912	−0.06 ± 0.88		0.00 ± 0.84	
Engaging in leisure activities with family/friends					
Always	102	−0.05 ± 0.89	0.601 [b]	0.00 ± 0.78	0.764 [b]
Often	498	−0.04 ± 0.92		0.03 ± 0.96	
Sometime	765	0.03 ± 0.94		−0.02 ± 0.77	
Seldom	238	0.02 ± 0.87		0.02 ± 0.93	
Never	12	−0.21 ± 0.59		−0.18 ± 0.33	
Education					
Master's degree or above	297	0.11 ± 0.99	0.034 [a]	−0.10 ± 0.24	<0.0001 [a]
University degree or below	1318	−0.03 ± 0.90		0.02 ± 0.94	
Sleep duration per day					
Less than 5 h	63	0.26 ± 1.04	<0.001 [b]	0.29 ± 1.88	0.069 [b]
Between 5 and 6 h	563	0.12 ± 1.00		0.01 ± 0.91	
Between 6 and 7 h	719	−0.06 ± 0.85		−0.04 ± 0.68	
Between 7 and 8 h	232	−0.14 ± 0.87		0.01 ± 0.82	
More than 8 h	38	−0.10 ± 0.75		0.01 ± 0.46	
Coffee intake per day					
More than 2 cups per day	26	0.61 ± 1.25	<0.001 [b]	−0.17 ± 0.20	0.853 [b]
2 cups per day	70	0.18 ± 0.97		−0.03 ± 0.62	
1 cup per day	556	0.06 ± 0.95		−0.01 ± 0.88	
Occasionally	678	−0.04 ± 0.90		0.02 ± 0.82	
Never	285	−0.13 ± 0.81		−0.00 ± 0.97	

Table 2. *Cont.*

Survey Variables	Individuals	Score on the Frequency of Musculoskeletal Pain			
		Mean ± SD			
		NBSP Score	*p*-Value	BAP Score	*p*-Value
Alcohol use					
Alcohol use in a month	609	0.10 ± 0.97	0.001 [a]	0.01 ± 0.84	0.857 [a]
No alcohol use in a month	1006	−0.06 ± 0.88		−0.00 ± 0.86	
Exercise at least once a week					
Yes	933	−0.07 ± 0.87	0.001[a]	−0.01 ± 0.80	0.705 [a]
No	682	0.09 ± 0.97		0.01 ± 0.93	
Overtime work in a month					
More than 80 h	5	0.54 ± 1.35	<0.001 [b]	−0.25 ± 0.41	0.587 [b]
45–80 h per month	54	0.44 ± 1.14		0.04 ± 1.46	
Fewer than 45 h	502	0.09 ± 0.96		0.04 ± 1.46	
Seldom	1054	−0.07 ± 0.87		−0.02 ± 0.73	
Shift schedules					
Irregular shifts	192	0.16 ± 1.05	0.075 [a]	−0.06 ± 0.49	0.445 [a]
Regular shifts	196	−0.04 ± 0.91		0.02 ± 0.88	
Night shifts	166	−0.05 ± 0.84		0.08 ± 1.13	
Day shifts	1061	−0.15 ± 0.91		−0.01 ± 0.85	
Profession					
Physicians	138	0.03 ± 1.01	0.036 [b]	−0.01 ± 0.80	0.889 [b]
Nurses	613	0.08 ± 0.94		0.02 ± 1.00	
Professional and technical personnel	283	−0.06 ± 0.84		−0.02 ± 0.59	
Administrative staff	581	−0.06 ± 0.90		−0.01 ± 0.82	
Suffering from chronic diseases					
Yes	638	0.20 ± 1.03	<0.0001 [a]	0.04 ± 1.16	0.195 [a]
No	977	−0.13 ± 0.81		−0.03 ± 0.57	

Note: SD, standard deviation; [a] *t* test; [b] one-way ANOVA; NBSP, neck and both shoulders pain; BAP, both ankles pain.

Since the number of individuals with a sleep duration of less than 5 h per day was only 63 (Table 2), the variables of sleep duration of less than 5 h per day and sleep duration between 5 and 6 h per day were combined into a new variable: sleep duration of less than 6 h per day (SLD < 6 h). Furthermore, since the number of individuals who drank more than two cups of coffee per day was only 26, the variables of drinking more than two cups of coffee per day or drinking just two cups of coffee per day were combined into a new variable: drinking multiple cups of coffee (MCC) per day.

As shown in Table 3, which presents the effects of sleep duration per day and drinking MCC per day on NBSP, drinking MCC per day was significantly associated with an increased level of NBSP in the simple or multiple linear regression models (B = 0.32, $p = 0.001$; 0.23, $p = 0.016$), while SLD < 6 h was significantly associated with an increased level of NBSP in the simple or multiple linear regression models (B = 0.21, $p < 0.0001$; 0.15, $p = 0.001$). The results in Table 3 confirm Hypotheses 1 and 2 (illustrated in the introduction), that coffee intake (more than two cups per day) and a shorter sleep duration (less than 6 h per day) are associated with MS pain (especially neck and both shoulders pain).

Finally, this study used mediation analysis to determine the existence of a mutual relationship between coffee, MS pain, and sleep. Figure 1.1 demonstrates that drinking MCC per day mediated the effect of SLD < 6 h on increased levels of NBSP ($Z_m = 2.27$, $p < 0.05$). Lack of sleep (<6 h) also caused individuals to drink more coffee per day, which led to more frequent neck and shoulder pain. Figure 1.2 illustrates that SLD < 6 h mediated the effect of drinking MCC per day on increased NBSP ($Z_m = 2.95$, $p < 0.01$). Overall, Figures 1 and 2 demonstrate that long-term coffee drinking and lack of sleep can further increase the occurrence of neck and shoulder pain.

Table 3. Effect of SLD and drinking MCC per day on NBSP.

Main Effect	Unstandardized Linear Regression Coefficient (B) for NBSP					
	Simple Regression			Multiple Regression[1]		
	B	SE	*p*	B	SE	*p*
Drinking MCC per day	0.32	0.10	0.001	0.23	0.10	0.016
SLD < 6 h per day	0.21	0.05	<0.0001	0.15	0.05	0.001

SE, standard error; B, unstandardized linear regression coefficient; [1] model was in the presence of adjusted variables, including gender, age, marriage, having children, education, alcohol use, exercise, overtime work, profession, and suffering from chronic diseases.

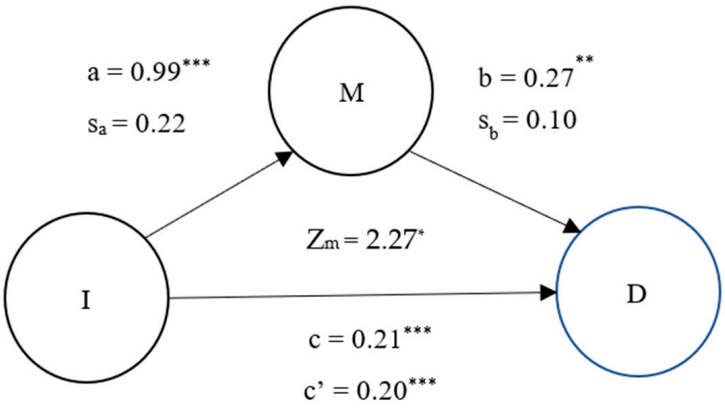

Figure 1. Mediation effect of MCC per day on SLD < 6 h and NBSP. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.0001$; M, mediation factor; I, independent variable; D, dependent variable.

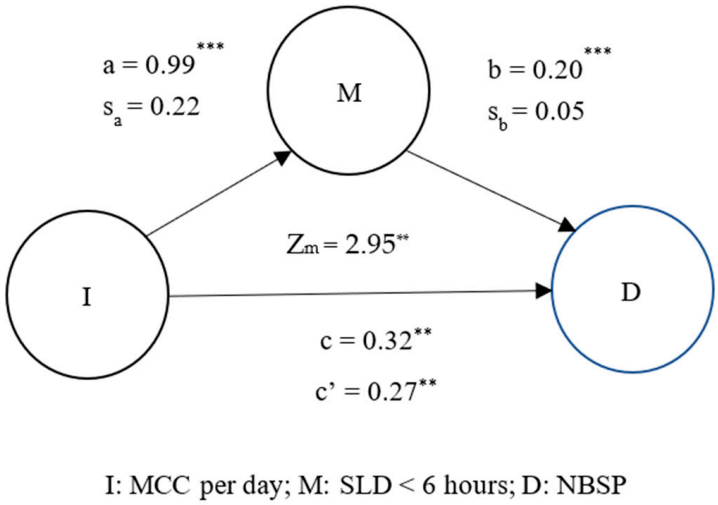

Figure 2. Mediation effect of SLD < 6 h on MCC per day and NBSP. ** $p < 0.01$; *** $p < 0.0001$; M, mediation factor; I, independent variable; D, dependent variable; c is the simple linear or logistic regression coefficient for the independent variable against dependent variable in the absence of mediation factor; c′ is the binary linear or logistic regression coefficient for the independent variable against dependent variable in the presence of mediation factor; a is the simple linear or logistic regression coefficient for the independent variable against the mediation factor; b is the regression coefficient for the mediation factor against the dependent variable in the binary linear or logistic regression model; s_a and s_b represent the standard deviations of a and b.

Figure 3 adopts SLD < 6 h and NBSP as dependent and independent variables for the mediation model, respectively. Based on the findings, drinking MCC per day mediated SLD < 6 h and increased NBSP ($Z_m = 2.5$, $p < 0.05$). Specifically, individuals who suffer from neck and should pain tend to drink coffee to cope with such pain. However, it eventually decreases their sleep duration per day. Figures 1–3 confirmed Hypothesis 3 and determined that coffee intake (more than two cups per day) really opens the vicious circle between lack of sleep (less than 6 h per day) and MS pain (especially neck and shoulders pain).

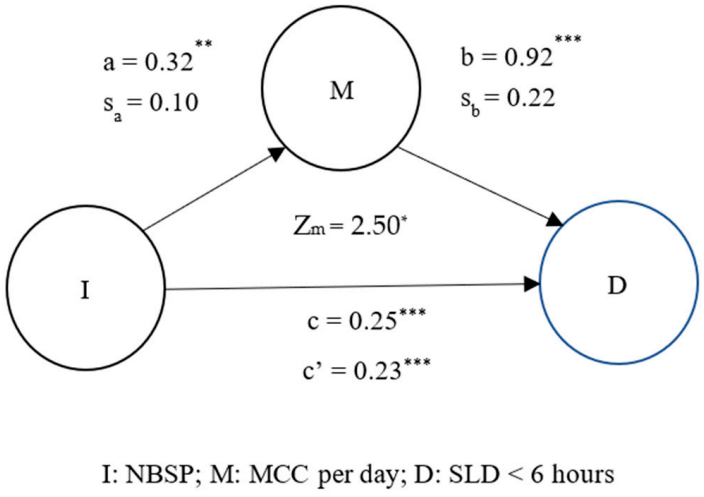

Figure 3. Mediation effect of MCC per day on NBSP and SLD < 6 h. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.0001$; M, mediation factor; I, independent variable; D, dependent variable; c is the simple linear or logistic regression coefficient for the independent variable against dependent variable in the absence of mediation factor; c′ is the binary linear or logistic regression coefficient for the independent variable against dependent variable in the presence of mediation factor; a is the simple linear or logistic regression coefficient for the independent variable against the mediation factor; b is the regression coefficient for the mediation factor against the dependent variable in the binary linear or logistic regression model; s_a and s_b represent the standard deviations of a and b.

4. Discussion

The present study confirms three hypotheses and determined that long-term heavy coffee intake (two cups per day) and a shorter sleep duration (<6 h per day) are associated with neck and shoulder pain. Notably, long-term heavy coffee intake plays a mediating factor in the vicious circle between shorter sleep duration and neck and shoulder pain. In addition, alcohol use, the lack of regular exercise at least once a week, overtime work in a month, and the presence of chronic diseases were significantly associated with pain in the neck/shoulders or ankles.

Related studies have illustrated that reduced alcohol use [18–21], physical activity [21], and fewer work hours [14] could reduce the risk of MS pain. In addition, individuals with chronic diseases [26,27] have a high risk for MS pain. These risk factors are consistent with our findings.

A literature review on healthcare workers demonstrated that MS pain occurred primarily in the lower and upper back, neck, and shoulders [53]. Our study found that the common pain sites were the shoulders (43.09%), neck (36.22%), waist or lower back (27.93%), and upper back (16.90%), which was consistent with the findings of a previous study.

Only 25% of adults achieve the recommended minimum sleep duration of 7 h per night for healthy adults [39]. However, only 16.72% of healthcare workers in the present study satisfy the 7 h sleep condition, as shown in Table 2. Therefore, the lack of sleep could be a common problem among healthcare workers in Taiwan, and this should be noted and further explored.

4.1. First Hypothesis: Coffee Intake Is Significantly Associated with an Increased Risk of MS Pain

Previous studies have found that individuals with a high caffeine intake (4–12 cups/day) had more severe pain than those with a low (0.25–1.5 cups/day) or moderate (2–3.5 cups/day) caffeine intake [54]. In addition, men who drink more than seven cups of coffee per day have an increased risk of knee osteoarthritis [7]. Our study determined that among healthy individuals, long-term drinking of more than two cups of coffee per day was associated with frequent neck and shoulder pain (Table 3, B = 0.23, $p = 0.016$). Since the half-life of caffeine is approximately 4 h [55], drinking two or more cups of coffee per day can reach the threshold of caffeine's effect on MS pain, depending on one's genetics [56]. Based on these results, we can confirm our first hypothesis.

4.2. Second Hypothesis: Individuals with Shorter Sleep Durations Are More Susceptible to MS Pain

Evidence suggests a close link between short sleep durations and impairments in several physiological responses, including pain [57]. A study on middle-aged adults in the U.S. demonstrated that a sleep duration of <6 h was associated with greater next-day pain [58]. In addition, individuals who reported >6 h of sleep were more likely to have improved pain conditions [59]. Our study found important evidence that sleep duration was associated with MS pain at specific sites. Individuals with sleep durations of <5 or 6 h tend to experience more neck and shoulder pain than others (Table 2; mean = 0.26 ± 1.04, 0.12 ± 1.00). Table 3 shows that a sleep duration of <6 h per day was significantly associated with increased neck and shoulder pain in the multiple regression model (B = 0.15, $p = 0.001$). These results confirm our second hypothesis.

4.3. Third Hypothesis: Coffee Intake Could Lead to a Vicious Circle between Lack of Sleep and MS Pain

A previous study showed that individuals who reported a sleep duration of <6 h consumed 3.6 times more caffeine per day than those who reported a sleep duration of >8 h [40]. Our study of healthcare workers found that individuals who reported a sleep duration of <6 h consumed 2.69 times (Figure 1.1, $\beta = 0.99$, odds ratio = e0.99 = 2.69, $p < 0.0001$) more caffeine per day than those who reported a sleep duration of >6 h. This close relationship between sleep duration and coffee intake indicates a causal relationship between sleep duration, NBSP, and coffee intake.

The mediation model in Figure 1.1 demonstrates that individuals who had shorter sleep durations tended to drink multiple cups of coffee, which can lead to increased MS pain (Zm = 2.27, $p < 0.05$). In addition, the mediation model in Figure 1.2 shows that individuals who chronically drink multiple cups of coffee generally experience shorter sleep durations and increased MS pain (Zm = 2.95, $p < 0.01$). These mediation models regarding coffee intake, MS pain, and sleep duration show that long-term heavy coffee intake (more than two cups per day) plays a mediating role in the two-way association of sleep duration <6 h and NBSP. Specifically, long-term heavy coffee intake will induce a vicious circle of sleep and neck and shoulder pain. These results are consistent with our third hypothesis.

This study has several limitations. First, we used the number of cups to measure the degree of caffeine intake per day. However, this is not an exact measurement method because cups have different volumes. Second, different coffee-brewing methods can lead to varied caffeine concentrations and errors in the dose–response of caffeine on MS pain. However, we believe that the differences in volume and caffeine concentration can be overcome. In addition, caffeine's effect on MS pain reaches the threshold depending on one's genetics [56]. Therefore, the threshold of more than two cups of coffee per day might not be suitable for other countries or races. Additionally, since sleep duration and sleep quality are subjective, future research should adopt other scales to measure sleep-related issues. Third, MS pain can be the result of workloads, work styles, or posture. Unfortunately, our study did not collect such data in the regression models. Fourth, the

effects of caffeine on individuals can be associated with genetics [56] and nationality. For example, the effects of coffee intake on MS pain in Europeans or Americans may differ from our results because our participants were Taiwanese.

Despite the adjustment for sex in the multiple linear regression, the results of the present study could be better suited to women because female participants accounted for >80% of the study population. Regarding the sex difference in MS pain, it could be caused by estrogen and progesterone. For instance, testosterone, the major male sex hormone, protects men from chronic MS pain [60]. Because the study population only included physicians, nurses, professional and technical personnel, and administrative staff, we added "healthcare workers" in the title to limit the applicability to occupational groups.

Notably, we could determine whether high work stress or emotional exhaustion caused by the pandemic affected the findings; thus, a similar study during the nonpandemic period should be replicated, and its results compared with those from the pandemic period. Finally, the mediation models in our study could be biased [61] because the relationship was based on a higher risk of judgment. Therefore, we excluded the phrase "causal relationship" to avoid confusion.

5. Conclusions

The present study determines that keeping good living habits (such as decreased alcohol use, regular exercise a week, and sufficient sleep), maintaining physical health (such as staying away from chronic diseases), and avoiding overtime work are ways to lower the risk of MS pain. We further examined the effects of frequent coffee drinking on individuals experiencing MS pain and lack of sleep. Based on the results, neck and shoulder pain was the most common among the healthcare workers. In addition, a sleep duration of less than 6 h and drinking more than two cups of coffee per day increased the occurrence of such pain, while controlling for other risk factors. Notably, long-term heavy coffee drinking created a vicious cycle between neck and shoulder pain and sleep duration of less than 6 h. The implication of the findings is that individuals who sleep less than 6 h, or who suffer from neck and shoulder pain, should limit their coffee intake to two cups per day.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/jpm13010025/s1, Table S1: the description of basic demography of 1615 participants; Table S2: The description of sleep duration per day for all individuals; Table S3: The description of coffee intake per day for all individuals.

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Data Availability Statement: The original contributions presented in this study are included in the article/Supplementary Material. Further inquiries can be directed to the corresponding author.

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Relationships between Alcohol Use, Musculoskeletal Pain, and Work-Related Burnout

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Abstract: *Background and Objectives*: Burnout affects approximately half of all nurses, physicians, and other clinicians. Alcohol use may impair performance in work-related tasks, leading to decreased productivity and morale. The present study's aim was to determine whether a causal relationship existed between alcohol use, work-related burnout (WB), and musculoskeletal pain. *Materials and Methods*: A total of 1633 members from a hospital affiliated with a medical university in Taichung, Taiwan, completed questionnaires in 2021, where 1615 questionnaires were declared valid. Questionnaires were used to obtain information on basic demographic variables, and the Nordic Musculoskeletal Questionnaire and Copenhagen Burnout Inventory were used. Statistical analyses were performed using SAS Enterprise Guide 6.1 software, and significance was set at $p < 0.05$. *Results*: Work experience, being married, parenthood, leisure activities with family and friends, and regular weekly exercise were negatively associated with WB. In addition, overtime work, irregular and regular shift work, the physician and nurse medical profession, chronic disease (heart disease, diabetes, etc.), neck and both shoulders pain (NBSP), both ankles pain (BAP), and alcohol use frequency (AUF) were positively associated with WB. NBSP could explain the residual effect of AUF on WB. AUF was determined to mediate the relationship between NBSP and WB. In addition, NBSP was found to mediate the relationship between AUF and WB. *Conclusions*: The individuals who used alcohol to cope with NBSP or those with NBSP who often consumed alcohol had worsened WB due to a vicious circle of musculoskeletal pain and alcohol use. Therefore, medical staff should not consider alcohol use as an option to reduce burnout.

Keywords: alcohol use; musculoskeletal pain; work-related stress; burnout

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1. Introduction

Burnout was first described in 1974 by the clinical psychologist Herbert Freudenberger, who borrowed the term from drug-addict slang [1]. Burnout refers to physical, emotional, and mental exhaustion resulting from long-term work situations [2]. To measure burnout, Christina Maslach proposed the Maslach Burnout Inventory in 1981, and the extent of an individual's symptoms in each dimension is measured on the basis of the three subscales of emotional exhaustion, depersonalization, and a diminished sense of personal accomplishment [3]. The Copenhagen Burnout Inventory (CBI) developed by researchers from Denmark is another scale used to measure burnout [4]. The CBI considers exhaustion as the core of the burnout concept and includes three scales, namely, the personal burnout scale,

work-related burnout (WB) scale, and client burnout scale, which can be separately used to measure burnout in different settings (not only for service professions); the questionnaire is developed in such a manner that it is suitable for individuals from all occupations [4]. In contrast with personal and client burnout, WB is defined in the CBI as the degree of physical and psychological fatigue and exhaustion that is perceived by the person as related to paid work of some kind [4].

The severe clinical presentations of burnout include emotional exhaustion, physical fatigue, cognitive impairments, disturbed sleep, and functional impairment [5,6]. A combination of stressors due to long-term work and nonwork on individuals often contribute to clinical burnout [7], which could lead to sleep disturbances, depression, or anxiety disorders [5]. Burnout affects approximately half of all nurses, physicians, and other clinicians [8]. Among them, one-tenth of the nurses worldwide suffer high burnout symptoms [9] and 48.7% of German clinicians meet the criteria for burnout [10]. Notably, clinical burnout is related to a reduced ability to work [7]. Burnout is responsible for high physician turnover and reduced clinical hours, which cause total losses of approximately USD 4.6 billion each year [11]. Notably, burnout also affects the patient-related quality of care [10].

In the United States, 13% of the total workforce loss is associated with body pain conditions and costs an estimated USD 61.2 billion per year [12]. A large study conducted in the Netherlands demonstrated that the top three self-reported musculoskeletal pain sites were the lower back, shoulder, and neck [13]. Moreover, studies reported diverse risk factors for musculoskeletal pain, including long work hours [14], occupational stress [15], alcohol consumption [16], sleep duration [17], and chronic diseases (CDs) [18].

Alcohol use contributes to around 4% of the global burden of disease [19] and is related to premature death, where the major causes are injury, alcoholic liver disease, heart disease and stroke, cancers, and gastrointestinal disease [20]. Alcohol use may impair performance in work-related tasks, leading to decreased productivity and morale [21] and an increased occupational injury risk [22]. Many individuals consume alcohol to alleviate stress caused by working overtime [23] and even to cope with pain [24].

Individuals commonly tend to adopt an alcohol consumption strategy to cope with pain, psychological, or physical troubles. Based on this, the present study asked questions about alcohol use, MS pain, and burnout to establish (1) whether a causal relationship exists between alcohol use, WB, and musculoskeletal pain, and (2) the role of alcohol use in the relationship between musculoskeletal pain and WB?

2. Methods

2.1. Study Population

In this observational and cross-sectional study, we included 2531 employees from a hospital affiliated with a medical university in Taichung, Taiwan, in 2021. The study protocol was approved by the institutional review board of Chung Shan Medical University Hospital on 25 August 2021 (no. CS1-21108).

2.2. Study Measures

The QR-code-linked questionnaires were sent to all eligible participants by email. Among the 2531 members, 1633 (64.52%) completed questionnaires. After exclusion due to missing data, 1615 (63.81%) questionnaires were determined to be valid. The questionnaires were used to obtain information on basic demographic variables, family factors, living habits, work-related factors, and physical health factors. In addition, we used the Nordic Musculoskeletal Questionnaire (NMQ) and the WB scale.

Regarding the education level, the response options were “below high school”, “Bachelor”, “Master”, and “PhD”. The response options for marriage status were “married” and “others”. In terms of family factors, we examined whether the respondents were parents by using the following response options: “without child”, “one child”, “two children”, “three children”, and “over three children”. Raising at least one child was reclassified as a new variable called “parenthood”.

Relationships with family and friends were also evaluated in the questionnaire. For the question "Whether participants engage in leisure activities with family or friends in vacation time?", the Likert scale method was used, where the response options were distinguished as "always", "often", "sometimes", "seldom", and" never"; these were scored as 100, 75, 50, 25, and 0 points, respectively. The data was an ordinal scale that could be suitable for parametric tests (such as *t*-tests, analysis of variance, Pearson correlations, and regression), even when statistical assumptions were violated (such as normal distribution of data) [25]. An item related to the presence of a listed CD was included in the questionnaire, and the presence of one or more diseases was classified as a "yes" response. Regarding AU in the past month, the response options were "always", "often", "sometimes", "seldom", and "never"; these responses were scored as 100, 75, 50, 25, and 0 points, respectively. Finally, the mean value was considered as the new variable AU frequency (AUF). The response options for the sleep duration (SLD) were classified as <5, 5–6, 6–7, 7–8, or >8 h per day; these were reclassified as SLD < 6 h and SLD > 6 h per day. The response options for exercise habit were "at least once a day", "at least once a week", "at least once a month", "less than once a month", or "never". Exercising at least once a day or week was reclassified as regular exercise weekly (REW). The response options for the question on overtime (OT) were "seldom", "less than 45 h per month", "45–80 h per month", and "more than 80 h per month". The responses were reclassified as seldom OT and experiencing OT (including less than 45 h, 45–80 h, and more than 80 h per month). The possible responses to the question on the shift schedule were "day shift work", "night shift work", "irregular shift (IRS) work", and "regular shift (RS) work".

We adopted the NMQ that was modified and translated by the Taiwan Institute of Occupational Safety and Health, which includes questions on the presence of pain attributable to work-related factors in the preceding year and at pain sites. The options for pain sites were the neck, left shoulder, right shoulder, upper back, waist or lower back, left elbow, right elbow, left wrist, right wrist, left hip/thigh/buttock, right hip/thigh/buttock, left knee, right knee, left ankle, and right ankle. If a participant answered "yes" to a question on the experience of work-related pain in the preceding year, they were required to indicate its occurrence frequency: every day, once a week, once a month, once every half year, or at least once every half year (100, 80, 60, 40, and 20 points, respectively).

We used the Chinese version of the CBI [26], which was reported to be a reliable and valid tool (the Cronbach's alpha value was over 0.84 for males and females) for the assessment of burnout and measuring WB. The seven items for measuring WB were as follows:

1. "Is your work emotionally exhausting?"
2. "Do you feel burnt out because of your work?"
3. "Does your work frustrate you?"
4. "Do you feel worn out at the end of the working day?"
5. "Are you exhausted in the morning at the thought of another day at work?"
6. "Do you feel that every working hour is tiring for you?"
7. "Do you have adequate energy for family and friends during leisure time?"

The response options were "always", "often", "sometimes", "seldom", and "never or almost never", and these were scored as 100, 75, 50, 25, and 0, respectively, except for item 7, which was inversely scored (i.e., the responses were scored as 0, 25, 50, 75, and 100, respectively); the calculated mean value indicated the WB level for the participants.

2.3. Data Analysis

Factor analysis [27] was conducted using the NMQ results to determine the underlying variables that explained most of the questionnaire. A univariate linear regression model was used to examine the associations between the dependent variables (DVs) and independent variables (IVs). Multiple linear regression was conducted to determine whether the adjustment for variables significantly affected the associations between IVs and DVs. Mediation effects were analyzed using the strategy proposed by Baron and Kenny [28], in

which (1) the IV significantly affects the mediator (first-stage effect), (2) the IV significantly affects the DV in the absence of the mediator, (3) the mediator exerts a significant unique effect on the DV (second-stage effect), and (4) the effect of the IV on the DV weakens upon the addition of a mediator to the model. Among them, item (2) is only recommended but not required [29]. The formulas are as follows:

$$Y = b_{01} + cX$$

$$M = b_{02} + aX$$

$$Y = b_{03} + c'X + bM$$

where X is an IV, Y is a DV, M is the adjusted variable (i.e., the mediating factor), a is the linear regression coefficient of X against M, b is the linear regression coefficient of M against Y, c is the linear regression coefficient of X against Y, and c' is the linear regression coefficient of X against Y with M as the adjusting variable. The standard errors of a and b are represented by s_a and s_b, respectively. The formula for the Sobel test is as follows:

$$Z = \frac{a \times b}{\sqrt{b^2 s_a{}^2 + a^2 s_b{}^2}}$$

The results exceeding $|1.96|$, $|2.57|$, and $|3.90|$ (for a two-tailed test) are significant at α = 0.05, 0.01, and 0.0001, respectively.

The mediation proportion is defined as the dimensionless proportion of the effect of an IV on a DV mediated through the mediation factor, whose formula is as follows [30]:

$$MP = \frac{a \times b}{c' + a \times b}$$

Analyses were performed using SAS Enterprise Guide 6.1 software (SAS Institute Inc., Cary, NC, USA), and significance was set at $p < 0.05$.

3. Results

3.1. Musculoskeletal Pain Sites and Factor Analysis of the Nordic Musculoskeletal Questionnaire

The prevalences of musculoskeletal pain in a year in both shoulders, the neck, the waist, the lower back, and the upper back were 43.09%, 36.22%, 27.93%, and 16.90%, respectively (Table 1). The mean frequency scores of neck, waist or lower back, right shoulder, left shoulder, and upper back pain were 26.76 ± 37.64, 20.20 ± 34.72, 17.64 ± 33.89, 15.07 ± 31.62, and 12.90 ± 29.77, respectively. According to the principle proposed by Hair and Anderson (1995) [27], factors 1 and 2 were retained because their vector values exceeded 1. Although the eigenvalue of factor 3 was lower than 1, factor 3 was retained to ensure the maximum ability to explain the questionnaire. The factor loadings were converted into standardized scoring coefficients through varimax rotation. The relatively large factor loading values for factors 1, 2, and 3 corresponded to frequency scores for the neck and both shoulder pain (NBSP), both ankle pain (BAP), and both knee pain (BKP), respectively.

Table 1. Musculoskeletal pain sites and factor analysis of the Nordic musculoskeletal questionnaire.

MS Pain Site	MS Pain Subjects	Prevalence (%)	Frequency Score	Factor Loading		
			Mean ± SD	Factor 1	Factor 2	Factor 3
Neck	585	36.22	26.76 ± 37.64	***0.33***	−0.02	−0.03
Left shoulder	325	20.12	15.07 ± 31.62	***0.33***	−0.01	−0.01
Right shoulder	371	22.97	17.64 ± 33.89	***0.33***	0.02	−0.07
Upper back	273	16.90	12.90 ± 29.77	0.17	0.00	−0.01
Waist or lower back	451	27.93	20.20 ± 34.72	0.08	−0.04	0.03
Left elbow	70	4.33	3.29 ± 16.26	−0.05	−0.04	−0.05
Right elbow	113	7.00	5.33 ± 20.43	−0.04	−0.04	−0.02

Table 1. *Cont.*

MS Pain Site	MS Pain Subjects	Prevalence (%)	Frequency Score	Factor Loading		
			Mean ± SD	Factor 1	Factor 2	Factor 3
Left wrist	77	4.77	3.72 ± 17.38	−0.05	0.00	0.01
Right wrist	162	10.03	7.51 ± 23.66	−0.03	−0.03	−0.02
Left hip/thigh/buttock	67	4.15	3.12 ± 15.64	−0.05	−0.07	−0.01
Right hip/thigh/buttock	68	4.21	3.17 ± 15.83	−0.02	−0.04	−0.06
Left knee	80	4.95	3.78 ± 16.98	−0.05	−0.07	***0.51***
Right knee	88	5.45	4.17 ± 18.05	−0.02	−0.04	***0.45***
Left ankle	29	1.80	1.26 ± 10.10	−0.02	***0.49***	−0.05
Right ankle	25	1.55	1.10 ± 9.58	−0.02	***0.54***	−0.05
			Eigenvalues	4.93	1.55	0.68
			Explained variation (%)	57.59	18.12	0.08

3.2. Statistical Results of Response Options for Every Work-Related Burnout Item

Table 2 presents the statistical results of the response options for every WB item. The Cronbach's alpha value of the WB scale was 0.87. The mean values of all items for measuring WB are shown below. The mean values and standard deviations of all items for the WB scale are shown below.

Table 2. Statistical results of the response options for each WB item.

Items for Measuring WB		Response Options for WB (Subjects/Proportion (%))					
		Always	Often	Sometimes	Seldom	Never/Almost Never	Mean ± SD
1.	Is your work emotionally exhausting?	38 (2.33)	98 (6.00)	549 (33.62)	715 (43.78)	233 (14.27)	34.58 ± 22.11
2.	Do you feel burnt out because of your work?	22 (1.35)	79 (4.84)	471 (28.84)	803 (49.17)	258 (15.80)	31.69 ± 20.77
3.	Does your work frustrate you?	14 (0.86)	43 (2.63)	543 (33.25)	810 (49.60)	223 (13.66)	31.86 ± 18.98
4.	Do you feel worn out at the end of the working day?	68 (4.16)	178 (10.90)	680 (41.64)	568 (34.78)	139 (8.51)	41.86 ± 23.16
5.	Are you exhausted in the morning at the thought of another day at work?	61 (3.74)	124 (7.59)	524 (32.09)	718 (43.97)	206 (12.61)	36.47 ± 23.41
6.	Do you feel that every working hour is tiring for you?	18 (1.10)	41 (2.51)	349 (21.37)	896 (54.87)	329 (20.15)	27.39 ± 19.46
7.	Do you have enough energy for family and friends during leisure time?	261 (15.98)	646 (39.56)	528 (32.33)	165 (10.10)	33 (2.02)	35.66 ± 23.56

Cronbach's alpha = 0.87; SD, standard deviation.

As presented in Table 3, work experience was negatively associated with WB (β = −0.23, $p < 0.0001$) and AUF (β = −0.21, $p < 0.01$). Married status and parenthood were protective factors against WB (β = −4.30 and −4.86, respectively; $p < 0.0001$ for both) and AUF (β = −2.68 and −3.10, respectively; $p < 0.05$ for both). Engaging in leisure activities with family and friends was negatively associated with WB (β = −0.14, $p < 0.0001$) but not with AUF (β = −0.00, $p > 0.05$). Regular weekly exercise was a protective factor against WB (β = −5.60, $p < 0.0001$); however, it was not significantly associated with AUF (β = 1.72, $p > 0.05$). SLD < 6 h per day was significantly positively associated with WB (β = 6.27, $p < 0.0001$) and AUF (β = 3.11, $p < 0.05$). The participants with a master's degree or above reported a lower level of WB (β = −2.21, $p < 0.05$) than those with a university or below university degree; however, having a master's degree or above was not significantly associated with AUF (β = 2.17, $p > 0.05$). OT work was a risk factor for WB (β = 8.88, $p < 0.0001$) and AUF (β = 4.33, $p < 0.001$). A significant difference in WB was noted between different shift schedules. IRS and RS work significantly increased WB (β = 8.87 and 6.23, respectively; $p < 0.0001$ for both). Regarding professional fields, physicians (β = 9.89, $p < 0.0001$) and nurses (β = 8.44, $p < 0.0001$) reported higher levels of WB. Moreover, the AUF was significantly higher in the physicians (β = 9.96, $p < 0.0001$). The presence of a CD was positively associated with WB (β = 3.47, $p < 0.0001$) and AUF (β = 3.01, $p < 0.05$). Regarding musculoskeletal pain, NBSP was closely associated with WB (β = 6.30, $p < 0.0001$) and AUF (β = 2.48, $p < 0.01$). In addition, BAP was associated with WB (β = 1.44, $p < 0.01$).

Table 3. Stratified analysis of work-related burnout and alcohol use.

		WB		AUF	
Survey Variables	**N**	**β**	***p***	**β**	***p***
Work experience					
WE	1615	−0.23	***	−0.21	**
Marriage state					
Married	779	−4.30	***	−2.68	*
Unmarried	836	1.00		1.00	
Parenthood					
Yes	703	−4.86	***	−3.10	*
No	912	1.00		1.00	
Leisure activity with family and friends					
mean score	1615	−014	***	−0.00	
Exercise habit weekly					
REW	933	−5.60	***	1.72	
None REW	682	1.00		1.00	
SLD (per day) ranks					
<6 h	626	6.27	***	3.11	*
>6 h	989	1.00		1.00	
Education degree					
Master's degree or above	297	−2.21	*	2.17	
University or below university degree	1318	1.00		1.00	
Overtime work per month					
Experience OT	561	8.88	***	4.33	**
Seldom OT	1054	1.00		1.00	
Shift schedules					
IRS work	192	8.87	***	3.02	
RS work	196	6.23	***	0.29	
Night shift work	166	3.24	*	3.66	
DS work	1061	1.00		1.00	
Professional fields					
Physicians	138	9.89	***	9.96	***
Nurses	613	8.44	***	1.30	
PTs	283	2.17		3.11	
ADs	581	1.00		1.00	

Table 3. *Cont.*

Survey Variables	N	WB		AUF	
		β	*p*	β	*p*
Suffering CD					
Yes	638	3.47	***	3.01	*
No	977	1.00		1.00	
MS pain					
NBSP	1615	6.30	***	2.48	**
BAP	1615	1.44	**	0.19	
BKP	1615	0.75		−0.44	

N, participants; β, the linear regression coefficient; * $p < 0.05$, ** $p < 0.01$, *** $p < 0.0001$.

3.3. The Association between Alcohol Use, Musculoskeletal Pain, and Work-Related Burnout

As presented for M_0 in Table 4, AUF was closely associated with WB (β = 0.07, $p < 0.0001$). After an adjustment for work experience, marriage status, parenthood, leisure activity with family and friends, exercise habit weekly, SLD, education degree, OT work per month, shift schedules, professional fields, and CD in the M_1 model, we observed that AUF was still associated with WB (β = 0.04, $p < 0.01$). In the M_2 model, the residual effect of AUF on WB could be fully explained by NBSP (β = 0.03, $p > 0.05$). Mediation analysis was performed (Table 5) to determine whether a causal relationship existed between WB, AUF, and NBSP.

Table 4. AU effect in the linear regression models of WB.

Main Effect	M_0		M_1		M_2	
	β	*p*	β	*p*	β	*p*
AUF	0.07	***	0.04	**	0.03	

β, the linear regression coefficient; ** $p < 0.01$, *** $p < 0.0001$; M_0, without adjustment for variables; M_1, adjustment for work experience, marriage status, parenthood, leisure activity with family and friends, exercise habit weekly, sleep duration, educational level, overtime work per month, shift schedules, professional fields, and CD; M_2, adjustment for all the variables included in M_1 and an additional variable, namely, NBSP.

Table 5. Mediation effect of AUF on the relationship between NBSP and WB.

IV	M	WB						
		c'	A	s_a	b	s_b	Z	MP (%)
NBSP	AUF	6.19 ***	2.46 **	0.67	0.05 **	0.02	2.07 *	1.95
AUF	NBSP	0.05 **	0.00 **	0.00	6.19 ***	0.41	3.25 **	27.08

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.0001$; M, mediation factor; c', the direct effect of NBSP on WB; a, the first-stage effect of NBSP on AU; s_a, the standard error for a; b, the second stage effect for AUF on WB; s_b, the standard error for b; MP, mediation proportion.

As presented in Table 5, AUF was determined to be a mediator (Z = 2.07, $p < 0.05$) of the relationship between NBSP and WB, with the mediation proportion being only 1.95%. In addition, NBSP was determined to be a mediator (Z = 3.25, $p < 0.01$) of the relationship between AUF and WB, with the mediation proportion being 27.08%.

4. Discussion

Our study's results suggested that alcohol use was associated with increased NBSP, and both were closely related to increased WB. According to the mediation models, alcohol use mediated the relationship between NBSP and WB, causing worse WB. In addition, NBSP was a mediation factor of alcohol use, causing worse WB. Based on this, in response to the two research aims posed in the Introduction: (1) a causal relationship existed between alcohol use, WB, and musculoskeletal pain, and (2) alcohol use was a mediation factor between musculoskeletal pain and WB that increased WB.

Previous studies reported various causes of burnout. For example, a systematic review of the literature on burnout revealed that inexperienced psychotherapists easily experienced burnout due to a sense of hopelessness and an inability to reach idealistic expectations and standards [31]. In this study, work experience was found to be a protective factor against WB ($\beta = -0.23$, $p < 0.0001$; Table 3).

Family members and friends play a vital role in preventing burnout [32]. For instance, health workers reported that they could minimize burnout by obtaining support from family [33]. As demonstrated in Table 3, being married ($\beta = -4.30$, $p < 0.0001$) and parenthood ($\beta = -4.86$, $p < 0.0001$) were negatively associated with WB. These results indicated that family members could effectively reduce the level of WB; this finding is consistent with those of previous studies. Participating in leisure activities can relieve stress, help cope with emotional stress, and moderately maintain physical and mental health [34]. The same finding was observed in this study: engaging in leisure activities with family and friends was negatively associated with WB ($\beta = -0.14$, $p < 0.0001$).

Physiological changes resulting from physical activity can reduce individuals' sensitivity to chronic stress [35]. Thus, engaging in physical activity can lead to faster recovery after experiencing a stressful situation, and thus, reduce the risk of burnout [36]. Our results revealed that regular weekly exercise effectively reduced WB ($\beta = -5.60$, $p < 0.0001$).

Burnout development was closely related to considerably less sleep (<6 h) [37] and disturbed sleep [38]. Similar to the findings of previous studies, our results revealed that the participants with SLD < 6 h/day reported a higher level of WB than those with SLD > 6 h/day ($\beta = 6.27$, $p < 0.0001$).

OT work hours are closely correlated with burnout development in a dose-dependent manner [39]. IRS work is related to a significantly higher level of burnout [40]. The same phenomena were observed in our study: OT ($\beta = 8.88$, $p < 0.0001$) and IRS work ($\beta = 8.87$, $p < 0.0001$) were significantly associated with WB.

Burnout was observed to be markedly higher among practicing physicians than individuals in other careers after adjustment for work hours and other factors [41]. The present study indicated that the physicians reported a higher level of WB than those employed in other fields (Table 3). This result is consistent with those of previous studies.

Burnout is an independent risk factor for coronary heart disease [42] and type 2 diabetes [43]. Similar findings are presented in Table 3. The participants who had at least one CD reported a higher level of WB than those without CD ($\beta = 3.47$, $p < 0.0001$).

The onset of regional neck/shoulder and/or low back pain was associated with an increased risk of burnout [44]. In the present study, NBSP was significantly related to WB ($\beta = 6.30$, $p < 0.0001$). Overall, the increased occurrence frequency of neck and shoulder pain increased WB.

Burnout was strongly associated with alcohol abuse or dependence among American surgeons [45] and was significantly positively associated with higher AU among doctors, nurses, and residents [46]. The present study demonstrated that AUF was significantly associated with work-related burnout in a univariate linear regression (Table 3; M_0: $\beta = 0.07$, $p < 0.0001$). Even after adjusting for other risk factors, we observed that this association was still significant (Table 3; M_1: $\beta = 0.04$, $p < 0.01$). However, this association did not become significant after the addition of an extra adjusted variable, namely, NBSP, in the M_1 model (M_2 model). NBSP fully explained the residual effect of AUF on WB after an adjustment for other risk factors.

Previous studies demonstrated a close relationship between musculoskeletal pain, burnout, and alcohol use. Musculoskeletal pain is associated with the frequency of drinking, and the association between alcohol consumption and pain is curvilinear [47]. For example, moderate alcohol consumption was associated with a decreased risk of disabling chronic back or neck pain [48] and chronic widespread pain [49]. Excessive alcohol use may cause the development of chronic pain by increasing the risk of traumatic injury and deleterious effects on the musculoskeletal system [50]. To determine the causal relationship between AUF, NBSP, and WB, three variables were modeled and the results are presented in Table 5.

The mediation model (Table 5) demonstrated that AUF mediated the relationship between NBSP and WB and that NBSP mediated the relationship between AUF and WB. Some individuals who often reported NBSP used alcohol to cope with pain; however, this strategy worsened their WB due to increased alcohol use (the mediation proportion was only 1.95%). In addition, the individuals who often consumed alcohol often reported NBSP, which further increased WB due to worsening musculoskeletal pain (the mediation proportion reached 27.08%). These relationships formed a vicious circle of WB for medical staff who used alcohol and had musculoskeletal pain.

The present study only surveyed the frequency of alcohol use in the past month and ignored the amount of alcohol intake per day by the participants. This could mean that alcohol's effects on burnout and musculoskeletal pain were weakened. The severity of musculoskeletal pain was also ignored since we could not further explore whether the dose–response relationship between alcohol use and musculoskeletal pain or burnout existed. Notably, our study was conducted during the COVID-19 pandemic. It was reported that over 50% of healthcare professionals reported burnout symptoms during the COVID-19 pandemic, which was mainly caused by contacting patients, supply shortages, and work impacting household activities [51]. However, our study's variables did not include these factors.

5. Conclusions

Work experience, marriage, and parenthood were negatively associated with WB and the frequency of alcohol use. A sleep duration of less than 6 h per day, overtime work, physician medical profession, suffering from CDs, and increased NBSP were positively associated with WB and frequency of alcohol use. Leisure activity with family and friends, regular exercise weekly, and a master's degree or above were negatively associated with WB. Shift work, nurse medical profession, and increased BAP were positively associated with WB.

Alcohol use and NBSP were closely associated, and both were independent risk factors for WB. Mediation models indicated that the individuals who used alcohol to cope with NBSP or those with NBSP who often consumed alcohol had worsened WB due to a vicious circle of musculoskeletal pain and alcohol use. Therefore, medical institutions should positively encourage that staff quit drinking or drink in moderation. In particular, individuals who suffer from neck and shoulder pain should not consider alcohol use to cope with burnout symptoms.

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ORIGINAL ARTICLE

Observational Study

Is burnout a mediating factor between sharps injury and work-related factors or musculoskeletal pain?

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Abstract

BACKGROUND

Burnout, musculoskeletal pain, and sharps injuries (SIs) affect medical workers.

AIM

To establish a model between SIs, burnout, and the risk factors to assess the extent to which burnout affects SIs.

METHODS

This questionnaire was used for an observational and cross-sectional study, which was based on members at a hospital affiliated with a medical university in Taichung, Taiwan, in 2020. The valid responses constituted 68.5% (1734 of 2531). The items were drawn from the Nordic Musculoskeletal Questionnaire and Copenhagen burnout inventory and concerned work experience, occupational category, presence of chronic diseases, sleep duration, overtime work, and work schedule. Factor analysis, chi-square test, Fisher exact test, Multiple linear, logistic regression and Sobel test were conducted. The present analyses were performed using SAS Enterprise Guide 6.1 software (SAS Institute Inc., Cary, NC, United States), and significance was set at $P < 0.05$.

RESULTS

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Personal and work-related burnout ranks, sex, work experience ranks, occupational groups, drinking in the past month, sleep duration per day, presence of chronic diseases, overtime work ranks, and work schedule were associated with SIs. Frequent upper limb and lower limb pain (pain occurring every day or once a week) determined to be related to SIs. High personal burnout (> Q3) and high work-related burnout (> Q3) mediated the relationship between SIs and frequent lower limb pain. Similarly, frequent lower limb pain mediated the relationship of SIs with high personal and high work-related burnout. High personal and high work-related burnout mediated the relationships of SIs with overtime work and irregular shift work. The mediating model provides strong evidence of an association between mental health and SIs.

CONCLUSION

Burnout was determined to contribute to SIs occurrence; specifically, it mediated the relationships of SIs with frequent musculoskeletal pain, overtime work, and irregular shift work.

Key Words: Personal burnout; Work-related burnout; Sharps injuries; Musculoskeletal pain; Mediating factor; Overtime work

Core Tip: Burnout affects approximately half of all nurses, physicians, and other clinicians. Sharps injuries, which frequently occur among health care workers, constitute a critical problem. Our study found burnout was determined to contribute to sharps injuries occurrence; specifically, it mediated the relationships of sharps injuries with frequent musculoskeletal pain, overtime work, and irregular shift work. Results from the present study suggest that if the problem of burnout is ignored, training or safe operation may not be sufficient to effectively prevent work-related injuries. To the best of our knowledge, this finding has never been reported.

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INTRODUCTION

In May 2018, burnout was recognized as an "occupational phenomenon" in the International Classification of Diseases, 11th Revision (ICD-11) of the World Health Organization. Burnout is a state of physical, emotional, and mental exhaustion that results from long-term involvement in work situations that are emotionally demanding[1]. The specific definition of burnout in the ICD-11 is "a syndrome conceptualized as resulting from chronic workplace stress that has not been successfully managed."

Burnout is responsible for high physician turnover and reduced clinical hours, which cause total losses of approximately 4.6 billion dollars in the United States each year[2]. Moreover, burnout affects approximately half of all nurses, physicians, and other clinicians[3]. Studies on resident physicians and nurses have indicated that most cases of burnout are personal or work-related. Studies have noted that work-related burnout (WB) and personal burnout (PB) occur in 30% and 50% of individuals with burnout, respectively[4]. Notably, burnout also affects the patient-related quality of care[5]. The numerous reasons for the development of burnout include basic demographic characteristics such as sex[4,6] and age[7]; occupational factors such as work experience (WE)[8], overtime (OT) work[9], and shift work[10]; lifestyle habits such as sleep duration (SLD)[10,11] and exercise[11]; and health status (*e.g.*, the presence of chronic diseases)[12].

In the United States, 13% of the workforce experience losses in productivity stemming from a painful physical condition, amounting to an estimated US$61.2 billion in pain-related lost productive time each year[13]. Musculoskeletal (MS) in the lower back, shoulders, and neck are most commonly reported[14]. In addition, myofascial pain syndromes from trigger points are among the main causes of MS pain due to traumatic/micro traumatic events (often secondary to occupational postures/attitudes/activities)[15].

The United States Centers for Disease Control and Prevention defines sharp injuries (SI) as an exposure event (blood/body fluid exposure) that occurs when a needle or other sharp object penetrates the skin. SI frequently occurs among health care workers and constitutes a critical infective problem upon contamination of the sharp object. As one study noted, 0.42 hepatitis B infections, 0.05 to 1.30 hepatitis C infections, and 0.04 to 0.32 human immunodeficiency virus (HIV) infections develop per 100 cases of SI per year. The literature review conducted in that study revealed that SIs led to mean costs of €1966 if the source patient was HIV positive and had coinfections of hepatitis B and hepatitis C[16]. SI occurrence has been reported to be associated with occupational factors such as WE[17], work hours[18], and shift work schedules[19] as well as demographic characteristics such as sex[20] and age[21]. Moreover, one article asserted that the experience of SIs was related to the mental health of health care workers[22]. Therefore, the relationship between burnout level (as measured using a routine questionnaire) and SI deserves scholarly attention with regard to the prevention of work-related injuries among medical personnel. In the present study, a model of causal relationships between SI, burnout, and work-related risk factors was established to assess the extent to which burnout affects SI. This investigation serves as a basis on which the impact of mental health on occupational injuries can be further explored in the future. Specifically, the present study examined the relationship between mental health and occupational injuries, with burnout and SI as agent variables.

MATERIALS AND METHODS

This questionnaire was used for an observational and cross-sectional study, which was based on members at a hospital affiliated with a medical university in Taichung, Taiwan, in 2020. Of the 2531 individuals to whom the questionnaire was sent, 1838 (72.6%) completed the questionnaire. After exclusion for missing data, 1734 questionnaires (68.5%) were determined to be valid.

The participants' WE (years) and occupational category were provided by the occupational safety department of the hospital. On the questionnaire, the participants were asked whether they had a listed chronic disease (CD), with the selection of one or more diseases classified as a "yes" response. The participants were also asked whether they had experienced a SI in the past year. In response to the question on smoking in the past month, "never" or "have quit smoking" were classified as "no." As for drinking in the preceding month, answers of "seldom" or "every day" were classified as "yes," whereas "never" was classified as "no." SLD was classified as < 5, 5–6, 6–7, 7–8, or > 8 h. The participants were asked whether they exercised at least once a day, at least once a week, at least once a month, less than once a month, or never. Possible responses to the question on OT work were the following: seldom, fewer than 45 h per month, 45–80 h per month, and more than 80 h per month. The responses were classified as seldom, < 45 h per month, and > 45 h per month accordingly. As for work schedule, the options given were day shift work, night shift work, irregular shift work, and regular shift work.

This study adopted the Nordic MS Questionnaire (NMQ) modified and translated by the Taiwan Institute of Occupational Safety and Health[23]. The NMQ, which is used in the investigation of the site and frequency of MS pain, was developed in a project funded by the Nordic Council of Ministers. The NMQ has acceptable reliability [23] and has been applied in a wide range of occupational groups, including nurses [24]. Items on the NMQ include questions on the presence of pain attributable to work-related factors in the preceding year and on the pain sites, the options for which were the neck (N1), left shoulder (N2), right shoulder (N3), upper back (N4), waist or lower back (N5), left elbow (N6), right elbow (N7), left wrist (N8), right wrist (N9), left hip/thigh/buttock (N10), right hip/thigh/buttock (N11), left knee (N12), right knee (N13), left ankle (N14), and right ankle (N15). If a participant answered "yes" to the question on the experience of work-related pain over the past year, they were instructed to indicate its frequency: every day, once a week, once a month, or once

every half year. Pain occurring every day or once a week was defined as frequent MS (FMS) pain and was scored as 1. Pain occurring once a month or once every half year was scored as 0.

In the present study, factor analysis was conducted on the NMQ results to determine the underlying variables that explained most of the questionnaire. According to the principle proposed by Hair *et al*[25], factors that should be retained have feature vector values exceeding 1. Through varimax rotation, the standardized scoring coefficients constituted new factor loadings and were defined as new factors according to the corresponding significance of the factor loadings.

The Copenhagen burnout inventory (CBI), which comprises three scales assessing PB, WB, and client-related burnout, has extremely high internal reliability and low nonresponse rate[26]. The present study used the Chinese version of CBI, which has proven to be a reliable and valid tool for assessment of burnout problems[27]; thus, it was used to evaluate burnout in the present study, with a focus on PB and WB. The first six items, which concern PB, are as follows: C1: "How often do you feel tired?" C2: "How often are you physically exhausted?" C3: "How often are you emotionally exhausted?" C4: "How often do you think 'I can't take it anymore'?" C5: "How often do you feel worn out?" C6: "How often do you feel weak and susceptible to illness?"

Items 7–13, which concern WB, are as follows: C7: "Is your work emotionally exhausting?" C8: "Do you feel burnt out because of your work?" C9: "Does your work frustrate you?" C10: "Do you feel worn out at the end of the working day?" C11: "Are you exhausted in the morning at the thought of another day at work?" C12: "Do you feel that every working hour is tiring for you?" C13: "Do you have enough energy for family and friends during leisure time?"

The response options-"always", "often", "sometimes", "seldom", and "never/almost never"-are scored as 100, 75, 50, 25, and 0 points, respectively, except for item C13, which is inverse scored (*i.e.*, the responses are scored as 0, 25, 50, 75, and 100 points, respectively). Levels of PB and WB are represented by the mean of the total PB and WB scores (the sum of scores on items C1–C6 and items C7–C13), respectively.

The categorical variables were subjected to the chi-square test or Fisher exact test. Significance in the differences among the means of continuous variables was determined using the *t* test or one-way ANOVA. Multiple linear or logistic regression was conducted to control the interference of potential risk factors in the association between the independent variables (IVs) and the dependent variable (DV)-specifically, to determine whether adjustments to variables significantly affected IV–DV associations. Mediation effects were analyzed on the basis of the strategy proposed by Baron and Kenny[28] in which: (1) The IV significantly affects the mediator (first-stage effect); (2) The IV significantly affects the DV in the absence of the mediator; (3) The mediator has a significant unique effect on the DV (second-stage effect); and (4) The effect of the IV on the DV weakens upon addition of the mediator to the model. A method for mediation suitable for a combination of categorical and continuous variables, developed by Iacobucci[29], was used; the (formula 1) are as follows.

$$\hat{Y} = b_{01} + cX$$

$$\hat{M} = b_{02} + aX$$

$$\hat{Y} = b_{03} + c'X + bM$$

$$Z_a = \hat{a}/\widehat{S_a}$$

$$Z_b = \hat{b}/\widehat{S_b}$$

Where *X* is an IV; *Y* is a DV; *M* is the adjusted variable (*i.e.*, the mediating factor) in a simple mediation model; *a* is a logistic/Linear regression coefficient of *X* against *M* when *M* and *X* are a DV and IV, respectively; *b* is the logistic/Linear regression coefficient of *M* against *Y* in a simple mediation model; *c* is the logistic/Linear regression coefficient of *X* against *Y*; and *c*' is the logistic/Linear regression coefficient of *X* against *Y* with *M* as the adjusting variable. The standard errors of *a* and *b* are represented by s_a and s_b, respectively.

The original formula of the Sobel test was rederived into formula 2.

$$Z_{mediation}\,(Z_m) = \frac{\frac{a}{s_a}\times\frac{b}{s_b}}{\sqrt{{Z_a}^2+{Z_b}^2+1}}$$

Results exceeding |1.96| and |2.57| (for a two-tailed test) are significant at α = 0.05 and α = 0.01, respectively. The present analyses were performed using SAS Enterprise Guide 6.1 software (SAS Institute Inc., Cary, NC, United States), and significance was set at $P < 0.05$.

RESULTS

As shown in Table 1, the mean PB and WB scores were 36.69 ± 17.59 and 34.19 ± 16.29, respectively. SI incidence was 8.42%. Q1, Q2, and Q3 represented the lower quartile, median, and upper quartile, respectively. The highest proportions of SIs (12.55% and 12.42%) corresponded to PB and WB (rank > Q3 for both), respectively. Differences in SI occurrence were significant among the PB or WB ranks. Women reported higher PB and WB than men (37.39 *vs* 33.64 and 34.89 *vs* 31.13, respectively; $P < 0.01$ for both), but SIs were more common in men (13.85% *vs* 7.17%; $P < 0.01$). Regarding WE, ranks > Q2 and ≤ Q3 corresponded to the highest PB level (mean = 38.94 ± 17.60), whereas a rank > Q3 corresponded to the lowest WB level (mean = 31.36 ± 15.46). Moreover, ranks > Q1 and ≤ Q2 with regard to WE corresponded to the highest proportion of SI occurrence (12.21%). Significant differences in the proportion of SI occurrence and in the levels of PB and WB were noted among occupational groups, with nurses experiencing the highest PB and WB (41.22 and 39.33). Notably, SIs occurred most commonly among physicians (15.86%). Levels of PB (mean = 39.51) and WB (mean = 36.17) were significantly higher in participants who reported drinking during the preceding month, as was SI occurrence (11.41%). SLD was significantly associated with PB level, WB level, and SI occurrence. The highest PB and WB (mean scores = 48.52 and 41.82, respectively) were observed in the participants who reported sleeping ≤ 5 h per night, as was the highest SI occurrence (14.52%). The participants who exercised daily reported significantly lower PB and WB (mean scores = 31.27 and 28.84, respectively) than those who exercised less frequently, but no significant difference in SI occurrence was noted. Compared with those without such conditions, the participants with CD had significantly higher levels of PB and WB (mean scores = 38.69 and 35.43, respectively) and were more likely to have sustained an SI (10.53%). Burnout levels and SI occurrence differed significantly according to the monthly number of OT hours. Specifically, the participants who worked > 45 h per month had the highest PB and WB (mean scores = 48.51 and 43.73, respectively). These individuals were also the most likely to have sustained an SI (16.98%). Burnout levels and SI occurrence also differed significantly with work schedule. Specifically, the participants who worked irregular shifts reported the highest PB and WB (mean scores = 43.54 and 40.90, respectively) as well as the highest SI occurrence (13.45%).

Table 2 presents information on the sites and occurrence of MS pain experienced over the 12 mo as well as the sites and proportion of MS pain that occurred at least once a week (*i.e.*, FMS pain). Because the eigenvalues of factors 1 and 2 exceeded 1, these factors were retained. Although the eigenvalue of factor 3 was lower than 1, it was retained for the maximum explaining questionnaire. The factor loadings were converted into standardized scoring coefficients through varimax rotation. The relatively large factor loading values in bold for factors 1, 2, and 3 correspond to pain in the upper trunk, lower limbs, and upper limbs, respectively. Frequent upper torso pain (FUTP) occurred in the neck, both shoulders, and upper back, and its standardized coefficient was defined as FUTP. As for frequent lower limb pain (FLLP), sites included both hip/thigh/buttocks, both knees, and both ankles, and its standardized coefficient was defined as FLLP. Frequent upper limb pain (FULP) occurred in both elbows and both wrists, and its standardized coefficient was defined as FULP. The explained variation in FUTP, FLLP, and FULP was 73.86%, 23.11%, and 8.67%, respectively. This indicated that the participants experienced upper trunk pain most frequently, followed by lower limb and upper limb pain. Although FULP had the smallest explained variation of the three, it was retained because the present study was focused on the relationship between SI and upper limb pain.

Table 3 shows that the participants who had experienced an SI in the preceding year had significantly higher FLLP and FULP scores than those who had not, but no significant differences were noted for the FUTP score. In short, FLLP and FULP were identified as risk factors for SIs.

Because of the extremely high proportion of SIs corresponding to PB or WB ranks > Q3 (Table 1), PB rank was reclassified as PB > Q3 and PB ≤ Q3, and WB rank was reclassified as WB > Q3 and WB ≤ Q3. PB > Q3 and WB > Q3 corresponded to high PB level (HPBL) and high WB level (HWBL), respectively. Similarly, the participants who worked irregular shifts had significantly higher PB and WB scores; therefore, the work schedule was reclassified as irregular work shifts (IRWS) and other work schedules. Moreover, because SIs were only reported by nine participants who worked > 45 h of OT per month, OT work was reclassified as an experience of OT (EOT) work and seldom worked OT.

Table 1 Descriptive statistics concerning the results of the Copenhagen burn inventory and occurrence of sharps injuries (*n* = 1734)

Characters	*n*	PB score	WB score	SI
		mean ± SD	mean ± SD	Subject (%)
SI in past one year	1734	36.69 ± 17.59	34.19 ± 16.29	146 (8.42)
PB ranks				[1,b]
> Q3	542	56.93 ± 12.20	-	68 (12.55)
> Q2 and ≤ Q3	482	37.22 ± 3.31	-	30 (6.22)
> Q1 and ≤ Q2	394	27.08 ± 2.09	-	29 (7.36)
≤ Q1	316	13.12 ± 6.79	-	19 (6.01)
WB ranks				[1,b]
> Q3	451	-	54.66 ± 9.45	56 (12.42)
> Q2 and ≤ Q3	572	-	36.70 ± 4.03	39 (6.82)
> Q1 and ≤ Q2	344	-	26.61 ± 1.78	25 (7.27)
≤ Q1	367	-	12.20 ± 7.27	26 (7.08)
Sex		[b]	[b]	[2,b]
Male	325	33.64 ± 16.48	31.13 ± 15.28	45 (13.85)
Female	1409	37.39 ± 17.77	34.89 ± 16.44	101 (7.17)
WE ranks		[b]	[b]	[1,b]
≤ Q1	375	36.23 ± 17.73	34.72 ± 17.37	34 (9.07)
> Q1 and ≤ Q2	434	37.29 ± 17.98	35.12 ± 16.10	53 (12.21)
> Q2 and ≤ Q3	487	38.94 ± 17.60	35.48 ± 16.06	38 (7.80)
> Q3	438	34.07 ± 16.73[c]	31.36 ± 15.46	21 (4.79)
Occupation groups		[c]	[c]	[1,b]
Doctors	145	37.10 ± 17.37	34.11 ± 16.78	23 (15.86)
Nurses	627	41.22 ± 17.27	39.33 ± 15.55	55 (8.77)
Others	962	33.67 ± 17.20	30.84 ± 15.82[c]	68 (7.07)
Right-handed				
Yes	1663	36.89 ± 17.64	34.31 ± 16.31	142 (8.54)
No	71	31.87 ± 15.62	31.34 ± 15.48	4 (5.63)
Drinking in past month		[c]	[b]	[2,b]
Yes	561	39.51 ± 17.05	36.17 ± 16.03	64 (11.41)
No	1173	35.34 ± 17.69	33.24 ± 16.33	82 (6.99)
Smoking in past month				
Yes	12	31.60 ± 16.80	25.89 ± 17.04	2 (16.67)
No	1722	36.72 ± 17.60	34.24 ± 16.27	144 (8.36)
SLD (per day) ranks		[c]	[c]	[1,a]
≤ 5 h	62	48.52 ± 20.62	41.82 ± 17.57	9 (14.52)
> 5 and ≤ 6 h	566	41.04 ± 17.91	38.26 ± 16.47	54 (9.54)
> 6 and ≤ 7 h	771	34.91 ± 16.38	32.35 ± 15.40	66 (8.56)
> 7 h	335	31.23 ± 16.47	29.89 ± 15.80	17 (5.07)
Exercise per day		[b]	[c]	
Yes	133	31.27 ± 18.88	28.84 ± 17.87	11 (8.27)
No	1601	37.14 ± 17.41	34.63 ± 16.08	135 (8.43)

Suffering chronic disease		[b]	[a]	[2,a]
Yes	608	38.69 ± 17.95	35.43 ± 16.70	64 (10.53)
No	1126	35.61 ± 17.31	33.51 ± 16.02	82 (7.28)
OT work ranks		[c]	[c]	[1,b]
> 45 h / mo	53	48.51 ± 19.78	43.73 ± 18.34	9 (16.98)
< 45 h / m	481	41.32 ± 17.21	39.27 ± 15.82	58 (12.06)
Seldom	1200	34.31 ± 17.07[c]	31.73 ± 15.75	79 (6.58)
Work schedule classes		[c]	[c]	[1,b]
Irregular shift	223	43.54 ± 18.63	40.90 ± 16.91	30 (13.45)
Regular shift	204	37.89 ± 17.15	35.19 ± 15.19	25 (12.25)
Night	204	37.77 ± 18.14	37.45 ± 16.26	17 (8.33)
Day	1103	34.88 ± 16.99	32.04 ± 15.89	74 (6.71)

[1]Chi-square test.
[2]Fisher exact test.
[a]$P < 0.05$.
[b]$P < 0.01$.
[c]$P < 0.0001$. OT: Over time; PB: Personal burnout; SD: Standard deviation; SI: Sharp injuries; SLD: Sleep duration; WB: Work-related burnout.

Table 2 Sites of musculoskeletal pain and factor analysis of the Nordic musculoskeletal questionnaire, *n* (%)

Pain site	Pain past 12 months	FMS pain	Factor loadings		
	Subjects	Subjects	Factor 1: Upper torso	Factor 2: Lower limb	Factor 3: Upper limb
Neck	636 (36.68)	405 (23.36)	0.29	-0.04	-0.05
Left shoulder	370 (21.34)	234 (13.49)	0.27	-0.06	-0.03
Right shoulder	444 (25.61)	283 (16.32)	0.29	-0.05	-0.02
Upper back	327 (18.86)	210 (12.11)	0.19	0	0.01
Waist or lower back	529 (35.01)	300 (17.30)	0.12	0.02	0
Left elbow	65 (3.75)	35 (2.02)	-0.03	-0.02	0.25
Right elbow	126 (7.27)	81 (4.67)	-0.01	-0.04	0.27
Left wrist	103 (5.94)	67 (3.86)	-0.03	0	0.24
Right wrist	205 (11.82)	110 (6.34)	-0.02	-0.04	0.31
Left hip/thigh/buttock	70 (4.04)	48 (2.77)	-0.04	0.19	0.04
Right hip/thigh/buttock	70 (4.04)	45 (2.60)	-0.04	0.19	0.05
Left knee	95 (5.48)	51 (2.94)	0.04	0.2	-0.09
Right knee	88 (5.08)	51 (2.94)	0.02	0.29	-0.11
Left ankle	42 (2.42)	31 (1.79)	-0.06	0.23	0
Right ankle	51(2.94)	39 (2.25)	-0.05	0.21	0
Eigenvalues			4.02	1.26	0.47
Explained variation (%)			73.86	23.11	8.67

The relatively large factor loading values were marked in bold for corresponding to musculoskeletal pain sites.

Figure 1 shows the mediation effect of burnout in the association between SIs and the risk factors. The value of *c* must be statistically significant and greater than that of *c*′. Moreover, the values of *a* and *b* must be statistically significant. In addition, $a \times b$ and c-c' must differ significantly and be able to be tested by calculating the $Z_{mediation}$ value (Z_m). HPBL partially mediated the relationships of SI with FLLP ($Z_m = 2.84$),

Table 3 Differences in frequent musculoskeletal pain scores between participants who had and had not experienced an sharps injury in the preceding year

FMS pain score	With SIs in past year	Without SIs in past year	*P* value
	mean ± SD	mean ± SD	
FUTP	0.11 ± 0.97	-0.01 ± 0.86	
FLLP	0.24 ± 1.17	-0.02 ± 0.78	[b]
FULP	0.16 ± 0.96	-0.02 ± 0.70	[a]

[a]$P < 0.05$.

[b]$P < 0.01$. FMS: Frequent musculoskeletal; FUTP: Frequent upper torso pain; Sis: Sharps injuries.

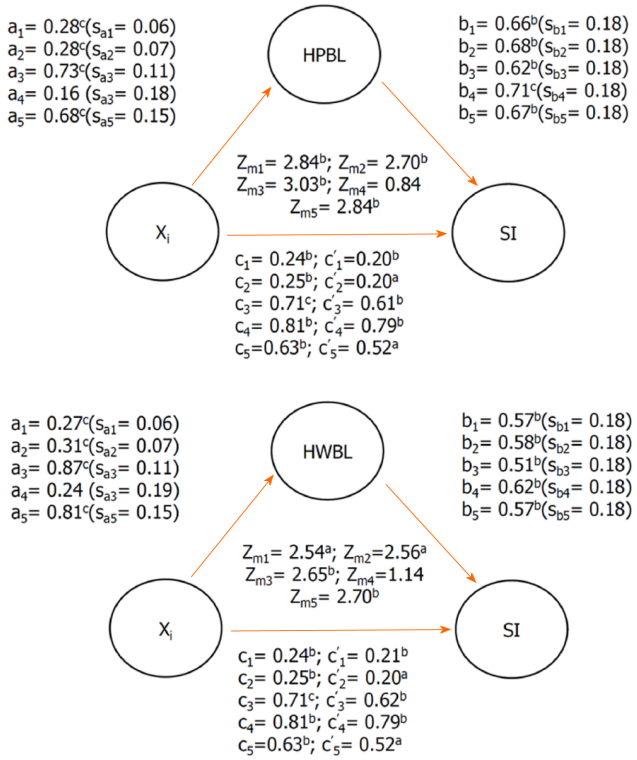

Figure 1 Mediation effects of high personal burnout level/high work-related burnout level in the association between sharps injuries and X_i. $^aP < 0.05$, $^bP < 0.01$, $^cP < 0.0001$. $_1$: Frequent lower limb pain; $_2$: Frequent upper limb pain; $_3$: Experience of overtime *vs* seldom worked overtime; $_4$: Doctors *vs* Nurses and others; $_5$: Irregular work shifts *vs* other work schedules; *ai*: The logistic regression coefficient of risk factors for the association between sharps injurie (SI) and risk factors; s_{ai}: The standard error of a_i; b_i: The logistic regression coefficient of burnout as an adjusted variable with regard to the association between SI and X_i; s_{bi}: The standard error of b_i. SI: Sharps injurie; HPBL: High personal burnout level; HWBL: High work-related burnout level.

FULP (Z_m = 2.70), EOT work (Z_m = 3.03), and IRWS (Z_m = 2.84). HWBL partially mediated the relationships of SI with FLLP (Z_m = 2.54), FULP (Z_m = 2.56), EOT work (Z_m = 2.65), and IRWS (Z_m = 2.70). A strong relationship between FMS pain and burnout was observed, but whether FMS pain also mediated the relationship between SI and burnout remains to be determined. Figure 2 shows FLLP significantly mediated the relationships of SI with HPBL (Z_m = 2.44) and HWBL (Z_m = 2.40). By contrast, the mediating effect of FULP was not significant. Neither FLLP nor FULP mediated the relationships of SI with EOT work, being a physician, and IRWS.

From the analytical results (Table 1-3, Figure 1 and 2), the following inferences can be made: an increase in the frequency of limb pain was closely correlated with an increase in SI incidence, and an increase in burnout level caused by an increase in the frequency of limb pain increased SI occurrence. The participants with HPBL accounted for a higher proportion of the SIs that occurred, and the increase in FLLP caused by HPBL also raised the proportion of SI occurrence. The participants with EOT work were more likely to sustain an SI, as were the participants experiencing serious burnout caused by OT work, which would increase the rate of SI occurrence. Similarly,

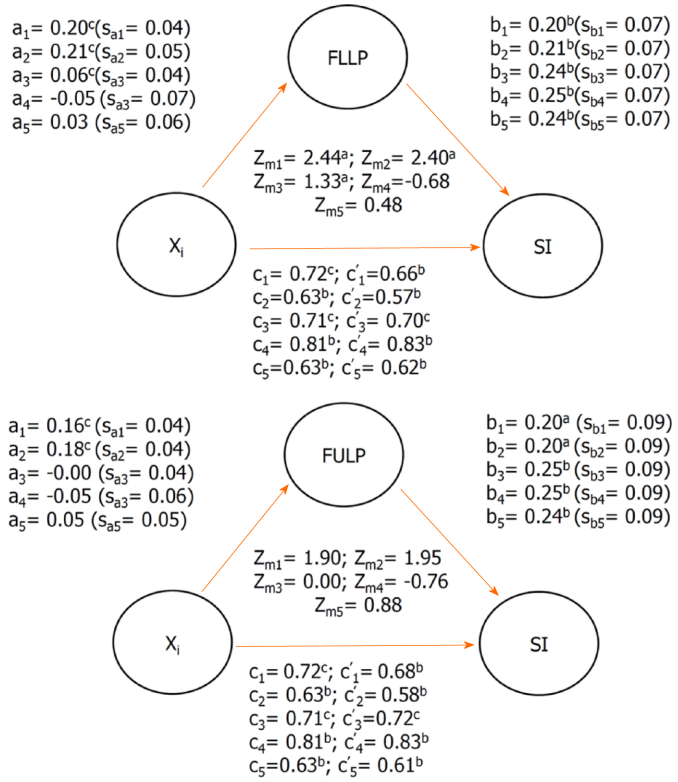

Figure 2 Mediation effects of frequent lower limb pain/frequent upper limb pain in the association between sharps injuries and X_i. $^aP <$ 0.05, $^bP < 0.01$, $^cP < 0.0001$. $_1$: High personal burnout level; $_2$: High work-related burnout level; $_3$: Experience of overtime *vs* seldom worked overtime; $_4$: Doctors *vs* Nurses and others; $_5$: Irregular work shifts *vs* other work schedules; a_i: The logistic regression coefficient of risk factors for the association between sharps injuries (SI) and risk factors; s_{ai}: The standard error of a_i; b_i: The logistic regression coefficient of burnout as an adjusted variable with regard to the association between SI and X_i; s_{bi}: The standard error of b_i. SI: Sharps injurie; FLLP: Frequent lower limb pain; FULP: Frequent upper limb pain.

the participants with IRWS were also more likely to sustain an SI, as were the participants experiencing serious burnout caused by IRWS, which would increase the rate of SI occurrence.

Constructed on the basis of the results presented in Figure 1 and 2 is a simple mediation model that indicates the existence of direct or mediating relationships between SI and FLLP, HPBL/HWBL, and EOT work or IRWS. HPBL and HWBL mediated the SI–FLLP relationship. Similarly, FLLP was a mediating factor in the relationships of SI with HPBL and HWBL. Furthermore, HPBL and HWBL mediated the relationships of SI with EOT work and IRWS.

DISCUSSION

In line with reports that both PB and WB levels are significantly higher among female resident physicians[4] and that male nurses experience burnout syndrome less commonly than female nurses[6], the women in the present sample reported significantly higher PB and WB than the men (Table 1). Regarding SIs, a study indicated that male health workers were 10 times more likely to sustain an SI than were female health workers[30]. The men in the present study were more likely to sustain SIs than the women (13.85% *vs* 7.17%).

Studies have reported that nurses and clinicians working OT are more likely to experience burnout[9]. In one study, an increase in weekly work hours increased the occurrence of SIs among nurses[31]. As shown in Table 1, a dose–response relationship between SI and OT work (> 45, < 45 h, or seldom) was observed. Similar results were noted for relationships of PB and WB with OT. Specifically, more OT work hours increased SI occurrence and the mean levels of PB and WB, and PB and WB was positively associated with SIs. These results suggest that OT work was related to PB and WB level as well as to SI occurrence. PB and WB may contribute critically to the relationship between SI and OT work; this possibility warrants further investigation. As shown in Figure 1, PB and WB partially mediated the relationship between SI and

EOT work; the effects were significant. These results suggest that EOT work affected SI directly or indirectly (through an unknown path). Studies have noted that increased OT was significantly associated with impairments in attention, executive function[32], and stress response[33]. Whether OT work affects SI incidence through these factors remains to be determined.

One study noted that burnout syndrome was more common among nurses working irregular shifts than among those working regular shifts[6]. In the same vein, studies have observed that working regular shifts exerted protective effects against Sis[19,21]. Consistent with results from other studies, in the present study, the highest mean PB and WB was reported by participants working irregular shifts (Table 1). As shown in Figure 1, PB and WB also partially mediated the relationship between SI and irregular shifts, indicating that irregular shifts may have affected SI through burnout in some participants; in others, irregular shifts may have exerted direct effects on SI through other routes.

A large study conducted in the Netherlands on MS pain occurring over 12 mo reported that lower back pain occurred the most frequently (43.9%), followed by shoulder pain (30.3%) and neck pain (31.4%)[14]. In line with these results, the corresponding occurrence of low back pain, shoulder pain, and neck pain in the present study was 35.01%, 46.95%, and 36.68%, respectively (Table 2). A study on seven occupational groups in Norway reported a significant association between burnout and MS pain[34]. In the present study, the frequency of limb pain (lower or upper) was positively associated with HPBL and HWBL (a = 0.28, P < 0.0001; a = 0.28, P < 0.0001; Figure 1). A cross-sectional study on burnout and occupational accidents in which the Maslach Burnout Inventory (MBI) questionnaire was administered to employees in the occupational medicine department of a hospital reported that each one-unit increase in the burnout score corresponded to a 9% increase in the risk of injury[35]. In a study on Chinese nurses in which the MBI questionnaire was again used, emotional exhaustion was positively associated with SI occurrence[36]. Regarding the present results obtained from the CBI, SI occurrence differed significantly in PB (P < 0.01) and WB ranks (P < 0.01) (Table 1). As shown in Figure 2, HPBL (c = 0.72, P < 0.001) and HWBL (c = 0.63, P < 0.01) were positively associated with SI occurrence. The present results are consistent with those from other studies that used the MBI. However, in an extension of the literature, we further explored the causal relationships between SI, work-related risk factors, and burnout through the analysis of mediating effects. As shown in Figure 2, FLLP also mediated the relationships of SI with HPBL and HWBL, indicating that FLLP and HPBL or HWBL form a vicious circle with SI (Figure 3). These findings serve as a valuable reference for SI prevention. To test for significance, we used the Z_m formula developed by Iacobucci[29], which can effectively test for mediating effects in samples exceeding 300 when X, Y, and M are categorical variables. The present sample size of 1734 more than meets this requirement. Therefore, the Z_m formula was suitable.

WE, drinking in the preceding year, SLD, exercise, and CD, variables adjusted in the model, were identified as risk factors for SI and burnout. The significant association of these variables with SI and burnout is supported by results from other studies. For example, studies have indicated that individuals with less WE are at a higher risk of sustaining SIs[17], and the report of burnout was significantly positively associated with higher alcohol consumption[37]. Moreover, PB has been demonstrated to be significantly associated with impaired sleep quality[11], and reductions in SLD increase the risk of occupational injury[38]. University students or nurses who engage in physical activity or exercise have been noted to report significantly lower levels of PB and fatigue[11], and individuals with burnout appear to be more susceptible to physical illness than those without burnout[39]. Therefore, the adjustment of these variables was both necessary and appropriate for reducing the impacts of possible confounders on the SI model.

The burnout mediation model regarding SI and occupational risk factors (*e.g.*, OT work, irregular shift, and MS pain) provides strong evidence of an association between mental health and SIs. The literature mostly examines the relationship between SI and the work process or the use of protective equipment; deeper psychological factors are seldom explored. The relationship between SIs and work-related injuries not induced by burnout warrants further investigation. A study on 112 workers in metal melting industries reported no significant association between occupational burnout and unsafe actions[40]. Despite the small sample size in that study, results from both that study and the present study suggest that if the problem of burnout is ignored, training or safe operation may not be sufficient to effectively prevent work-related injuries. Therefore, to mitigate the problem of work-related injuries, institutions should take effective countermeasures to alleviate burnout among medical personnel.

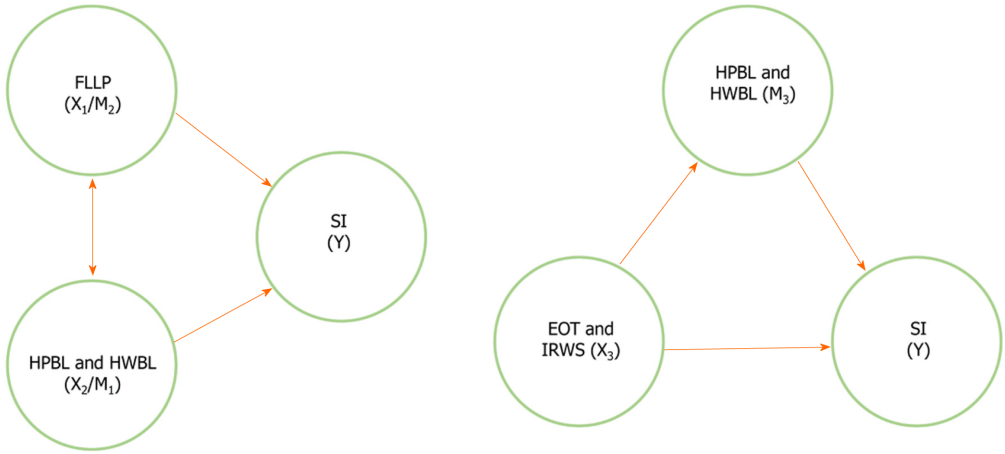

Figure 3 Simple mediation model for burnout and frequent lower limb pain. X_i and Y are the independent and dependent variables, respectively, whereas M_i is the mediating factor of sharps injuries (Y) and X_i. FLLP: Frequent lower limb pain; HPBL: High personal burnout level; HWBL: High work-related burnout level; EOT: The experience of overtime (work); IRWS: Irregular work shifts.

This study was performed in the context of the coronavirus disease 2019 pandemic, which may have been more demanding on medical personnel than the non-pandemic period. Therefore, a similar study that assesses the regular work conditions and exposure of health care workers during the non-pandemic period should be replicated and compared with the result of the pandemic period.

CONCLUSION

Burnout was determined to contribute to SI occurrence; specifically, it mediated the relationships of SI with FUTP, FLLP, EOT, and IRWS. FLLP also mediated the relationship between SI and burnout, forming a vicious circle of burnout and FLLP that further increased the frequency of SIs. To the best of our knowledge, this finding has never been reported. The present findings serve as a reference for the management of mental health and the prevention of SIs among medical personnel worldwide.

ARTICLE HIGHLIGHTS

Research background

Burnout affects approximately half of all nurses, physicians, and other clinicians. Sharps injuries, which frequently occur among health care workers, constitute a critical problem in the hospital.

Research motivation

Studies conducted in many countries revealed the relationship between burnout level (as measured using a routine questionnaire) and sharps injury deserves scholarly attention with regard to the prevention of work-related injuries among medical personnel. However, studies assessing the extent to which burnout affects sharps injuries are scarce.

Research objectives

To be established a model between sharps injuries, burnout, and the risk factors to assess the extent to which burnout affects sharps injuries.

Research methods

A questionnaire was used for an observational and cross-sectional study, which was based on members at a hospital affiliated with a medical university in Taichung, Taiwan, in 2020. The valid responses constituted 68.5% (1734 of 2531). The items were drawn from the Nordic Musculoskeletal Questionnaire and Copenhagen burnout inventory and concerning work experience, occupational category, presence of chronic diseases, sleep duration, overtime work, and work schedule. Factor analysis, chi-

square test, Fisher exact test, multiple linear, logistic regression, and Sobel test were conducted.

Research results

Our study found burnout was determined to contribute to sharps injuries occurrence; specifically, it mediated the relationships of sharps injuries with frequent musculoskeletal pain, overtime work, and irregular shift work.

Research conclusions

Burnout was determined to contribute to SIs occurrence; specifically, it mediated the relationships of sharps injuries with frequent musculoskeletal pain, overtime work, and irregular shift work.

Research perspectives

A similar study that assesses the regular work conditions and exposure of health care workers during the non-pandemic period should be replicated and compared with the result of the pandemic period.

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ORIGINAL ARTICLE

Observational Study

Association of overtime work and obesity with needle stick and sharp injuries in medical practice

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Author contributions: Chen YH and Yeh CJ conceived and designed this manuscript; Jong GP and Yeh CJ analyzed and interpreted the data of this study; Chen YH wrote the original draft; Jong GP and Yeh CJ reviewed and edited the manuscript; Jong GP and Yeh CJ also share equal contribution; all authors were contributed to drafting and/or revising the article, and all authors approved the final version to be published.

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Abstract

BACKGROUND

Needle stick and sharps injuries (NSIs) may cause infections among medical personnel. Obesity and overtime work among medical personnel increase the incidence of work injuries.

AIM

To investigate whether overtime work and obesity increase the risk of NSIs.

METHODS

This cross-sectional study used the data of 847 hospital personnel, including 104 doctors, 613 nurses, 67 medical laboratory scientists, 54 specialist technicians, and nine surgical assistants. Of them, 29 participants notified the hospital of having at least one NSI in 2017. The data collected included age, overtime work, body mass index, medical specialty such as doctor or nurse, and professional grade such as attending physician or resident. The χ^2 and Fisher's exact tests were used to compare categorical variables. Multiple logistic regression analysis and the Sobel test were used to assess the risk of NSIs.

RESULTS

Overtime work, body weight, and medical specialty were significantly associated with NSIs ($P < 0.05$). After adjustment for risk factors, heavy overtime work was an independent risk factor for NSIs, and healthy body weight and nursing specialty were independent protective factors against NSIs. After adjustment for risk factors, medical personnel with healthy body weight has half as many NSIs as

and revised according to the STROBE statement.

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those with unhealthy body weight; the proportion of NSIs in doctors with healthy body weight was 0.2 times that in doctors with unhealthy body weight; the proportion of injuries among residents was 17.3 times higher than that among attending physicians; the proportion of injuries among junior nurses was 3.9 times higher than that among experienced nurses; the proportion of injuries among nurses with heavy overtime work was 6.6 times higher than that among nurses with mild overtime work; and the proportion of injuries among residents was 19.5 times higher than that among junior nurses. Heavy overtime work mediated the association of medical specialty with NSIs.

CONCLUSION
In addition to promoting the use of safety needles and providing infection control education, managers should review overtime schedules, and medical personnel should be encouraged to maintain a healthy weight.

Key Words: Medical staff; Needle stick and sharps injuries; Overtime work; Healthy body weight; Obesity

Core tip: Needle stick and sharp injuries (NSIs) are complex multifactorial processes that are commonly observed in physical, psychological, and environmental fields. Therefore, preventing NSIs in medical personnel remains a critical health issue. To reduce the risk of NSIs, other factors affecting their incidence, such as medical specialty and body weight, should be analyzed. We investigated whether overtime and obesity increase the risk of NSIs. We also aimed to provide insights into the development of more effective prevention plans for NSIs. To the best of our knowledge, these findings have never been reported.

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INTRODUCTION

Needlestick and sharp injuries (NSIs) carry the risk of various infections, such as hepatitis B, hepatitis C, and human immunodeficiency virus (HIV) infections[1,2]. In 2000, occupational exposure to percutaneous injuries caused by medical personnel resulted in 16000 cases of hepatitis C, 66000 cases of hepatitis B, and 1000 cases of HIV worldwide[3]. The mean number of NSIs per 100 occupied beds per year was 4.8–7.6 from 2009 to 2011 in Japan[4]. Poor organizational climate and high workloads are associated with NSIs and near-misses in nurses[5]; however, the incidence of NSIs remains higher among doctors, commonly due to stress or overwork, followed by careless attitude[6]. This careless attitude can be effectively reduced by providing preventive education[7-10] and supplying protective equipment for procedures such as intravenous access or blood draws[5]. Some occupational factors, such as long working hours and overtime, can increase the risk of NSIs among medical personnel [11,12]; the risk of work-related injuries due to overtime has also been observed in other occupations[13]. According to the Survey of Occupational Injuries and Illnesses compiled by the United States Department of Labor, overtime work increased the injury hazard rate by 61%. In particular, the injury hazard rate was increased by 37% and 23% for work that lasted more than 12 h daily and 60 h, respectively, per week [13]. To ensure that medical services are promptly delivered, medical personnel routinely extend their working hours in cases of personnel shortage or sudden spikes in demand at the medical site. In Taiwanese hospitals, medical personnel working overtime mainly comprise doctors, 40% of whom work more than 60 h per week. In particular, 97% and 83% of doctors in medical centers and regional hospitals, respectively, work overtime[14].

Obesity has been significantly associated with diseases such as type 2 diabetes, cardiovascular diseases, and several forms of cancer[15] and occupational injuries[16]. Occupational injuries caused by obesity generally comprise sprains, strains, lower limb injuries, and falls[17]. However, a study found no significant relationship between obesity and contact with sharp material agents without adjusting for medical specialty and overtime work[16]. Male health workers were found to be 10 times more likely than female health workers to encounter NSIs[18]. Furthermore, low work experience was associated with high NSI incidence among nurses[9], and resident doctors (RDs) have a higher incidence of NSIs than do attending physicians (APs)[19]. NSI incidence among doctors differed from that among nurses[7], and RDs had a higher incidence than APs and nurses[19].

NSIs are complex multifactorial processes that are related to physical, psychological and environmental fields. Therefore, preventing NSIs in medical personnel remains a critical health issue. To further reduce the risk of NSIs, other factors affecting NSI incidence should be analyzed, such as medical specialty and body weight (BW), and an effective prevention plan should be developed accordingly.

MATERIALS AND METHODS

This cross-sectional study used data regarding doctors, nurses, and medical laboratory scientists working in Chung Shan Medical University Hospital, Taichung, Taiwan, recorded during 2017. The following data were collected: sex, age, height, weight, intensity of overtime work, medical specialty (doctor, nurse, medical laboratory scientist, specialist, or surgical assistant), professional level (AP or RD for doctors and N, N1, N2, N3 or N4 for nurses based on The Guidelines of Nursing Clinical Ladder System Program in Hospital). In this study, nurses with the professional level of N, which represents < 1 year of clinical work, were categorized as junior nurses (JNs) and nurses with higher levels were categorized as experienced nurses. We defined a medical laboratory scientist as a professional technician (excluding pathology laboratory personnel), a specialized technician as a specialist nurse in some medical specialty, and a surgical assistant as a person who assists a doctor in performing a surgical operation.

This study included 847 participants (104 doctors, 613 nurses, 67 medical laboratory scientists, 54 specialist technicians, and nine surgical assistants). Among them, 29 notified the hospital of having at least one NSI in 2017; NSIs were recorded by the hospital's occupational safety and health department. In this study, the aforementioned data were analyzed after depersonalization. Body weight was classified according to the definition of overweight or obesity by the Health Promotion Administration, Ministry of Health and Welfare. Specifically, body mass index (BMI) between 18.5 and 24.0 was considered a healthy BW (HBW), and any other BMI outside this range was considered an unhealthy BW (UHBW). Overtime work was classified according to the workload levels in the *Guidelines for Prevention of Diseases Caused by Abnormal Workloads (Second Edition)* from the Occupational Safety and Health Administration, Ministry of Labor. Specifically, extra work (both overtime and non-overtime) was categorized as slight (< 45 h/mo), moderate (45–80 h/mo), and heavy (> 80 h/mo) overtime work, respectively.

All statistical analyses were conducted using SAS v6.1 (SAS Institute, Cary, NC, United States). In addition, the χ^2 and Fisher's exact tests were used to compare categorical variables. Multiple logistic regression analysis was used to analyze the correlation of NSI with the study's main variables. The mediation effect was determined using the following approach proposed by Baron and Kenny (1986)[20]: (1) The independent variable (IV) significantly affects the mediator (first-stage effect); (2) The IV significantly affects the dependent variable (DV) in the absence of the mediator; (3) The mediator has a significant unique effect on the DV (second-stage effect); and (4) The effect of the IV on the DV decreases upon the addition of the mediator to the model. Finally, the Sobel test[21] was conducted to determine the significance of this mediation effect, for which the sample size was required to be at least 200[22]. Before performing the Sobel test, if the IV, mediator, or DV was not continuous, the logistic regression coefficient was standardized: X is an independent variable, Y is a dependent variable and M is an adjusting variable (mediating factor) in a simple mediating model. a is the unary logistic regression coefficient of X against M when M is the dependent variable and X is the independent variable. b is the logistic regression coefficient of M against Y in a simple mediating model. c is the unary logistic regression coefficient of X against Y, and c' is the logistic regression coefficient

of X against Y with M as the adjusting variable. Moreover, S_a and S_a were the standard errors of a and b, respectively. Mediation analysis for categorical variables was conducted following the method recommended by Iacobucci (2012)[23].

$$\hat{Y} = b_{01} + cX$$

$$\hat{M} = b_{02} + aX$$

$$\hat{Y} = b_{03} + c'X + bM$$

$$Z_a = \hat{a}/\widehat{S_a}$$

$$Z_b = \hat{b}/\widehat{S_b}$$

The original Sobel test formula was modified as follows:

$$Z_{mediation} = \frac{\frac{a}{s_a} \times \frac{b}{s_b}}{\sqrt{Z_a{}^2 + Z_b{}^2 + 1}}$$

It was considered significant at the α = 0.05 Level if its value exceeded |1.96| (for a two-tailed test with α = 0.05). In this study, statistical significance was indicated by $P < 0.05$.

This study was approved by Institutional Review Board of Chung Shan Medical University Hospital on December 2, 2019 (CSMUH No: CS19137).

RESULTS

Table 1 presents the participant characteristics, including sex, body weight, and level of overtime work. If the χ^2 test's assumptions were violated, Fisher's exact test was performed. Medical personnel were classified as doctors, nurses, and others (which included medical laboratory scientists, specialist nurses, and surgical assistants). Different types of medical personnel differed significantly in terms of NSI, sex, age, and moderate or heavy overtime (Table 1). Among them, the proportion of NSIs was the highest among doctors (7.7%). Furthermore, our cohort had an exceptionally low proportion of male nurses, with 95.9% of nurses being female; by contrast, the proportion of female doctors was lower (26.9%). Among the medical specialties, nurses were the youngest, with a mean age of 33.6 years. Moreover, no significant differences were observed in HBW between the three groups. The proportions of moderate and heavy overtime work among doctors (29.8% and 16.3%, respectively) were significantly higher than those among nurses and others.

Among doctors, APs and RDs differed significantly in terms of NSIs, sex, age, and moderate and heavy overtime, but not in terms of HBW. The proportion of NSIs among RDs (21.2%) was considerably higher than that among APs (21.2% *vs* 1.4%, $P < 0.01$). The significant difference in age between RDs and APs was expected due to the training system (45.5 *vs* 31.0, $P < 0.0001$). The proportion of moderate overtime was higher among APs than RDs (31.0% *vs* 27.3%, $P < 0.01$) but that of heavy overtime was considerably higher among RDs than APs (33.3% *vs* 8.5%, $P < 0.01$).

Nurses of different professional grades (N1–N4) differed significantly in terms of age ($P < 0.0001$) and moderate overtime ($P < 0.05$). Nurses with the professional level of N had the highest proportion of NSIs (6.2%). Age increased with the professional grade, which was expected due to the nursing clinical ladder system. Among nurses, nurses with the professional level of N had the highest proportion of moderate overtime work (32.6%), but the proportion of heavy overtime work was not the highest in this group (4.7%).

As presented in Table 2, the proportion of NSIs in participants with HBW was 0.5 times [odds ratio (OR) = 0.5, $P < 0.05$] that in participants with UHBW in the M_1 model of all participants. The proportion of NSIs in doctors with HBW was 0.2 times (OR = 0.2, $P < 0.05$) that in doctors with UHBW in the M_2 model of doctors. In addition, the proportion of NSIs in nurses with HBW was 0.5 times that in nurses with UHBW, but the difference was not significant.

Table 2 presents a clear effect of heavy overtime work on NSIs: medical personnel with heavy overtime work were 4.3–5.7 times more likely to experience an NSI than those with mild overtime work, and the difference was significant. Similarly, NSIs occurred 5.4 times more proportion in doctors with heavy overtime work (OR = 5.4, $P < 0.05$) than in those with slight overtime work; however, this effect could be

Table 1 Characteristics of study participants according to their medical specialty and professional grade

Variable	Total*n*	NSIs			Female			Age		HBW			Moderate OT			Heavy OT		
		n	%	*P*[1]	*n*	%	*P*[1]	mean ± SD	*P*[2]	*n*[3]	%	*P*[1]	*n*	%	*P*	*n*	%	*P*[1]
Profession groups																		
Doctors	104	8	7.7	[a]	28	26.9	[c]	40.9 ± 10.4	[c]	53	51.0	NS	31	29.8	[b]	17	16.3	[c]
Nurses	613	16	2.6		588	95.9		33.6 ± 8.3		354	57.8		147	24.0		28	4.6	
Others	130	5	3.9		95	73.1		40.6 ± 7.1		64	49.2		15	11.5		0	0.0	
Profession grade (doctor)																		
AP	71	1	1.4	[b]	14	19.7	[a]	45.5 ± 9.3	[c]	33	46.5	NS	22	31.0	[b]	6	8.5	[b]
RD	33	7	21.2		14	42.4		31.0 ± 2.9		20	60.6		9	27.3		11	33.3	
Profession grade (nurse)																		
N	129	8	6.2	[3]	119	92.2	NS	25.3 ± 3.3	[c]	78	60.5	NS	42	32.6	[a]	6	4.7	NS
N1	134	1	0.8		128	95.5		29.0 ± 4.9[b]		70	52.2		35	26.1		3	2.2	
N2	145	3	2.1		140	96.6		34.6 ± 6.7		84	57.9		24	16.6		9	6.2	
N3	143	4	2.8		140	97.9		40.5 ± 6.5		86	60.1		29	20.3		6	4.2	
N4	62	0	0		61	98.4		42.3 ± 4.8		36	58.1		17	27.4		4	6.5	

[a]$P < 0.05$.
[b]$P < 0.01$.
[c]$P < 0.0001$.
NS: Not significant.
[1]Chi-square test or Fisher's exact test.
[2]Moderate overtime work is 45–80 h/mo, and heavy overtime work is > 80 h/mo.
[3]Overweight/Obesity.
OT: Overtime; NSIs: Needle stick and sharps injuries.

explained by the other effects such as HBW (OR = 0.2, $P < 0.05$) and RDs (OR = 17.3, $P < 0.05$). Although nurses with heavy overtime work experienced more NSIs (OR = 3.7 and 3.8) than others, the difference was not significant.

Doctors experienced more NSIs incidence than other types of medical personnel, but the difference was nonsignificant (OR = 1.3–2.1, $P > 0.05$). After adjustment for other variables (M_1 model), the nurse specialty was identified as an independent protective factor for NSIs (OR = 0.3, $P < 0.05$). Among doctors, regardless of whether adjustments were made for other variables, being an RD was an independent risk factor for NSIs (OR = 18.9, $P < 0.01$ and OR = 17.3, $P < 0.05$). Similarly, among nurses, being a JN was also an independent risk factor for NSIs regardless of whether adjustments were made for variables (both OR = 3.9, $P < 0.01$).

Consequently, RDs and JNs were added to the logistic regression model in Table 3 for further exploring the relationships of BW and overtime work with NSI in professional experience. HBW was a protective factor against NSI occurred regardless of whether adjustments were made for variables (M_0, M_1, and M_2). However, after adjustment for HBW and RD effects, the effect of heavy overtime work was no longer significant (M_2, OR = 1.9, $P > 0.05$). The proportion of NSIs among RDs was 4.1 times (M_1, OR = 4.1, $P < 0.05$) higher than that among JNs without adjustment for variables; this increased to 19.5 times (M_2, OR = 19.5, $P < 0.05$) after adjustment for sex, age, overtime work, and body weight. Therefore, UHBW was determined to be an independent risk factor for NSIs in RDs and JNs.

Table 4 presents the results of multiple logistic regressions after adjusting for age for NSI because experienced nurses have a wider age distribution. The results indicated that the proportion of NSIs among nurses with heavy overtime work was 6.6 times (OR = 6.6, $P < 0.05$) higher than that among nurses with mild overtime work, and the difference was significant. However, the proportion of NSIs in nurses with HBW was 1.2 times (M_1, OR = 1.2, $P > 0.05$) that of nurses with UHBW, but the difference was not significant.

Table 5 illustrates the significant mediation effects ($Z_m = 2.5$, $P < 0.05$) of heavy overtime work on the relationship between NSIs and doctors. No mediation effects were noted for the other five combinations.

Table 2 Main effects on needle stick and sharps injuries in different models for all participants

Main effect		ORs of NSIs for All participants				ORs of NSIs for doctors				ORs of NSIs for nurses			
		N	*n*	M_0	M_1	*N*	*n*	M_0	M_2	*N*	*n*	M_0	M_2
Body weight level	HBW	471	11	0.5[NS]	0.5[a]	53	2	0.3	0.2[a]	354	7	0.6	0.5
	UHBW	376	18	1.0	1.0	51	6	1.0	1.0	259	9	1.0	1.0
OT work	Heavy	45	6	5.7[b]	4.3[a]	17	4	5.4[a]	2.0	28	2	3.7	3.8
	Moderate	193	7	1.4	1.2	31	1	0.6	0.5	147	5	1.7	1.4
	Mild	609	16	1.0	1.0	56	3	1.0	1.0	438	9	1.0	1.0
Type of medical personnel	Doctors	104	8	2.1	1.3	-	-	-	-	-	-	-	-
	Nurses	613	16	0.7	0.3[a]	-	-	-	-	-	-	-	-
	Others	130	5	1.0	1.0	-	-	-	-	-	-	-	-
Professional grade (Doctors)	RD	-	-	-	-	33	7	18.9[b]	17.3[a]	-	-	-	-
	AP	-	-	-	-	71	1	1.0	1.0	-	-	-	-
Professional grade (Nurses)	Junior	-	-	-	-	-	-	-	-	129	8	3.9[b]	3.9[b]
	experiencing	-	-	-	-	-	-	-	-	484	8	1.0	1.0

[a]$P < 0.05$.
[b]$P < 0.01$.
[c]$P < 0.0001$.
NS: Not significant.
Odds ratio = 1.0 indicates the reference; ORs: Odds ratios; *N*: Participants; *n*: Participants for needle stick and sharps injuries; M_0: Model only including main effect; M_1: Model adjusted for sex, age, overtime work, and medical specialty; M_2: Model adjusted for sex (only doctors), overtime work, professional grade, and body weight; HBW: Healthy body weight; UHBW: Unhealthy body weight; OT: Overtime; NSIs: Needle stick and sharps injuries.

Table 3 Main effects on needle stick and sharps injuries in various models for resident doctors and junior nurses

Main effect		*N*	ORs for NSIs			
			n	M_0	M_1	M_2
Body weight level	HBW	95	3	0.1[b]	0.1[b]	0.1[b]
	UHBW	52	12	1.0	1.0	1.0
OT work	Heavy	13	4	4.5[a]	4.5[a]	1.9
	Moderate	46	5	1.6	1.6	1.7
	Mild	88	6	1.0	1.0	1.0
Professional subfield	RD	26	7	4.1[a]	12.7[b]	19.5[a]
	JN	121	8	1.0	1.0	1.0

[a]$P < 0.05$.
[b]$P < 0.001$.
Odds ratio = 1.0 indicates the reference. ORs: Odds ratios; *N*: Participants; *n*: Participants for needle stick and sharps injuries; M_0: Model only including the main effect; M_1: Model adjusted for sex and age; M_2: Model adjusted for sex, age, and main effects; RD: Resident doctor; JN: Junior nurse; HBW: Healthy body weight; UHBW: Unhealthy body weight; OT: Overtime; NSIs: Needle stick and sharps injuries.

DISCUSSION

A cross-sectional study evaluating NSI incidence among 29 doctors and 51 nurses demonstrated that the proportion of NSIs among nurses was 0.2 times that among doctors[6]. A study including NSI data from 2002 to 2007 in a university hospital in Pakistan demonstrated that the number of NSIs has higher in junior doctors than in nurses[7]. The differences between doctors and nurses may stem from differences in their work patterns or attitudes. For example, doctors often experience NSIs during wound irrigation, sutures, incisions, handling body fluids, and tissue sample

Table 4 Main effects on needle stick and sharps injuries for experienced nurses

Main effect		Participants	ORs for NSIs		
			n	M_0	M_1
Body weight level	HBW	276	5	1.3	1.2
	UHBW	208	3	1.0	1.0
OT work	Heavy	22	2	7.0[a]	6.6[a]
	Moderate	105	1	0.7	0.7
	Mild	357	5	1.0	1.0

[a]*P* <0.05.

Odds ratio = 1.0 indicates the reference. ORs: Odds ratios; HBW: Healthy body weight; OT: Overtime; NSIs: Needle stick and sharps injuries; *n*: Participants for needle stick and sharps injuries; M_0: Model only including the main effect; M_1: Model adjusted for age, sex, body weight, and overtime work.

Table 5 Mediation effect of heavy overtime work and healthy body weight for needle stick and sharps injuries and the main effect

IV	Mediator factor												
	Heavy OT work[4]							HBW[5]					
	c	c'	a	s_a	b	s_b	Z_m	c'	a	s_a	b	s_b	Z_m
All participants													
Doctors[1]	1.1[a]	0.8	1.6[c]	0.3	1.4[b]	0.5	2.5*	1.0[a]	-0.2	0.2	-0.7[NS]	0.4	0.8
Doctors effect													
RD[2]	2.9[b]	2.6[a]	1.7[b]	0.6	1.1	0.8	1.2	3.3[b]	0.6	0.4	-1.8[a]	0.9	-1.1
Nurse effect													
JN[3]	1.4[b]	1.4[b]	0	0.5	1.2	0.8	0	1.4[b]	0.1	0.2	-0.6	0.5	-0.4

[a]*P* < 0.05.
[b]*P* < 0.01.
[c]*P* < 0.0001.
NS: Not significant.
[1]Reference variable includes nurses and others.
[2]Reference variable is Aps.
[3]Reference variable is experienced nurses.
[4]Reference variable includes moderate overtime and slight overtime.
[5]Reference variable is unhealthy body weight.
IV: Independent variable; RD: Resident doctor; JN: Junior nurse; HBW: Healthy body weight.

collection. By contrast, for nurses, injuries often occur during injections, intravenous infusions, heparin cap sealing, intravenous connections, and venous or arterial blood collection[24]. In addition, some studies have determined that the NSI risk is affected by education and work experience[9,10,25] among nurses and by stress and carelessness[6] among doctors. Consistent with this finding, our study indicated that doctors experienced more NSIs than nurses did (7.7% *vs* 2.6%). In addition, nurses who intensively contact patients were the protective factor of NSIs (OR = 0.3, $P < 0.05$). Our analysis revealed that the proportion of NSIs 4.1 times (OR = 4.1, $P < 0.05$) higher among RDs than among JNs; this increased to 19.5 times after adjusting for age and overtime work. Therefore, the NSI risk among RDs may be more serious than expected and has often been ignored in the past.

A cross-sectional survey of staff physicians, RDs, staff dentists, nurses, and laboratory technicians illustrated that RDs were significantly associated with NSIs; NSIs were three times more common among RDs than among APs[19]. The present data indicate a difference of 17.3 times between RDs and APs (21.2% *vs* 1.4%), which was markedly higher than in past studies. This may be because the numbers of NSIs among APs were low ($n = 1$), which may have led to the overestimation of this result. Nevertheless, the risk of NSIs among RDs was higher than that among other types of

medical personnel; for example this risk was 19.5 times higher in RDs than that in JNs.

Nurses with less work experience have a higher risk of NSIs[5,9]; in particular, nursing work experience of < 5 years was associated with significantly more NSIs than nursing work experience of > 5 years[5,11]. Consistent with these results, our study demonstrated that JNs have a higher risk of NSIs (OR = 3.9, P < 0.001) than experienced nurses after adjustment for other variables.

A cohort study including 11 728 employees revealed that claims costs were 7–11 times higher among those with BMI ≥ 40 compared with those within the recommended weight range[26]. A prospective cohort study of nearly 70 000 public sector employees demonstrated that, compared with employees whose BMI was in the healthy range, overweight or obese employees had an 11%–62% excess risk of occupational injury[16]. In addition, a study involving 7690 employees aged 18–65 years of an aluminum manufacturing company in the USA revealed that the proportion of injuries of participants with overweight or obesity was 1.3–2.2 times higher than those with normal weight[27]. The present results were in agreement with these findings and revealed that the proportion of NSIs among medical personnel with HBW was 0.5 times (OR = 0.5, P < 0.05) that among medical personnel with UHBW. Although we observed a relationship between NSIs and BW, the present study structure and data collected was insufficient to illustrate how BW affects NSIs. However, studies have demonstrated that fatigue increases the risk of NSIs among nurses and medical interns [28,29], and studies on grip strength have identified that, all things being equal, young people with obesity use more energy, have reduced endurance, and have accelerated power loss compared with nonobese young people. However, these obesity-related differences were not observed in the older age group[30]. These studies may explain the positive correlation between obesity and NSIs; obese people are more likely to use their poorer muscle strength improperly and be more prone to fatigue when performing clinical tasks, thus increasing their risk of NSIs.

A strong dose–response effect was noted between work hours and hazard rate[13], and working hours before injury will increase significantly compared to the past[31]. The positive trend between work hours and NSIs was observed in medical personnel: nurses with work hours of > 8 h/d[11] or > 40 h/wk[8] had higher risk of NSIs than those working < 8 h/d or < 40 h/wk. Our study found that the proportion of NSIs in participants with heavy overtime work was 4.3 times (OR = 4.3, P < 0.05) that in those with mild overtime work, but moderate overtime work effect (OR = 1.2, P > 0.05) was not significant; therefore, only heavy overtime work increased the risk of NSIs. Heavy overtime work was a risk factor for NSIs among doctors (OR = 5.4, P < 0.05) without adjustment for any variable, but this relationship was not significant when adjustments were made for sex, overtime work, professional grade, and BW; this was probably due to the higher proportion of heavy overtime work in RDs (33.3%) than in APs (8.5%). A dose–response effect was also noted between overtime work and NSIs for nurses, but it was not significant. However, experienced nurses engaged in heavy overtime work had 6.6 times (OR = 6.6, P < 0.05) more NSIs than those engaged in mild overtime work (Table 4); the effect of moderate overtime work on NSIs was not significant. Therefore, even among experienced nurses, only heavy overtime work affected the risk of NSIs. The proportion of NSIs was related to overtime work, but this relationship was not significant among nurses (Table 2); however, the association between NSIs and overtime work (OR = 6.6–7.0, P < 0.05) was significant among experienced nurses (Table 4). In addition, the mediation analysis (Table 5) demonstrated that heavy overtime work mediated (Z_m = 2.5, P < 0.05) the relationship between NSIs and medical specialty, confirming the impact of heavy overtime work on NSI. However, heavy overtime work and HBW were not mediation factors for the relationship between NSIs and experience level for doctors or nurses, indicating that low experience among medical personnel might itself be the cause of NSIs. A study indicated that the incidence of NSIs among first-year RDs was higher than expected—more than 60% during the first 6 mo[32]—implying that education and training may influence the risk of NSIs. Burnout also increases the risk of occupational accidents and its sequelae[33], and it was also a factor influencing NSIs among nurses [34]. Burnout decreases with an increase in professional experience[35]; this may also explain by burnout why RDs experience higher NSIs incidence than Aps. Future studies should comprehensively assess the burnout level of participants.

Because this study only collected data from one hospital, its findings are limited by the data collection method, sample size, as well as the hospital's environmental facilities, education, and training systems. In addition, because the number of reported NSIs was low, slight variations in the sample could have considerable influence on the conclusions. Moreover, factors such as hospital employees' work patterns, workload, burnout level, work stress, and willingness to report occupational injuries were not

considered in this study. These factors should be incorporated in the questionnaire design of future studies to further control for and discuss these effects on NSI risk. Although our results regarding NSI risk were consistent with those of past studies, this study compared the NSI risk between doctors and nurses, which has been rarely discussed in the literature. The findings can guide NSI prevention strategies in the medical practice.

CONCLUSION

This study revealed that heavy overtime work and low professional experience were associated with an increased NSI risk, particularly among RDs. Moreover, the present data indicated that HBW may reduce the risk of NSIs, which has rarely been evaluated in other studies. Maintaining an HBW had a protective effect against NSI for RDs and JNs. Therefore, in addition to promoting the use of safety needles and strengthening education and training related to infection control, the overtime schedule of medical personnel should be regularly reviewed; long work hours and excessive overtime should be avoided. Furthermore, strategies aimed at promoting the maintenance of HBW among employees should be implemented, which could further reduce NSI incidence.

ARTICLE HIGHLIGHTS

Research background

Needle stick and sharp injuries (NSIs) may cause infections among medical personnel. Obesity and overtime work among medical personnel increase the incidence of work injuries.

Research motivation

The associations of overtime work and obesity with NSIs are unclear.

Research objectives

The study aimed to investigate whether overtime work and obesity increase the risk of NSIs.

Research methods

This cross-sectional study used the data of 847 hospital personnel, including 104 doctors, 613 nurses, 67 medical laboratory scientists, 54 specialist technicians, and nine surgical assistants. Of them, 29 participants notified the hospital of having at least one NSI in 2017. The χ^2 and Fisher's exact tests were used to compare categorical variables. Multiple logistic regression analysis and the Sobel test were used to assess the risk of NSIs.

Research results

Overtime work, body weight (BW), and medical specialty were significantly associated with NSIs. After adjustment for risk factors, heavy overtime work was an independent risk factor for NSIs, and healthy BW (HBW) and nursing specialty were independent protective factors against NSIs. Also, after adjustment for risk factors, medical personnel with HBW had half as many NSIs as those with unhealthy BW (UHBW); the proportion of NSIs in doctors with HBW was 0.2 times that in doctors with UHBW; the proportion of injuries among residents was 17.3 times higher than that among attending physicians; the proportion of injuries among junior nurses was 3.9 times higher than that among experienced nurses; the proportion of injuries among nurses with heavy overtime work was 6.6 times higher than that among nurses with mild overtime work; and the proportion of injuries among residents was 19.5 times higher than that among junior nurses. Heavy overtime work mediated the association of medical specialty with NSIs.

Research conclusions

Heavy overtime work and low professional experience were associated with an increased NSI risk, particularly among resident doctors. Maintaining HBW had a protective effect against NSI for resident doctors and junior nurses.

Research perspectives

In addition to promoting the use of safety needles and providing infection control education, managers should review overtime schedules, and medical personnel should be encouraged to maintain an HBW.

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Sodium-glucose co-transporter-2 inhibitors reduce the risk of new-onset stroke in patients with type 2 diabetes: A population-based cohort study

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Background: Epidemiological evidence suggests the association of diabetes with an increased risk of stroke. Clinical studies have investigated the effects of sodium-glucose co-transporter-2 (SGLT2) inhibitors on new-onset stroke (NOS), but the results are inconsistent.

Objectives: To determine the association between the use of SGLT2 inhibitors and NOS in patients with type 2 diabetes mellitus (DM).

Methods: We conducted a retrospective longitudinal cohort study based on the Taiwan Health Insurance Review and Assessment Service database (2016–2019). The primary outcome of the assessment was the risk of incident stroke by estimating hazard ratios (HRs) and 95% confidence intervals (CIs). Multiple Cox regression was applied to estimate the adjusted HR of NOS. Subgroup analysis was also conducted.

Results: Among the 232,101 eligible patients with type 2 DM aged ≥ 20 years, SGLT2-inhibitor users were compared with non-SGLT2-inhibitor users based on age, sex, and the duration of type 2 DM matching at a ratio of 1:2. The event rate per 10 000 person-months was 9.20 (95% CI 8.95 to 9.45) for SGLT2-inhibitor users and 10.5(10.3–10.6) for non-SGLT2-inhibitor users. There was a decreased risk of NOS for SGLT2-inhibitor users (adjusted HR 0.85, 95% CI 0.82–0.88) compared with non-SGLT2-inhibitor users. Results for the propensity score-matched analyses showed similar results (adjusted HR 0.87, 95% CI 0.84–0.91 for both SGLT2-inhibitor users and non-SGLT2-inhibitor users).

Conclusion: The risk of developing NOS was lower in patients with SGLT2-inhibitor users than in non-SGLT2-inhibitor users. The decreased risk of NOS in patients with type 2 DM was greater among patients with concurrent use of statins, biguanides, thiazolidinediones, and glucagon-like peptide-1 receptor agonists. We, therefore, suggest that the long-term use of SGLT2 inhibitors may help reduce the incidence of NOS in patients with type 2 DM.

KEYWORDS

new-onset stroke, SGLT2 inhibitor, type 2 DM, concurrent medication, ischemic stroke, hemorrhagic stroke

Introduction

The global incidence and prevalence of type 2 diabetes mellitus (DM) have increased over the past two decades and caused much health burden across the world (1, 2). Past studies have demonstrated that type 2 DM is associated with an elevated risk of stroke (3, 4). Stroke in patients with type 2 DM has a poor prognosis, which is marked by worse mortality outcomes relative to that in several other diabetes-related comorbidities, including coronary heart diseases (4). It affects approximately 40% of patients with ischemic stroke who had been diagnosed with diabetes in the United States (5). A study reported that controlling glucose levels with intensive diabetes therapy could reduce the risk of stroke by 57% (6).

Sodium-glucose co-transporter-2 (SGLT2) inhibitors are used in patients with type 2 DM as glucose-lowering therapies targeting SGLT2 (7, 8). Although these drugs are primarily indicated for diabetes, several studies have examined their use in the primary and secondary prevention of stroke (9, 10). Animal studies have demonstrated a neuroprotective effect of SGLT2 inhibitors, which play an important role in antioxidant, anti-inflammatory, and anti-apoptotic mechanisms (11–13). SGLT2 inhibitors also improve the endothelial function, prevent remodeling, and exert a protective effect on the neurovascular unit and the blood–brain barrier, which can be promising in stroke therapy (14). However, the results of previous studies are inconsistent in a clinical setting (15–17). Therefore, the objective of the present study was to evaluate the risk of new-onset stroke (NOS) associated with the prescription of SGLT2 inhibitors in a nationwide cohort study of patients with type 2 DM in Taiwan.

Materials and methods

Study design

This is a retrospective study conducted on a population-based cohort using data from the insurance claims provided by the Taiwanese Bureau of National Health Insurance (TBNHI) from January 2004 to December 2019. This database contains anonymized longitudinal medical records that store the claims' information forms in two tables: a visit table and a prescription table. The visit tables contain the patient's identification numbers, sex, age, three diagnostic codes for outpatient and five for inpatient visits, medications, drug doses, medical expenditures, and hospital and physician information. The prescription table contains the quantity and expenditure for all administered drugs, operations, and treatments undertaken.

Patients included in this study were of age at least 20 years, with a newly diagnosed case of type 2 DM with or without prescribed SGLT2 inhibitors between May 2016 and December 2019. SGLT2-inhibitor users were defined as patients who received at least an SGLT2 inhibitor prescription for 180 days during the study period. In contrast, non-SGLT2 inhibitor users were patients who did not receive an SGLT2 inhibitor prescription throughout the study period.

Study population

The study population comprised patients with type 2 DM (ICD-10-CM, E11) who were admitted to the hospital or visited the hospital as an outpatient between May 1, 2016 and December 31, 2019. At least one of the following enrollment criteria was required to be met for inclusion in this study: (1) two or more outpatient visits within 6 months, (2) all antidiabetic drugs were continuously prescribed to the patients for >6 months during the follow-up period, or (3) one or more inpatient admissions with a diagnosis of type 2 DM. The primary endpoint was the development of stroke, which was defined by the time a stroke (ICD-10-CM codes I60, I61, I62, I63, I65, I66, I67.84, G45, G46) code first appeared in the inpatient or outpatient claim records. Comorbidities related to stroke were defined according to the ICD-10-CM code and included coronary heart disease (ICD-10-CM code I20–I25), hypertension (ICD-10-CM code I10), hyperlipidemia (ICD-9-CM code E78.1–E78.5), chronic kidney disease (ICD-10-CM code N18), chronic liver disease (ICD-10-CM code K71, K75, K76), chronic obstructive pulmonary disease (ICD-10-CM code J44), atrial fibrillation and flutter (ICD-10-CM code I48), and rheumatoid arthritis (ICD-9-CM code M05). Patients who fulfilled any of the following criteria

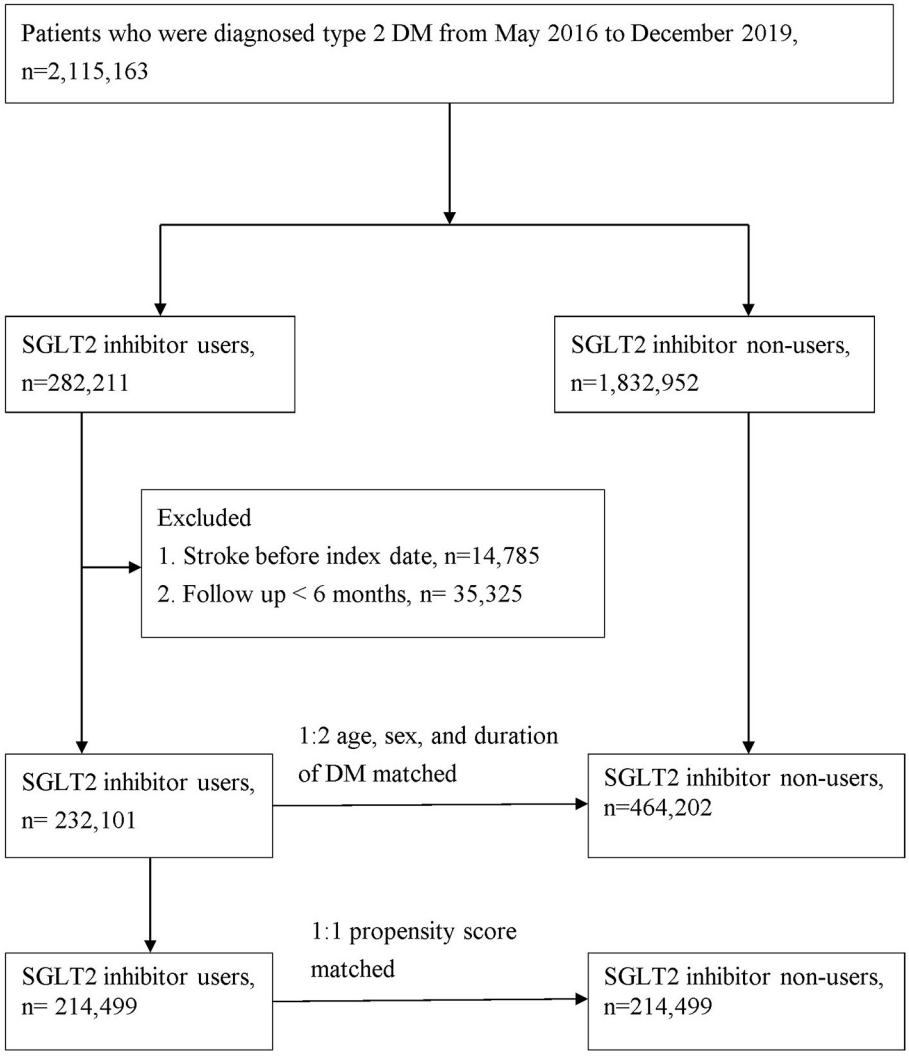

FIGURE 1
Patient flow chart.

were excluded from the study: (1) prior history of stroke before May 1, 2016 and (2) patient age of <20 years. Considering the differences in the baseline characteristics and stroke risk between the SGLT2-inhibitor users and non-SGLT2-inhibitor users, we applied age-, sex-, and type 2 DM duration matching at a ratio of 1:2 for patients with type 2 DM with and without SGLT2 inhibitor use. Finally, the study group comprised 232,101 participants with type 2 DM who were SGLT2 inhibitor users, and the control group included 464,202 randomly selected participants with type 2 DM who were non-SGLT2-inhibitor users (Figure 1). We also conducted propensity score matching with age, sex, duration of type 2 DM, comorbidities, and drug index date at a ratio of 1:1 for sensitivity analysis in patients with type 2 DM with and without the use of an SGLT2 inhibitor (Figure 1).

Statistical analysis

Data were presented as valid percentages and the mean values with a standard deviation. Differences in the demographic data and clinical characteristics between SGLT2-inhibitor users and non-SGLT2-inhibitor users were examined using a *t*-test for continuous variables, whereas Chi-square tests were performed for categorical variables. The Cox proportional hazard regression model was applied to compare the risk of developing study events between the SGLT2 inhibitor group and the non-SGLT2 inhibitor group. Adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated after adjusting for important risk factors toward developing the study events, including age, sex, concurrent medication, and comorbidities. The risk of study outcomes over time for the

TABLE 1 Baseline characteristics of all patients.

Characteristics		2:1 sex, age matching			1:1 Propensity score matching		
		Non- SGLT2 ($n = 464,202$)	SGLT2 ($n = 232,101$)	*P*	Non-SGLT2 ($n = 214,499$)	SGLT2 ($n = 214,499$)	ASD
Sex				1.0000			0.00177
Female		204,534 (44.06%)	102,267 (44.06%)		94,518 (44.06%)	94,707 (44.15%)	
Male		259,668 (55.94%)	129,834 (55.94%)		119,981 (55.94%)	119,792 (55.85%)	
Age				1.0000			0.00000
<50		114,804 (24.73%)	57,402 (24.73%)		53,466 (24.93%)	53,131 (24.77%)	
51–60		138,494 (29.83%)	69,247 (29.83%)		64,132 (29.90%)	64,128 (29.90%)	
61–70		142,538 (30.71%)	71,269 (30.71%)		66,008 (30.77%)	65,896 (30.72%)	
>70		68,366 (14.73%)	34,183 (14.73%)		30,893 (14.4%)	31,344 (14.61%)	
Years (Mean ± SD)		58.34 ± 12.21	58.34 ± 12.21	1.0000	58.44 ± 11.89	58.29 ± 12.23	
DM history				<0.0001			0.02967
<=2 years		133,455 (28.75%)	59,608 (25.68%)		54,688 (25.50%)	55,752 (25.99%)	
3-4 years		243,394 (52.43%)	126,088 (54.32%)		115,391 (53.80%)	115,875 (54.02%)	
≥5 years		87,353 (18.82%)	46,405 (19.99%)		44,420 (20.71%)	42,872 (19.99%)	
Comorbidities							
dv11	Hypertension	250,659 (54%)	139,336 (60.03%)	<0.0001	128,819 (60.06%)	12,738 5(59.39%)	0.01363
dv13	Coronary artery disease	51,129 (11.01%)	41,448 (17.86%)	<0.0001	33,966 (15.84%)	35,030 (16.33%)	0.01350
dv14	Hyperlipidemia	257,784 (55.53%)	153,956 (66.33%)	<0.0001	142,463 (66.42%)	140,575 (65.54%)	0.01858
dv19	Chronic kidney disease	104,962 (22.61%)	59,599 (25.68%)	<0.0001	57,593 (26.85%)	54,907 (25.60%)	0.02847
dv20	Chronic liver disease	50,928 (10.97%)	26,537 (11.43%)	<0.0001	24,725 (11.53%)	24,501 (11.42%)	0.00328
dv66	COPD	15,910 (3.43%)	8,446 (3.64%)	<0.0001	7,301 (3.40%)	7,631 (3.56%)	0.00839
dv29	Atrial fibrillation and flutter	4,902 (1.06%)	3,824 (1.65%)	<0.0001	3,087 (1.44%)	3,149 (1.47%)	0.00242
	Rheumatoid arthritis	3,188 (0.69%)	1,285 (0.55%)	0.01696	1,168 (0.54%)	1,202 (0.56%)	0.00214
Concurrent medication							
Dr1	NSAIDs	263,337 (56.73%)	133,108 (57.35%)	<0.0001	122,355 (57.04%)	122,768 (57.23%)	0.00389
Dr2	Corticosteroids	88,850 (19.14%)	45,398 (19.56%)	<0.0001	41,286 (19.25%)	41,608 (19.40%)	0.00380
Dr3	PPIs	35,647 (7.68%)	18,410 (7.93%)	0.0002	16,619 (7.75%)	16,739 (7.80%)	0.00209
Dr4	H2-receptor antagonists	120,629 (25.99%)	61,091 (26.32%)	0.0027	55,435 (25.84%)	56,109 (26.16%)	0.00716
Dr5	Aspirins	92,245 (19.87%)	63,518 (27.37%)	<0.0001	55,176 (25.72%)	55,748 (25.99%)	0.00609
Dr25	Statins	240,244 (51.75%)	162,084 (69.83%)	<0.0001	147,212 (68.63%)	146,131 (68.13%)	0.01084
Dr13	Biguanides	242,784 (52.3%)	151,068 (65.09%)	<0.0001	134,691 (62.79%)	136,345 (63.56%)	0.01599
Dr14	Sulfonylureas	155,979 (33.6%)	101,140 (43.58%)	<0.0001	91,743 (42.77%)	90,022 (41.97%)	0.01624
Dr15	Alpha glucosidase inhibitors	45,540 (9.81%)	43,008 (18.53%)	<0.0001	34,432 (16.05%)	35,391 (16.50%)	0.01211
Dr16	Thiazolidinediones	43,754 (9.43%)	41,938 (18.07%)	<0.0001	34,607 (16.13%)	34,857 (16.25%)	0.00316
Dr17	DPP4 inhibitors	99,152 (21.36%)	93,734 (40.39%)	<0.0001	80,445 (37.50%)	79,384 (37.01%)	0.01023
Dr18	Insulins	71,925 (15.49%)	57,020 (24.57%)	<0.0001	48,358 (22.54%)	48,840 (22.77%)	0.00537
Dr26	GLP-1 receptor agonists	5,101 (1.1%)	4,244 (1.83%)	<0.0001	3,763 (1.75%)	3,665 (1.71%)	0.00350

COPD, chronic obstructive pulmonary disease; DPP4, Dipeptidyl peptidase 4; GLP-1, Glucagon-like peptide-1; NSAID, Non-steroid anti-inflammatory drug; PPI, proton pump inhibitor; ASD, absolute standardized difference; PSM, propensity score matching; SD, standard deviation.

SGLT2 inhibitor group compared with the non-SGLT2 inhibitor group was determined by survival analysis using the Kaplan–Meier method.

We also conducted a sensitivity analysis to test the robustness of our primary findings. Initially, a propensity score was calculated for each patient to minimize confounding by indication, when patients with other risk factors between the SGLT2 inhibitor user group and non-SGLT2 inhibitor user group. Then, the propensity score matching (1:1) and absolute standardized difference (ASD) were performed to estimate the difference between the two groups. An ASD of <0.10 implied a negligible

TABLE 2 Incidence rate of stroke.

	2:1 sex age matching		1:1 Propensity score matching	
	Non- SGLT2	SGLT2	Non- SGLT2	SGLT2
N	464,202	232,101	214,499	214,499
Follow up person months	11,135,130	5,634,359	5,177,840	5,191,193
New case	11,701	5,186	5,328	4,678
Incidence rate*(95% C.I.)	10.50 (10.30–10.60)	9.20 (8.95–9.45)	10.20 (10.00–10.50)	9.01 (8.75–9.27)
Crude Relative risk (95% C.I.)	Reference	0.88 (0.85–0.91)	Reference	0.88 (0.84–0.91)
Adjusted HR* (95% C.I.)†	Reference	0.85 (0.82–0.88)	Reference	0.87 (0.84–0.91)

*Incidence rate, per 10,000 person-months. †adjusted hazard ratio, the covariates including duration of DM history, sex, age, co-morbidities, and medication at baseline.

difference in the potential confounders between the two groups.

In addition, we conducted subgroup analyses stratified by sex, age, duration of type 2 DM, presence of comorbidities, and concurrent medication at baseline for the primary outcomes of NOS. Statistical significance was considered at $P < 0.05$. All statistical calculations were performed using the statistical analysis software, version 9.3 (SAS Institute, Inc., Cary, NC, USA).

Results

Study population and baseline characteristics

A total of 696,303 patients were enrolled in the present study, with the SGLT2-inhibitor user group consisting of 232,101 individuals from the NHIRD who were diagnosed with type 2 DM from May 2016 through December 2019. This group was compared with 464,202 control patients who were non-SGLT2-inhibitor users at a 1:2 ratio (Figure 1). There were more men (55.94%) than women (44.06%) in this study. At the baseline, patients receiving SGLT2 inhibitor had more comorbidities, except for rheumatoid arthritis, and they used more concurrent medication than those not receiving SGLT2 inhibitor (Table 1).

Analysis of the main TBNHI cohort

During the follow-up, 5,186 and 11,701 NOSs events were recorded in the SGLT2-inhibitor user and non-SGLT2-inhibitor user groups, respectively. The event rate was 9.20 per 10 000 person-months (95% CI 8.95–9.45) for SGLT2-inhibitor users when compared with 10.50 (95% CI 10.30–10.60) for non-SGLT2-inhibitor users. There was a significantly lower the incidence rate of NOS after adjusting for the duration of type 2 DM history, sex, age, comorbidities, and concurrent medication among the SGLT2-inhibitor users when compared to that among the non-SGLT2-inhibitor users (adjusted HR: 0.85; 95% CI: 0.82–0.88) (Table 2). The cumulative incidence rate of developing stroke was also lower in the SGLT2-inhibitor users than in the non-SGLT2-inhibitor in the Kaplan–Meier survival analysis ($P < 0.0001$; Figure 2A).

Propensity score-matched analysis

We included 428,998 patients (214,499 in the SGLT2-inhibitor group and 214,499 in the non-SGLT2-inhibitor group) in the propensity score matching, and the baseline characteristics of sex, age, and duration of type 2 DM did not differ (Table 1). At the baseline, the non-SGLT2-inhibitor group had more comorbidities, except for coronary artery disease, chronic obstructive pulmonary disease, atrial fibrillation and flutter, and rheumatoid arthritis than the SGLT2-inhibitor group. However, the SGLT2 inhibitor users used more concurrent medication, except statins, sulfonylureas, dipeptidyl peptidase 4 inhibitors, and glucagon-like peptide-1 receptor agonists than the non-SGLT2 inhibitor users (Table 1).

There were 4,678 and 5,328 NOS events recorded in the SGLT2-inhibitor and non-SGLT2-inhibitor groups, respectively, in the follow-up period. The event rate was 9.01 per 10 000 person-months (95% CI 8.75–9.27) for the SGLT2-inhibitor group compared with 10.20 (95% CI 10.00–10.50) for the non-SGLT2-inhibitor group. The relative risk of NOS after adjusting the duration of type 2 DM history, sex, age, comorbidities, and concurrent medication demonstrated a decreasing risk of incident stroke in the SGLT2 inhibitor group when compared to those in the non-SGLT2-inhibitor group (adjusted HR: 0.87; 95% CI: 0.84–0.91) (Table 2). Similarly, the SGLT2-inhibitor group revealed a significantly lower cumulative incidence rate of developing stroke than the non-SGLT2-inhibitor group as per the Kaplan–Meier survival analysis ($P < 0.0001$, Figure 2B).

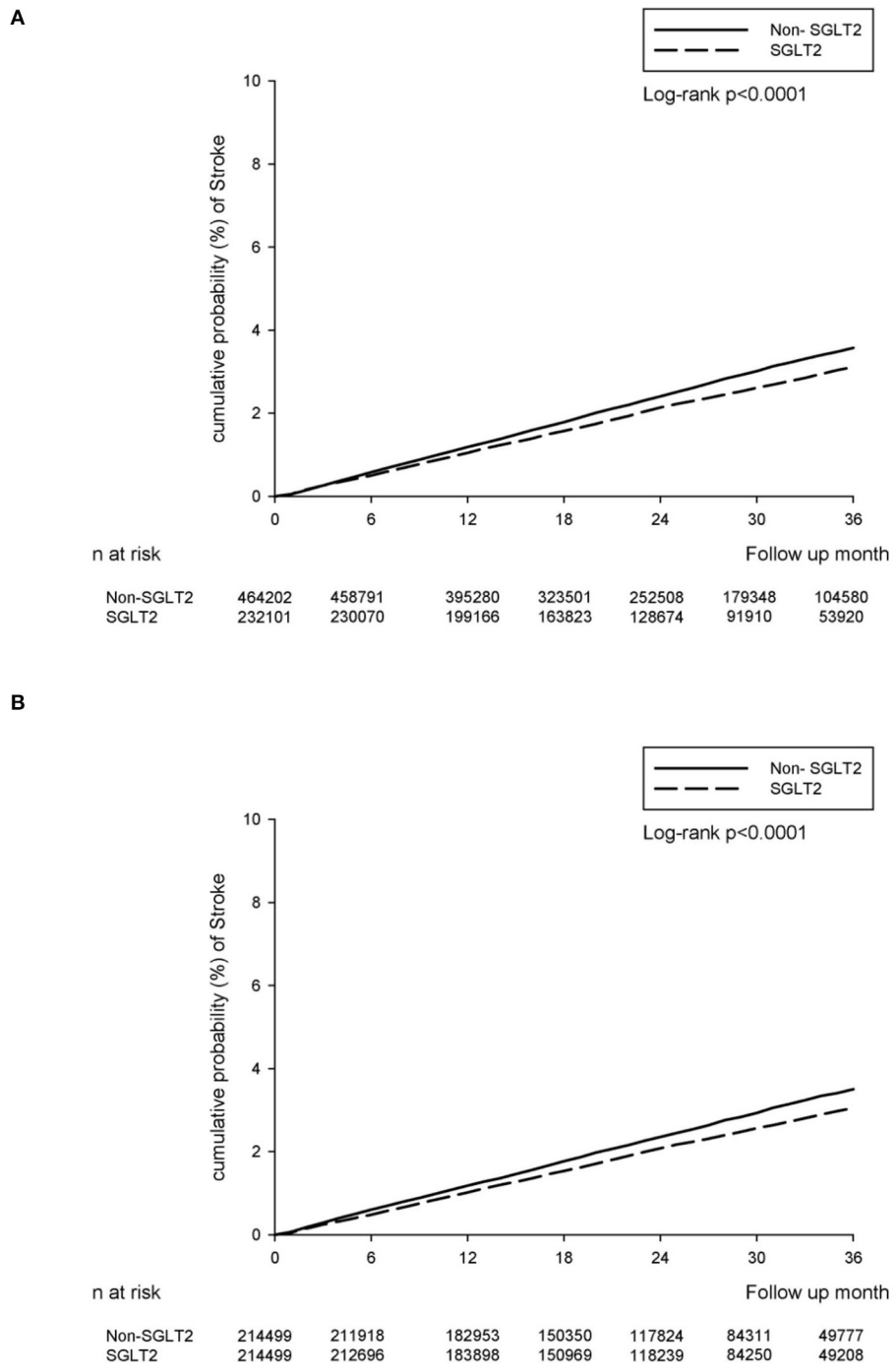

FIGURE 2
The cumulative incidence rate of developing stroke between SGLT2-inhibitor group and non-SGLT2-inhibitor group. **(A)** The main TBNHI Cohort. **(B)** The propensity score-matched cohort.

Subgroup analysis

The results of the subgroup analyses revealed that, after adjusting for the duration of type 2 DM history, sex, age, comorbidities, and concurrent medication were partly consistent with the results of the main analyses (Table 3). The two groups were different in terms of their incidental stroke, with the SGLT2 inhibitor users exhibiting a substantially high risk of NOS with male, an adjusted HR = 1.34 (95% CI: 1.30 to 1.39) than female. Compared with younger patients (aged < 50),

TABLE 3 Multiple Cox regression to estimate the hazard ratio for subgroup analysis.

	aHR (95% CI)	
	2:1 sex, age matching	**1:1 propensity score matching**
Sex		
Female	reference	reference
Male	1.34(1.30–1.39)	1.33(1.27–1.38)
Age		
<50	reference	reference
51–60	1.59(1.51–1.68)	1.51(1.41–1.63)
61–70	2.24(2.13–2.36)	2.17(2.02–2.32)
>70	3.67(3.48–3.88)	3.55(3.31–3.82)
Duration of type 2 DM history		
<=2 years	1.21(1.14–1.28)	1.27(1.11–1.37)
2–4 years	1.16(1.11–1.23)	1.20(1.12–1.28)
>=4 years	reference	reference
Comorbidity(ref: non-comorbidity)		
Hypertension	1.22(1.18–1.26)	1.28(1.23–1.34)
Coronary artery disease	1.02(0.97–1.06)	1.02(0.97–1.07)
Hyperlipidemia	0.77(0.74–0.79)	0.80(0.77–0.83)
Chronic kidney disease	1.17(1.13–1.21)	1.16(1.11–1.21)
Chronic liver disease	0.81(0.77–0.85)	0.79(0.74–0.85)
Malignancy	1.02(0.96–1.08)	1.03(0.95–1.13)
COPD	1.08(1.01–1.16)	1.06(0.97–1.15)
Atrial fibrillation and flutter	1.79(1.64–1.95)	1.82(1.64–2.02)
Rheumatoid Arthritis	1.23(1.04–1.44)	1.15(0.91–1.45)
Medication (reference: non-medication)		
NSAIDs	1.00(0.97–1.04)	1.05(1.01–1.09)
Corticosteroids	1.07(1.03–1.11)	1.08(1.02–1.13)
PPIs	1.19(1.13–1.25)	1.20(1.12–1.28)
H2-receptor antagonists	1.05(1.02–1.09)	1.07(1.02–1.12)
Aspirins	1.53(1.48–1.59)	1.55(1.49–1.62)
Statins	0.84(0.81–0.86)	0.88(0.84–0.92)
Biguanides	0.77(0.75–0.79)	0.85(0.82–0.89)
Sulfonylureas	1.09(1.06–1.13)	1.14(1.10–1.19)
Alpha glucosidase inhibitors	1.03(0.98–1.07)	1.06(1.01–1.12)
Thiazolidinediones	0.89(0.85–0.93)	0.93(0.88–0.98)
DPP4 inhibitors	1.05(1.02–1.09)	1.08(1.03–1.12)
Insulins	1.62(1.56–1.68)	1.67(1.60–1.74)
GLP-1 receptor agonists	0.84(0.71–0.98)	0.77(0.63-y0.93)

COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; DPP4, Dipeptidyl peptidase 4; GLP-1, Glucagon-like peptide-1; NSAID, Non-steroid anti-inflammatory drug; PPI, proton pump inhibitor.

elderly patients exhibited a significantly higher risk of NOS (aHR 1.59, 95% CI 1.51–1.68 for patients aged 50–60; aHR 2.24, 95% CI 2.13–2.36 for patients aged 60–70; aHR 3.67, 95% CI 3.48–3.88 for patients aged > 70). The duration of type 2 DM history were higher in the <=2 or 2–4 years than in the ≥4 years. Patients with hypertension, chronic kidney disease, chronic obstructive pulmonary disease, atrial fibrillation and flutter, and rheumatoid arthritis were also at significantly higher risks of NOS (aHR = 1.22, 1.17, 1.08, 1.79, and 1.23, respectively). However, patients with hyperlipidemia and chronic liver disease have significantly lower risks of NOS (aHR = 0.77, and 0.81, respectively). Similar findings were also noted for concurrent medication of statins (aHR 0.84, 95% CI 0.81–0.86 in the main TBNHI cohort; aHR 0.88, 95% CI 0.84–0.92 in the propensity score matching), biguanides (aHR 0.77, 95% CI 0.75–0.79 in the main TBNHI cohort; aHR 0.85, 95% CI 0.82–0.89 in the propensity score matching), thiazolidinediones (aHR 0.89, 95% CI 0.85–0.93 in the main TBNHI cohort; aHR 0.93, 95% CI 0.88–0.98 in the propensity score matching), and glucagon-like peptide-1 receptor agonists (aHR 0.84, 95% CI 0.71–0.98 in the main TBNHI cohort; aHR 0.77, 95% CI 0.63–0.93 in the propensity score matching). However, an increased risk of NOS was noted for concurrent medication with non-steroid anti-inflammatory drugs (aHR 1.01, 95% CI 0.98–1.05 in the main TBNHI cohort; aHR 1.05, 95% CI 1.01–1.05 in the propensity score matching), corticosteroids (aHR 1.07, 95% CI 1.03–1.11 in the main TBNHI cohort; aHR 1.08, 95% CI 1.02–1.13 in the propensity score matching), proton pump inhibitors (aHR 1.19, 95% CI 1.13–1.25 in the main TBNHI cohort; aHR 1.20, 95% CI 1.12–1.20 in the propensity score matching), H2-receptor antagonists (aHR 1.05, 95% CI 1.02–1.09 in the main TBNHI cohort; aHR 1.07, 95% CI 1.02–1.12 in the propensity score matching), aspirins (aHR 1.53, 95% CI 1.48–1.59 in the main TBNHI cohort; aHR 1.55, 95% CI 1.49–1.62 in the propensity score matching), sulfonylureas (aHR 1.09, 95% CI 1.06–1.13 in the main TBNHI cohort; aHR 1.14, 95% CI 1.10–1.19 in the propensity score matching), alpha-glucosidase inhibitors (aHR 1.03, 95% CI 0.98–1.07 in the main TBNHI cohort; aHR 1.06, 95% CI 1.01–1.12 in the propensity score matching), Dipeptidyl peptidase 4 inhibitors (aHR 1.05, 95% CI 1.02–1.09 in the main TBNHI cohort; aHR 1.08, 95% CI 1.03–1.12 in the propensity score matching), and insulins (aHR 1.62, 95% CI 1.56–1.68 in the main TBNHI cohort; aHR 1.67, 95% CI 1.60–1.74 in the propensity score matching) (Table 3).

Discussion

The present findings suggest that the incidence of NOS was decreased in type 2 DM patients who were SGLT2-inhibitor users compared with those who were not. Sensitivity analysis was also consistent with the main analysis. The subgroups analysis identified the concurrent use of statins, biguanides, thiazolidinediones, and glucagon-like peptide-1 receptor agonists as having a protective effect against developing NOS. However, we observed the increased risk based on whether non-steroid anti-inflammatory drugs, corticosteroids,

proton pump inhibitors, H2-receptor antagonists, aspirins, sulfonylureas, alpha-glucosidase inhibitors, dipeptidyl peptidase 4 inhibitors, and insulins were prescribed for concurrent use with an SGLT2 inhibitor.

Hypertension, type 2 DM, and obesity are identified as the most important risk factors for stroke (18). Several experimental studies reported improvements in these risk factors in diabetic and obese or stroke-prone mice and rats after treatment with SGLT2 inhibitors (11–13, 19). *In vitro* data has shown that the SGLT2 inhibitor significantly increased survival (67%) of spontaneously hypertensive stroke-prone rats when compared with controls (13). The authors observed that SGLT2 inhibitor-treated rats had weight and blood pressure reduction, which could explain the reduced stroke risk and increased survival. However, the effects of SGLT2 inhibitors on stroke prevention were contradictory in different clinical trials. In the Empagliflozin Cardiovascular Outcomes and Mortality in Type 2 Diabetes (EMPA-REG OUTCOME) trial (17), empagliflozin users were found to be associated with an insignificantly increased risk of stroke when compared to empagliflozin non-users (HR, 1.18; 95% CI, 0.89–1.56; $P = 0.26$). On the other hand, canagliflozin users were found to be associated with an insignificantly decreased risk of stroke relative to canagliflozin non-users (HR, 0.87; 95% CI, 0.69–1.09) in the Cardiovascular and Renal Events in Type 2 Diabetes (CANVAS) trial (20). However, several meta-analyses have demonstrated that SGLT2 inhibitors may lower the risk of embolic stroke (9, 21, 22). Their results were the same as ours and they suggested a possible protective effect of SGLT2 inhibitors including different populations and the level of renal functions.

In our study, subgroups analyses demonstrated that the patients' concurrent use of statins, biguanides, thiazolidinediones, and glucagon-like peptide-1 receptor agonists had a protective effect against developing NOS, whereas patients' concurrent use of non-steroid anti-inflammatory drugs, corticosteroids, proton pump inhibitors, H2-receptor antagonists, aspirins, sulfonylureas, alpha-glucosidase inhibitors, dipeptidyl peptidase 4 inhibitors, and insulins showed an increased risk of developing NOS. This result demonstrates that different drugs may play a major role in lowering or increasing the risk of NOS when combined with SGLT2 inhibitors for patients with type 2 DM, which conforms to previous reports (23–27).

Other than antidiabetic effects, SGLT2 inhibitors also promoted natriuresis and osmotic diuresis to lower blood pressure in patients with cardiovascular disease and heart failure (28–30). As evidence of the efficacy of SGLT-2 inhibitors continued to grow, many trails and meta-analysis on these drugs have expanded their prescriptions from diabetes patients only to also include patients with HF without type 2 DM (28–32). Furthermore, the safety and dose-response relationship of SGLT2 inhibitors were recommended in the clinical practice (33–35).

In summary, there is negative association between the use of SGLT2 inhibitors and the risk of NOS in patients with type 2 DM. The decreased risk of NOS in patients with type 2 DM was greater among patients with concurrent use of statins, biguanides, thiazolidinediones, and glucagon-like peptide-1 receptor agonists. Therefore, we suggest that the long-term use of SGLT2 inhibitors may help reduce the incidence of NOS in patients with type 2 DM.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

This study was approved by the Ethics Committee of the Chung Shan Medical University Hospital (CS1-21037). Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

Author contributions

T-KL and M-CC: conceptualization, methodology, formal analysis, and writing–original draft. Y-HC and J-YH: formal analysis and validation. P-LL: formal analysis. T-KL, Y-HC, J-YH, and M-CC: data curation. L-FP and G-PJ: conceptualization, investigation, writing–review and editing, supervision, project administration, and funding acquisition. All authors read the study and approved the manuscript for publication.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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Table 4 The association between burnout and MS pain

MS pain	The unary linear regression coefficient c		
	PB	WB	CB
NBSP	8.27***	6.49***	3.79***
BAP	1.59**	1.49**	0.92
BKP	2.29**	1.57**	1.19

*, P < 0.05; **, P < 0.01; ***, P < 0.0001; c, the linear regression coefficient of MS pain against burnout.

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Table 5 The linear regression models of three burnout scales

Main effect/DV	The linear regression coefficients (c)					
	PB		WB		CB	
	ULR	MLR[1]	ULR	MLR[1]	ULR	MLR[1]
WE	-0.11*	-0.14**	-0.19**	-0.11*	-0.14**	-0.01
Parenthood	-0.30	2.41*	-4.19***	-1.38	-5.12***	-3.00**
Not parenting	1.00	1.00	1.00	1.00	1.00	1.00
LAFF	-0.13***	-0.06**	-0.16***	-0.09***	-0.14***	-0.08**
SSLD	8.11***	4.25***	6.52***	2.78**	3.84**	1.17
SLD > 6h	1.00	1.00	1.00	1.00	1.00	1.00
Working OT	10.53***	6.91***	9.50***	6.18***	6.51***	3.95***
Seldom working OT	1.00	1.00	1.00	1.00	1.00	1.00
IRS work	7.76***	3.32*	8.48***	3.97**	6.05***	2.19
RS work	5.20**	4.00**	6.16***	3.88**	6.37***	3.93**
NS work	3.05	1.17	4.36**	1.27	5.31***	1.43
DS work	1.00	1.00	1.00	1.00	1.00	1.00
Physician	10.17***	7.75***	9.94***	7.69***	6.07**	4.01*
Nurse	9.01***	5.29***	8.38***	4.44***	7.74***	4.65***
PTs	2.95*	3.43**	2.42	3.52**	2.20	3.06*
ADs	1.00	1.00	1.00	1.00	1.00	1.00
NBSP	8.27***	6.86***	6.49***	5.51***	3.79***	3.23***
BAP	1.59**	1.38**	1.49**	1.33**	0.92	0.81
BKP	2.29**	1.68**	1.57**	1.16*	1.19	1.01

*, P < 0.05; **, P < 0.01; ***, P < 0.0001; DV, dependent variable; URL, unary linear regression; MRL, multiple linear regression; [1], MRL models adjusted sex, education degree, REW, CD, ever AU and all main effects.

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Table 5-1 The effect of parenthood against PB after adjusting single risk factor

AV	the linear regression coefficient parenthood effect (AV)
-	-0.30
LAFF	0.66 (-0.13***)
SSLD	0.17 (8.12***)
working OT	0.42 (10.56***)
IRS work	1.08 (7.99***)
RS work	1.08 (5.51**)
NS work	1.08 (3.43*)
Physician	0.97 (10.29***)
Nurse	0.97 (9.14***)
PTs	0.97 (2.85)
NBSP	-1.28 (8.32***)
BAP	-0.31 (1.59**)
BKP	-0.45 (2.31**)

*, P < 0.05; **, P < 0.01; ***, P < 0.0001; AV, adjusted variable.

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Table 5-2 The effect of sex against WB after adjusting single risk factor

AV	the linear regression coefficient c of women for WB women vs men	AV
Not adjusted	8.42*	-
WE	-0.11	-0.18*
Parenthood	6.37	-5.05
LAFF	8.71*	-0.20*
SSLD	8.35*	9.72**
working OT	8.95*	8.83**
IRS work	5.04	8.52
RS work	5.04	15.86**
NS work	5.04	17.66
NBSP	-1.85	6.50***
BAP	-1.85	0.47
BKP	-1.85	1.88*

*, P < 0.05; **, P < 0.01; ***, P < 0.0001; AV, adjusted variable.

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Table 6 The first-stage effect in the mediation model for

IV/DV		first-stage effect (a)							
		mar.[1]	pare.[1]	LAFF[2]	REW[1]	CD[1]	AU[1]	SSLD[1]	OT[1]
WE	a	0.10***	0.11***	0.12*	0.03***	0.03***	-0.03***	-0.00	-0.01
	s_a	0.01	0.01	0.06	0.01	0.01	0.01	0.01	0.01
mar.	a	-	4.43***	7.28***	0.26*	0.36**	-0.23*	-0.35**	-0.36**
	s_a	-	0.20	1.14	0.12	0.12	0.12	0.12	0.12
pare.	a	4.43***	-	7.42***	0.22	0.39**	-0.30*	-0.25*	-0.30*
	s_a		-	1.15	0.12	0.12	0.12	0.12	0.12
OT	a	-0.36**	-0.30*	-4.26**	-0.37**	0.18	0.46**	0.52***	-
	s_a	0.12	0.12	1.20	0.12	0.12	0.12	0.12	-
IRS	a	-0.53**	-0.54**	-0.70	-0.68**	-0.21	0.17	0.60**	0.42*
	s_a	0.18	0.18	1.76	0.17	0.18	0.18	0.17	0.17
DS	a	1.26***	1.22***	3.70**	0.78***	0.16	-0.25*	-0.27*	-0.20
	s_a	0.13	0.13	1.20	0.12	0.12	0.12	0.12	0.12
Phy.	a	-0.23	-0.35	1.56	0.65**	-0.04	0.90***	0.44*	0.60**
	s_a	0.20	0.21	2.03	0.22	0.20	0.20	0.20	0.20
Nurse	a	-0.52***	-0.59***	-4.51**	-0.82***	-0.09	-0.10	0.21	0.55***
	s_a	0.12	0.12	1.17	0.12	0.12	0.12	0.12	0.12

*, $P < 0.05$; **, $P < 0.01$; ***, $P < 0.0001$; a, logistic/linear regression coefficient, s_a, standard error of
parenting; [1], the corresponding field value is logistic regression coefficient; [2], the corresponding fiel

Table 6-1 The tested results of mediation effect for PB

IV/M		direct effect and second-stage effect												
		mar.[1]	pare.[1]	LAFF[2]	REW[1]	CD[1]	AU[1]	SSLD[1]	OT[1]	IRS[1]	DS[1]	NBSP[2]	BAP[2]	BKP[2]
WE	c'	-0.12*	-0.13*	-0.09	-0.08	-0.15**	-0.09	NCF	NCF	-0.10	-0.05	NCF	NCF	-0.14*
	b	0.52	0.73	-0.12***	-5.88***	5.83***	4.16***	-	-	6.32***	-5.17***	-	-	2.51**
	S_b	1.12	1.14	0.03	1.03	1.05	1.06	-	-	1.56	1.08	-	-	0.67
	Z	0.31	0.64	1.79	**-2.62****	**2.61****	**-2.33***	-	-	**-2.80****	**-3.42****	-	-	**3.75****
OT	c'	NA	NA	10.09***	10.06***	NCF	10.17***	9.66***	-	10.27***	NCF	8.88***	NCF	NCF
	b	-	-	-0.10***	-5.19***		3.25**	6.92***	-	5.56**	-	7.75***	-	-
	S_b	-	-	0.02	0.99		1.02	1.00	-	1.49	-	0.49	-	-
	Z	-	-	**2.89****	**2.62****		**2.40***	**3.65****	-	**2.01***	-	**4.06*****	-	-
IRS	c'	NA	NA	NCF	5.64**	NCF	NCF	5.45**	5.56**	-	NA	4.99**	NCF	NCF
	b	-	-	-	-5.63***	-	-	7.74***	10.27***	-	-	8.15***	-	-
	S_b	-	-	-	1.02	-	-	1.03	1.02	-	-	0.51	-	-
	Z	-	-	-	**3.20****	-	-	**3.17****	**2.39***	-	-	**2.47***	-	-
DS	c'	NA	NA	-4.96***	-4.40***	NCF	-5.15***	-4.89***	NCF	NA	-	NCF	NCF	NCF
	b	-	-	-0.12***	-5.25***	-	4.05**	7.80***	-	-	-	-	-	-
	S_b	-	-	0.03	1.03	-	1.04	1.02	-	-	-	-	-	-
	Z	-	-	**-2.44***	**-3.98*****	-	-1.79	**-2.14***	-	-	-		-	-
Phy.	c'	NCF	NCF	NCF	6.48**	NCF	4.64**	4.68**	4.02*	NCF	NCF	NCF	NCF	NCF
	b	-	-	-	-6.37***	-	4.00**	7.94***	10.32***	-	-	-	-	-

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S_b	-	-	-	1.02	-	1.06	1.03	1.02	-	-	-	-	-
Z	-	-	-	**-2.64****	-	**2.85****	**2.10***	**2.86****	-	-	-	-	-

*, P < 0.05; **, P < 0.01; ***, P < 0.0001; c', linear regression coefficient of IV to PB in the exist of mediated factor. M, mediated factor; [1], b is a logistic regression coefficient and Z is a value calculated by $Z_{mediation}$ [61]; 2, b is a linear regression coefficient and Z is value calculated by the original formula of the Sobel test; NCF, Non-compliance with the first-stage effect; NA, not applicable

Table 6-2 The tested results of mediation effect for WB

		direct effect and the second-stage effect												
IV/M		mar.[1]	pare.[1]	LAFF[2]	REW[1]	CD[1]	AU[1]	SSLD[1]	OT[1]	IRS[1]	DS[1]	NBSP[2]	BAP[2]	BKP[2]
WE	c'	-0.13*	-0.11*	-0.17**	-0.15**	-0.22***	-0.17**	NCF	NCF	-0.16**	-0.12*	NCF	NCF	-0.21***
	b	-2.71**	-3.25**	-0.15***	-5.54***	4.65***	3.09**	-	-	6.49***	-5.86***	-	-	1.89**
	S_b	1.00	1.02	0.02	0.92	0.94	0.95	-	-	1.39	0.96	-	-	0.60
	Z	**-2.60****	**-3.05****	-1.93	**-2.65****	**2.53***	**-2.15***	-	-	**-3.00****	**-3.84****	-	-	**3.15****
Mar.	c'	-	-1.12	-2.65**	-3.34**	-4.07***	-3.52**	-3.19**	-2.94**	-3.33**	-2.08*	-4.67***	NCF	NCF
	b	-	-3.30*	-0.15***	-5.66***	4.37***	3.27**	6.25***	9.24***	6.56***	-5.75***	6.69***	-	-
	S_b	-	1.50	0.02	0.92	0.94	0.94	0.93	0.92	1.39	0.98	0.47	-	-
	Z	-	**-2.19***	**-4.86*****	**-2.02***	**2.48***	-1.63	**-2.65****	**-2.86****	**-2.46****	**-5.00*****	**2.94****	-	-
Par.	c'	NA	-	-3.13**	NCF	-4.60***	-3.96***	-3.82***	-3.56***	-3.85***	-2.66**	-4.67***	NCF	NCF
	b	-	-	-0.14***	-	4.45***	3.18***	6.29***	9.25***	6.50***	-5.62***	6.66***	-	-
	S_b	-	-	0.02	-	0.93	0.94	0.93	0.92	1.39	0.98	0.46	-	-
	Z	-	-	**-4.74*****	-	**2.65****	**-1.96***	**-1.97***	**-2.42***	**-2.49***	**-4.87*****	**2.37***	-	-
OT	c'	NA	NA	8.93***	9.05***	NCF	9.23***	8.82***	-	9.22***	NCF	8.22***	NCF	NCF
	b	-	-	-0.14***	-5.11***	-	2.47**	5.44***	-	6.07***	-	6.01***	-	-
	S_b	-	-	0.02	0.89	-	0.92	0.91	-	1.34	-	0.46	-	-
	Z	-	-	**3.17****	**2.69****	-	**2.15***	**3.48****	-	**2.13***	-	**4.00*****	-	-
IRS	c'	NA	NA	NCF	6.08***	NCF	NCF	6.09***	6.07***	-	NA	5.75***	NCF	NCF
	b	-	-	-	-5.43***	-	-	6.11***	9.22***	-	-	6.35***	-	-
	S_b	-	-	-	0.92	-	-	0.93	0.91	-	-	0.47	-	-

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	Z	-	-	-	**3.28****	-	-	**3.08****	**2.39***	-	-	**2.46***	-	-
DS	c'	NA	NA	5.85***	-5.45***	NCF	-6.20***	-5.99***	NCF	NA	-	NCF	NCF	NCF
	b	-	-	-0.14***	-4.90***	-	3.11**	6.14***	-	-	-	-	-	-
	S_b	-	-	0.02	0.92	-	0.93	0.92	-	-	-	-	-	-
	Z	-	-	**-2.82****	**-4.09*****	-	-1.71	**-2.11***	-	-	-	-	-	-
Phy.	c'	NCF	NCF	NCF	6.62***	NCF	5.00**	5.01**	4.33**	NCF	NCF	NCF	NCF	NCF
	b	-	-	-	-6.21***	-	3.09**	6.34***	9.28***	-	-	-	-	-
	S_b	-	-	-	0.92	-	0.95	0.93	0.92	-	-	-	-	-
	Z	-	-	-	**-2.68****	-	**2.59****	**2.07***	**2.86****	-	-	-	-	-

*, $P < 0.05$; **, $P < 0.01$; ***, $P < 0.0001$; c', linear regression coefficient of IV to PB in the exist of mediated factor. M, mediated factor; [1], b is a logistic regression coefficient and Z is a value calculated by $Z_{mediation}$ [61]; 2, b is a linear regression coefficient and Z is value calculated by the original formula of the Sobel test; NCF, Non-compliance with the first-stage effect; NA, not applicable

Table 6-3 The tested results of mediation effect for CB

		direct effect and the second-stage effect												
IV/M		mar.[1]	pare.[1]	LAFF[2]	REW[1]	CD[1]	AU[1]	SSLD[1]	OT[1]	IRS[1]	DS[1]	NBSP[2]	BAP[2]	BKP[2]
WE	c'	-0.08*	-0.04	-0.13*	-0.11*	-0.16**	-0.12*	NCF	NCF	-0.13*	-0.08	NCF	NCF	-0.16**
	b	-3.03**	-4.83***	-0.14***	-5.19***	1.62	3.40**	-	-	4.00**	-5.59***	-	-	1.44*
	S_b	1.06	1.07	0.02	0.98	1.01	1.00	-	-	1.48	1.02	-	-	0.64
	Z	**-2.74****	**-4.16*****	-1.92	**-2.58****	1.36	**-2.20***	-	-	**-2.19***	**-3.66****	-	-	**2.25***
Mar.	c'	-	0.97	-2.67**	-3.30**	-3.76**	-3.44**	-3.34**	-3.12**	-3.41**	-2.15*	-4.21***	NCF	NCF
	b	-	-5.88**	-0.13***	-5.22***	1.51	3.48**	3.55**	6.24***	3.96**	-5.29***	3.97***	-	-
	S_b	-	1.57	0.02	0.97	1.00	1.00	0.99	0.99	1.48	1.04	0.52	-	-
	Z	-	**-3.69****	**-4.56*****	**-1.98***	1.29	-1.63	**-2.21***	**-2.68****	-1.92	**-4.49*****	**2.79****	-	-
Par.	c'	NA	-	-4.18***	NCF	-5.27***	-4.88***	-4.91***	-4.69***	-4.91***	-3.81**	-5.58***	NCF	NCF
	b	-	-	-0.13***	-	1.68	3.32**	3.54**	6.17***	3.78*	-4.85***	3.98***	-	-
	S_b	-	-	0.02	-	0.99	0.99	0.99	0.99	1.47	1.03	0.51	-	-
	Z	-	-	**-4.58*****	-	1.45	-1.95	-1.75	**-2.30***	-1.89	**-4.19*****	**2.29***	-	-
OT	c'	NA	NA	5.96***	6.07***	NCF	6.18***	6.13***	-	6.34***	NA	5.78***	NCF	NCF
	b	-	-	-0.13***	-4.92***	-	3.00**	3.08**	-	3.77**	-	3.45***	-	-
	S_b	-	-	0.02	0.96	-	0.99	0.99	-	1.46	-	0.52	-	-
	Z	-	-	**3.12****	**2.61****	-	**2.32***	**2.50***	-	1.72	-	**3.55***	-	-
DS	c'	NA	NA	-5.45***	-5.08***	NCF	-5.74***	-5.72***	NCF	NA	-	NCF	NCF	NCF
	b	-	-	-0.13***	-4.52***		3.34**	3.48**	-	-	-	-	-	-
	S_b	-	-	0.02	0.98		0.99	0.99	-	-	-	-	-	-

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	Z	-	-	**-2.79****	**-3.73****		-1.72	1.84	-	-	-	-	-	-
Nur.	c'	NA	NA	5.55***	5.26***	NCF	NCF	NCF	5.39***	5.83***	4.72***	5.62***	NCF	NCF
	b	-	-	-0.13***	-4.40***	-	-	-	5.79***	3.11*	-4.33***	3.55***	-	-
	S_b	-	-	0.02	0.98	-	-	-	0.99	1.47	1.05	0.52	-	-
	Z	-	-	**3.32****	**3.73****	-	-	-	**3.58****	1.92	3.89**	2.75**	-	-

*, $P < 0.05$; **, $P < 0.01$; ***, $P < 0.0001$; c', linear regression coefficient of IV to PB in the exist of mediated factor. M, mediated factor; [1], b is a logistic regression coefficient and Z is a value calculated by $Z_{mediation}$ [61]; 2, b is a linear regression coefficient and Z is value calculated by the original formula of the Sobel test; NCF, Non-compliance with the first-stage effect; NA, not applicable

Table 7 Mediation and suppression models of burnout

			Mediation or suppression effect											
IV	DV	c'	1.mar.	2.pare.	3.LAFF	4.REW	5.CD	6.AU	7.SSLD	8.OT	9.IRS	10.DS	11. NBSP	12.BAP	13.BKP
1.WE	PB	-	NS	NS	NS	(+) **m****	(+) S**	(-) **m***	NCF	NCF	(-) **m****	(+) **m****	NCF	NCF	(+) S**
2.OT	PB	+	NA	NA	(-) m**	(-) m**	N	(+) m*	(+) m**	X	(+) m*	NCF	(+) m***	NCF	NCF
3.IRS	PB	+	NA	NA	NCF	(-) m**	NCF	NCF	(+) m**	(+) m*	X	NA	(+) m*	NCF	NCF
DS	PB	-	NCF	NCF	(+) m*	(+) m***	NCF	NS	(-) m*	NCF	NCF	-	NCF	NCF	NCF
4.Phy.	PB	+	NCF	NCF	NCF	(+) S**	N	(+) m**	(+) m*	(+) m**	NCF	NCF	NCF	NCF	NCF
5.WE	WB	-	(+) m**	(+) m**	NS	(+) m**	(+) S*	(-) m*	NCF	NCF	(-) m**	(+) m**	NCF	NCF	(+) S**
6.mar.	WB	-	X	(+) ***m****	(+) m***	(+) m*	(+) S*	NS	(-) m**	(-) m**	(-) m**	(+) m***	(+) S**	NCF	NCF
7.pare.	WB	-	NA	X	(+) m***	NCF	(+) S**	(-) m*	(-) m*	(-) m*	(-) m*	(+) m***	(+) S*	NCF	NCF
8.OT	WB	+	NA	NA	(-) m**	(-) m**	NCF	(+) m*	(+) m**	X	(+) m*	NCF	(+) m***	NCF	NCF
9.IRS	WB	+	NA	NA	NCF	(-) m**	NCF	NCF	(+) m**	(+) m*	X	NA	(+) m*	NCF	NCF
10.DS	WB	-	NA	NA	(+) m**	(+) m***	NCF	NS	(-) m*	NCF	NA	X	NCF	NCF	NCF
11.Phy.	WB	+	NCF	NCF	NCF	(+) S**	NCF	(+) m**	(+) m*	(+) m**	NCF	NCF	NCF	NCF	NCF
12.WE	CB	-	(+) m**	(+) ***m******	NS	(+) m**	NS	(-) m*	NCF	NCF	(-) m*	(+) **m****	N	N	(+) S*
13.mar.	CB	-	X	(+) **m****	(+) m***	(+) m*	NS	NS	(-) m*	(-) m**	NS	(+) m***	(+) S**	N	N
14.pare.	CB	-	NA	X	(+) m***	NCF	NS	NS	NS	(-) m*	NS	(+) m***	(+) S*	N	N
15.OT	CB	+	NA	NA	(-) m**	(-) m**	NCF	(+) m*	(+) m*	X	NS	NA	(+) m*	N	N
16.DS	CB		NA	NA	(+)m**	(+)m**	NCF	NS	NS	N	NA	X	NCF	NCF	NCF

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17.Nur.	CB	NA	NA	(-) m**	(-) m**	NCF	NCF	NCF	(+) m**	NS	(-) m**	(+) m**	NCF	NCF

*, $P < 0.05$; **, $P < 0.01$; ***, $P < 0.0001$; phy., physician; mar., married; pare., parenting; +/-, positive/negative relationship for IV and DV; (+/-), positive/negative relationship for IV and mediated factor; m, mediated effect; s, suppressed effect; NA, not applicable; NS, not statistically significant; NCF, Non-compliance with the first-stage effect

Table 8 Identification of risk factors for WRIs and SIs

IV/DV	subjects	WRIs mean ± SD	WRIs c	SIs mean ± SD	SIs c
Sex					
Women	1016	16.61±18.97	0.69	7.19±13.18	-2.22*
Men	234	15.92±17.19	1.00	9.40±14.91	1.00
Work experience[1]					
WE	1250	-	0.07	-	-0.05
Education degree					
Master's degree or above[1]	210	15.83±17.01	-0.78	6.67±12.36	-1.12
University or below university degree[2]	1040	16.61±18.97	1.00	7.79±13.77	1.00
Marriage state					
Married	612	16.95±18.91	0.93	7.19±13.39	-0.80
others	638	16.03±18.39	1.00	7.99±13.68	1.00
Raising the child					
Parenting[3]	553	17.04±18.80	1.01	7.41±13.68	-0.33
Not Parenting	697	16.03±18.53	1.00	7.75±13.44	1.00
Engaging in LAFF[1]					
LAFF	1250	-	-0.04	-	-0.22
Exercise frequency					
REW	711	16.10±18.41	-0.87	7.60±13.74	-0.01
Not REW	539	16.98±18.96	1.00	7.61±13.29	1.00
With CD					
Yes	491	19.30±19.45	4.64***	8.66±14.60	1.74*
No	759	14.66±17.89	1.00	6.92±12.77	1.00
The frequency for drink coffee[1]					
Coffee intake score	1250	-	-0.00		0.01
Alcohol use habit in a month					
Ever AU	474	18.41±19.37	3.10**	9.60±14.73	3.22***
Never AU	776	15.30±18.10	1.00	6.38±12.62	1.00
Sleeping duration					

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per day					
SSLD	481	18.76±19.23	3.71**	9.15±14.59	2.52**
Not SSLD	769	15.05±18.09	1.00	6.63±12.75	1.00
Experiencing OT work per month					
Work OT	459	20.64±20.50	6.58***	10.40±15.91	4.43***
seldom work OT	791	14.07±17.03	1.00	5.97±11.66	1.00
Shift work schedule[2]					
irregular shift	154	20.29±19.76	5.08**	10.88±15.11	4.03**
regular shift	165	18.18±22.49	2.97	8.64±14.78	1.79
Night shift	142	17.43±18.83	2.22	7.04±12.76	0.20
day shift	789	15.21±17.36	1.00	6.84±12.99	1.00
Professional field[2]					
physicians	112	14.96±18.21	1.26	6.92±11.24	-0.37
Nurses	512	19.34±19.59	5.64***	9.03±14.34	1.75
PTs	228	15.68±17.51	1.99	5.26±10.48	-2.02
ADs	398	13.69±17.68	1.00	7.29±14.43	1.00
MS pain[1]					
NBSP	1250	-	5.89***	-	1.78***
BAP	1250	-	1.78**	-	0.39
BKP	1250	-	3.10***	-	1.02*

*, P < 0.05; **, P < 0.01; ***, P < 0.0001; [1], They are all continuous variables and are added to model individually; [2], All dummy variables were added to model at the same time.

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Table 8-1 The impact of burnout against WRIs

risk factor		the adjusting variable for WRIs					
		PB		WB		CB	
	c	c'	d (%)	c'	d (%)	c'	d (%)
CD	4.64***	2.52*	45.69	2.95**	36.42	4.33***	6.68
AU	3.10**	1.37	NC	1.62	NC	2.13*	31.29
SSLD	3.71**	0.46	NC	0.93	NC	2.70*	27.22
Work OT	6.58***	2.53*	61.55	2.69*	59.12	4.98***	24.32
IRS work[1]	4.35**	1.72	NC	1.36	NC	3.18*	26.90
Nurses[2]	4.84***	2.26*	53.31	2.27	53.10	3.28**	32.23
NBSP	5.89***	3.09***	47.54	3.56***	39.56	5.07***	13.92
BAP	1.78**	1.14*	35.96	1.14*	35.96	1.53**	14.04
BKP	3.10***	2.20**	29.03	2.44**	21.29	2.79***	10.00

*, P < 0.05; **, P < 0.01; ***, P < 0.0001; c, the linear regression coefficient for risk factor without adjusting burnout.; c', the linear regression coefficient for risk factor after adjusting burnout; $d(\%) = c - c'/c \times 100$; NC, not calculated; [1], reference variable is other participants except to subjects who work irregular shift; [2], reference variable is other participants except to nurses.

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Table 8-2 The mediation effect of burnout against WRIs

IV/M	PB					WB					CB				
	a	s_a	b	s_b	Z	a	s_a	b	s_b	Z	a	s_a	b	s_b	Z
CD	5.39***	1.04	0.39***	0.03	***4.81*****	4.01***	0.94	0.42***	0.03	4.08***	1.17	1.00	0.27***	0.03	1.16
AU	4.35***	1.05	0.40***	0.03	3.96***	3.47**	0.95	0.43***	0.03	***3.54****	3.68**	1.00	0.27***	0.03	3.41**
SSLD	8.11***	1.03	0.40***	0.03	***6.78*****	6.52***	0.93	0.43***	0.03	***6.30*****	3.84**	1.00	0.26***	0.03	3.51**
OT	10.53***	1.02	0.39***	0.03	8.08***	9.50***	0.92	0.41***	0.03	8.24***	6.51***	0.99	0.25***	0.03	5.16***
IRS[1]	6.58***	1.55	0.40***	0.03	***4.05*****	6.98***	1.39	0.43***	0.03	4.74***	4.40**	1.48	0.27***	0.03	2.82**
Nurses[2]	6.56***	1.03	0.39***	0.03	5.72***	6.12***	0.92	0.42***	0.03	6.01***	6.14***	0.98	0.26***	0.03	5.08***
NBSP	8.27***	0.51	0.34***	0.03	9.29***	6.49***	0.47	0.36***	0.03	9.06***	3.79***	0.52	0.22***	0.03	5.17***
BAP	1.59**	0.59	0.40***	0.03	2.64**	1.49**	0.53	0.43***	0.03	2.76**	0.92	0.56	0.27***	0.03	1.62
BKP	2.29**	0.66	0.40***	0.03	3.36**	1.57**	0.60	0.42***	0.03	2.57**	1.19	0.63	0.26	0.03	1.85

*, P < 0.05; **, P < 0.01; ***, P < 0.0001; M, mediated factor; a, the linear regression coefficient of IV against M; s_a, the standard error for a; b, the linear regression coefficient of M against PB/WB/CB; s_b, the standard error for b; Italic bold font represented fully mediated effect; ; [1], reference variable is other participants except to subjects who work irregular shift; [2], reference variable is other participants except to nurses.

Table 8-3 The impact of burnout against SIs

risk factor	the adjusting variable for SIs							
	PB			WB			CB	
	c	c'	d (%)	c'	d (%)	c'	d (%)
Women	-2.22*	-2.54**	NE	-2.50**	NE	-2.41*	NE
CD	1.74*	1.02	NC	1.16	NC	1.59*	8.62
AU	3.22***	2.66**	17.39	2.74**	14.91	2.79**	13.35
SSLD	2.52**	1.47	NC	1.61*	36.11	2.06**	18.25
Work OT	4.43***	3.23***	27.09	3.28***	25.96	3.73***	15.80
IRS work[1]	3.74**	2.87*	23.26	2.76*	26.20	3.21**	14.17
Nurses[2]	2.43**	1.57*	35.39	1.58*	34.98	1.71*	29.63
NBSP	1.78***	0.78	NC	0.95*	46.63	1.36**	23.60
BKP	1.02*	0.71	NC	0.79	NC	0.87	NC

*, P < 0.05; **, P < 0.01; ***, P < 0.0001; c, the linear regression coefficient for risk factor without adjusting burnout.; c', the linear regression coefficient for risk factor after adjusting burnout; $d(\%) = c - c'/c \times 100$; NE, not estimate; NC, not calculated; [1], reference variable is other participants except to subjects who work irregular shift. [2], reference variable is other participants except to nurses.

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Table 8-4 The mediation effect of burnout against SIs

	PB					WB					CB				
IV/M	a	s_a	b	s_b	Z	a	s_a	b	s_b	Z	a	s_a	b	s_b	Z
CD	5.39^{***}	1.04	0.13^{**}	0.02	***4.05*****	4.01^{**}	0.94	0.14^{**}	0.02	***3.64*****	1.17	1.00	0.12^{***}	0.02	1.15
AU	4.35^{***}	1.05	0.13^{**}	0.02	3.49^{**}	3.47^{**}	0.95	0.14^{**}	0.02	3.24^{**}	3.68^{**}	1.00	0.12^{***}	0.02	3.14^{**}
SSLD	8.11^{***}	1.03	0.13^{**}	0.02	***5.01*****	6.52^{**}	0.93	0.14^{**}	0.02	4.95^{***}	3.84^{**}	1.00	0.12^{***}	0.02	3.23^{**}
OT	10.53^{***}	1.02	0.11^{**}	0.02	4.85^{**}	9.50^{**}	0.92	0.12^{**}	0.02	5.19^{***}	6.51^{***}	0.99	0.11^{***}	0.02	4.22^{***}
IRS[1]	6.58^{***}	1.55	0.13^{**}	0.02	3.55^{**}	6.98^{**}	1.39	0.14^{**}	0.02	4.08^{***}	4.40^{**}	1.48	0.12^{***}	0.02	2.66^{**}
Nurses[2]	6.56^{***}	1.03	0.13^{**}	0.02	4.55^{**}	6.12^{**}	0.92	0.14^{**}	0.02	4.82^{***}	6.14^{***}	0.98	0.12^{***}	0.02	4.33^{***}
NBSP	8.27^{***}	0.51	0.12^{**}	0.02	***5.63*****	6.49^{**}	0.47	0.13^{**}	0.03	4.13^{***}	3.79^{***}	0.52	0.11^{***}	0.02	4.39^{***}
BKP	2.29^{**}	0.66	0.14^{**}	0.02	***3.11*****	1.57^{**}	0.60	0.15^{**}	0.02	***2.47****	1.19	0.63	0.12^{***}	0.02	1.80

*, $P < 0.05$; **, $P < 0.01$; ***, $P < 0.0001$; Italic bold font represented fully mediated effect; [1], reference variable is other participants except to subjects who work irregular shift. [2], reference variable is other participants except to nurses.

Table 9 The mediation models of burnout, risk factors and WRIs/SIs

		DV								
		WRIs				SIs				
		mediation factor				mediation factor				
IV	c	PB	WB	CB	c	PB	WB	CB		
CD	+	(+) m^{***}	(+) m^{*}	NA	+	(+) m^{***}	(+) m^{**}	NA		
AU	+	(+) m^{***}	(+) m^{**}	(+) m^{**}	+	(+) m^{**}	(+) m^{**}	(+) m^{**}		
SSLD	+	(+) ***m^{***}***	(+) m^{***}	(+) m^{**}	+	(+) m^{**}	(+) m^{***}	(+) m^{**}		
OT	+	(+) m^{***}	(+) m^{***}	(+) m^{***}	+	(+) m^{***}	(+) m^{***}	(+) m^{***}		
IRS	+	(+) m^{***}	(+) m^{***}	(+) m^{**}	+	(+) m^{***}	(+) m^{***}	(+) m^{**}		
Nurse	+	(+) m^{***}	(+) m^{***}	(+) m^{***}	+	(+) m^{***}	(+) m^{***}	(+) m^{***}		
NBSP	+	(+) m^{***}	(+) m^{***}	(+) m^{***}	+	(+) m^{***}	(+) m^{***}	(+) m^{***}		
BAP	+	(+) m^{**}	(+) m^{**}	NA	NS	NA	NA	NA		
BKP	+	(+) m^{**}	(+) m^{**}	NA	+	(+) m^{**}	(+) m^{*}	NA		

*, $P < 0.05$; **, $P < 0.01$; ***, $P < 0.0001$; +/-, positive/negative relationship c: (+/-), positive/negative relationship between IV and mediated factor; m, mediation effect; s, suppression effect; NA, not applicable; NS, not statistically significant.

doi:10.6834/csmu202200004

7. Figures

Figure 1 Development and impacting factors of Burnout

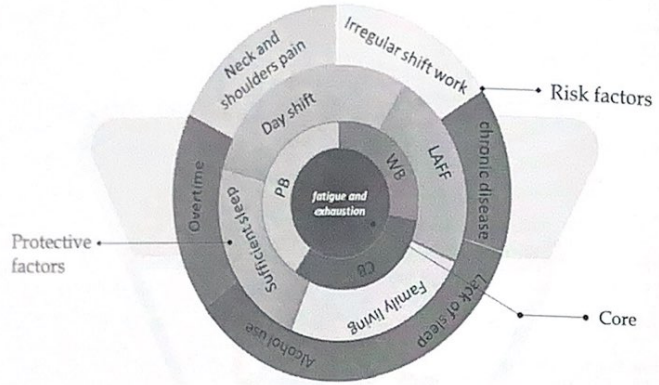
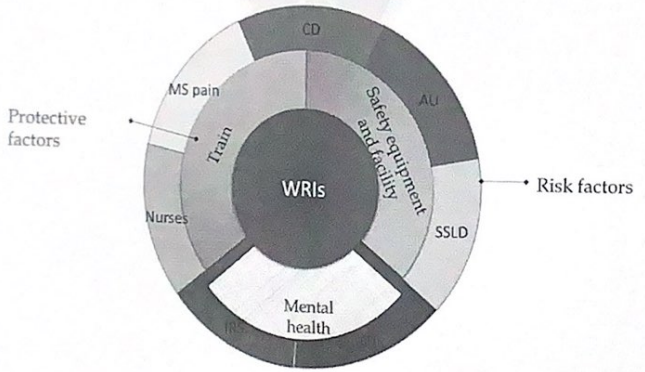


Figure 2 Development and impacting factors of Work-related injuries



doi:10.6834/csmu202200004

8. Appendix

Appendix A. Permission of Research Proposal for CS1-21108

中山醫學大學附設醫院第一人體研究倫理審查委員會

The Institutional Review Board
Chung Shan Medical University Hospital
No.110, Sec.1, Chien-Kuo N. Road, Taichung, Taiwan 402
Phone: 04-24739595 Fax: 04-35073516

研究計畫許可書

CSMUH No: CS1-21108

計畫名稱： 醫療工作場所職業倦怠發展的探索
計畫主持人及服務機構： 陳詠昕／中山醫學大學附設醫院
經費來源： 主持人自行支付
會議日期： NA
版　　本：【計畫書：Version 1.0，日期：2021/06/23；Waiver 1：V1.0，日期：2021 年 6 月 23 日】
許可書有效期間： 自民國 110 年 08 月 25 日至民國 113 年 08 月 24 日
期中報告繳交頻率：每年(12 個月)繳交一次，若需申請延長試驗，請於效期屆滿前申請。
上述計畫已於 110 年 08 月 25 日經本院人體研究倫理審查委員會依據簡易審查作業基準同意執行，有關計畫主持人的職責、義務、及注意事項均詳列於背面，請參閱並遵守。

主任委員 曹承孝

中　華　民　國　一　一　〇　年　八　月　二　十　五　日

Permission of Research Proposal
Chung Shan Medical University Hospital

Date: Aug 25, 2021

Protocol Title: Exploration on the Development of Burnout in Medical Workplace
Principle Investigator & Affiliated Institution: Yong-Hun Chen／Chung Shan Medical University Hospital
Date of meeting: NA
Version: 【see above】
Effective duration approved: 2021/08/25 to 2024/08/24
Frequency of Interim Report: every 12 months. Please file an extension before the expiry date, if you need.
Above study has been approved with the expedited review by Institutional Review Board of the Chung Shan Medical University Hospital on Aug 25, 2021. About the essential duties, obligations and responsibilities of the principal investigator please refer to the back page.

Thomas Chang-Yao TSAO

Thomas Chang-Yao TSAO, MD/PhD.
Chairman
The Institutional Review Board

本委員會組織與執行皆符合 ICH-GCP 規範及赫爾辛基宣言之精神
This Committee has been organized and operated in conformance with ICH-GCP requirements and the essence of Declaration of Helsinki.

doi:10.6834/csmu202200004

Appendix B. Permission of Research Proposal for CS19137

中山醫學大學附設醫院第一人體研究倫理審查委員會

The Institutional Review Board
Chung Shan Medical University Hospital
No.110, Sec.1, Chien-Kuo N. Road, Taichung, Taiwan 402
Phone: 04-24739595 Fax: 04-35073516

研究計畫許可書

CSMUH No:CS19137

計畫名稱：超時工作與肥胖問題對醫療人員尖銳物扎傷的影響
計畫主持人及歸屬機構：陳詠心／中山醫學大學附設醫院
會議日期：108/11/28
版　本：【計畫書：V001，日期：2019/11/21；Waiver1：V001，日期：2019/11/21】
許可書有效期間：自民國 108 年 12 月 2 日至民國 109 年 12 月 1 日
期中報告繳交頻率：每年 12 個月繳交一次，若需申請延長試驗，請於效期屆滿前申請。
上述計畫已於 108 年 12 月 2 日經本院人體研究倫理審查委員會依據一般(全會)審查作業程序審查通過同意執行，有關計畫主持人的職責、義務、及注意事項均詳列於背面，請參閱並遵守。

主任委員 韓志平

中　華　民　國　一　〇　八　年　十　二　月　五　日

Permission of Research Proposal
Chung Shan Medical University Hospital

Date: Dec.5, 2019

Protocol Title: The effect of overtime work and obesity to medical staff sharps injury
Principle Investigator & Affiliated Institution: YongHsin Chen／Chung Shan Medical University Hospital

Date of meeting：2019/11/28
Version:【see above】
Effective duration approved: 2019/12/2 to 2020/12/1
Frequency of Interim Report: every 12 months. Please file an extension before the expiry date, if you need.
Above study has been approved with the full-board review by Institutional Review Board of the Chung Shan Medical University Hospital on Dec.2, 2019. About the essential duties, obligations and responsibilities of the principal investigator, please refer to the back page.

Chib-Ping Han,MD/PhD.
Chairman
The Institutional Review Board

本委員會組織與執行皆符合 ICH-GCP 規範及赫爾辛基宣言之精神
This Committee has been organized and operated in conformance with ICH-GCP requirements and the essence of Declaration of Helsinki.

doi:10.6834/csmu202200004

Appendix C. Permission of Research Proposal for CS19150

中山醫學大學附設醫院第一人體研究倫理審查委員會　複本

The Institutional Review Board
Chung Shan Medical University Hospital
No.110, Sec.1, Chien-Kuo N. Road, Taichung 40201, Taiwan
Phone: 04-24739595 Fax: 04-35073516

研究計劃免除審查證明書

CSMUH No: CS19150

計畫名稱：過度疲勞是否是尖銳物扎傷的危險因子?
計畫主持人及歸屬機構：陳詠心／中山醫學大學附設醫院
經費來源：主持人自行支付
版　本：【計畫書：V0617，日期：2020/06/17；Waiver 1：V0722，日期：2020 年 7 月 22 日】
許可書有效期間：自民國 109 年 08 月 19 日至民國 112 年 08 月 18 日
效期屆滿，自動失效；若計畫仍未執行完畢，主持人須重新提出申請。

上述計畫已於 109 年 08 月 19 日經本院人體研究倫理審查委員會依簡免除審查流程決議同意執行，有關計畫主持人的職責、義務及注意事項均詳列於背面，請參閱並遵守。

主任委員　曹昌堯

中　華　民　國　一　〇　九　年　八　月　十　九　日

Certification of Exempt Review
Chung Shan Medical University Hospital

Date: Aug 19, 2020

Protocol Title: Whether is overfatigue the risk factor of sharps injury?
Principle Investigator & Affiliated Institution: Yong-Hsin Chen／Chung Shan Medical University Hospital
Version:【see above】
Effective duration approved: 2020/08/19 to 2023 /08/18
This certificate will be automatically void after the validity period. The principal investigator should resubmit a new application, if the research is not yet completed.

Above study has been approved with the exempt review by Institutional Review Board of the Chung Shan Medical University Hospital on Aug 19, 2020. About the essential duties, obligations and responsibilities of the principal investigator, please refer to the back page.

Thomas Chang-Yao TSAO, MD/PhD.
Chairman
The Institutional Review Board

本委員會組織與執行皆符合 ICH-GCP 規範及赫爾辛基宣言之精神
This Committee has been organized and operated in conformance with ICH-GCP requirements and the essence of Declaration of Helsinki.

doi:10.6834/csmu202200004

IRS work, and often DS work were mediation factors of relationship between increased work experience and reduced level for burnout. Therefore, the present study could determine that burnout level could be improved for junior or young medical employee by effectively work-related interventions including avoided AU, often IRS work, and increased proportion of DS work. Due to BKP was suppression factor between WE and burnout, junior or young medical employee should specially note the problem for BKP.

3.8.2-1 Association between overtime / shift work and burnout

As shown in Table 1, the subjects who work overtime (OT) more than 80h and work OT between 45 and 80h per month were only 5 and 43 persons, respectively, therefore, which and subjects who work OT < 45h per month were combined to a new dummy variable – "work OT ", and the subjects who seldom work OT was as a reference variable. Table 2 demonstrated work OT was significantly relevant to PB (c = 10.53, P < 0.0001), WB (c = 9.50, P < 0.0001), and CB (c = 6.51, P < 0.0001). Participants who work OT reported high PB (42.67±18.25 vs 32.14±16.87, P < 0.0001), WB (40.22±15.69 vs 30.72±15.65, P < 0.0001), and CB (33.98±17.83 vs 27.47±16.39, P < 0.0001) than those who seldom work OT. There was significant difference of PB, WB, and CB level (for all P < 0.0001) among shift work schedules. Participants with irregular shift (IRS) work reported highest PB (41.78±18.08; c = 7.76, P < 0.0001) and WB (40.33±15.82; c = 8.48, P < 0.0001), however, participants with regular shift (RS) work report high CB (34.04±16.53; c = 6.37, P < 0.0001) than others. Participants with day shift (DS) work reported lowest PB, WB, and CB, therefore, the present study found DS work was a protective factor for burnout.

In MLR model (Table 5), work OT was independent risk factors of PB (c= 6.91, P < 0.0001), WB (c= 6.18, P < 0.0001), and CB (c= 3.95, P < 0.0001). According to mediation models in Table 7, the causes that participants who work OT sustained high

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level for burnout were negatively engaging in LAFF (impacting PB/WB/CB), without keeping REW (impacting PB/WB/CB), reporting AU (impacting PB/WB/CB), experiencing SSLD (impacting PB/WB/CB), IRS work (impacting PB/WB), and sustaining high NBSP (impacting PB/WB/CB).

In MLR model (Table 5), IRS work (c= 3.32, P < 0.05; c= 3.97, P < 0.01) and RS work (c=4.00, P < 0.01; c= 3.88, P < 0.01) were independent risk factors for PB and WB. However, RS work (c= 3.93, P < 0.01) was an independent risk factor of CB. The mediation/suppression models in Table 7 demonstrated reduced REW, SSLD, work OT, and high level for NBSP were one of causes that participant with IRS work sustained high level for PB and WB. Participants who were DS worker seem to report low burnout than others. According to mediation/suppression models in Table 7, positively engaging LAFF, keeping REW, and seldom experienced SSLD were one of causes that participants whose work's schedule were DS sustained low level for WB/CB than others.

3.8.2-2 Discussion for the relationship between overtime work and burnout

Many studies had determined work OT or long work hours were closely to burnout development. Nurses and clinicians working OT are more likely to experience burnout[93]. A study for 182 clinicians demonstrated participants working overtime reported significantly increased burnout.[94] A cross-sectional survey for 1560 full-time employees in Taiwan found long working hours (working over 40 hours per week) are correlated with burnout.[39] Furthermore, nurses working shifts of ten hours or longer were up to two and a half times more likely than nurses working shorter shifts to experience burnout[93]. The present study found participants who work OT sustained significantly high level of PB/WB/CB than those who seldom work OT. Our another a study (shown in Table 1, doi: 10.12998/wjcc.v9.i25.7391) at a hospital affiliated with a medical university in Taichung, Taiwan, in 2020, that also

doi:10.6834/csmu202200004

demonstrated participants who work OT more than 45 h per month reported highest level for PB and WB. There was a significant dose-response between OT work and PB or WB.

The past study demonstrated participants who experienced overtime and decreased interaction with family or friends were easily the deterioration of mental well-being[95]. In addition, participants whose working hours exceed standard recommendations are more likely to increase their alcohol use[96] for alleviating stress [32, 33]. From the view for medicine, the long working hours aggravates risk factors of atherosclerosis to cause circulatory system diseases, probably through its harmful effects to worsen workers' lifestyle, to cause lack of sleep[97]. The previous study also observed short sleep duration and overtime degree were in dose- response[98]. A survey of 2,617 registered nurses demonstrated extended work schedules were associated with musculoskeletal injury/disorders[99]. The shortening of regular workdays from over 7 hours to 6 hours may considerably reduce the prevalence of neck-shoulder pain[100]. The mediation models in Table 7 further found participants who work OT would negatively engage in LAFF, and often experienced SSLD, and didn't keep REW, and often reported short sleep duration, and measured high NBSP. That could cause burnout to worse for participants who work OT. These models were consistent with the previous research studies.

3.8.2-3 Discussion for the relationship between shift work and burnout

Shift work especially IRS work has been approved unfavorable to burnout by many studies. A cross-sectional study of health care workers demonstrated burnout was found more frequently among shift workers than those who did not work shifts[90]. Nurses who have irregular shift work schedule had high level of burnout syndrome than those have RS work schedule[40]. Other occupation also observed similar trend such

doi:10.6834/csmu202200004

as irregular schedules and increased night shifts were related to higher burnout risk in police[41]. Our another a study in 2020 (shown in Table 1, doi: 10.12998/wjcc.v9.i25.7391) also demonstrated participants with irregular shift work reported high level PB and WB than others. In addition, we found SSLD and NBSP play mediated role between IRS work and PB/WB. The previous Section has determined sleep problem is an important that IRS work impacts burnout. Another study for nurses also demonstrated adverse schedules are significantly related to MS disorders [99]. Above results represented IRS really impacts physical health for medical staff which could further damage mental health including burnout

3.8.3-1 Burnout difference among different professional fields

Table 2 illustrated there was significant difference of burnout among professional fields. Among them, the physician reported high PB (41.03±20.89; c = 10.17; both for $P < 0.0001$) and WB (39.38±18.45; c = 9.94; both for $P < 0.0001$) than others. Nurse reported high CB (33.48±17.62; c = 7.74; both for $P < 0.0001$) than others.

Table 7 demonstrated AU, SSLD, and OT were one of the causes of worsen PB/WB for physician. In addition, keep REW could against worsen PB/WB in physicians. As shown in Table 7, the causes that nurse's professional field easily worsen CB were that nurses didn't positive engage in LAFF, didn't keep REW, work OT, work IRS, and increased NBSP.

3.8.3-2 Discussion for the relationship between professional field and burnout

The present study found physicians' professional field itself still impacted burnout after adjusting the problems for LAFF, alcohol use, lack of sleep, work OT, shift work, MS pain. The past study also demonstrated the burnout is markedly higher amongst practicing physicians than individuals in other careers after adjusting for work

doi:10.6834/csmu202200004

hours and other factors[101, 102]. Attributed to reasons, work-related stressors[103, 104], excessive workloads[105], and work–home conflicts[106] were associated with burnout amongst physicians. Another, the present study had extra found different from past that physician's PB/WB sustained high level that also could be caused by AU, SSLD, and work OT. It is worth mentioning, according to mediation or suppression effect in Table 7, physicians common reported regular exercise weekly which also was often helpful to relieve PB/WB. Alcohol abuse and dependence is a significant problem in US surgeons, that were strongly associated with burnout [85]. According to the mediation model for burnout/AU/physicians in Table 7, physicians always adopted AU to face burnout, however, that is in vain.

One of the reasons for the high rate of insufficient sleep for physicians is the medical training culture. Trained physicians are instilled in the idea that sleep is optional, because they continue to work long shifts even when working hours are limited[107]. Table 7 demonstrated SSLD was mediation factor between physicians and PB/WB that also confirmed the medical training culture about physicians ignored sleep problem. It's this culture to cause high burnout for physicians than others.

Nurse professional field seem to bear high CB than other professional fields that would be explained by so-call "medical model"[108], whose statement is "people are not held responsible for either the origin of their problems or the solution to their problems". Patients are seen as ill or incapacitated, they are expected to accept their state as well as the diagnosis and the advice and treatment of an expert. It is clear that the expectation of investments of the patients are quite low, even lower than those of the professional. Therefore, nurses had a low level of burnout when interacting with a low investor patient and a high level of burnout when interacting with a high investor patient[109]. Corresponds to the practice of clinic, physicians have powerful professional authority to patient than nurses in ordinary people's minds, therefore, that

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could be the possible cause that nurses experienced high CB than physicians.

Generally speaking, the physical activity level of nurses is generally insufficient[110] and over 50% of nurses were insufficiently active[111] . A recent study of nurses found that many nurses did not participate in leisure-time physical activity[112]. Physical activity at work may not have the same positive impact on health as leisure activities[113]. Table 6 also demonstrated nurse is negative related to LAFF ($c = -4.51$, $P < 0.01$) and REW ($c = -0.82$, $P < 0.0001$) that is consistent with past studies. Table 7 further linked nurses, LAFF/REW, and burnout from client and determined LAFF/REW could improve burnout level for nurses.

Stressors had significant effect on increasing musculoskeletal discomforts of organs such as neck, shoulders and back for nurses [114]. Burnout impacting MS pain was similar, Mediation/suppression models in Table 7 found nurses often report high NBSP (neck or shoulders pain degree) which would cause burnout caused by client to sustain high level. Therefore, the strategy and resource of relieved MS pain for nurses is important for improvement of burnout.

3.9 Physical Health and Burnout

3.9.1-1 Association between chronic diseases / musculoskeletal pain and burnout

As shown in Table 2, participants who suffered chronic diseases (CD) sustained high level for PB (39.27±18.59 vs 33.89±17.48, $P < 0.0001$) and WB (36.64±16.84 vs 32.63±15.78, $P < 0.0001$). CD was a risk factor for PB and WB ($c = 5.39$ and 4.01; both for $P < 0.0001$).

As shown in Table 4, NBSP was positive relevant to PB ($c = 8.27$, $P < 0.0001$), WB ($c = 6.49$, $P < 0.0001$), and CB ($c = 3.79$, $P < 0.0001$). In addition, BAP was positive relevant to PB ($c = 1.59$, $P < 0.01$) and WB ($c = 1.49$, $P < 0.01$). There was positive relationship between BKP and PB ($c = 2.29$, $P < 0.01$) or WB ($c = 1.57$, $P < 0.01$).

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As shown in Table 5, NBSP (c= 6.86; c= 5.51, for both P < 0.0001), BAP (c= 1.38; c= 1.33, for both P < 0.01), and BKP (c= 1.68, P < 0.01; c= 1.16, P < 0.05) were independent risk factor for PB and WB. However, only NBSP (c= 3.23, P < 0.0001) was independent factor risk for CB. Apparently, NBSP obviously and directly sustained high burnout.

In addition, MS pain also played a bridge role (mediation effect) between risk factors and burnout. According to mediation effect in Table 7, NBSP was one of the reasons work OT sustained PB/WB/CB, IRS work sustained PB/WB, and nurses' professional field sustained CB. We had determined married/parenthood were closely relevant to WB and CB, however, married/parenthood also caused sustained high NBSP that will offset the relieved effect of married/parenthood for WB/CB. Increased WE was negative relevant to PB/WB/CB, however, BKP increased accompanied by work experience increased that also partially offset the protective effect of WE for burnout. Therefore, improvement plan of burnout should more note knee health problem for older senior staff.

3.9.1-2 Discussion for chronic diseases / musculoskeletal pain and burnout

The past study had demonstrated there are positive association between burnout and MS pain, too[43]. We also determined NBSP, BAP, and BKP were related to sustained PB and WB, too. It is worth mentioning that MS pain often play mediation factor for sustaining high burnout. According to MLR models in Table 5, NBSP was an independent risk factor for PB/WB/CB. In addition, we also determined the relationship of OT, NBSP and burnout by mediation models in Table 7 those participants who work OT often suffered pains from neck or both shoulders which would further worse burnout degree caused by overtime work. A prospective study in apparently healthy individuals demonstrated baseline levels of burnout predict the onset of regional

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neck/shoulder and/or low back pain and burnout symptoms were associated with a 1.67-fold increased risk of MS pain[115]. Another prospective study demonstrated nurses who reported low mood or stress at baseline were more likely to develop neck/shoulder pain later[116]. Despite the present study is a cross-sectional study, which through MLR and mediation models to confirm direct impacting and the mediation effect of neck and both shoulders pain for burnout. These results are highly consistent with the past study and determined the importance role for MS pain on burnout development.

The previous studies also found the shortening of regular workdays from over 7 hours to 6 hours may considerably reduce the prevalence of neck-shoulder pain[100]. Compared with fixed shift work, the irregular shift workers for male were associated with shoulders and neck pain and those for female were associated with neck pain[117]. The present study had further linked OT/IRS, burnout and MS pain by mediation models in Table 7 those participants who work OT or work IRS easily suffered neck or both shoulders pain which would cause burnout degree to further worse. Therefore, the relieve neck and both shoulders pain also should be included in improvement plan of burnout for medical employee.

The previous study demonstrated work experience significantly increases the morbidity of pain [118]. However, the present study determined WE was only relevant to BKP. Moreover, BKP suppressed the protective effect WE to PB/WB/CB.

Participants who were parenthood (c= 0.12, P < 0.05) and married (c= 0.15, P < 0.01) would increase NBSP. The relationship was similar to past study that domestic work and stress from overload further exacerbate musculoskeletal disorders because they interfere with the recovery process[119]. The present study has illustrated parenthood was closely related to worsen PB and NBSP that could imply closely relationship among both. According to Table 7, We determined NBSP will cause WB/CB for people married or parented to worsen by suppressed effect. This finds

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coincidentally with the previous study that poor psychological status may predict neck and shoulders pain [120, 121].

The three highest prevalence rates of MS pain for nurses were found for the neck, shoulders and back[122]. Compared with other professional fields, nurses' professional field was closely related to NBSP (Table 6, c= 0.15, P < 0.01).

3.10 Burnout and Work-Related / Sharps Injuries

3.10.1 Statistical test for association

Table 2 demonstrated work-related injuries (WRIs) was significantly relevant to PB (c = 0.38, P < 0.0001), WB (c = 0.33, P < 0.0001), and CB (c = 0.23, P < 0.0001). Similarly, Sharps injuries (SIs) was closely relevant to PB (c = 0.25, P < 0.0001), WB (c = 0.22, P < 0.0001), and CB (c = 0.20, P < 0.0001), too.

The past studies for administrative services[48] and forest industry employees[49] demonstrated burnout was relevant to risk of injuries. The present study demonstrated linear regression coefficients of 3 sub-burnout dimension to WRIs were between 0.23-0.38. Regarding forest industry employees, each one-unit increase in the burnout score was related to a 9% increase in the risk of injury[49] which is obviously lower than medical employee compared with the present study. In line with reports for nurses and the healthcare employees that there was association between burnout and SIs[123, 124].

The present research confirmed that there were positive dose-response between burnout and WRIs/SIs for medical employee.

3.10.2 Risk factors of work-related and sharps injuries

As shown in Table 8, CD (c= 4.64, P < 0.0001), AU (c= 3.10, P < 0.01), SSLD (c= 3.71, P < 0.01), work OT (c= 6.58, P < 0.0001), IRS work (c= 5.08, P < 0.0001),

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Nurse (c= 5.64, P < 0.0001), NBSP (c= 5.89, P < 0.0001), BAP (c= 1.78, P < 0.01), and BKP (c= 3.10, P < 0.0001) were risk factors of WRIs. In addition, As shown in Table 8, CD (c= 1.74, P < 0.05), AU (c= 3.22, P < 0.0001), SSLD (c= 2.52, P < 0.01), work OT (c= 4.43, P < 0.0001), IRS work (c= 4.03, P < 0.01), NBSP (c= 1.78, P < 0.01), and BKP (c= 1.02, P < 0.05) were risk factors for SIs. However, women (c= -2.22, P < 0.05) was a protective factor of SIs compared to men.

Followed Sections will further explore association between risk factors and burnout and model risk factors, burnout, and WRIs/SIs to assess.

3.10.3 Sex difference of WRIs and SIs

As shown in Table 8, there was not difference of WRIs between men and women (c= 0.69, P > 0.05). However, the sex difference was found in SIs. Women sustained low correlation for SIs than men (c= -2.22, P < 0.05).

A study indicated that male health workers were 10 times more likely to sustain an SI than were female health workers[125] that is consistent with the present study.

3.10.4 Role of burnout between chronic diseases and work-related / sharps injuries

The index for ability of explanation was "d", which is defined the reduced proportion for regression coefficient of risk factor to WRIs before and after adjusting variable. If the regression coefficient before adjusting variable was statistically significant and which was not statistically significant after adjusting variable, that was call "fully explanation the effect " and "d" value would not be calculated. If the regression coefficient before adjusting variable was not statistically significant, the ability of explanation did not be estimated. If the regression coefficient before adjusting variable was statistically significant and which was also statistically significant after

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adjusting variable, that was call "partial explanation the effect" and "d" value would be calculated. "d" value is higher, the ability of explanation is stronger.

As shown in Table 8-1, CD was significant related to WRIs (c= 4.64, P < 0.0001) that could be explained by PB, WB, and CB effect and ability of explanation is 45.69% (d=45.69), 36.42% (d=36.42), and 6.68% (d=6.68), respectively. Table 8-2 presented the mediation effect that PB (Z= 4.81, P < 0.0001) and WB (Z= 4.08, P < 0.0001) mediated the relationship between WRIs and CD.

As shown in Table 8-3, PB and WB effect could fully explain the relationship between CD and SIs. CB effect only could explain 8.62% (d= 8.62) the relationship between CD and SIs. Table 8-4 demonstrated PB (Z= 4.05, P < 0.0001) and WB (Z= 3.64, P < 0.01) were mediation factors for the relationship between CD and SIs.

Persons with chronic health conditions, such as chronic heart disease, diabetes, arthritis, blindness, or difficulty seeing, and asthma and depression confer an increased risk work-related injury[126, 127]. In addition, burnout is related to CD, such as coronary heart disease[46], cardiovascular disease[128], and type 2 diabetes[47]. The present study linked CD, burnout, and WRIs by mediated model (Table 7) which determined PB/WB is one of causes that CD sustained high WRIs. Therefore, physical diseases could impact people psychology which caused work-related injuries occurrence. The mental health promoting for medical worker suffering CD is demand immediate attention in preventing of work-related injuries.

As shown in Table 8 and Table 8-4, participants who suffer CD sustain high level for SIs (c= 1.74, P < 0.05) and PB/WB (c= 5.39/4.01, P < 0.0001). The mediated models further demonstrated PB/WB (Z= 4.05, P < 0.0001; Z= 3.64, P < 0.01) is a mediated factor. Therefore, this is an important find that mental health could play a positive and helpful role of SIs caused by physical disease.

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3.10.5 Role of burnout between alcohol use and work-related / sharps injuries

Table 8-1 demonstrated AU was significantly related to WRIs (c= 3.10, P < 0.01). The relationship could be fully explained by PB/WB effect and could be explained 31.29% proportion by CB effect. Table 8-2 presented PB (Z= 3.96, P < 0.0001), WB (Z= 3.54, P < 0.01), and CB (Z= 3.41, P < 0.01) mediated the relationship between WRIs and AU.

As shown in Table 8-3, PB, WB and CB could explain 17.39% (d= 17.39), 14.91% (d= 14.91), and 13.35% (d= 13.35) the relationship between SIs and AU, respectively. Table 8-4 demonstrated PB (Z= 3.49, P < 0.01), WB (Z= 3.24, P < 0.01), and CB (Z= 3.14, P < 0.01) mediated the relationship between AU and SIs.

There were a significant association between alcohol consumption and work-related injuries among farmers.[129, 130] The odds of injury also significantly increased with increased frequency of drinking per week[130]. However, for young U.S. workers in early research, common occupational injuries (excluding sprains and strains) may not be strongly associated with alcohol dependence[131]. Despite there were different results about the association for alcohol use and WRIs in past studies, the difference in the formal reported injuries and self-report injuries could be the one of main reasons. The present study adopted self-report questionnaire of WRIs that demonstrated AU were closely relevant to WRIs. The mediation models further determined the relationship among AU, burnout, and WRIs that burnout (PB/WB/CB) was one of causes that AU sustained high WRIs that seldom be mentioned in past studies.

As shown in Table 8-4, the mediation models further demonstrated burnout (PB/WB/CB) mediated the relationship between AU and SIs which determined AU is also through burnout to impact SIs. This is new evidence which is seldom mentioned in past studies. The find could extend new vision for SIs prevention of medical worker

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and highlight the importance for quitting alcohol use.

3.10.6 Role of burnout between short sleep duration and work-related / sharps injuries

Table 8-1 demonstrated, the relationship between short sleeping duration (SSLD) and WRIs (c= 3.71, P < 0.01) could be fully explained by PB/WB effect, and CB effect could only explain 27.22% (d=27.22). Table 2 showed PB (Z= 6.78, P < 0.0001), WB (Z= 6.30, P < 0.0001), and CB (Z= 3.51, P < 0.01) mediated the relationship between SSLD and WRIs.

As shown in Table 8-3, The relationship between SSLD and SIs could be fully explained by PB effect, however, WB and CB only explained 36.11% (d= 36.11) and 18.25% (d= 18.25). Table 8-4 demonstrated PB (Z= 5.01, P < 0.0001), WB (Z= 4.95, P < 0.0001), and CB (Z= 3.23, P < 0.01) mediated the relationship between SSLD and SIs.

People with sleep insufficiency often reported frequent physical distress, frequent mental distress, activity limitations, depressive symptoms, anxiety, and pain[132]. The determined relationship for burnout and SSLD in previous section has been fully discussion. The National Health Interview Survey for USA suggested the work-related injury risk significant increases with decreasing usual daily self-reported sleep hours[133]. In addition, A systematic literature search demonstrated workers with sleep problems had a 1.62 times higher risk of being injured than workers without sleep problems[134]. Therefore, the association between sleep and work injuries was confirmed. According to mediation model, we further determine burnout (PB/WB/CB) was one of reasons for SSLD sustained high WRIs, too.

Despite reduction in SLD increase the risk of occupational injury[135], the present study also confirmed SIs is same as occupational injury that sleep duration less

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than 6 h easier sustained high SIs (Table 8, c= 2.52, P < 0.01). Table 8-4 determined PB/WB/CB mediated the relationship between SSLD and SIs which represented burnout play an important role between SSLD and SIs. Among them, only PB fully mediated the relationship between SSLD and SIs that represented participants who experienced SIs that caused by SSLD commonly sustained higher PB level. This could be proofed by Table 8-4 that SSLD impacting PB (a= 8.11, P < 0.0001) was strong than WB (a= 6.52, P < 0.0001) and CB (a= 3.84, P < 0.01). The previous study also found same trend that PB were significantly associated with impaired sleep quality[136].

3.10.7 Role of burnout between overtime work and work-related / sharps injuries

Table 8-1 demonstrated the relationship between work OT and WRIs (c= 6.58, P < 0.0001) could be partially explained by PB, or WB, or CB and the ability of explanation were 61.55% (d=61.55), 59.12% (d=59.12), and 24.32% (d=24.32), respectively. Table 8-2 illustrated PB (Z= 8.08, P < 0.0001), WB (Z= 8.24, P < 0.0001), CB (Z= 5.16, P < 0.0001) mediated the relationship between WRIs and OT.

As shown in Table 8-3, PB, WB and CB could partially explain 27.09% (d= 27.09), 25.96% (d= 25.96) and 15.08% (d= 15.08) the relationship between work OT and SIs, respectively. Table 8-4 demonstrated PB (Z= 4.85, P < 0.0001), WB (Z= 5.19, P < 0.0001), and CB (Z= 4.22, P < 0.0001) mediated the relationship between work OT and SIs.

The working in jobs with OT schedules was associated with a 61% higher injury hazard rate compared to jobs without overtime[137]. The present study confirmed the adverse relations of working OT with WRIs (Table 8, c= 6.58, P < 0.0001), too. Further study in mediated models (Table 9) found participants who work OT sustained high WRIs due to worsen PB/WB/CB. It represented work OT could through mental factor such as burnout to impact WRIs. This is an important find and view to preventing WRIs

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in future.

In one study, an increase in weekly work hours increased the occurrence of SIs among nurses[138]. The present study further also confirmed work OT was significant relevant to SIs (Table 8, c= 4.43, P < 0.0001) for participants including physician, nurse, and other professional fields. It represented OT impacting WRIs could be a widely problem among different medical professional fields. PB/WB/CB only explained 15%~28% the relationship between work OT and SIs (Table 8-3) and partially mediated the relationship between work OT and SIs (Table 8-4, Z= 4.85, P < 0.0001; Z= 5.19, P < 0.0001; Z= 4.22, P < 0.0001). These results suggested that work OT affected SIs directly or indirectly (through an unknown path). Studies have noted that increased OT was significantly associated with impairments in attention, executive function[139], and stress response[140]. Whether OT work affects SI incidence through these factors remains to be determined. However, the present study confirmed burnout was one of causes that working OT sustained high SIs.

3.10.8 Role of burnout between irregular shift work and work-related / sharps injuries

Table 8-1 demonstrated the relationship between irregular shift (IRS) work and WRIs (c=4.35, P < 0.01) could be fully explained by PB and WB effect. CB could partially explain 26.90% (d=26.90). Table 8-2 demonstrated PB (Z= 4.05, P < 0.0001), WB (Z= 4.74, P < 0.0001), and CB (Z= 2.82, P < 0.01) mediated the relationship between WRIs and IRS work.

As shown in Table 8-3, The relationship between IRS work and SIs could be explained through PB, WB, and CB effect, their explained proportion were 23.26% (d= 23.26), 26.20% (d= 26.20%), and 14.17% (d= 14.17), respectively. Table 8-4 illustrated PB (Z= 3.55, P < 0.01), WB (Z= 4.08, P < 0.0001), and CB (Z= 2.66, P < 0.01) mediated

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the relationship between IRS work and SIs.

The working shifts repeated disruption of the circadian system[141], in addition, the misalignment of circadian rhythms of body functions is responsible of the so-called "jet lag" syndrome, which could cause feelings of fatigue, sleepiness, insomnia, digestive troubles, irritability, poorer mental agility, and reduced performance efficiency[142]. Above these damages from "jet lag" syndrome could be related to burnout such as feelings of fatigue and insomnia. Shift work had a statistically difference with work-related injuries compared to non-shift work[143, 144]. Therefore, there could be a connection among shift work, burnout, and WRIs. The present study found only IRS work was significantly relevant to WRIs among people who work shift work. RS work was not statistical significantly relevant to WRIs. Burnout including PB, WB, and CB paly mediation factors between IRS work and WRIs that demonstrated burnout obviously sustains high WRIs for participants who have IRS work. The present study confirmed mental health also impacts WRIs occurrence for people with IRS work.

In the same vein, studies have observed that working regular shifts exerted protective effects against SIs compared with irregular shift work [51, 54]. Consistent with results from other studies, Table 8 demonstrated irregular shift work was significantly associated with SIs (c= 4.03, P < 0.01), but regular shift work was not significant (c= 1.79, P > 0.05). Table 8-4 shown PB (Z= 3.55, P < 0.01), WB (Z= 4.08, P < 0.0001), and CB (Z= 2.66, P < 0.05) partially mediated the relationship between IRS work and SIs, indicating that burnout was also one of causes that IRS work sustains SIs; in others, irregular shifts may have exerted effects on SIs through other routes.

3.10.9 Role of burnout between nurses and work-related / sharps injuries

Table 8-1 shown the relationship between nurse and WRIs (c=4.84, P < 0.0001)

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that could be partially explained by PB, WB, and CB effect could partially explain 53.31% (d= 53.31), 53.10% (d= 53.10), and 32.23% (d= 32.23). Table 8-2 showed PB (Z= 5.72, P < 0.0001), WB (Z= 6.01, P < 0.0001), and CB (Z= 5.08, P < 0.0001) mediated the relationship between WRIs and nurses.

Table 8-3 demonstrated the relationship between nurse and SIs (c= 2.43, P < 0.01) that could be partially explained by PB, WB, and CB effect could partially explain 35.39% (d= 35.39), 34.98% (d= 34.98), and 29.63% (d= 29.63). Table 8-4 presented PB (Z= 4.55, P < 0.0001), WB (Z= 4.82, P < 0.0001), and CB (Z= 4.33, P < 0.0001) mediated the relationship between nurses and SIs.

Nurses' inclination to report injuries was higher in organizations with onsite health programs[145]. The Occupational Health Safety Network (OHSN) to collect detailed injury data included falls, patient handling, and workplace violence demonstrated nurse assistants and nurses had the highest injury rates of all occupations examined according to injuries occurring from January 1, 2012–September 30, 2014[146]. Our study found that nurses were significantly relevant to WRIs compared with other professional fields (Table 7, c= 5.64, P < 0.0001). The further analysis in Table 8-1 found the relationship between nurses and WRIs could be fully explained by PB and WB effect and be partially explained by CB effect (d= 34.93%). The mediation analysis (Table 8-2) also determined nurses' burnout really play a pivotal role in WRIs.

The reasons of SIs occurrence were complex and multiple such as younger than 25 years of age, irregular shift work, significant fatigue after work, and suboptimal staffing levels[147]. In addition, there were significant differences of SIs among departments[54]. The present study demonstrated nurses through burnout (PB/WB/CB) to increase SI occurrence that suggests that mental health factors also could cause SIs occurrence for nurses. Therefore, a full prevention plan of SIs should include improvement plans for mental health.

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3.10.10 Role of burnout between MS pain and work-related / sharps injuries

Table 8-1 demonstrated the relationship between NBSP and WRIs (c= 5.89, P < 0.0001) that could be explained by PB effect, WB effect, and CB effect, respectively. Among them, the ability of explanation for PB, WB, and CB was 47.54% (d= 47.54), 39.57% (d= 39.57), and 13.92% (d= 13.92), respectively. The relationship between BAP and WRIs (c= 1.78, P < 0.01) that could be explained by PB effect (35.96%), WB effect (35.96%), and CB effect (14.04%). The relationship between BKP and WRIs (c= 3.10, P < 0.0001) that could be explained by PB effect (29.03%), or WB effect (21.29%), or CB effect (10.00%). As shown in Table 8-2, PB (Z= 9.29, P < 0.0001), WB (Z= 9.06, P < 0.0001), and CB (Z= 5.17, P < 0.0001) mediated the relationship between WRIs and NBSP. PB (Z= 2.64, P < 0.01), WB (Z= 2.76, P < 0.01) mediated the relationship between WRIs and BAP. PB (Z= 3.36, P < 0.01) and WB (Z= 2.57, P < 0.01) mediated the relationship between WRIs and BKP.

Table 8-3 demonstrated PB could fully explain the relationship between FNBS pain and SIs. However, WB and CB could partially explain 46.63% (d= 46.63), and 23.60% (d= 23.60) the relationship between FNBS pain and SIs, respectively. In addition, PB, WB, and CB could fully explain the relationship between BKP and SIs. Table 8-4 presented PB (Z= 5.63, P < 0.0001), WB (Z= 4.13, P < 0.0001), and CB (Z= 4.39, P < 0.0001) mediated the relationship between FNBS and SIs. Among them, PB and WB fully mediated the relationship between SIs and NBSP. PB (Z= 3.11, P < 0.01) and WB (Z= 2.47, P < 0.05) fully mediated the relationship between BKP and SIs.

The previous Section had illustrated MS pain was associated with burnout. Table 8 demonstrated FNBS and FBK pain were significantly relevant to SIs (c= 1.78, P < 0.0001; c= 1.02, P < 0.05). Based on these results, we further explored the relationships among SIs, burnout, and MS pain. As shown in Table 8-4, PB fully mediated the

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relationship between SIs and NBSP or BKP ($Z= 5.63$, $P < 0.0001$; $Z= 3.11$, $P < 0.01$). WB partially mediated the relationship between SIs and NBSP or BKP ($Z= 4.13$, $P < 0.0001$; $Z= 2.47$, $P < 0.01$). In addition, CB partially mediated the relationship between SIs and NBSP ($Z= 4.39$, $P < 0.0001$). NBSP and BKP seem to be closely related to PB, WB, and CB when exploring the causes of SIs occurrence.

The past study also really found severity of pain in the neck / shoulder area were associated with an increased risk of burnout[148] and psychosocial elements of work were more involved in the persistence of the symptoms in the knee[149]. Our study confirms previous studies that neck/shoulders/knee pain sites seem to be associated with mental health and linked the relationship between SIs and neck/shoulders/knee pain through mediation effect of burnout. These results more extend views for preventing of SIs that SIs is not only an education and safety culture problem which also could be an outcome of complex influence process for physiology and psychology.

3.10.11 Difference of burnout effect for WRIs and SIs

SIs was one of WRIs, too. Is there difference for burnout impacting them? Table 9 showed that there was not obvious difference in both except to BAP. SIs for nurse was not significantly different compared with other professional fields. However, nurses reported high WRIs incidence than other professional fields. The regression coefficient for nurse to SIs was 1.75, but which is not statistically significant. It represented there could be obviously difference for SIs occurrence among different nurses' departments. In addition, the cause could come from education or train. The previous study also illustrated a continuous educational effort leads to a reduction of sharps injuries[150]. Despite pain site difference, MS pain did not only impact WRIs and impacted SIs, too. Therefore, burnout's mediated effect had consistent effect on occurrence for WRIs and SIs.

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4. Conclusion

4.1 Summary

The present study has determined the reasons of burnout development by three burnout scales and statistical methods. In addition, we also determined increased work-related (WRIs) and sharps injuries (SIs) will result from high burnout level caused by sex-dominated occupations, negative family role, lack of sleep and increased alcohol use (AU), overtime (OT) and shift, chronic diseases (CD), and musculoskeletal (MS) pain.

Sex difference for burnout

The proportion of man is high than women in physician's field, women physicians significantly experience high burnout from work than man physicians. The proportion of woman is markedly high than man in nurse's field. Despite of not statistically significant, men nurse common reported high burnout level than women nurses. The present study suggest sex difference of burnout was associated with sex-dominated occupations.

Family factors and burnout

People married or parenthood is relevant to lower work-related burnout (WB) and client burnout (CB). Parent's role itself instead be unfavorable factor to personal burnout (PB) after adjusting other risk factors. Positively engaging in leisure activity with family and friends (LAFF) is helpful for a successful role of parents which can further enhance the role quality of staff or service provider which could sustain lower level of WB and CB.

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Living habits and burnout

People who experience short sleep duration (SSLD) common reported high level for PB and WB than others. OT and irregular shift (IRS) work could lead to SSLD which will further sustain high level of PB and WB. The one of reasons for physicians reporting high PB and WB than others is lack of sleep. Sufficient sleep duration is one of causes that day shift (DS) staffs sustain low PB and WB level than others.

AU can't alleviate burnout which is instead an unfavorable factor of burnout. People who work OT adopt AU, which is unhelpful to relieve burnout and instead sustain high level for PB, WB and CB. In addition, AU is one of reasons for physicians reporting high PB and WB than others, too.

Work-related factors and burnout

Young or junior employee reported lower burnout level in three burnout scales. Increased work experience was negatively relevant to burnout. Compared with seldom OT, medical employee who work OT sustained high level of PB, WB, and CB. People who work shift sustain high PB, WB, and CB than others, but people who work IRS experienced higher PB and WB than those who work regular shift work. People who work OT or IRS could experience shorter sleep duration or often report neck or both shoulders pain that could further worse PB and WB.

DS was a protective factor of PB, WB, and CB whose protective effect resulted from people who have DS work could often engaged in leisure activity with family and friends or had habit of regular exercise weekly (REW), or sufficient sleep duration per day (> 6 h). There was difference of burnout among professional fields. Among them, the main reasons for physicians reporting high PB and WB than others were AU, OT, and lack of sleep. Physicians and nurses reported high CB than others. Physicians have powerful professional authority to patient than nurses that cause markedly high-level

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CB for nurses compared with physicians.

Physical health and burnout

Compared with people without CD, people who reported suffered at least one CD sustained significantly high burnout level in personal and work-related burnout scales. There was dose-response between MS pain (neck and both shoulders pain (NBSP), both ankle pain (BAP), and both knee pain (BKP)) and PB or WB, however, CB was only relevant to NBSP. The one of reasons for nurses sustained high CB was NBSP.

Work-related injuries and burnout

CD, AU, SSLD, work OT, IRS work, Nurses, MS pain including NBSP, BAP, and BKP are unfavorable factors for WRIs. Burnout is also closely relevant to these unfavorable factors and mediated bridges in these risk factors and WRIs, too. SIs is one of WRIs for medical staff common and there are almost same risk factors with WRIs except to Nurse professional field and BAP. In addition, burnout plays mediated roles in risk factors and SIs, too.

Finally, summarized present study's results with two Figures which is presented in Figure 1 and Figure 2 that are very valuable to preventing burnout and work-related injuries.

Suggestions

Burnout impacts every medical employee and causes hugely hidden loss for personal, family, and institutions. More important, it could harm patient safety. Regarding preventing burnout, medical institutions should encourage employees to increase parent-child interaction and positively engage in LAFF and keep regularly

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exercise after getting off work is necessary. The courses of quit alcohol use should be arranged to staff and avoid long workhours, OT, and irregular shift. In addition, the problem for physician on alcohol use, sleep, and overtime work should be paid attention much more. Based on the markedly relationship between burnout and MS pain, employee relief plans (including resource or education courses) of neck and both shoulders pain should be supplied.

Poor personal health, bad living habits damage mental health and further causes injuries in workplace. It represents the prevention plans for WRIs and SIs should include the work plan for the high-risk identification of burnout to early find the high-risk employee for work injuries and relieve burnout symptoms, and effectively reduce the incidence for WRIs/SIs.

4.2 Evaluation

The present study is 3rd research plan for SIs and burnout, which was approved by the Institutional Review Board of Chung Shan Medical University Hospital on Aug 25, 2021 (CSMUH NO: CS1-21108) whose license was on Appendix A. The first research was approved by the Institutional Review Board of Chung Shan Medical University Hospital on December 2, 2019 (CSMUH No: CS19137) whose license and published manuscript by journal were on Appendix B and doi: 10.12998/wjcc.v9.i35.10937. That was focus on the relationship among SIs, OT work and healthy body weight. The result indicated heavy overtime work (> 80 h/month) was associated with needle and SIs risk. Compared with the present study that work OT sustained high SIs, both results were consistent. However, we must indicate there is difference in SIs definition and sample collected come from different years. The definition of NSI in CS19137 was at least one NSI notified hospital by employee in past one year (yes/no), but the present study was SIs occurrence frequency (always

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/often / sometimes / seldom /never) in past year for employee's self-reported questionnaire. The self-reported advantage is the sample size could be extended, which could reduce the problem for employee not notifying hospital for sharps injuries. Therefore, we changed the method of collected data to self-report of participants.

The second research was approved by the Institutional Review Board of Chung Shan Medical University Hospital on July 22, 2020 (CSMUH No: CS19150) whose license and published manuscript by journal were on Appendix C and doi: 10.12998/wjcc.v9.i25.7391. The study had added new theme for burnout and more new variables. It demonstrated burnout was determined to contribute to SIs occurrence; specifically, burnout mediated the relationships of SIs with frequent MS pain, work OT, and IRS work. Despite second study's SIs is categorical variables and the present study's SIs is continuous variable which is occurrence frequency of SIs, both conclusions are still consistency. In addition, a new variable CB measured by client burnout scale was added to present study and could sufficiently illustrate the profile of burnout than previous studies. Same to PB and WB, CB mediated the relationships of SIs with frequent MS pain, work OT, and IRS work, too. The present study also found burnout was a mediated factor in SIs and CD, or AU, or SSLD. The second research CS19150 illustrated there was significant difference of burnout among WE rank, occupation groups, drinking in past month, sleep duration ranks, exercise per day, chronic disease, overtime work ranks, and work schedule classes that were consistent with the present study. Our study has special, interesting, and important new finds compared with research CS19150 that people who married or parenting or people engage in leisure activities with family or friends in vacation time sustained low level for work-related burnout.

The present study adopted mediation analysis could further find the reasons for burnout that different from other studies that only explored the association between risk

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factors and burnout by multiple linear regression method. Burnout is closely relevant to WRIs and SIs which is seldom mentioned in other studies. In addition, married and parenting was associated with burnout were interesting discoveries. Despite parenthood itself worsens PB, it instead relieves WB and CB. This leads to an interesting point that successful family live and successful career is not necessarily conflict in mental health that is a new find that is seldom mentioned in past studies, too. A find seldom mentioned in other studies that leisure activity with family and friends is favorable for relieved burnout and even reduces occurrence for WRIs/SIs.

Except to the association between neck/shoulders pain and burnout have been determined in present study, we also determined burnout is a key that workplace factors such as work OT and IRS work cause specific body pain.

4.3 Limitation

Despite we have got excellent and significantly results for the relationship between burnout and married or parenting, the duration of marriage and the child's age are lack. We don't determine whether long marriage relationship will cause burnout to sustain? Whether will parent's burnout gradually relieve by adulthood of children? These could cause interference to study's results. LAFF was as an index for successful family role seem to be insufficient which should seek more rigorous questionnaire to strengthen measured index. Although sex-dominated occupations could affect burnout development for men or women in our study and other studies, The proportion of men or women is as a basis of determined sex-dominated occupations is not sufficient in present study. Therefore, we should collect more variables (such as supervisor position or pressure of sexism) to determine this result. The types of occupational injuries are multiple which could have different occurrence reasons. The present study only adopted "work-related" to include these injuries. Therefore, we cannot know the relationship

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between other different injuries and burnout. Despite we have determined a specific injuries SIs are closely relevant to burnout, we cannot determine other injuries (such as falling, slipping and cutting) are relevant to burnout, too. The present study's data collected didn't include department information for participants, that could cause results to be interfered by work style or type. In addition, workload for participants and frequency of contact with patients or visitors are not be included in the present study which could not truly reflect busy condition for employee despite work OT had be included.

4.4 Future Work

This study was performed in the context of the coronavirus disease 2021 pandemic, which may have been more demanding on medical personnel than the non-pandemic period. Therefore, a similar study that assesses the regular work conditions and exposure of health care workers during the non-pandemic period should be replicated and compared with the result of the pandemic period. In addition, this study is a cross-section study that unable to capture the progress and changes of participants or environment. We have planned to conduct a series questionnaire about burnout for same group in the next few years which will be favorable for prospective cohort study. New questionnaires for social support, family relationship and parent burnout will be adopted by reviewing literatures and workplace bullying survey also will be added which will be contributed for further exploring new reasons for burnout. In Taiwan, care of elderly parents is a common problem that adult children must face. Therefore, raising elderly parents' options should be added in questionnaire to future explore the relationship between burnout and raising elderly parents.

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6. Tables

Table 1 The basic variables descriptions for all 1250 participants

Basic variables	subjects	proportion %
Sex		
Women	1016	81.28
Men	234	18.72
Married state		
Married	612	48.96
others	638	51.04
Raising the child		
without child	697	55.76
one child	185	14.80
two children	307	24.56
three children	57	4.56
over three children	4	0.32
Leisure activities with family or friends		
always	78	6.24
often	383	30.64
sometimes	592	47.36
seldom	186	14.88
never	11	0.88
Exercise frequency		
At least once a day	126	10.08
At least once a week	585	46.80
At least once a month	226	18.08
Less than once a month	244	19.52
Never	69	5.52
Frequency for drink coffee		
at least two cups a day (100 points)	16	1.28
two cups a day (75 points)	47	3.76
one cup a day (50 points)	444	35.52
sometimes (25 points)	520	41.60
never (0 points)	223	17.84
Alcohol use in a month		
everyday	4	0.32
occasionally	470	37.60
never	776	62.08
Sleep duration per day		
less 5 hours	46	3.68
between 5 and 6 hours	435	34.80
between 6 and 7 hours	558	44.64
between 7 and 8 hours	180	14.40
above 8 hours	31	2.48
Work experience (10.88±9.51)		
less 1 years	162	12.96
1-5 years	356	28.48
5-10 years	169	13.52
10-15 years	199	15.92
15-20 years	125	10.00
20-25 years	142	11.36
25-30 years	41	3.28
over 30 years	56	4.48
Education degree		
Below high school	55	4.40
Bachelor	985	78.80
Master	171	13.68
PhD	39	3.12
Work OT per month		
> 80 h	5	0.40
45-80 h	43	3.44
< 45 h	411	32.88
seldom	791	63.28
Shift work schedule		
Irregular shift work	154	12.32
regular shift work	165	13.20
Night shift work	142	11.36
Day shift work	789	63.12
Professional field		
Attending physician	57	4.56
Resident physician	55	4.40
Nurses	512	40.96
Respiratory therapist	12	0.96

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Physical therapist	35	2.8
Social worker	10	0.8
Nurse Practitioner	50	4.00
Nutritionist	12	0.96
Occupational Therapist	30	2.40
Medical Radiation Technologist	39	3.12
Medical technologist	37	2.96
Psychologist	3	0.24
Administration Staff and others	398	31.84
With chronic disease		
Yes	491	39.28
No	759	60.72
Experienced work-related injuries in a year		
always (100 points)	4	0.32
often (75 points)	18	1.44
sometimes (50 points)	129	10.32
seldom (25 points)	496	39.68
never (0 points)	603	48.24
Experienced sharps injuries in a year		
always (100 points)	0	0.00
often (75 points)	4	0.32
sometimes (50 points)	39	3.12
seldom (25 points)	290	23.20
never (0 points)	917	73.36

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Table 2 The association between burnout and surveyed variables

		PB		WB		CB	
Surveyed variables	subjects	mean ±SD	c	mean ±SD	c	mean ±SD	c
Sex							
Women	1016	36.43±17.84	2.30	34.56±16.33	1.88	30.14±16.96	1.53
Men	234	34.14±19.16	1.00	32.68±16.22	1.00	28.62±18.28	1.00
Marriage state				***		**	
Married	612	35.80±17.64	-0.40	32.32±15.41	-3.70***	28.00±16.28	-3.63**
Unmarried	638	36.20±18.56	1.00	36.02±16.96	1.00	31.64±17.90	1.00
Raising the child				***		***	
Parenthood	552	35.84±18.42	-0.30	31.87±15.74	-4.19***	27.00±16.48	-5.12***
Not parenthood	697	36.14±17.87	1.00	36.06±16.54	1.00	32.12±17.46	1.00
Leisure activities with family or friends							
LAFF	1250	-	-0.13***	-	-0.16***	-	-0.14***
Exercise frequency		***		***		***	
Regular exercise every week	711	33.40±17.30	-6.04***	31.67±16.15	-5.88***	27.51±17.21	-5.43***
No weekly regular exercise[7]	539	39.44±18.59	1.00	37.55±15.95	1.00	32.95±16.74	1.00
The frequency for coffee consumption							
Coffee consumption score	1250		0.02		-0.02		-0.02

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Alcohol use habit in a month		***		**		**	
Ever AU	474	38.70±17.84	4.35***	36.36±15.53	3.47**	32.15±17.11	3.68**
Never alcohol use	776	34.35±18.08	1.00	32.89±16.65	1.00	28.46±17.14	1.00
Sleeping duration per day		***		***		**	
SLD < 6h (SSLD)	481	40.99±19.00	8.11***	38.22±17.03	6.52***	32.22±17.80	3.84**
SLD > 6h	769	32.88±16.80	1.00	31.70±15.34	1.00	28.38±16.68	1.00
Work experience							
WE (years)	1250	-	-0.11*	-	-0.19**	-	-0.14**
Education degree				*		**	
Master's degree or above	210	36.09±18.36	0.11	32.08±16.36	-2.56*	26.98±15.77	-3.45**
University or below university degree	1040	35.99±18.07	1.00	34.64±16.28	1.00	30.44±17.44	1.00
Experiencing overtime work per month		***		***		***	
Work OT	459	42.67±18.25	10.53***	40.22±15.69	9.50***	33.98±17.83	6.51***
seldom work OT	791	32.14±16.87	1.00	30.72±15.65	1.00	27.47±16.39	1.00
Work schedule		***		***		***	
IRS work	154	41.78±18.08	7.76***	40.33±15.82	8.48***	33.71±18.50	6.05***
RS work	165	39.22±19.55	5.20**	38.01±17.26	6.16***	34.04±16.53	6.37***
Night shift	142	37.06±18.85	3.05	36.22±16.21	4.36**	32.98±19.12	5.31**
DS work	789	34.02±17.33	1.00	31.85±15.74	1.00	27.67±16.36	1.00
Professional field		***		***		***	
physician	112	41.03±20.89	10.17***	39.38±18.45	9.94***	31.81±18.91	6.07**
Nurses	512	39.88±17.85	9.01***	37.82±16.05	8.38***	33.48±17.62	7.74***
PTs	228	33.81±17.11	2.95*	31.86±15.41	2.42	27.94±16.30	2.20
Ads	398	30.86±16.63	1.00	29.44±15.00	1.00	25.74±15.61	1.00
Suffering CD		***		***			
Yes	491	39.27±18.59	5.39***	36.64±16.84	4.01***	30.57±18.30	1.17
No	759	33.89±17.48	1.00	32.63±15.78	1.00	29.40±16.47	1.00
Experienced work-related injuries							
WRIs score	1250	-	0.38***	-	0.33***	-	0.23***
Experienced sharps injuries							
SIs score	1250	-	0.25***	-	0.22***	-	0.20***

*, P < 0.05; **, P < 0.01; ***, P < 0.0001; PB, personal burnout; WB, work-related; CB, client burnout; c, the linear regression coefficient of independent variable; AU, alcohol use; OT, overtime; IRS, irregular shift work; RS, regular shift; DS, day shift; c, the linear regression coefficient of surveyed variable against burnout.

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Table 2-1 Sex difference of burnout for physicians

Character	subjects	PB		WB		CB	
		mean ±SD	c	mean ±SD	c	mean ±SD	c
Sex							
Women	39	46.05±23.67	7.69	44.87±20.46	8.42*	36.43±17.25	7.09
Men	73	38.36±18.88	-	36.45±16.69	-	29.35±19.40	

*, P < 0.05; **, P < 0.01; ***, P < 0.0001; PB, personal burnout; WB, work-related; CB, client burnout; c, the linear regression coefficient of surveyed variable against burnout.

Table 2-2 Sex difference of burnout for nurses

Character	subjects	PB		WB		CB	
		mean ±SD	c	mean ±SD	c	mean ±SD	c
Sex							
Women	494	39.77±17.62	-3.06	37.68±16.08	-3.90	33.22±17.31	-7.53
Men	18	42.82±23.82	-	41.67±15.00	-	40.74±24.19	-

*, P < 0.05; **, P < 0.01; ***, P < 0.0001; PB, personal burnout; WB, work-related; CB, client burnout; c, the linear regression coefficient of surveyed variable against burnout.

Table 3 MS pain sites and factor analysis of the Nordic musculoskeletal questionnaire

MS pain site	MS pain subjects	Prevalence %	frequency score	Factor loading		
			mean ±SD	Factor 1	Factor 2	Factor 3
Neck	445	35.60	26.21±37.41	***0.33***	-0.02	-0.03
left shoulder	251	20.08	15.15±31.87	***0.33***	0.01	-0.02
right shoulder	277	22.16	16.96±33.42	***0.33***	0.02	-0.07
upper back	209	16.72	12.86±29.81	0.17	-0.01	-0.00
waist or lower back	364	29.12	20.90±35.01	0.08	-0.03	0.01
left elbow	56	4.48	3.44±16.67	-0.05	-0.04	-0.05
right elbow	84	6.72	5.22±20.33	-0.03	-0.05	-0.00
left wrist	65	5.20	4.08±18.21	-0.05	-0.02	-0.02
right wrist	129	10.32	7.65±23.88	-0.05	-0.06	-0.02
left hip/thigh/buttock	56	4.48	3.36±16.25	-0.05	-0.09	-0.00
right hip/thigh/buttock	56	4.48	3.34±16.19	-0.02	-0.07	-0.06
left knee	69	5.52	3.94±17.14	-0.05	-0.08	***0.51***
right knee	74	5.92	4.51±18.69	-0.02	-0.07	***0.47***
left ankle	27	2.16	1.52±11.12	-0.01	***0.51***	-0.01
right ankle	22	1.76	1.28±10.39	-0.04	***0.58***	-0.03
		eigenvalues		5.18	1.60	0.66
		explained variation %		59.03	18.17	7.51

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中山醫學大學公共衛生學系博士班

博士論文

Doctoral Thesis, Department of Public Health,

Chung Shan Medical University

從家庭、生活習慣、工作相關因素、肌肉骨骼疼痛探討職業倦怠的原因及其與工作相關傷害的關係

To explore the causes of burnout and association with work-related injuries from family, living habits, work-related factors, and musculoskeletal pain

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Yong-Hsin Chen
January 2022

中文摘要

引言

倦怠(Burnout) 於 1974 年由臨床心理學家 Herbert Freudenberger 首次描述。倦怠(burnout) 是一種身體的、情緒的及心理的耗竭狀態，它是由於長期參與對情緒有要求的工作環境所導致。Maslach Burnout Inventory (MBI)以及 Copenhagen Burnout Inventory (CBI)是最常被使用去評估倦怠的工具。倦怠在美國每年至少造成了近 46 億美元的損失並且影響了將近一半的醫生、護士及其他的醫療人員。此外，倦怠也會影響與病人相關的照護品質。過去的研究已經表明了倦怠與工作相關傷害(work-related injuries, WRIs)有關而且也會增加受傷的風險。本研究將建立職業倦怠的模型，以識別職業倦怠的危險因素，並探討職業倦怠與醫務人員的 WRI/銳器傷 (SI) 之間的關係。

方法與材料

本研究是在 2021 年以台灣台中一所醫學大學員工為調查基礎所做的一個觀察型及橫斷面研究，總共有 1633 人完成了包含北歐肌肉骨骼問卷(Nordic MS Questionnaire, NMQ)及哥本哈根倦怠問卷(Copenhagen burnout inventory, CBI)在內的調查，CBI 包含了個人倦怠(PB)、工作相關倦怠(WB)及客戶倦怠(CB)等三個尺度。在排除了資料漏失的問卷後共有 1250 份為有效問卷。統計分析採用了 t 檢定、 卡方(chi-square test)或費雪精確檢定、因子分析(factor analysis)、線性回歸及索博中介分析(Sobel test)。統計分析軟體是使用 SAS Enterprise Guide 6.1，統計顯著水準訂為 $P < 0.05$。

結果

研究表明了工作經驗(WE)、教育程度、已婚、為人父母、在假日積極與朋友及家人參與休閒活動(LAFF)、每週定期運動習慣(REW)、慢性病(CD)、一個月內

飲酒(AU)、每天睡眠時間短於 6 小時(SSLD)、加班(OT)、不定期輪班 (IRS)、不同的專業職域、常常頸部與肩膀疼痛(NBSP)、常常腳踝疼痛(BAP)以及常常雙膝疼痛(BKP)都與倦怠顯著相關。職業倦怠的性別差異與性別主導職業有關，女醫師的 WB 明顯高於男醫師。PB、WB、CB 與工作相關傷害(WRIs)及尖銳物扎傷(SIs)密切正相關。SSLD、OT、IRS、護士職業、NBSP 等也都與 WRIs/SIs 相關，其中 PB、WB 及 CB 也是這些關係的中介因子。CD、BKP 也與 WRIs/SIs 有顯著關係，PB 及 WB 是這些關係的中介因子。BAP 與 WRIs 緊密相關但與 SI 沒有顯著相關，PB 及 WB 為 BAP 與 WRIs 的中介因子。

結論

本研究通過三種職業倦怠量表和統計方法確定了職業倦怠發展的原因。 此外我們還確定很少與家人和朋友進行休閒活動，睡眠不足、AU、OT 和輪班、CD 和 MS 疼痛會增加倦怠程度，這將進一步增加 WRIs/SIs 的發生率。 因此，WRI 的預防計劃應包括職業倦怠的高危識別機制，及早發現工傷高危員工，進一步緩解職業倦怠症狀，有效避免工傷的發生。

關鍵字: 個人倦怠、工作相關倦怠、顧客倦怠、中介效應、工作相關傷害、尖銳物扎傷

Abstract

Introduction

Burnout was first described in 1974 by the clinical psychologist Herbert Freudenberger. Burnout is a state of physical, emotional, and mental exhaustion that results from long-term involvement in work situations that are emotionally demanding. Maslach Burnout Inventory (MBI) and Copenhagen Burnout Inventory (CBI) were most used instruments to assess burnout.

Burnout cause total losses of US$4.6 billion in the United States each year and affects approximately half of all nurses, physicians, and other clinicians. In addition, burnout also affects patient-related quality of care. The previous studies demonstrated burnout is related to work-related injuries (WRIs) and increase in the risk of injury. The present study would establish the relationship models of burnout to identify risk factors of burnout and explore the relationship between burnout and WRIs/sharps injuries (SIs) for medical worker.

Methods and materials

This is an observational and cross-sectional study which was based on members at a hospital affiliated with a medical university in Taichung, Taiwan, in 2021. 1633 individuals completed the questionnaires including Nordic Musculoskeletal Questionnaire (NMQ) and the Copenhagen burnout inventory (CBI). CBI included three burnout scales that are personal burnout (PB), work-related burnout (WB) and client burnout (CB), respectively. Among them, 1250 questionnaires were determined to be valid after exclusion for missing data. Statistical methods included t test, chi-square test or fisher exact test, factor analysis, linear regression, and Sobel test. Analysis was conducted using SAS Enterprise Guide 6.1 software, and significance was set at P

< 0.05.

Results

The present study demonstrated participants with master's degree or above or married or parenthood significantly reported low level for WB and CB than others and those with regular exercise every week (REW) reported low level for PB, WB and CB than others. Participants with chronic diseases (CD) or ever alcohol use (AU) or sleep duration per day less than 6 h (SSLD) or work overtime (OT) or shift work including irregular shift (IRS) and regular shift (RS) work or physicians/nurses reported high level for PB, WB and CB than others. Work experience (WE) and engaging in leisure activities with family or friends (LAFF) in vacation were negatively related to PB, WB and CB. Neck and both shoulders pain (NBSP) was positively related to PB, WB and CB. Both ankles pain (BAP) and both knees pain (BKP) was positively related to PB and WB. Sex difference of burnout was associated with sex--dominated occupations. Under low proportion of women than men in physician field, women physicians significantly reported high WB than man physicians. PB/WB/CB was closely relevant to WRIs/SIs and was mediation factors between WRIs/SIs and SSLD, or work OT, or IRS work, or Nurse, or NBSP. PB/WB mediated the relationship between WRIs/SIs and CD or BKP, too. However, PB/WB only mediated the relationship between WRIs and BAP.

Conclusion

The present study has determined the reasons of burnout development by three burnout scales and statistical methods. In addition, we also determined seldom engaging in leisure activity with family and friends, lack of sleep, AU, OT and shift, CD, and MS pain will increase burnout degree, which will further raise incidence of WRIs/SIs. Therefore, the prevention plans of WRIs should include the high-risk identification mechanism of burnout and early find the high-risk employee of work injuries to further relieve burnout symptoms and effectively avoid occurrence for injuries.

Keywords: Personnel Burnout, Work-Related Burnout, Client-related Burnout, Mediation Effect, Work-Related Injuries, Sharps Injuries.

Contents

Abbreviation

ADS, **AD**ministration Staff
AU, **A**lcohol **U**se
BAP: Both **A**nkles **P**ain
BKP: Both **K**nees **P**ain
CB: Client-related **B**urnout
CBI: **C**openhagen **B**urnout **I**nventory
CD: **C**hronic **D**iseases
DS: **D**ay **S**hift
IRS: **I**r**R**egular **S**hift
LAFF: **L**eisure **A**ctivities with **F**amily or **F**riends
MLR: **M**ultiple **L**inear **R**egression
MS: **M**usculo**S**keletal
NBSP: **N**eck and **B**oth **S**houlders **P**ain
NMQ: **N**ordic **M**usculoskeletal **Q**uestionnaire
OT: **O**ver**T**ime
PB: **P**ersonal **B**urnout
PTs: **P**rofessional and **T**echnical personnel
REW: **R**egular **E**xercise per **W**eek
RS: **R**egular **S**hift
SIs: **S**harps **I**njuries
SLD: **SL**eeping **D**uration
SSLD: **S**hort (less 6 hours per day) **SLD**
ULR: **U**nary **L**inear **R**egression
WB: **W**ork-related **B**urnout
WE: **W**ork **E**xperience
WRIs: **W**ork-**R**elated **I**njuries.

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1.Introduction

1.1 History, Measured Methods and Definition of Burnout

Burnout was first described in 1974 by the clinical psychologist Herbert Freudenberger, who found emotional depletion and accompanying psychosomatic symptoms among the clinic's volunteer staff. He called the phenomenon "burnout" which borrowed the term from drug-addict slang. In addition, he defined burnout as exhaustion resulting from "excessive demands on energy, strength, or resources" in the workplace, characterizing it by a set of symptoms including malaise, fatigue, frustration, cynicism, and inefficacy[1]. The social psychologist Christina Maslach and her colleagues came across the same term "burnout" in California when interviewing a variety of human services workers and developed a model of burnout consisting of three dimensions: emotional exhaustion, depersonalization, and a diminished sense of personal accomplishment[2]. In 1981, she proposed the Maslach Burnout Inventory (MBI), which consists of three subscales including emotional exhaustion, depersonalization, and a diminished sense of personal accomplishment to measure the extent of an individual's symptoms along each dimension[2]. The MBI remains the one of most used instruments to assess burnout to this day. However. MBI has been cast doubted on its temporal and sequential consistency[3] and has been pointed to difficulties when it is used outside of a human service setting[4]. In addition, the depersonalization and exhaustion subscale items are all negatively keyed, the personal accomplishment subscale items are all positively keyed. This structure has been criticized as leading to artificial factor solutions[5], and inflated intrascale correlations[6].

Considering exhaustion as the core of the burnout concept, researchers from

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Denmark developed the Copenhagen Burnout Inventory (CBI) [7] which is a new burnout questionnaire and allows measuring burnout in different settings (not just the service professions) and higher accuracy than MBI. In addition, CBI also overcomes the limitations of MBI and satisfies the need to measure burnout suitably[7]. CBI has extremely high internal reliability and low nonresponse rate, a questionnaire with three sub-dimensions. The three separate parts of the questionnaire including personal burnout (PB), work-related burnout (WB) and client burnout (WB) were designed to be applied in different domains. PB dimension is defined in the following way: "PB is the degree of physical and psychological fatigue and exhaustion experienced by the person", whose questionnaire were formulated in a way so that all human beings can answer them[7]. WB dimension was defined as "The degree of physical and psychological fatigue and exhaustion that is perceived by the person as related to his/her work", which assume that the respondent has paid work of some kind[7]. CB dimension was defined as "The degree of physical and psychological fatigue and exhaustion that is perceived by the person as related to his/her work with clients", whose questionnaire includes the term client (or a similar term such as patient, student, inmate, etc.)[7]. CBI possesses excellent psychometric properties and seems to be an more appropriate measure of burnout in populations of health professionals compared with Maslach Burnout Inventory[8]. Except to English version, CBI has been translated several language versions such as Malay[9], Greek[10], Chinese[11] [12], Portuguese[13], Korean[14], and Spanish[15] etc.

In May 2018, burnout was recognized as an "occupational phenomenon" in the *International Classification of Diseases, 11th Revision* (*ICD-11*) of the World Health Organization. Burnout is a state of physical, emotional, and mental exhaustion that results from long-term involvement in work situations that are emotionally

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demanding.[16] The specific definition of burnout in the *ICD-11* is "a syndrome conceptualized as resulting from chronic workplace stress that has not been successfully managed." A harmonized definition of occupational burnout approved by experts from 29 countries within the Network on the Coordination and Harmonization of European Occupational Cohorts, which demonstrated "In a worker, occupational burnout or occupational physical and emotional exhaustion state is an exhaustion due to prolonged exposure to work-related problems"[17].

1.2 Background

Burnout is responsible for high physician turnover and reduced clinical hours, which cause total losses of approximately US$4.6 billion in the United States each year[18]. Moreover, burnout affects approximately half of all nurses, physicians, and other clinicians[19]. A study about burnout and self-reported quality of health care in a nationwide sample of 1311 clinicians in surgery in Germany illustrated about 48.7% of the clinicians meet the criteria for burnout[20]. A systematic review and meta-analysis for 45,539 nurses across 49 countries suggested one-tenth of the nurses worldwide suffered high burnout symptoms[21]. Studies on resident physicians and nurses have indicated that most cases of burnout are personal or work related. Studies have noted that WB and PB occur in 30% and 50% of individuals with burnout, respectively[22]. Notably, burnout also affects patient-related quality of care[20].

1.3 Literature Review

According to numerous literatures, the influence ranges were very widely for burnout which included sex, family, living habits, workplace, and physical health etc. The present study will review literatures about burnout following above order step by step and further determined research objective.

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Sex difference for burnout

There were numerous reasons for the development of burnout according to previous studies. An early study suggested the sex of the employee is not a major factor in burnout [23]. However, studies in human service professionals have demonstrated higher burnout in women than in men [24], and that the burnout level is significantly higher among female resident physicians [22]. A previous study reported that women in male-dominated occupations experience higher psychological distress than women in female-dominated occupations [25].

Burnout and family factors

Marital state and parenthood also impact developing burnout and 57.26% health workers reported that they could minimize burnout by getting support from family[26]. Aimed women nurses study found family members and friend play a vital role for developing burnout which could predict 29% of the variance of burnout[27]. A cross-sectional study of 563 working doctors suggested disturbance of home and family life by work is related to high burnout.[28]

Burnout and living habits

Short sleep duration (SSLD) impacts several domains of psychological health such as stress and burnout. A study in USA for 32,749 people aged 18 years or older found association between sleep duration per day less than 6 hours and high self-reported stress[29]. A study for 2268 full-time nurses in 39 hospitals demonstrated nurses who slept less than 6 h per working day experienced higher risk for PB (odds ratio= 3.0, $P < 0.05$), WB (odds ratio= 3.4, $P < 0.05$), and CB (odds ratio= 2.0, $P < 0.05$) than those who slept more than 7 h per working day[30].

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Although some study think alcohol use (AU) is helpless to improve stress[31], many people adopted AU to alleviate stress which caused by working overtime,[32, 33] even drinking for pain-coping.[34] A multinational study of 2623 doctors, nurses and residents for exploring the associations between burnout and alcohol consumption, which suggested burnout is significantly positively associated with higher alcohol consumption[35].

Burnout and work-related factors

Work experience (WE) was also related to burnout. Some previous studies demonstrated lack of WE therapists faced with increasingly complex work conditions and demands, they may develop a sense of hopelessness in relation to their inability to reach their own idealistic expectations and standards, ultimately leading to disillusionment and burnout[36, 37].

In Taiwan, 97% and 83% of doctors in medical centers and regional hospitals, respectively, work overtime (OT)[38]. In addition, an OT work's study for 1560 full-time employees found less than 40 , between 40 and 60 , and more than 60 weekly work hours were significantly correlated with burnout in a dose-dependent manner (odds ratios for upper against lower tertile were 1.58 and 2.29, $P < 0.01$) [39].

Shift work is a common work schedule for hospital worker to support 24 hours service. In total, 684 nurses study demonstrated irregular shift (IRS) working schedule was also related to a significantly higher burnout syndrome[40]. The positive relationship between burnout and shift work was also observed in policemen. A burnout's study about 3140 police officers found irregular schedules and long shifts were associated with increased risk of overall burnout[41].

Burnout and physical health

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Physical health is also related to burnout, including musculoskeletal (MS) pain and chronic diseases (CD). Lower back (26.9%), shoulders (20.9%) and neck (20.6%) were most reported one of pain sites based on the point prevalence[42]. A study aimed to 4507 lawyers, physicians, nurses, teachers, church ministers, bus drivers, and information technology workers in Norway suggested burnout is related to MS pain[43]. In addition, a prospective study for 650 employed men and women found burnout symptoms were associated with a 1.67-fold increased risk of MS pain which illustrated burnout is a risk factor for the development of MS pain in seemingly healthy individuals[44].

A Finland's survey for 3368 employees aged 30–64 years suggested the prevalence of diseases was related to the severity of burnout; about half (54%) of those with no burnout had at least one physical illness compared to 63% of those with mild burnout and 71% of those with severe burnout[45]. In specific chronic diseases, burnout is an independent risk factor for future incidence of coronary heart disease[46] and type 2 diabetes[47], too.

Burnout and work-related injuries

There was evidence shown burnout is related to work-related injuries. In USA, 682 employees in cross-units of the administrative services completed survey of burnout found that workload and exhaustion was related to the incidence of injuries during the subsequent year[48]. A prospective cohort study for a total of 10,062 forest industry employees in Finnish demonstrated each one-unit increase in the burnout score was related to a 9% increase in the risk of injury[49] which shown burnout could be closely relevant to WRIs.

Sharps injuries (SIs), which frequently occur among health care workers, constitute a critical problem. SI occurrence has been reported to be associated with

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occupational factors such as WE[50], work hours[51], and shift work schedules[52] as well as demographic characteristics such as sex[53] and age[54]. Moreover, one article asserted that the experience of SIs was related to the mental health of health care workers[55].

1.4 Research Objectives

A systematic review and meta-analysis for physician demonstrated organizational and individual interventions are effective at reducing burnout[56]. Based on this, the study would model the relationship of burnout to explore the cause of burnout and affect the work-related injuries for medical worker. We believe these findings could suggest effective strategies for hospital to improve burnout and work-related injuries for medical worker in further.

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2. Materials and Methods

2.1 Source and Valid Samples for Participants

This manuscript is an observational and cross-sectional study, which was based on members at a hospital affiliated with a medical university in Taichung, Taiwan, in 2021 and had been approved with the expedited review by Institutional Review Board of the Chung Shan Medical University Hospital on Aug 25, 2021 (No: CS1-21108). Of the 2531 individuals to whom the questionnaires including Copenhagen Burnout Inventory (CBI) and Nordic Musculoskeletal Questionnaire (NMQ) were sent, 1633 (64.52%) completed the questionnaires. After exclusion for missing data, 1250 questionnaires (49.39%) were determined to be valid.

2.2 Questionnaires Design

The questionnaire separated several sections including the general basic demographic variables, family variables, living habits variables, work-related variables, physical health variables, variables for NMQ, CBI, and work-related injuries.

Demographic and family factors

The general basic demographic and living/work-related variables questionnaire included the participants' work experience, occupational category, height (cm), and body weight (kg). The education degree was also included in questionnaire that the response options are “Below high school”, “Bachelor”, “Master”, and “PhD”. Participants were asked whether he/she has married? The responses' options were "married" and “others”. In addition, participants also were asked whether he/she raises the children? The responses' options were “without child”, “one child”, “two children”, “three children”, and “over three children”. The questionnaire also surveys whether

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participants engage in **leisure activities with family or friends (LAFF)** in vacation time? The responses' options were "always", "often", "sometimes", "seldom", and "never" -are scored as 100, 75, 50, 25, and 0 points, respectively. Regarding **exercise frequency** in questionnaire, the responses' options were "at least once a day", "at least once a week", "at least once a month", "less than once a month", and "never", respectively.

Variables for living habits

The participants were also asked whether they drunk coffee frequently? The responses' options to the question were "never", "sometimes", "one cup a day", "two cups a day", "at least two cups a day" -are scored as 0, 25, 50, 75, and 100 points. In response to the question on smoking habit, option was "smoking in past month", "never" or "have quit smoking". Alcohol Use (AU) habit in past month also was included, the responses' options were "everyday", "occasionally", and "never". In response to the question on sleep duration (SLD) per day for participants, options were classified to "less 5 hours", "between 5 and 6 hours", "between 6 and 7 hours", "between 7 and 8 hours", and "above 8 hours".

Variables for work-related factors

Possible responses to the question on **overtime (OT)** work was the following: seldom, fewer than 45 h per month, 45–80 h per month, and more than 80 h per month. As for **work schedule**, the options given were **day shift (DS)** work, **night shift** work, **irregular shift (IRS)** work, and **regular shift (RS)** work.

Variables for physical health

On the questionnaire, the participants were asked whether they had a listed

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chronic disease (CD), with the selection of one or more diseases classified as a "yes" response.

Nordic MS Questionnaire (NMQ)

This study adopted the NMQ modified and translated by the Taiwan Institute of Occupational Safety and Health[57]. The NMQ, which is used in the investigation of the site and frequency of MS pain, was developed in a project funded by the Nordic Council of Ministers. The NMQ has acceptable reliability[57] and has been applied in a wide range of occupational groups, including nurses[58].

Items on the NMQ include questions on the presence of pain attributable to work-related factors in the preceding year and on the pain sites, the options for which were the:

neck (N1), left shoulder (N2), right shoulder (N3),
upper back (N4), waist or lower back (N5),
left elbow (N6), right elbow (N7), left wrist (N8), right wrist (N9),
left hip/thigh/buttock (N10), right hip/thigh/buttock (N11),
left knee (N12), right knee (N13),
left ankle (N14), and right ankle (N15).

If a participant answered "yes" to the question on the experience of work-related pain over the past year, they were instructed to indicate its frequency: every day, once a week, once a month, or once every half year, or at least once every half year -are scored as 100, 80, 60, 40, and 20 points, respectively.

In the present study, factor analysis was conducted on the NMQ results to

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determine the underlying variables that explained most of the questionnaire. According to the principle proposed by Hair *et al.*[59] factors that should be retained have feature vector values exceeding 1. Through varimax rotation, the standardized scoring coefficients constituted new factor loadings and were defined as new factors according to the corresponding significance of the factor loadings.

Variables for work-related and sharps injuries

The participants were also asked whether they had experienced **work-related injuries (WRIs)** or **sharps injuries (SIs)** in the past year. The response options to the two questions were "always", "often", "sometimes", "seldom", and "never"-are scored as 100, 75, 50, 25, and 0 points, respectively.

Variables for three burnout scales

Copenhagen burnout inventory (CBI) questionnaire

The present study used the Chinese version of CBI, which has proven to be a reliable and valid tool for assessment of burnout problems; [11, 12] thus, it was used to evaluate burnout in the present study. Regarding CB, client was defined as patient and had been denoted on questionnaire.

The first six items, which concern PB, are as follows:

C1: "How often do you feel tired?"

C2: "How often are you physically exhausted?"

C3: "How often are you emotionally exhausted?"

C4: "How often do you think 'I can't take it anymore'?"

C5: "How often do you feel worn out?"

C6: "How often do you feel weak and susceptible to illness?"

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Items 7–13, which concern WB, are as follows:

C7: "Is your work emotionally exhausting?"

C8: "Do you feel burnt out because of your work?"

C9: "Does your work frustrate you?"

C10: "Do you feel worn out at the end of the working day?"

C11: "Are you exhausted in the morning at the thought of another day at work?"

C12: "Do you feel that every working hour is tiring for you?"

C13: "Do you have enough energy for family and friends during leisure time?"

Items 14–19, which concern CB, are as follows:

C14:" Do you find it hard to work with clients?"

C15:" Does it drain your energy to work with clients?"

C16:" Do you find it frustrating to work with clients?"

C17:" Do you feel that you give more than you get back when you work with clients?"

C18:" Are you tired of working with clients?"

C19:" Do you sometimes wonder how long you will be able to continue working with clients?"

Regarding the calculated method for three burnout scales

The response options—"always", "often", "sometimes", "seldom", and "never/almost never"—are scored as 100, 75, 50, 25, and 0 points, respectively, except for item C13, which is inverse scored (ie, the responses are scored as 0, 25, 50, 75, and 100 points, respectively). Levels of PB, WB, and CB are represented by the mean of the total PB, WB, and CB scores (the sum of scores on items C1–C6, items C7–C13, and items C14-C19), respectively.

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2.3 Statistical Methods

The categorical variables were subjected to the chi-square test or Fisher exact test. Significance in the differences among the means of continuous variables was determined using the *t* test or one-way ANOVA. Multiple linear or logistic regression was conducted to control the interference of potential risk factors in the association between the independent variable (IV) and the dependent variable (DV)-specifically, to determine whether adjustments to variables significantly affected IV–DV associations.

Mediation analysis

Mediation effects were analyzed on the basis of the strategy proposed by Baron and Kenny [60], in which:

(1) the IV significantly affects the mediator (first-stage effect)

(2) the IV significantly affects the DV in the absence of the mediator

(3) the mediator has a significant unique effect on the DV (second-stage effect)

(4) the effect of the IV on the DV weakens upon addition of a mediator to the model (direct effect).

A mediation model suitable for the combination of categorical and continuous variables was developed by Iacobucci (2012) [61]; the formulas are as follows:

$$\hat{Y} = b_{01} + cX$$

$$\hat{M} = b_{02} + aX$$

$$\hat{Y} = b_{03} + c'X + bM$$

$$Z_a = \hat{a}/\widehat{S_a}$$

$$Z_b = \hat{b}/\widehat{S_b}$$

where X is an independent variable; $\hat{Y}$ is a dependent variable; $\hat{M}$ is the adjusted variable (i.e., the mediating factor); a is a logistic or linear regression coefficient of X against $\hat{M}$ when $\hat{M}$ and X are a DV and an IV, respectively; b is the logistic or linear regression coefficient of $\hat{M}$ against $\hat{Y}$; c is the logistic or linear regression coefficient of X against $\hat{Y}$; and c' is the logistic or linear regression coefficient of X against $\hat{Y}$ with $\hat{M}$ as the adjusting variable. The standard errors of a and b are represented by s_a and s_b, respectively.

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If $\hat{M}$ and $\hat{Y}$ are all continuous variables, the original formula of the Sobel test is applicable:

$$Z = \frac{a \times b}{\sqrt{b^2 {s_a}^2 + a^2 {s_b}^2}}$$

If $\hat{M}$ and $\hat{Y}$ are categorical variables or a combination of categorical and continuous variables, the original formula of the Sobel test is rederived into a new formula:

$$Z_{mediation}\,(Z_m) = \frac{\frac{a}{s_a} \times \frac{b}{s_b}}{\sqrt{{Z_a}^2 + {Z_b}^2 + 1}}$$

The results exceeding |1.96|, |2.57|, and |3.90| (for a two-tailed test) are significant at $\alpha = 0.05$, 0.01, and 0.0001, respectively.

Suppression effect

The traditional mediation effect is generally recognized as a, b, c, and c' in the same direction. However, a suppression effect would be present when the direct and mediated effects of an IV on a DV have opposite signs [62, 63], and the suppression variable would increase the predictive validity of another variable (or a set of variables) by its inclusion in a regression equation [62]. For clearly judging the suppression effect, a study examining statistical similarities among mediating, confounding, and suppression variables indicated that when $a \times b$ has the opposite sign to that of c', $a \times b$ is an estimate of the suppressor effect [63], whose statistical significance could be verified using the Sobel test.

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Analysis was performed using SAS Enterprise Guide 6.1 software (SAS Institute Inc., Cary, NC, USA), and significance was set at $P < 0.05$.

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3. Results and Discussion

3.1 Basic Variables Descriptions

Sex and family factors

As shown in Table 1, Women was much higher proportion (81.28%) than men for participants. The proportion of married was 48.96% for all participants. Participants without child reached 55.76%. The proportion of raising two children (24.56%) was highest among participants with raising the child. There were 84.24% participants for sometimes, or often, or always engaging in leisure activities with family or friends (LAFF) in vacation.

Living habits

The proportion of exercise frequency at least once a week was highest and was 46.80%, next to at less than once a month was 19.52%. The proportion was 17.84% for participants who never have drunk coffee in a month and was 40.56% for those who have drunk coffee at least one cup a day. The mean of drink coffee frequency score was 32.26±21.15. The proportion was 62.08% for participants who never reported alcohol use (AU) in a month and was 37.92% for those who reported AU occasionally or every day in a month. The proportion was highest for participants with sleep duration (SLD) per day between 6 and 7 h and reached 44.64%, next to those with SLD per day between 5 and 6 h and reached 34.80%. The proportion was only 3.68% for participants with SLD per day less 5 h.

Work-related factors

The mean of work experience (WE) is 10.88±9.51 years for all participants. The highest proportion of WE were in 1-5 years, which reaches 28.48%. The proportion was

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12.96% for WE less than 1 year and was over 40% for WE less than 5 years. For education degree, 78.80% participants had bachelor's degree. The proportion was 16.80% for above master's degree. The participants who seldom work overtime (OT) per month were 63.28% for all participants. The participants who work OT per month was less 45h, or between 45 and 80h, or more than 80h were 36.72% for all participants. The participants with day shift (DS) work were 63.12% for all participants, which is highest proportion, next to was regular shift (RS) work, irregular shift (IRS) work, and night shift work, which were 13.20%, 12.32%, and 11.36%, respectively.

Professional fields

The professional fields were classified to 13 fields, respectively. Among them, Nurses were largest group and were 40.96% for all participants, next to Administration (ADS) staff and others and were 31.84% for all participants. Physician including attending and resident were third big group and were 8.96% for all participants. The other professional fields were reclassified to professional and technical personnel (PTs) and were 18.24% for all participants.

Healthy factors

The proportion was 39.28% for participants with at least one listed chronic disease (CD).

Work-related and sharps injuries

The proportion was 48.24% for participants who never have experienced work-related injuries (WRIs) in past year. The proportion for participants who always/often/sometimes/ seldom experienced WRIs was 51.76%. The mean of WRIs score was 16.48±18.65. In past year, the proportion was 73.36% for participants who never experienced sharps injuries (SIs) and was 26.24% for those who ever have experience SIs. The mean of SIs score was 7.60±13.54.

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3.2 Factor Analysis for NMQ

Table 3 demonstrated Musculoskeletal (MS) pain's incidence in a year for both shoulders, neck, waist or lower back, upper back was 42.24%, 35.60%, 29.12%, and 16.72%, respectively. The mean score of frequency for neck, waist or lower back, right shoulders, left shoulder, and upper back was 26.21±37.41, 20.90±35.01, 16.96±33.42, 15.15±31.87, and 12.86±29.81, respectively. Because the eigenvalues of factors 1 and 2 exceeded 1, these factors were retained. Although the eigenvalue of factor 3 was lower than 1, it was retained for maximum explaining questionnaire. The factor loadings were converted into standardized scoring coefficients through varimax rotation. The relatively large factor loading values in bold for factors 1, 2, and 3 correspond to frequency score for neck and both shoulders pain (NBSP), both ankles pain (BAP), and both knees pain (BKP), respectively. The explained variation in FNBS pain, FBA pain, and FBK pain was 73.86%, 23.11%, and 8.67%, respectively.

3.3 Association Between Burnout and Surveyed Variables

Synthesized Table 2 and Table 4 that AU (c= 4.35, P < 0.001), SSLD (c= 8.11, P < 0.0001), work OT (c= 10.53, P < 0.0001), IRS work (c= 7.66, P < 0.0001), CD (c= 5.39, P < 0.0001), physician (c= 10.17, P < 0.0001), and NBSP (c= 8.27, P < 0.0001), BAP (c= 1.59, P < 0.01), and BKP (c= 2.29, P < 0.01) are risk factors of PB. The risk factors of WB included AU (c= 3.47, P < 0.01), SSLD (c= 6.52, P < 0.0001), work OT (c= 9.50, P < 0.0001), CD (c= 4.01, P < 0.0001), physician (c= 9.94, P < 0.0001), NBSP (c= 6.49, P < 0.0001), BAP (c= 1.49, P < 0.01), and BKP (c= 1.57, P < 0.01). AU (c= 3.68, P < 0.01), SSLD (c= 3.84, P < 0.01), work OT (c= 6.51, P < 0.0001), RS work (c=

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6.36, P < 0.0001), nurses (c= 7.74, P < 0.0001), and NBSP (c= 3.79, P < 0.0001) were risk factors of CB. It is worth mentioning that WE (c= -0.11, P < 0.05), LAFF (c= -0.13, P < 0.0001), and REW (c= -6.04, P < 0.0001) were protective factors of PB. WE (c= -0.19, P < 0.01), Master's degree or above (c= -2.56, P < 0.05), married (c= -3.70, P < 0.0001), parenthood (c= -4.19, P < 0.0001), LAFF (c= -0.16, P < 0.0001), and REW (c= -5.88, P < 0.0001) were protective factors of WB. WE (c=-0.14, P < 0.01), Master's degree or above (c= -3.45, P < 0.01), married (c= -3.63, P < 0.01), parenthood (c= -5.12, P < 0.0001), LAFF (c= -0.14, P < 0.0001), and REW (c= -5.43, P < 0.0001) were protective factors of CB. No matter PB, WB and CB were risk factors of WRIs and SIs. Therefore, these risk and protective factors would be added to models of MLR and mediation/suppression for burnout to further explore the reasons for developing or relieving burnout and whether burnout play a key role for WRIs and SIs.

3.4 Models of Burnout Established

3.4.1 Linear regression models

Table 5 showed the independent risk factor of PB/WB/CB in ULR and multiple linear regression (MLR) models. In MLR model, WE, parenthood, LAFF, SSLD, working OT, IRS work, RS work, Physician, Nurse, PTs, NBSP, BAP, and BKP were independent risk/protective factors for PB. WE, LAFF, SSLD, working OT, IRS work, RS work, Physician, Nurse, PTs, NBSP, BAP, and BKP were independent risk/protective factors for WB. Parenthood, LAFF, working OT, RS work, Physician, Nurse, PTs, and NBSP were independent risk/protective factors for CB.

3.4.2 First-stage effect of mediation and suppression model

Mediated/suppressed models would be established to explore possible causes for agent variables affect burnout. Table 6 shown WE was statistically associated with

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parenthood, LAFF, REW, suffering CD, ever AU, IRS work, DS work, and BKP, that met so-call "the first-stage effect". (1) Parenthood was statistically associated with LAFF, suffering CD, EAU, SSLD, working OT, IRS work, DS work, and NBSP, that met so-call "the first-stage effect", too; (2) Working OT was statistically associated with parenthood, LAFF, REW, ever AU, SSLD, IRS work, and NBSP, that met so-call "the first-stage effect", too; (3) IRS work was statistically associated with parenthood, REW, SSLD, working OT, and NBSP, that met so-call "the first-stage effect", too; (4) DS work was statistically associated with parenthood, LAFF, REW, ever AU, and SSLD, that met so-call "the first-stage effect", too; (5) Physician was statistically associated with REW, ever AU, SSLD, working OT, that met so-call "the first-stage effect", too; (6) Nurse was statistically associated with parenthood, LAFF, REW, working OT, IRS work, DS work, and NBSP, that met so-call "the first-stage effect", too. All variables satisfied the first-stage effect would be selected to as possible mediated factors to further test.

3.4.3 Direct / second-stage effect of mediation and suppression effect

Table 6-1, Table 6-2, and Table 6-3 shown the direct effect and the second-stage effect for PB/WB/CB. According to a, s_a, b, and s_b values in Table 6-1~6-3, P value was calculated by Z or $Z_{mediation}$ [61] formulates to test the statistic significant of mediated/suppressed effect. If b is a logistic regression coefficient, Z is a value calculated by $Z_{mediation}$ [61]. If b is a linear regression coefficient, Z is value calculated by the original formula of the Sobel test.

3.4.4 Simple mediated and suppressed models for burnout

Table 7 showed all models of mediation and suppression effect for PB/WB/CB. The sign in "()" represents the positive or negative relationship between independent

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variable (IV) and mediated factor. "m" represents mediated effect is exist in IV and dependent variable (DV) and "S" represents suppressed effect is exist in IV and DV. "NS" represents mediated or suppressed effect is not statistically significant in IV and DV. The presentation of Table 7 is advantage to descript full picture for mediation and suppression effect. Follow chapters will through these models to explore the relationship between risk factors and burnout.

Followed Sections will further explore the association between burnout and women/men, family, living habits, personal health, and workplace. In addition, study also will assess whether burnout will impact work-related injuries and will try by statistical methods to identify whether there are existed significant relationship between mental health and work-related injuries.

3.5 Sex Difference for Burnout

3.5.1 Association between sex and burnout

As shown in Table 2, there was not statistically significant sex difference for PB (c= 2.30, P > 0.05), WB (c= 1.88, P > 0.05) and CB (c= 1.53, P > 0.05) despite women reported high PB, WB, and CB level than men. As shown in Table 2-1, compared with man physicians, woman physicians were significantly relevant to WB (c= 8.42, P < 0.05). Table 2-2 presented there were not significant differences of PB (c= -3.06, P > 0.05), WB (c= -3.90, P > 0.05), and CB (c= -7.53, P > 0.05) between man's nurses and woman's nurses.

3.5.2 Discussion for sex difference of burnout

Was there different level for burnout between women and men? An early study suggested the sex of the employee is not a major factor in burnout [23]. Despite women

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reported high PB/WB/CB than men in Table 2, there was not significant difference in statistic. However, studies in human service professionals have demonstrated higher burnout in women than in men [24]. The studies seemed different results. However, another study reported that women in male-dominated occupations experience higher psychological distress than women in female-dominated occupations [25]. Table 2-1 presented that the proportion of women physician was only 34.82% which is a few groups. In addition, despite woman physicians common reported high level for PB (c= 7.69, P > 0.05), WB (c= 8.42, P < 0.05), and CB (c= 7.09, P > 0.05) than man physicians, only WB was statistically significant. Regarding nurses, the proportion of woman nurses was 96.48%, which instead is a very majority. As shown in Table 2, despite there were not statistically significant, woman nurses common reported low level of PB (c= -3.06, P > 0.05), WB (c= -3.99, P > 0.05) and CB (c= -7.53, P > 0.05) than man nurses. That could result from the samples of men were only 18 persons which were much less than women. Therefore, nurse occupation to be in female-dominated occupation.

Table 5-2 presented the effect of woman physicians for WB could be fully explained by WE (c= -0.18, P < 0.05), RS work (c= 15.86, P < 0.01), and NBSP (c= 6.50, P < 0.0001). Woman physicians had less WE, more RS work, and reported high NBSP than man physicians. According to a prospective cohort study of workers from industrial and service companies in Denmark illustrated a high level of distress predicted subsequent neck/shoulder pain[64] that might imply woman physicians could bear more distress than men physicians in present study. In addition, WE was low for woman physicians than man physicians (6.53±7.03 vs 10.28±11.06, P < 0.05) and woman physicians had more RS work compared with man physicians (odds ratio= 3.35, P <0.05, not in the Table). The difference for work experience and stress between women and men imply physician professional field could be a male-dominated

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occupation. The previous study also demonstrated even when women constitute a high proportion of the physician workforce, they may continue to be underrepresented in positions of leadership and prestige[65]. Based on this, we suggested sex difference of burnout was associated with sex--dominated occupations.

3.6 Family-Related Factors and Burnout

3.6.1-1 Association between burnout, marriage state, and parenthood

As shown in Table 2, participants who have married reported low WB (32.32±15.41 vs 36.02±16.96, $P < 0.0001$) and CB (28.00±16.28 vs 31.64±17.90, $P < 0.01$) than those who have not married. Compared to unmarried, married was a protective factor for WB ($c = -3.70$, $P < 0.0001$) and CB ($c = -3.63$, $P < 0.01$).

The raising one child, two children, three children, and over three children were reclassified to a new variable "**parenthood**" due to less sample number for every group. Table 2 shown participants who are parenthood sustained lower WB (31.87±15.74 vs 36.06±16.54, $P < 0.0001$) and CB (27.00±16.48 vs 32.12±17.46, $P < 0.0001$), respectively. Therefore, parenthood was a protective factor for WB and CB ($c = -4.19$, -5.12; both for $P < 0.0001$).

As shown in Table 5, the regression coefficient c for parenthood was -0.30 ($P > 0.05$) in ULR model for PB, however, which was 2.41 ($P < 0.05$) in MLR model for PB. That demonstrated that parenthood was an independent risk factor for PB instead of protective factor after adjusting other risk factors.

As shown in Table 5-1, after respectively adjusting LAFF, SSLD, OT, three shift work dummy variables, and three professional field dummy variables, the regression coefficient c (original value was -0.30) of "parenthood" were to 0.66, 0.17, 0.42, 1.08, and 0.97, their c symbol is all opposite before and after. Despite not statistical signification, these adjusting variables could interference the positive or negative

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relationship between parenthood itself and PB.

ULR and MLR models (Table 5) of parenthood to WB/CB shown that parenthood effect to WB/CB could be explained by other risk factors due to the c absolute value was reduced. The mediated/suppressed models in Table 7 could further explore relationship among WB/CB, parenthood and explain variable. As shown in Table 7, under mediation effect, the reasons of parenthood sustaining low level for WB/CB were positively engaging in LAFF (impacting WB and CB), less AU (impacting WB), less reporting SSLD (impacting WB), less work OT (impacting WB and CB), less IRS work (impacting WB), and more DS work (impacting WB and CB). However, under suppression effect, participants who were parenthood would easily suffer CD (impacting WB) and sustain high NBSP (impacting WB and CB) which would further increase level of WB or CB.

Parenthood was an important stage to life. However, the present study found that the process seems to impact differently development for PB/WB/CB, respectively. These results seem to imply the complex and different relationship among burnout, work, family, and children.

3.6.1-2 Discussion for the relationship between burnout and parenthood

A multidimensional conception of burnout implies a work-restricted scope is deconstructed. In addition, the burnout is a chronic, unresolvable stress according to the putative cause of burnout, which is not limited to work[66]. Personal burnout is the degree of physical and psychological fatigue and exhaustion experienced by the person[7]. In addition, parenthood is a both complex and stressful activity, which causes parents enduring exposure to chronic parenting stress and form so-call "parental burnout" and there was statistically significant and positive correlations between parental burnout and professional burnout in emotion exhaustion dimension [67]. These

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results imply parental burnout and personal burnout could have impacted each other or have common outcomes or damages for parents.

The present study also found parenthood was an independent risk factor for PB which obviously be related to worsen PB. This important find is echo each other with previous study's' results regarding parent burnout. In addition, parenthood was instead favorable to relieve CB. We reviewed the definition about CB, the definition follow: "The degree of physical and psychological fatigue and exhaustion that is perceived by the person as related to his/her work with clients". The source for fatigue and exhaustion come from client and do not come from child. Participants played two roles – parent and service provider. According to a theory of work-family enrichment[68] illustrated that participation in one role may enrich the quality of life in the other role. Therefore, the role for parent would enrich the role for service provider, that was consistent with our find in present study.

3.6.2-1 Association between leisure activities and burnout

The frequency for engaging in leisure activities with family or friends was scored by 100, 75, 50, 25, and 0 points and was defined as a new continuous variable – leisure activities with family or friends (LAFF). The result in Table 2 presented LAFF was negative relevant to PB ($c = -0.13$, $P < 0.0001$), WB ($c = -0.16$, $P < 0.0001$), and CB ($c = -0.14$, $P < 0.0001$). It was a protective factor for PB/WB/CB.

As shown in Table 5, LAFF was an independent protective factor for PB ($c = -0.06$, $P < 0.01$), WB ($c = -0.09$, $P < 0.0001$), and CB ($c = -0.08$, $P < 0.01$). This result represented that LAFF itself could play an important role for relieving burnout. The mediation/suppression models (Table 7) could help us to further understand the possible reasons for LAFF relieving burnout. As shown in Table 7, under mediation effect, negatively engaging in LAFF is one of causes for work OT worsening PB/WB/CB.

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Positively engaging in LAFF is one of causes for married/parenthood relieving WB/CB. According to mediation effect in Table 7, participants with DS work could positively engage in LAFF which could help participants to further relieve WB/CB. However, nurse reported highest CB level which could result from nurses negatively engaged in LAFF (Table 7, mediation effect).

3.6.2-2 Discussion for the relationship between burnout and leisure activities

The present study found positively engaging in LAFF had important function for relieving burnout from personal, work-related, and client. According to questionnaire's content, LAFF included two element, leisure activities and interaction/support with friends and family. Greater friend-based and colleague-based social support were both indirectly associated with lower personal and work-related burnout scores[69]. People feel more stress, participating in leisure activities will relieve the stress and cope with emotion, and moderately maintain physical and mental health [70, 71]. By providing leisure benefits, organizations can facilitate employees to better manage work pressure, boost employee morale, help to reduce role conflict, and enhance employee's satisfaction with life[72]. A study for flight attendants in Taiwan demonstrated leisure coping strategies can regulate job demands—burnout—health problems and when flight attendants suffer from burnout, they can adopt leisure coping strategies to improve their negative emotions.[73]. Therefore, the present study's evidence supported the opinion that leisure activities combined friendly interaction with friends and family would be an effective strategy for relieving burnout.

The previous study[74] also illustrated that assume a fixed amount of time and human energy, people participate in multiple roles inevitably will experience conflict and stress that detract from their quality of life. Based on this view, people would have not enough energy to engage in leisure activities with family or friends due to heavy

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work or overtime work. Table 6 shown working OT was negative related to LAFF (c= -4.26, P < 0.01). The present study's results support previous studies opinion that participants who work OT really reduce opportunity for engaging in LAFF.

Despite married individuals spent significantly less time for leisure activities than did single individuals[75], the various aspects of positive parental functioning were related to increases in overall leisure time and leisure time spent with spouse for both mothers and fathers[76]. In addition, the cohesion, adaptability, family functioning, and satisfaction with family life were positive related to family leisure[77]. Therefore, common leisure activity with family is key for positive parenthood role and satisfaction with family life. The mediated models in present study demonstrated participants who married or were parenthood would positive engage LAFF which is advantageous for relieving WB and CB. We revisit the questionnaire content about LAFF. The content was "Whether participants engage in leisure activities with family or friends in vacation time?". The premise of leisure activities is to spend the holiday with family or friends and not alone. Therefore, the LAFF should be as a family leisure instead of pure personal leisure activities. The successful family role (husband, or wife, or parents) for participants enhanced by family leisure activity that will further enhance the role of service provider that would relieve WB and CB at the same time. Above result was consistent with theory of work-family enrichment. [68].

The previous study illustrated the shift workers and dayworkers showed significant differences (p<0.0001) on almost leisure activity[78]. The present study also found participants who were DS work would positively engage in LAFF than others. Table 7 determined LAFF mediated the relationship between DS work and relieved WB/CB which represented positive family role also will enhance staff or service-provider roles.

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3.7 Living Habits and Burnout

3.7.1-1 Association between regular exercise and burnout

As shown in Table 1, the participants who exercise at least once a day or a week was 56.88% for all participants, therefore, both were reclassified as a new variable "regular exercise every week" (REW) and other frequency class was classified as a reference variable – "No weekly regular exercise". As shown in Table 2, REW was negative relevant to PB, WB, and CB (c =-6.04, -5.88 -5.43, respectively; for all P < 0.0001) and participants with REW sustained low PB (33.40±17.30 vs 39.44±18.59, P < 0.0001), WB (31.67±16.15, P < 0.0001), and CB (27.51±17.21 vs 32.95±16.74, P < 0.0001) than others. According to Table 7, REW was effectively protective factors. REW was a mediation factor which could effectively against the unfavorable effect of OT and IRS work for PB and WB according to mediation effect in Table 7. In addition, under mediation effect for REW, Participants who had day shift work easily kept REW which could effectively sustain low level for PB/WB/CB. Although physicians common reported high PB and WB, REW seemed to effectively relieve PB and WB due to suppression effect. However, the same effect was not observed on nurses.

3.7.1-2 Discussion for the relationship between burnout and regular exercise

Physiological changes by physical activity could reduce the persons' physiological sensitivity to chronic stress[79], that could lead to faster physical recovery after a stressful experienced situation and therefore to a reduction of the risk of burnout[80]. There is a positive dose-response relationship between physical activity and emotional well-being[81]. A systematic review study demonstrated physical activity seems to be effective in reducing burnout[82]. Healthy exercise habits are associated with lower risk of burnout[83].

The present study demonstrated participants who report REW experienced low

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PB, WB and CB. It is consistent with the previous studies regarding REW and burnout.

3.7.2-1 Association between coffee assumption / alcohol use and burnout

As shown in Table 2, participants also reported the habits for coffee consumption and alcohol use. The frequency for coffee consumption was not significantly related to PB ($c = 0.02$, $P > 0.05$), WB ($c = -0.02$, $P > 0.05$), and CB ($c = -0.02$, $P > 0.05$). Alcohol use (AU) every day or occasionally were combined to a new dummy variable – "ever AU". "Never AU" is as a reference variable. Participants who have reported ever AU experienced high PB (38.70±17.84 vs 34.35±18.08, $P < 0.0001$), WB (36.36±15.53 vs 32.89±16.65, $P < 0.01$), and CB (32.15±17.11 vs 28.46±17.14, $P < 0.01$) than others. Therefore, AU was a risk factor for PB ($c = 4.35$, $P < 0.0001$), WB ($c = 3.47$, $P < 0.01$), and CB ($c = 3.68$, $P < 0.01$). According to mediation effect of AU in Table 7, AU was one of reasons that physicians and participants who work OT sustained high level of PB/WB.

3.7.2-2 Discussion for the relationship between burnout and alcohol use

Whether alcohol actually reduces stress is debatable[31]. One study illustrated AU should increase stress and would be ineffective for negative reinforcement[84]. The burnout were strongly associated with alcohol abuse or dependence among American surgeons[85]. Burnout was significantly positively associated with higher AU among doctors, nurses and residents[35]. The present study found same results with the past studies that participants who report AU sustained higher level for PB, WB and CB.

3.7.3-1 Association between sleep duration per day and burnout

Because of subjects for sleep duration (SLD) less 5 hours per day being less, the ranks of SLD per day were reclassified to two ranks – SLD less 6 hours per day (SSLD)

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and SLD over 6 hours per day. SSLD was as a dummy variable and SLD over 6 hours was as a reference variable. SSLD was significantly associated with PB ($c = 8.11$, $P < 0.0001$), WB ($c = 6.52$, $P < 0.0001$), and CB ($c = 3.84$, $P < 0.01$) and participants who have reported SSLD experienced high PB (40.99±19.00 vs 32.88±16.80, $P < 0.0001$), WB (38.22±17.03 vs 31.70±15.34, $P < 0.0001$), and CB (32.22±17.80 vs 28.38±16.68, $P < 0.01$) than others.

As shown in Table 5, SSLD was associated with PB ($c = 8.11$, $P < 0.0001$), WB ($c = 6.52$, $P < 0.0001$), and CB ($c = 3.84$, $P < 0.01$). In MLR model, SSLD was an independent risk factor for PB ($c = 4.25$, $P < 0.0001$) and WB ($c = 2.78$, $P < 0.01$). However, the effect of SSLD impacting CB could been explained by other risk factors due to absolute value of c for SSLD reduced after adjusting variables.

The mediation/suppression models (Table 7) noted that sleep problem plays the important role between OT/IRS work and burnout. Specifically, SSLD mediated the relationship between OT and PB/WB/CB and the relationship between IRS work and PB/WB. In addition, Table 7 further illustrated that physicians often reported SSLD which was the one of reasons for physicians sustained high level for PB/WB. Parenthood reported low level for WB which was partially resulted from SSLD.

3.7.3-2 Discussion for the relationship between burnout and sleep duration

The past many studies had demonstrated the relationship for sleep, burnout, and OT work. Such as too little sleep (< 6 h) was as the main risk factor for burnout development[86] and burnout is also associated with disturbed sleep[87] . Some studies also illustrated the working OT is related to short or disturbed sleep, too[88, 89]. The present study has observed the same result that SSLD was significantly relevant to burnout. It is worth mentioning that the present study successfully through mediation/suppression models established in Table 7 to link the relationship for OT

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work, sleeping duration, and burnout that hint the lack of sleep could be a bridge for shift work and burnout. The past studies demonstrated that burnout was associated with shift or irregular shift work[40] [90]. In addition, the prevalence of insomnia, sleep deprivation depended significantly on the shift system[91]. The reason that shift work impacts sleep could be explained by "shift work sleep disorder". Shift work sleep disorder is a common yet under-recognized and undertreated sleep disorder caused by a sleep/wake pattern that is misaligned with the endogenous circadian rhythm[92]. A study for full-time nurses in 39 hospitals found compared with those slept longer than 7 h, nurse who slept less than 6 h per working day had higher risk for personal burnout, work-related burnout, and client-related burnout[30]. Despite our participants do not just include nurses and included doctors and other medical staff and adjusting variables were not exactly same, however, we found SSLD worsen PB, WB, and CB for participants still was obviously. Synthesize past literature and present research results, we could determine SSLD is a key that IRS work sustained high level for burnout.

3.8 Work-Related Factors and Burnout

3.8.1-1 Association between work experience / education degree and burnout

As shown in Table 2, work experience (WE) was as a continuous variable according to questionnaire. The present study demonstrated WE was significantly relevant to PB ($c = -0.11, P < 0.05$), WB ($c = -0.19, P < 0.01$), and CB ($c = -0.14, P < 0.01$). The education degrees were reclassified to "master's degree or above" and "university or below university degree" due to the participants with PhD or below high school were seldom (39 and 55 samples). Participants with university or below university degree reported high WB (34.64±16.28 vs 32.08±16.36, P < 0.05) and CB (30.44±17.44 vs 26.98±15.77, P < 0.01) than those with master's degree or above. Compared with University or below university degree, Master's degree or above was a

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protective factor for WB (c =-2.56, P < 0.05) and CB (c =-3.45, P < 0.01).

As shown in Table 5, WE (c= -0.14, P < 0.01; c= -0.11, P < 0.05) was an independent protective factor for PB/WB. The regression coefficient c for WE was -0.14 (P < 0.01) in ULR model for CB, but which was -0.01 (P > 0.05) in MLR model for CB. That represented WE effect to CB was explained by other risk factors. Table 7 further illustrated the relationships of burnout, risk factors, and WE by mediated/suppressed models. Burnout (including PB/WB/CB) would gradually be relieved followed increasing work experience, under mediation effect, these causes of relieving burnout included married (impacting WB/ CB), parenting (impacting WB/CB), REW (impacting PB/WB/CB), seldom AU (impacting PB/WB/CB), not often IRS work (impacting PB/WB/CB), often DS work (impacting PB/WB/CB). However, under suppression effect, CD and BKP would offset the advantage that WE relieve PB/WB. In addition, BKP also offset the advantage that WE relieve CB.

3.8.1-2 Discussion for the relationship between work experience and burnout

A study for a systematic review of the literature for burnout among psychotherapists make a description for the relationship in work experience and burnout. The original description follows "it is possible that as inexperienced psychotherapists are faced with increasingly complex work conditions and demands, they may develop a sense of hopelessness in relation to their inability to reach their own idealistic expectations and standards, ultimately leading to disillusionment, depersonalization, and burnout."[37] As shown in Table 5, increased WE was closely related to relieved PB (= -0.11, P < 0.05)/WB (c= -0.19, P < 0.01)/CB (c= -0.14, P < 0.01) and was independent protective factors for PB (c= -0.14, P < 0.01) and WB (c= -0.11, P < 0.05), respectively. The present research result for medical employee was consistent with above study for psychotherapists. According to Table 7, REW, seldom AU, not often

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The Effects of Frequent Coffee Drinking on Female-Dominated Healthcare Workers Experiencing Musculoskeletal Pain and a Lack of Sleep

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Abstract: Previous research has demonstrated that chronic diseases can occur due to musculoskeletal (MS) pain and poor sleep. It is also worth noting that the caffeine in coffee can reduce overall sleep duration, efficiency, and quality. Thus, the present study examines the effects of frequent coffee drinking (two cups per day) on individuals experiencing MS pain and a lack of sleep during the COVID-19 period. This observational and cross-sectional study recruited 1615 individuals who completed the self-reported (Nordic musculoskeletal) questionnaire. Long-term, frequent coffee drinking and a sleep duration of less than 6 h per day were significantly associated with neck and shoulder pain among healthy individuals. The mediation model demonstrated that the shorter sleep duration and drinking multiple cups of coffee per day had a two-way relationship that worsened such pain over the long term. Specifically, individuals who experienced such pain frequently drank multiple cups of coffee per day, which, in turn, shortened their sleep durations. In summary, long-term coffee drinking creates a vicious cycle between MS pain and sleep duration. Therefore, the amount of coffee should be fewer than two cups per day for individuals who sleep less than 6 h per day or suffer from MS pain, especially neck and shoulder pain.

Keywords: coffee; musculoskeletal pain; sleep; Nordic musculoskeletal questionnaire; neck and shoulder pain

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1. Introduction

Coffee is one of the most popular beverages for people of many ages. It is a complex chemical mixture that contains caffeine, which is a purine alkaloid that is naturally found in coffee beans [1] and contributes to its bitterness [2]. Caffeine stimulates the central nervous system, which can increase alertness, blood circulation, and respiration [3]. However, caffeine has biphasic effects, i.e., lower doses can provide some behavioral stimulation, whereas higher doses can lead to anxiety, aversion, irritability, and discomfort [4]. Despite clinical studies demonstrating the adjuvant analgesic effects of caffeine [5], long-term coffee drinking can negatively affect health and musculoskeletal (MS) pain. In health, individuals drinking more than five cups of coffee per day can have an increased risk of myocardial infarction or unstable angina [6]. In MS pain, related research showed that drinking more than seven cups of coffee per day was associated with a higher risk of knee osteoarthritis among Korean men [7]. Interestingly, patients with chronic back pain tend to drink two times as much caffeine as those without such pain [8], whereas individuals with

chronic daily headaches were generally high caffeine consumers before the onset of such headaches [9].

MS pain is common in many occupations, and it is one of the main reasons for long-term sick leave [10]. In the United States, 13% of the total workforce experienced a loss caused by body pains, with lost productive time costs estimated at USD 61.2 billion annually [11]. Although different occupations can affect MS pain at various anatomical sites and have diverse risk factors [12], a recent study in the Netherlands showed that the top three self-reported MS pains include lower-back pain, shoulder pain, and neck pain [13]. In addition, previous studies have demonstrated that work hours [14,15], occupational stress [16,17], alcohol consumption [18–21], sleep duration [22–24], exercise habits [25], and chronic diseases [26,27] contribute to MS pain.

Poor sleep quality is a common health problem among medical staff [28,29]. Reduced sleep duration and poor sleep quality have become more common during the past decades [30], leading to poor health outcomes [31] and even increased mortality [32]. Despite the recommended minimum sleep duration of 7 h per night for healthy adults, only 25% of adults achieve this amount [33]. Notably, lack of sleep can lead to impaired daytime function [34], increased occupational injury [35], and reduced productivity [36].

Overall, a close relationship was found between sleep and MS pain. For instance, because sleep problems can significantly reduce pain tolerance [37], individuals with chronic pain are more likely to experience insomnia [38]. Caffeine in coffee can also reduce total sleep duration, efficiency, and quality [39]. In addition, frequent consumption of caffeinated drinks can negatively affect habitual sleep duration [40].

From a micro and physiological perspective, adenosine is a purine nucleoside and a ubiquitous endogenous neurotransmitter that signals through four receptors (A1R, A2AR, A2BR, and A3R) in the brain to inhibit arousal and increase drowsiness [41]. Among these four receptors, A1R may be related to pain-sensing neurons [42]. Some evidence has demonstrated that A1R activation can produce antinociception of postoperative [43], neuropathic [44], and inflammatory [45] pain. In this regard, one study of mice found that acupuncture causes the release of nucleotides and adenosine to relieve pain [46]. However, these antinociceptive effects can be blocked by caffeine [47]. Notably, individuals with chronic insomnia were found to have reduced adenosine [48]. Moreover, impaired sleep significantly increases the risk of reduced pain tolerance [39]. These results suggest that the effects of caffeine on adenosine could play a pivotal role in pain development. Based on previous research, we propose the following hypotheses:

Hypothesis 1: *Coffee intake is significantly associated with increased risk of MS pain.*

Hypothesis 2: *Individuals with shorter sleep durations are more susceptible to MS pain.*

Hypothesis 3: *Coffee intake could lead to a vicious circle between lack of sleep and MS pain.*

2. Materials and Methods

This observational and cross-sectional study was initially conducted from a hospital affiliated with a medical university in Taichung, Taiwan, from March to April 2021. All 2531 healthcare workers who had served for one year in the hospital were distributed a QR code for a Google Forms-linked questionnaire by email. Among them, 1633 (64.52%) individuals completed the self-reported questionnaire, after which 1615 (63.81%) were deemed valid after those with missing data were excluded. Specifically, we used questionnaires, including the Nordic musculoskeletal questionnaire (NMQ), to obtain the participants' basic demographic variables, family factors, living habits, work, physical health, and MS pain. The study protocol was approved by the Institutional Review Board of Chung Shan Medical University Hospital on 25 August 2021 (No: CS1-21108).

This study adopted the NMQ, modified and translated by the Taiwan Institute of Occupational Safety and Health [49], to survey the presence of pain attributable to work-

related factors in the preceding year. The pain sites on the NMQ were classified as the neck, left or right shoulder, upper back, waist or lower back, left or right elbow, left or right wrist, left hip/thigh/buttock, right hip/thigh/buttock, left or right knee, and left or right ankle. The options for the frequency of each pain site were every day, once a week, once a month, once every half a year, and at least once every half a year, scored as 100, 80, 60, 40, and 20 points, respectively. Factor analysis was also adopted in the NMQ to determine the underlying variables that could effectively explain most of the questionnaire items. Through varimax rotation, the standardized scoring coefficients constituted new factor loadings and were defined according to their corresponding significance. The new factors that featured vector values exceeding 1 were retained according to the principle proposed by Hair et al. [50].

In the questionnaire, the basic response options included male or female for gender; age; "married" or "other" for marriage; and "without child," "one child," "two children," "three children," and "more than three children" for having children. The survey also asked if the participants engaged in leisure activities with family/friends during vacation time. The response options included "always," "often," "sometimes," "seldom," and "never." Regarding their education, the response options were "master's degree or above" and "university degree or below," while the response options for self-reported sleep duration per day included "less than 5 h," "between 5 and 6 h," "between 6 and 7 h," "between 7 and 8 h," and "more than 8 h." As for their coffee intake per day, the response options were "more than 2 cups per day," "2 cups per day," "1 cup per day," "occasionally," and "never." Regarding their alcohol use, the response options included "alcohol use in a month" and "no alcohol use in a month," while the response options were "yes" and "no" for exercising at least once a week. As for their overtime work, the response options were "seldom," "fewer than 45 h per month," "45 to 80 h per month," and "more than 80 h per month," while "irregular," "regular," "night," and "day" were the response options for shift schedules. Finally, the participants were classified as physicians, nurses, professional and technical personnel, and administrative staff. They were also asked about the presence of chronic diseases. In this regard, the presence of one or more diseases was classified as a "yes" response.

Regarding the statistical methods, factor analysis [50] was adopted for the NMQ to determine new underlying variables, while a *t*-test or one-way ANOVA was adopted to examine the differences between the continuous variables. Additionally, a chi-square test or Fisher's exact test was conducted to determine the significant differences in the categorical variables, while simple/multiple linear or logistic regression was used to examine the correlation between the dependent variable (DV) and the independent variable (IV), in the absence (or presence) of the controlled variables. The mediation effects among the IV, DV, and mediator were based on the following strategy proposed by Baron and Kenny [51]: 1) in the presence of the first-stage effect, the IV significantly affects the mediation factor; 2) in the absence of the mediation factor, the IV significantly affects the DV; 3) in the presence of the second-stage effect, the mediation factor has a significant effect on the DV; and 4) the effect of the IV on the DV weakens upon the addition of a mediation factor in the model.

A mediation model suitable for combining the categorical and continuous variables was developed by Iacobucci (2012) [52]. The formulas are as follows:

If the mediation factor and dependent variables are continuous variables, then the original formula of the Sobel test is applicable:

$$Z = \frac{a \times b}{\sqrt{b^2 {s_a}^2 + a^2 {s_b}^2}}$$

If the mediation factor or dependent variables are categorical variables, then the original formula of the Sobel test is rederived into a new formula:

$$Z_{mediation}\ (Z_m) = \frac{\frac{a}{s_a} \times \frac{b}{s_b}}{\sqrt{\left(\frac{a}{s_a}\right)^2 + \left(\frac{b}{s_b}\right)^2 + 1}}$$

Among them, a is the simple linear or logistic regression coefficient for the independent variable against the mediation factor, while b is the regression coefficient for the mediation factor against the dependent variable in the binary linear or logistic regression model. Additionally, s_a and s_b represent the standard deviations of a and b, respectively, while the results exceeding $|1.96|$, $|2.57|$, and $|3.90|$ (for the two-tailed test) are significant at $\alpha = 0.05$, 0.01, and 0.0001, respectively. In this study, the analyses were performed using SAS Enterprise Guide 7.1 software (SAS Institute Inc., Cary, NC, USA), and the significance was set at $p < 0.05$.

3. Results

Regarding the detailed description, the description of the basic demographics, sleep duration per day, and coffee intake of 1615 participants are shown in the Supplementary Information Tables S1–S3. The results demonstrated that marriage ($p = 0.016$), engaging in leisure activities with family/friends ($p < 0.0001$), coffee intake per day ($p < 0.0001$), exercise at least once a week ($p = 0.008$), overtime work in a month ($p < 0.0001$), shift schedules ($p < 0.0001$), and profession ($p = 0.005$) were associated with sleep duration per day. In addition, gender ($p = 0.024$), age ($p < 0.0001$), marriage ($p < 0.0001$), having children ($p < 0.0001$), education ($p < 0.0001$), alcohol use ($p < 0.0001$), exercise at least once a week ($p = 0.002$), and profession ($p = 0.001$) were related to coffee intake.

Table 1 illustrates that the common pain sites included both shoulders (43.09%), neck (36.22%), waist or lower back (27.93%), and upper back (16.90%). According to the principle proposed by Hair and Anderson (1995) [50], Factors 1 and 2 were retained because their vector values exceeded 1. In addition, the factor loadings were converted into standardized scoring coefficients through varimax rotation. The relatively large factor loading values for Factors 1 and 2 corresponded to the neck and both shoulder pain and both ankle pain sites, respectively. Thus, Factors 1 and 2 were redefined into two new variables: the neck and both shoulder pain (NBSP) score and the both ankle pain (BAP) score.

Table 1. MS pain sites and factor analysis of the NMQ.

MS Pain Sites	N	%	Score	Factor Loading	
			Mean ± SD	Factor 1	Factor 2
Neck	585	36.22	26.76 ± 37.64	0.33	−0.02
Left shoulder	325	20.12	15.07 ± 31.62	0.33	−0.01
Right shoulder	371	22.97	17.64 ± 33.89	0.33	0.02
Upper back	273	16.90	12.90 ± 29.77	0.17	0.00
Waist or lower back	451	27.93	20.20 ± 34.72	0.08	−0.04
Left elbow	70	4.33	3.29 ± 16.26	−0.05	−0.04
Right elbow	113	7.00	5.33 ± 20.43	−0.04	−0.04
Left wrist	77	4.77	3.72 ± 17.38	−0.05	0.00
Right wrist	162	10.03	7.51 ± 23.66	−0.03	−0.03
Left hip/thigh/buttock	67	4.15	3.12 ± 15.64	−0.05	−0.07
Right hip/thigh/buttock	68	4.21	3.17 ± 15.83	−0.02	−0.04
Left knee	80	4.95	3.78 ± 16.98	−0.05	−0.07
Right knee	88	5.45	4.17 ± 18.05	−0.02	−0.04
Left ankle	29	1.80	1.26 ± 10.10	−0.02	0.49
Right ankle	25	1.55	1.10 ± 9.58	−0.02	0.54
			Eigenvalues	4.93	1.55
			Explained variation %	57.59	18.12

N, individuals; %, the proportion of individuals suffering from MS pain.

According to Table 2, there were significant differences in the NBSP scores for gender ($p < 0.001$), age ($p = 0.003$), marriage ($p = 0.003$), having children ($p = 0.006$), education ($p = 0.034$), sleep duration per day ($p < 0.001$), coffee intake per day ($p = < 0.001$), alcohol use ($p = 0.001$), exercise at least once a week ($p = 0.001$), overtime work per month ($p < 0.0001$), profession ($p = 0.036$), and suffering from chronic diseases ($p < 0.0001$). There were no significant differences in the BAP scores among the survey variables, except for education ($p < 0.0001$). Regarding the other survey variables, the females obtained higher NBSP scores than the males (0.04 ± 0.93 vs. −0.17 ± 0.84). Moreover, individuals who were 38–45 years of age (0.15 ± 0.96), were married (0.07 ± 0.96), were parents (0.07 ± 0.96), had a master's degree or above (0.11 ± 0.99), had a sleep duration of less than 5 h (0.26 ± 1.04), drank more than two cups of coffee per day (0.61 ± 1.25), used alcohol in a month (0.10 ± 0.97), had no weekly exercise (0.09 ± 0.97), worked overtime more than 45 h per month (0.54 ± 1.35/ 0.44 ± 1.14), were nurses (0.08 ± 0.94), or suffered from chronic diseases (0.20 ± 1.03) achieved higher NBSP scores than the others. Simple multiple linear or logistic regression was also used to examine the correlation between the dependent and independent variables in the absence (or presence) of the controlled variables.

Table 2. Differences in the frequency of pain among the survey variables.

		Score on the Frequency of Musculoskeletal Pain			
		Mean ± SD			
Survey Variables	**Individuals**	**NBSP Score**	***p*-Value**	**BAP Score**	***p*-Value**
Gender					
Female	1314	0.04 ± 0.93	<0.001 [a]	−0.01 ± 0.85	0.643 [a]
Male	301	−0.17 ± 0.84		0.02 ± 0.90	
Age					
Less than or equal to 29	412	−0.11 ± 0.86	0.003 [b]	−0.00 ± 0.81	0.420 [b]
Between 29 and 38	433	0.01 ± 0.90		−0.06 ± 0.41	
Between 38 and 45	302	0.15 ± 0.96		0.04 ± 1.01	
More than or equal to 45	468	−0.01 ± 0.95		0.03 ± 1.06	
Marriage					
Married	779	0.07 ± 0.96	0.003 [a]	−0.02 ± 0.79	0.330 [a]
Other	836	−0.07 ± 0.87		0.02 ± 0.91	
Having children					
Parents	703	0.07 ± 0.96	0.006 [a]	−0.00 ± 0.88	0.914 [a]
Not parents	912	−0.06 ± 0.88		0.00 ± 0.84	
Engaging in leisure activities with family/friends					
Always	102	−0.05 ± 0.89	0.601 [b]	0.00 ± 0.78	0.764 [b]
Often	498	−0.04 ± 0.92		0.03 ± 0.96	
Sometime	765	0.03 ± 0.94		−0.02 ± 0.77	
Seldom	238	0.02 ± 0.87		0.02 ± 0.93	
Never	12	−0.21 ± 0.59		−0.18 ± 0.33	
Education					
Master's degree or above	297	0.11 ± 0.99	0.034 [a]	−0.10 ± 0.24	<0.0001 [a]
University degree or below	1318	−0.03 ± 0.90		0.02 ± 0.94	
Sleep duration per day					
Less than 5 h	63	0.26 ± 1.04	<0.001 [b]	0.29 ± 1.88	0.069 [b]
Between 5 and 6 h	563	0.12 ± 1.00		0.01 ± 0.91	
Between 6 and 7 h	719	−0.06 ± 0.85		−0.04 ± 0.68	
Between 7 and 8 h	232	−0.14 ± 0.87		0.01 ± 0.82	
More than 8 h	38	−0.10 ± 0.75		0.01 ± 0.46	
Coffee intake per day					
More than 2 cups per day	26	0.61 ± 1.25	<0.001 [b]	−0.17 ± 0.20	0.853 [b]
2 cups per day	70	0.18 ± 0.97		−0.03 ± 0.62	
1 cup per day	556	0.06 ± 0.95		−0.01 ± 0.88	
Occasionally	678	−0.04 ± 0.90		0.02 ± 0.82	
Never	285	−0.13 ± 0.81		−0.00 ± 0.97	

Table 2. *Cont.*

Survey Variables	Individuals	Score on the Frequency of Musculoskeletal Pain			
		Mean ± SD			
		NBSP Score	*p*-Value	BAP Score	*p*-Value
Alcohol use					
Alcohol use in a month	609	0.10 ± 0.97	0.001 [a]	0.01 ± 0.84	0.857 [a]
No alcohol use in a month	1006	−0.06 ± 0.88		−0.00 ± 0.86	
Exercise at least once a week					
Yes	933	−0.07 ± 0.87	0.001[a]	−0.01 ± 0.80	0.705 [a]
No	682	0.09 ± 0.97		0.01 ± 0.93	
Overtime work in a month					
More than 80 h	5	0.54 ± 1.35	<0.001 [b]	−0.25 ± 0.41	0.587 [b]
45–80 h per month	54	0.44 ± 1.14		0.04 ± 1.46	
Fewer than 45 h	502	0.09 ± 0.96		0.04 ± 1.46	
Seldom	1054	−0.07 ± 0.87		−0.02 ± 0.73	
Shift schedules					
Irregular shifts	192	0.16 ± 1.05	0.075 [a]	−0.06 ± 0.49	0.445 [a]
Regular shifts	196	−0.04 ± 0.91		0.02 ± 0.88	
Night shifts	166	−0.05 ± 0.84		0.08 ± 1.13	
Day shifts	1061	−0.15 ± 0.91		−0.01 ± 0.85	
Profession					
Physicians	138	0.03 ± 1.01	0.036 [b]	−0.01 ± 0.80	0.889 [b]
Nurses	613	0.08 ± 0.94		0.02 ± 1.00	
Professional and technical personnel	283	−0.06 ± 0.84		−0.02 ± 0.59	
Administrative staff	581	−0.06 ± 0.90		−0.01 ± 0.82	
Suffering from chronic diseases					
Yes	638	0.20 ± 1.03	<0.0001 [a]	0.04 ± 1.16	0.195 [a]
No	977	−0.13 ± 0.81		−0.03 ± 0.57	

Note: SD, standard deviation; [a] *t* test; [b] one-way ANOVA; NBSP, neck and both shoulders pain; BAP, both ankles pain.

Since the number of individuals with a sleep duration of less than 5 h per day was only 63 (Table 2), the variables of sleep duration of less than 5 h per day and sleep duration between 5 and 6 h per day were combined into a new variable: sleep duration of less than 6 h per day (SLD < 6 h). Furthermore, since the number of individuals who drank more than two cups of coffee per day was only 26, the variables of drinking more than two cups of coffee per day or drinking just two cups of coffee per day were combined into a new variable: drinking multiple cups of coffee (MCC) per day.

As shown in Table 3, which presents the effects of sleep duration per day and drinking MCC per day on NBSP, drinking MCC per day was significantly associated with an increased level of NBSP in the simple or multiple linear regression models (B = 0.32, $p = 0.001$; 0.23, $p = 0.016$), while SLD < 6 h was significantly associated with an increased level of NBSP in the simple or multiple linear regression models (B = 0.21, $p < 0.0001$; 0.15, $p = 0.001$). The results in Table 3 confirm Hypotheses 1 and 2 (illustrated in the introduction), that coffee intake (more than two cups per day) and a shorter sleep duration (less than 6 h per day) are associated with MS pain (especially neck and both shoulders pain).

Finally, this study used mediation analysis to determine the existence of a mutual relationship between coffee, MS pain, and sleep. Figure 1.1 demonstrates that drinking MCC per day mediated the effect of SLD < 6 h on increased levels of NBSP ($Z_m = 2.27$, $p < 0.05$). Lack of sleep (<6 h) also caused individuals to drink more coffee per day, which led to more frequent neck and shoulder pain. Figure 1.2 illustrates that SLD < 6 h mediated the effect of drinking MCC per day on increased NBSP ($Z_m = 2.95$, $p < 0.01$). Overall, Figures 1 and 2 demonstrate that long-term coffee drinking and lack of sleep can further increase the occurrence of neck and shoulder pain.

Table 3. Effect of SLD and drinking MCC per day on NBSP.

Main Effect	Unstandardized Linear Regression Coefficient (B) for NBSP					
	Simple Regression			Multiple Regression[1]		
	B	SE	*p*	B	SE	*p*
Drinking MCC per day	0.32	0.10	0.001	0.23	0.10	0.016
SLD < 6 h per day	0.21	0.05	<0.0001	0.15	0.05	0.001

SE, standard error; B, unstandardized linear regression coefficient; [1] model was in the presence of adjusted variables, including gender, age, marriage, having children, education, alcohol use, exercise, overtime work, profession, and suffering from chronic diseases.

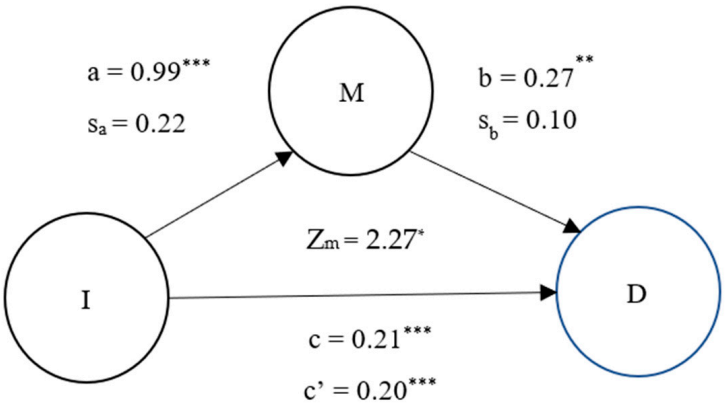

Figure 1. Mediation effect of MCC per day on SLD < 6 h and NBSP. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.0001$; M, mediation factor; I, independent variable; D, dependent variable.

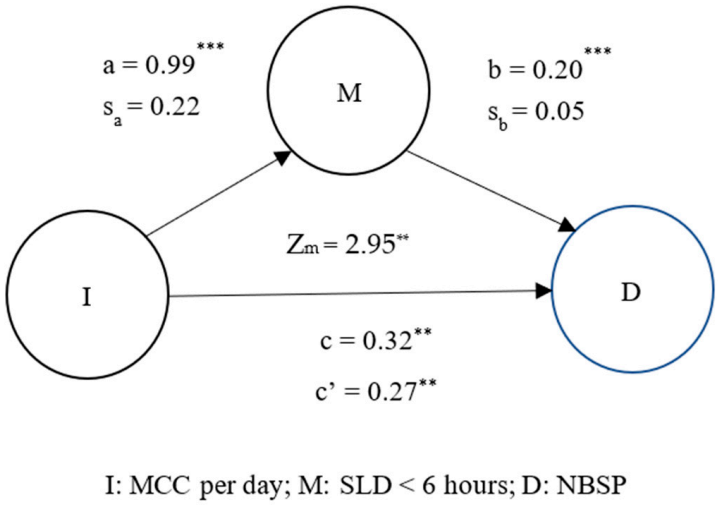

Figure 2. Mediation effect of SLD < 6 h on MCC per day and NBSP. ** $p < 0.01$; *** $p < 0.0001$; M, mediation factor; I, independent variable; D, dependent variable; c is the simple linear or logistic regression coefficient for the independent variable against dependent variable in the absence of mediation factor; c′ is the binary linear or logistic regression coefficient for the independent variable against dependent variable in the presence of mediation factor; a is the simple linear or logistic regression coefficient for the independent variable against the mediation factor; b is the regression coefficient for the mediation factor against the dependent variable in the binary linear or logistic regression model; s_a and s_b represent the standard deviations of a and b.

Figure 3 adopts SLD < 6 h and NBSP as dependent and independent variables for the mediation model, respectively. Based on the findings, drinking MCC per day mediated SLD < 6 h and increased NBSP ($Z_m = 2.5$, $p < 0.05$). Specifically, individuals who suffer from neck and should pain tend to drink coffee to cope with such pain. However, it eventually decreases their sleep duration per day. Figures 1–3 confirmed Hypothesis 3 and determined that coffee intake (more than two cups per day) really opens the vicious circle between lack of sleep (less than 6 h per day) and MS pain (especially neck and shoulders pain).

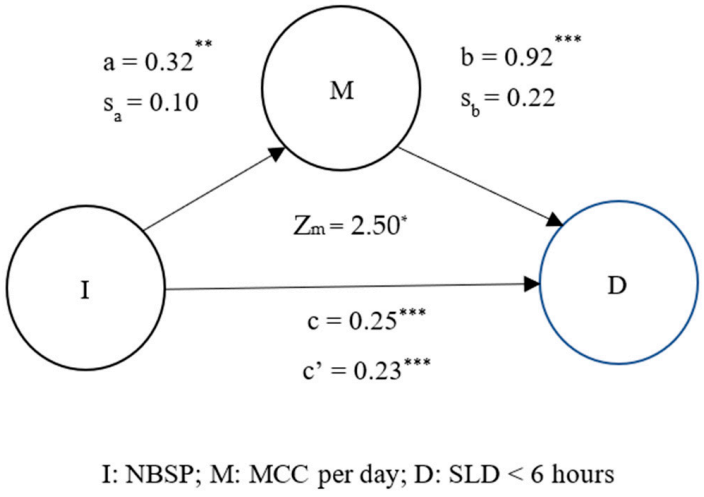

Figure 3. Mediation effect of MCC per day on NBSP and SLD < 6 h. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.0001$; M, mediation factor; I, independent variable; D, dependent variable; c is the simple linear or logistic regression coefficient for the independent variable against dependent variable in the absence of mediation factor; c′ is the binary linear or logistic regression coefficient for the independent variable against dependent variable in the presence of mediation factor; a is the simple linear or logistic regression coefficient for the independent variable against the mediation factor; b is the regression coefficient for the mediation factor against the dependent variable in the binary linear or logistic regression model; s_a and s_b represent the standard deviations of a and b.

4. Discussion

The present study confirms three hypotheses and determined that long-term heavy coffee intake (two cups per day) and a shorter sleep duration (<6 h per day) are associated with neck and shoulder pain. Notably, long-term heavy coffee intake plays a mediating factor in the vicious circle between shorter sleep duration and neck and shoulder pain. In addition, alcohol use, the lack of regular exercise at least once a week, overtime work in a month, and the presence of chronic diseases were significantly associated with pain in the neck/shoulders or ankles.

Related studies have illustrated that reduced alcohol use [18–21], physical activity [21], and fewer work hours [14] could reduce the risk of MS pain. In addition, individuals with chronic diseases [26,27] have a high risk for MS pain. These risk factors are consistent with our findings.

A literature review on healthcare workers demonstrated that MS pain occurred primarily in the lower and upper back, neck, and shoulders [53]. Our study found that the common pain sites were the shoulders (43.09%), neck (36.22%), waist or lower back (27.93%), and upper back (16.90%), which was consistent with the findings of a previous study.

Only 25% of adults achieve the recommended minimum sleep duration of 7 h per night for healthy adults [39]. However, only 16.72% of healthcare workers in the present study satisfy the 7 h sleep condition, as shown in Table 2. Therefore, the lack of sleep could be a common problem among healthcare workers in Taiwan, and this should be noted and further explored.

4.1. First Hypothesis: Coffee Intake Is Significantly Associated with an Increased Risk of MS Pain

Previous studies have found that individuals with a high caffeine intake (4–12 cups/day) had more severe pain than those with a low (0.25–1.5 cups/day) or moderate (2–3.5 cups/day) caffeine intake [54]. In addition, men who drink more than seven cups of coffee per day have an increased risk of knee osteoarthritis [7]. Our study determined that among healthy individuals, long-term drinking of more than two cups of coffee per day was associated with frequent neck and shoulder pain (Table 3, B = 0.23, $p = 0.016$). Since the half-life of caffeine is approximately 4 h [55], drinking two or more cups of coffee per day can reach the threshold of caffeine's effect on MS pain, depending on one's genetics [56]. Based on these results, we can confirm our first hypothesis.

4.2. Second Hypothesis: Individuals with Shorter Sleep Durations Are More Susceptible to MS Pain

Evidence suggests a close link between short sleep durations and impairments in several physiological responses, including pain [57]. A study on middle-aged adults in the U.S. demonstrated that a sleep duration of <6 h was associated with greater next-day pain [58]. In addition, individuals who reported >6 h of sleep were more likely to have improved pain conditions [59]. Our study found important evidence that sleep duration was associated with MS pain at specific sites. Individuals with sleep durations of <5 or 6 h tend to experience more neck and shoulder pain than others (Table 2; mean = 0.26 ± 1.04, 0.12 ± 1.00). Table 3 shows that a sleep duration of <6 h per day was significantly associated with increased neck and shoulder pain in the multiple regression model (B = 0.15, $p = 0.001$). These results confirm our second hypothesis.

4.3. Third Hypothesis: Coffee Intake Could Lead to a Vicious Circle between Lack of Sleep and MS Pain

A previous study showed that individuals who reported a sleep duration of <6 h consumed 3.6 times more caffeine per day than those who reported a sleep duration of >8 h [40]. Our study of healthcare workers found that individuals who reported a sleep duration of <6 h consumed 2.69 times (Figure 1.1, $\beta = 0.99$, odds ratio = e0.99 = 2.69, $p < 0.0001$) more caffeine per day than those who reported a sleep duration of >6 h. This close relationship between sleep duration and coffee intake indicates a causal relationship between sleep duration, NBSP, and coffee intake.

The mediation model in Figure 1.1 demonstrates that individuals who had shorter sleep durations tended to drink multiple cups of coffee, which can lead to increased MS pain (Zm = 2.27, $p < 0.05$). In addition, the mediation model in Figure 1.2 shows that individuals who chronically drink multiple cups of coffee generally experience shorter sleep durations and increased MS pain (Zm = 2.95, $p < 0.01$). These mediation models regarding coffee intake, MS pain, and sleep duration show that long-term heavy coffee intake (more than two cups per day) plays a mediating role in the two-way association of sleep duration <6 h and NBSP. Specifically, long-term heavy coffee intake will induce a vicious circle of sleep and neck and shoulder pain. These results are consistent with our third hypothesis.

This study has several limitations. First, we used the number of cups to measure the degree of caffeine intake per day. However, this is not an exact measurement method because cups have different volumes. Second, different coffee-brewing methods can lead to varied caffeine concentrations and errors in the dose–response of caffeine on MS pain. However, we believe that the differences in volume and caffeine concentration can be overcome. In addition, caffeine's effect on MS pain reaches the threshold depending on one's genetics [56]. Therefore, the threshold of more than two cups of coffee per day might not be suitable for other countries or races. Additionally, since sleep duration and sleep quality are subjective, future research should adopt other scales to measure sleep-related issues. Third, MS pain can be the result of workloads, work styles, or posture. Unfortunately, our study did not collect such data in the regression models. Fourth, the

effects of caffeine on individuals can be associated with genetics [56] and nationality. For example, the effects of coffee intake on MS pain in Europeans or Americans may differ from our results because our participants were Taiwanese.

Despite the adjustment for sex in the multiple linear regression, the results of the present study could be better suited to women because female participants accounted for >80% of the study population. Regarding the sex difference in MS pain, it could be caused by estrogen and progesterone. For instance, testosterone, the major male sex hormone, protects men from chronic MS pain [60]. Because the study population only included physicians, nurses, professional and technical personnel, and administrative staff, we added "healthcare workers" in the title to limit the applicability to occupational groups.

Notably, we could determine whether high work stress or emotional exhaustion caused by the pandemic affected the findings; thus, a similar study during the nonpandemic period should be replicated, and its results compared with those from the pandemic period. Finally, the mediation models in our study could be biased [61] because the relationship was based on a higher risk of judgment. Therefore, we excluded the phrase "causal relationship" to avoid confusion.

5. Conclusions

The present study determines that keeping good living habits (such as decreased alcohol use, regular exercise a week, and sufficient sleep), maintaining physical health (such as staying away from chronic diseases), and avoiding overtime work are ways to lower the risk of MS pain. We further examined the effects of frequent coffee drinking on individuals experiencing MS pain and lack of sleep. Based on the results, neck and shoulder pain was the most common among the healthcare workers. In addition, a sleep duration of less than 6 h and drinking more than two cups of coffee per day increased the occurrence of such pain, while controlling for other risk factors. Notably, long-term heavy coffee drinking created a vicious cycle between neck and shoulder pain and sleep duration of less than 6 h. The implication of the findings is that individuals who sleep less than 6 h, or who suffer from neck and shoulder pain, should limit their coffee intake to two cups per day.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/jpm13010025/s1, Table S1: the description of basic demography of 1615 participants; Table S2: The description of sleep duration per day for all individuals; Table S3: The description of coffee intake per day for all individuals.

Author Contributions: Conceptualization, Y.-H.C. (Yong-Hsin Chen), T.-Y.Y. and G.-P.J.; methodology, Y.-H.C. (Yong-Hsin Chen), T.-Y.Y. and G.-P.J.; data curation, Y.-H.C. (Yong-Hsin Chen), T.-Y.Y. and G.-P.J.; formal analysis, Y.-H.C. (Yong-Hsin Chen) and Y.-H.C. (Ying-Hsiang Chou); resources, Y.-H.C. (Ying-Hsiang Chou); supervision, T.-Y.Y. and G.-P.J.; writing—original draft preparation, Y.-H.C. (Yong-Hsin Chen); writing—review and editing, T.-Y.Y. and G.-P.J. All authors have read and agreed to the published version of the manuscript.

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Relationships between Alcohol Use, Musculoskeletal Pain, and Work-Related Burnout

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Abstract: *Background and Objectives*: Burnout affects approximately half of all nurses, physicians, and other clinicians. Alcohol use may impair performance in work-related tasks, leading to decreased productivity and morale. The present study's aim was to determine whether a causal relationship existed between alcohol use, work-related burnout (WB), and musculoskeletal pain. *Materials and Methods*: A total of 1633 members from a hospital affiliated with a medical university in Taichung, Taiwan, completed questionnaires in 2021, where 1615 questionnaires were declared valid. Questionnaires were used to obtain information on basic demographic variables, and the Nordic Musculoskeletal Questionnaire and Copenhagen Burnout Inventory were used. Statistical analyses were performed using SAS Enterprise Guide 6.1 software, and significance was set at $p < 0.05$. *Results*: Work experience, being married, parenthood, leisure activities with family and friends, and regular weekly exercise were negatively associated with WB. In addition, overtime work, irregular and regular shift work, the physician and nurse medical profession, chronic disease (heart disease, diabetes, etc.), neck and both shoulders pain (NBSP), both ankles pain (BAP), and alcohol use frequency (AUF) were positively associated with WB. NBSP could explain the residual effect of AUF on WB. AUF was determined to mediate the relationship between NBSP and WB. In addition, NBSP was found to mediate the relationship between AUF and WB. *Conclusions*: The individuals who used alcohol to cope with NBSP or those with NBSP who often consumed alcohol had worsened WB due to a vicious circle of musculoskeletal pain and alcohol use. Therefore, medical staff should not consider alcohol use as an option to reduce burnout.

Keywords: alcohol use; musculoskeletal pain; work-related stress; burnout

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1. Introduction

Burnout was first described in 1974 by the clinical psychologist Herbert Freudenberger, who borrowed the term from drug-addict slang [1]. Burnout refers to physical, emotional, and mental exhaustion resulting from long-term work situations [2]. To measure burnout, Christina Maslach proposed the Maslach Burnout Inventory in 1981, and the extent of an individual's symptoms in each dimension is measured on the basis of the three subscales of emotional exhaustion, depersonalization, and a diminished sense of personal accomplishment [3]. The Copenhagen Burnout Inventory (CBI) developed by researchers from Denmark is another scale used to measure burnout [4]. The CBI considers exhaustion as the core of the burnout concept and includes three scales, namely, the personal burnout scale,

work-related burnout (WB) scale, and client burnout scale, which can be separately used to measure burnout in different settings (not only for service professions); the questionnaire is developed in such a manner that it is suitable for individuals from all occupations [4]. In contrast with personal and client burnout, WB is defined in the CBI as the degree of physical and psychological fatigue and exhaustion that is perceived by the person as related to paid work of some kind [4].

The severe clinical presentations of burnout include emotional exhaustion, physical fatigue, cognitive impairments, disturbed sleep, and functional impairment [5,6]. A combination of stressors due to long-term work and nonwork on individuals often contribute to clinical burnout [7], which could lead to sleep disturbances, depression, or anxiety disorders [5]. Burnout affects approximately half of all nurses, physicians, and other clinicians [8]. Among them, one-tenth of the nurses worldwide suffer high burnout symptoms [9] and 48.7% of German clinicians meet the criteria for burnout [10]. Notably, clinical burnout is related to a reduced ability to work [7]. Burnout is responsible for high physician turnover and reduced clinical hours, which cause total losses of approximately USD 4.6 billion each year [11]. Notably, burnout also affects the patient-related quality of care [10].

In the United States, 13% of the total workforce loss is associated with body pain conditions and costs an estimated USD 61.2 billion per year [12]. A large study conducted in the Netherlands demonstrated that the top three self-reported musculoskeletal pain sites were the lower back, shoulder, and neck [13]. Moreover, studies reported diverse risk factors for musculoskeletal pain, including long work hours [14], occupational stress [15], alcohol consumption [16], sleep duration [17], and chronic diseases (CDs) [18].

Alcohol use contributes to around 4% of the global burden of disease [19] and is related to premature death, where the major causes are injury, alcoholic liver disease, heart disease and stroke, cancers, and gastrointestinal disease [20]. Alcohol use may impair performance in work-related tasks, leading to decreased productivity and morale [21] and an increased occupational injury risk [22]. Many individuals consume alcohol to alleviate stress caused by working overtime [23] and even to cope with pain [24].

Individuals commonly tend to adopt an alcohol consumption strategy to cope with pain, psychological, or physical troubles. Based on this, the present study asked questions about alcohol use, MS pain, and burnout to establish (1) whether a causal relationship exists between alcohol use, WB, and musculoskeletal pain, and (2) the role of alcohol use in the relationship between musculoskeletal pain and WB?

2. Methods

2.1. Study Population

In this observational and cross-sectional study, we included 2531 employees from a hospital affiliated with a medical university in Taichung, Taiwan, in 2021. The study protocol was approved by the institutional review board of Chung Shan Medical University Hospital on 25 August 2021 (no. CS1-21108).

2.2. Study Measures

The QR-code-linked questionnaires were sent to all eligible participants by email. Among the 2531 members, 1633 (64.52%) completed questionnaires. After exclusion due to missing data, 1615 (63.81%) questionnaires were determined to be valid. The questionnaires were used to obtain information on basic demographic variables, family factors, living habits, work-related factors, and physical health factors. In addition, we used the Nordic Musculoskeletal Questionnaire (NMQ) and the WB scale.

Regarding the education level, the response options were “below high school”, “Bachelor”, “Master”, and “PhD”. The response options for marriage status were “married” and “others”. In terms of family factors, we examined whether the respondents were parents by using the following response options: “without child”, “one child”, “two children”, “three children”, and “over three children”. Raising at least one child was reclassified as a new variable called “parenthood”.

Relationships with family and friends were also evaluated in the questionnaire. For the question "Whether participants engage in leisure activities with family or friends in vacation time?", the Likert scale method was used, where the response options were distinguished as "always", "often", "sometimes", "seldom", and" never"; these were scored as 100, 75, 50, 25, and 0 points, respectively. The data was an ordinal scale that could be suitable for parametric tests (such as *t*-tests, analysis of variance, Pearson correlations, and regression), even when statistical assumptions were violated (such as normal distribution of data) [25]. An item related to the presence of a listed CD was included in the questionnaire, and the presence of one or more diseases was classified as a "yes" response. Regarding AU in the past month, the response options were "always", "often", "sometimes", "seldom", and "never"; these responses were scored as 100, 75, 50, 25, and 0 points, respectively. Finally, the mean value was considered as the new variable AU frequency (AUF). The response options for the sleep duration (SLD) were classified as <5, 5–6, 6–7, 7–8, or >8 h per day; these were reclassified as SLD < 6 h and SLD > 6 h per day. The response options for exercise habit were "at least once a day", "at least once a week", "at least once a month", "less than once a month", or "never". Exercising at least once a day or week was reclassified as regular exercise weekly (REW). The response options for the question on overtime (OT) were "seldom", "less than 45 h per month", "45–80 h per month", and "more than 80 h per month". The responses were reclassified as seldom OT and experiencing OT (including less than 45 h, 45–80 h, and more than 80 h per month). The possible responses to the question on the shift schedule were "day shift work", "night shift work", "irregular shift (IRS) work", and "regular shift (RS) work".

We adopted the NMQ that was modified and translated by the Taiwan Institute of Occupational Safety and Health, which includes questions on the presence of pain attributable to work-related factors in the preceding year and at pain sites. The options for pain sites were the neck, left shoulder, right shoulder, upper back, waist or lower back, left elbow, right elbow, left wrist, right wrist, left hip/thigh/buttock, right hip/thigh/buttock, left knee, right knee, left ankle, and right ankle. If a participant answered "yes" to a question on the experience of work-related pain in the preceding year, they were required to indicate its occurrence frequency: every day, once a week, once a month, once every half year, or at least once every half year (100, 80, 60, 40, and 20 points, respectively).

We used the Chinese version of the CBI [26], which was reported to be a reliable and valid tool (the Cronbach's alpha value was over 0.84 for males and females) for the assessment of burnout and measuring WB. The seven items for measuring WB were as follows:

1. "Is your work emotionally exhausting?"
2. "Do you feel burnt out because of your work?"
3. "Does your work frustrate you?"
4. "Do you feel worn out at the end of the working day?"
5. "Are you exhausted in the morning at the thought of another day at work?"
6. "Do you feel that every working hour is tiring for you?"
7. "Do you have adequate energy for family and friends during leisure time?"

The response options were "always", "often", "sometimes", "seldom", and "never or almost never", and these were scored as 100, 75, 50, 25, and 0, respectively, except for item 7, which was inversely scored (i.e., the responses were scored as 0, 25, 50, 75, and 100, respectively); the calculated mean value indicated the WB level for the participants.

2.3. Data Analysis

Factor analysis [27] was conducted using the NMQ results to determine the underlying variables that explained most of the questionnaire. A univariate linear regression model was used to examine the associations between the dependent variables (DVs) and independent variables (IVs). Multiple linear regression was conducted to determine whether the adjustment for variables significantly affected the associations between IVs and DVs. Mediation effects were analyzed using the strategy proposed by Baron and Kenny [28], in

which (1) the IV significantly affects the mediator (first-stage effect), (2) the IV significantly affects the DV in the absence of the mediator, (3) the mediator exerts a significant unique effect on the DV (second-stage effect), and (4) the effect of the IV on the DV weakens upon the addition of a mediator to the model. Among them, item (2) is only recommended but not required [29]. The formulas are as follows:

$$Y = b_{01} + cX$$

$$M = b_{02} + aX$$

$$Y = b_{03} + c'X + bM$$

where X is an IV, Y is a DV, M is the adjusted variable (i.e., the mediating factor), a is the linear regression coefficient of X against M, b is the linear regression coefficient of M against Y, c is the linear regression coefficient of X against Y, and c' is the linear regression coefficient of X against Y with M as the adjusting variable. The standard errors of a and b are represented by s_a and s_b, respectively. The formula for the Sobel test is as follows:

$$Z = \frac{a \times b}{\sqrt{b^2 s_a{}^2 + a^2 s_b{}^2}}$$

The results exceeding $|1.96|$, $|2.57|$, and $|3.90|$ (for a two-tailed test) are significant at α = 0.05, 0.01, and 0.0001, respectively.

The mediation proportion is defined as the dimensionless proportion of the effect of an IV on a DV mediated through the mediation factor, whose formula is as follows [30]:

$$MP = \frac{a \times b}{c' + a \times b}$$

Analyses were performed using SAS Enterprise Guide 6.1 software (SAS Institute Inc., Cary, NC, USA), and significance was set at $p < 0.05$.

3. Results

3.1. Musculoskeletal Pain Sites and Factor Analysis of the Nordic Musculoskeletal Questionnaire

The prevalences of musculoskeletal pain in a year in both shoulders, the neck, the waist, the lower back, and the upper back were 43.09%, 36.22%, 27.93%, and 16.90%, respectively (Table 1). The mean frequency scores of neck, waist or lower back, right shoulder, left shoulder, and upper back pain were 26.76 ± 37.64, 20.20 ± 34.72, 17.64 ± 33.89, 15.07 ± 31.62, and 12.90 ± 29.77, respectively. According to the principle proposed by Hair and Anderson (1995) [27], factors 1 and 2 were retained because their vector values exceeded 1. Although the eigenvalue of factor 3 was lower than 1, factor 3 was retained to ensure the maximum ability to explain the questionnaire. The factor loadings were converted into standardized scoring coefficients through varimax rotation. The relatively large factor loading values for factors 1, 2, and 3 corresponded to frequency scores for the neck and both shoulder pain (NBSP), both ankle pain (BAP), and both knee pain (BKP), respectively.

Table 1. Musculoskeletal pain sites and factor analysis of the Nordic musculoskeletal questionnaire.

MS Pain Site	MS Pain Subjects	Prevalence (%)	Frequency Score	Factor Loading		
			Mean ± SD	Factor 1	Factor 2	Factor 3
Neck	585	36.22	26.76 ± 37.64	***0.33***	−0.02	−0.03
Left shoulder	325	20.12	15.07 ± 31.62	***0.33***	−0.01	−0.01
Right shoulder	371	22.97	17.64 ± 33.89	***0.33***	0.02	−0.07
Upper back	273	16.90	12.90 ± 29.77	0.17	0.00	−0.01
Waist or lower back	451	27.93	20.20 ± 34.72	0.08	−0.04	0.03
Left elbow	70	4.33	3.29 ± 16.26	−0.05	−0.04	−0.05
Right elbow	113	7.00	5.33 ± 20.43	−0.04	−0.04	−0.02

Table 1. *Cont.*

MS Pain Site	MS Pain Subjects	Prevalence (%)	Frequency Score	Factor Loading		
			Mean ± SD	Factor 1	Factor 2	Factor 3
Left wrist	77	4.77	3.72 ± 17.38	−0.05	0.00	0.01
Right wrist	162	10.03	7.51 ± 23.66	−0.03	−0.03	−0.02
Left hip/thigh/buttock	67	4.15	3.12 ± 15.64	−0.05	−0.07	−0.01
Right hip/thigh/buttock	68	4.21	3.17 ± 15.83	−0.02	−0.04	−0.06
Left knee	80	4.95	3.78 ± 16.98	−0.05	−0.07	***0.51***
Right knee	88	5.45	4.17 ± 18.05	−0.02	−0.04	***0.45***
Left ankle	29	1.80	1.26 ± 10.10	−0.02	***0.49***	−0.05
Right ankle	25	1.55	1.10 ± 9.58	−0.02	***0.54***	−0.05
			Eigenvalues	4.93	1.55	0.68
			Explained variation (%)	57.59	18.12	0.08

3.2. Statistical Results of Response Options for Every Work-Related Burnout Item

Table 2 presents the statistical results of the response options for every WB item. The Cronbach's alpha value of the WB scale was 0.87. The mean values of all items for measuring WB are shown below. The mean values and standard deviations of all items for the WB scale are shown below.

Table 2. Statistical results of the response options for each WB item.

Items for Measuring WB		Response Options for WB (Subjects/Proportion (%))					
		Always	Often	Sometimes	Seldom	Never/Almost Never	Mean ± SD
1.	Is your work emotionally exhausting?	38 (2.33)	98 (6.00)	549 (33.62)	715 (43.78)	233 (14.27)	34.58 ± 22.11
2.	Do you feel burnt out because of your work?	22 (1.35)	79 (4.84)	471 (28.84)	803 (49.17)	258 (15.80)	31.69 ± 20.77
3.	Does your work frustrate you?	14 (0.86)	43 (2.63)	543 (33.25)	810 (49.60)	223 (13.66)	31.86 ± 18.98
4.	Do you feel worn out at the end of the working day?	68 (4.16)	178 (10.90)	680 (41.64)	568 (34.78)	139 (8.51)	41.86 ± 23.16
5.	Are you exhausted in the morning at the thought of another day at work?	61 (3.74)	124 (7.59)	524 (32.09)	718 (43.97)	206 (12.61)	36.47 ± 23.41
6.	Do you feel that every working hour is tiring for you?	18 (1.10)	41 (2.51)	349 (21.37)	896 (54.87)	329 (20.15)	27.39 ± 19.46
7.	Do you have enough energy for family and friends during leisure time?	261 (15.98)	646 (39.56)	528 (32.33)	165 (10.10)	33 (2.02)	35.66 ± 23.56

Cronbach's alpha = 0.87; SD, standard deviation.

As presented in Table 3, work experience was negatively associated with WB (β = −0.23, $p < 0.0001$) and AUF (β = −0.21, $p < 0.01$). Married status and parenthood were protective factors against WB (β = −4.30 and −4.86, respectively; $p < 0.0001$ for both) and AUF (β = −2.68 and −3.10, respectively; $p < 0.05$ for both). Engaging in leisure activities with family and friends was negatively associated with WB (β = −0.14, $p < 0.0001$) but not with AUF (β = −0.00, $p > 0.05$). Regular weekly exercise was a protective factor against WB (β = −5.60, $p < 0.0001$); however, it was not significantly associated with AUF (β = 1.72, $p > 0.05$). SLD < 6 h per day was significantly positively associated with WB (β = 6.27, $p < 0.0001$) and AUF (β = 3.11, $p < 0.05$). The participants with a master's degree or above reported a lower level of WB (β = −2.21, $p < 0.05$) than those with a university or below university degree; however, having a master's degree or above was not significantly associated with AUF (β = 2.17, $p > 0.05$). OT work was a risk factor for WB (β = 8.88, $p < 0.0001$) and AUF (β = 4.33, $p < 0.001$). A significant difference in WB was noted between different shift schedules. IRS and RS work significantly increased WB (β = 8.87 and 6.23, respectively; $p < 0.0001$ for both). Regarding professional fields, physicians (β = 9.89, $p < 0.0001$) and nurses (β = 8.44, $p < 0.0001$) reported higher levels of WB. Moreover, the AUF was significantly higher in the physicians (β = 9.96, $p < 0.0001$). The presence of a CD was positively associated with WB (β = 3.47, $p < 0.0001$) and AUF (β = 3.01, $p < 0.05$). Regarding musculoskeletal pain, NBSP was closely associated with WB (β = 6.30, $p < 0.0001$) and AUF (β = 2.48, $p < 0.01$). In addition, BAP was associated with WB (β = 1.44, $p < 0.01$).

Table 3. Stratified analysis of work-related burnout and alcohol use.

		WB		AUF	
Survey Variables	**N**	**β**	***p***	**β**	***p***
Work experience					
WE	1615	−0.23	***	−0.21	**
Marriage state					
Married	779	−4.30	***	−2.68	*
Unmarried	836	1.00		1.00	
Parenthood					
Yes	703	−4.86	***	−3.10	*
No	912	1.00		1.00	
Leisure activity with family and friends					
mean score	1615	−014	***	−0.00	
Exercise habit weekly					
REW	933	−5.60	***	1.72	
None REW	682	1.00		1.00	
SLD (per day) ranks					
<6 h	626	6.27	***	3.11	*
>6 h	989	1.00		1.00	
Education degree					
Master's degree or above	297	−2.21	*	2.17	
University or below university degree	1318	1.00		1.00	
Overtime work per month					
Experience OT	561	8.88	***	4.33	**
Seldom OT	1054	1.00		1.00	
Shift schedules					
IRS work	192	8.87	***	3.02	
RS work	196	6.23	***	0.29	
Night shift work	166	3.24	*	3.66	
DS work	1061	1.00		1.00	
Professional fields					
Physicians	138	9.89	***	9.96	***
Nurses	613	8.44	***	1.30	
PTs	283	2.17		3.11	
ADs	581	1.00		1.00	

Table 3. *Cont.*

Survey Variables	N	WB		AUF	
		β	*p*	β	*p*
Suffering CD					
Yes	638	3.47	***	3.01	*
No	977	1.00		1.00	
MS pain					
NBSP	1615	6.30	***	2.48	**
BAP	1615	1.44	**	0.19	
BKP	1615	0.75		−0.44	

N, participants; β, the linear regression coefficient; * $p < 0.05$, ** $p < 0.01$, *** $p < 0.0001$.

3.3. The Association between Alcohol Use, Musculoskeletal Pain, and Work-Related Burnout

As presented for M_0 in Table 4, AUF was closely associated with WB (β = 0.07, $p < 0.0001$). After an adjustment for work experience, marriage status, parenthood, leisure activity with family and friends, exercise habit weekly, SLD, education degree, OT work per month, shift schedules, professional fields, and CD in the M_1 model, we observed that AUF was still associated with WB (β = 0.04, $p < 0.01$). In the M_2 model, the residual effect of AUF on WB could be fully explained by NBSP (β = 0.03, $p > 0.05$). Mediation analysis was performed (Table 5) to determine whether a causal relationship existed between WB, AUF, and NBSP.

Table 4. AU effect in the linear regression models of WB.

Main Effect	M_0		M_1		M_2	
	β	*p*	β	*p*	β	*p*
AUF	0.07	***	0.04	**	0.03	

β, the linear regression coefficient; ** $p < 0.01$, *** $p < 0.0001$; M_0, without adjustment for variables; M_1, adjustment for work experience, marriage status, parenthood, leisure activity with family and friends, exercise habit weekly, sleep duration, educational level, overtime work per month, shift schedules, professional fields, and CD; M_2, adjustment for all the variables included in M_1 and an additional variable, namely, NBSP.

Table 5. Mediation effect of AUF on the relationship between NBSP and WB.

IV	M	WB						
		c'	A	s_a	b	s_b	Z	MP (%)
NBSP	AUF	6.19 ***	2.46 **	0.67	0.05 **	0.02	2.07 *	1.95
AUF	NBSP	0.05 **	0.00 **	0.00	6.19 ***	0.41	3.25 **	27.08

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.0001$; M, mediation factor; c', the direct effect of NBSP on WB; a, the first-stage effect of NBSP on AU; s_a, the standard error for a; b, the second stage effect for AUF on WB; s_b, the standard error for b; MP, mediation proportion.

As presented in Table 5, AUF was determined to be a mediator (Z = 2.07, $p < 0.05$) of the relationship between NBSP and WB, with the mediation proportion being only 1.95%. In addition, NBSP was determined to be a mediator (Z = 3.25, $p < 0.01$) of the relationship between AUF and WB, with the mediation proportion being 27.08%.

4. Discussion

Our study's results suggested that alcohol use was associated with increased NBSP, and both were closely related to increased WB. According to the mediation models, alcohol use mediated the relationship between NBSP and WB, causing worse WB. In addition, NBSP was a mediation factor of alcohol use, causing worse WB. Based on this, in response to the two research aims posed in the Introduction: (1) a causal relationship existed between alcohol use, WB, and musculoskeletal pain, and (2) alcohol use was a mediation factor between musculoskeletal pain and WB that increased WB.

Previous studies reported various causes of burnout. For example, a systematic review of the literature on burnout revealed that inexperienced psychotherapists easily experienced burnout due to a sense of hopelessness and an inability to reach idealistic expectations and standards [31]. In this study, work experience was found to be a protective factor against WB ($\beta = -0.23$, $p < 0.0001$; Table 3).

Family members and friends play a vital role in preventing burnout [32]. For instance, health workers reported that they could minimize burnout by obtaining support from family [33]. As demonstrated in Table 3, being married ($\beta = -4.30$, $p < 0.0001$) and parenthood ($\beta = -4.86$, $p < 0.0001$) were negatively associated with WB. These results indicated that family members could effectively reduce the level of WB; this finding is consistent with those of previous studies. Participating in leisure activities can relieve stress, help cope with emotional stress, and moderately maintain physical and mental health [34]. The same finding was observed in this study: engaging in leisure activities with family and friends was negatively associated with WB ($\beta = -0.14$, $p < 0.0001$).

Physiological changes resulting from physical activity can reduce individuals' sensitivity to chronic stress [35]. Thus, engaging in physical activity can lead to faster recovery after experiencing a stressful situation, and thus, reduce the risk of burnout [36]. Our results revealed that regular weekly exercise effectively reduced WB ($\beta = -5.60$, $p < 0.0001$).

Burnout development was closely related to considerably less sleep (<6 h) [37] and disturbed sleep [38]. Similar to the findings of previous studies, our results revealed that the participants with SLD < 6 h/day reported a higher level of WB than those with SLD > 6 h/day ($\beta = 6.27$, $p < 0.0001$).

OT work hours are closely correlated with burnout development in a dose-dependent manner [39]. IRS work is related to a significantly higher level of burnout [40]. The same phenomena were observed in our study: OT ($\beta = 8.88$, $p < 0.0001$) and IRS work ($\beta = 8.87$, $p < 0.0001$) were significantly associated with WB.

Burnout was observed to be markedly higher among practicing physicians than individuals in other careers after adjustment for work hours and other factors [41]. The present study indicated that the physicians reported a higher level of WB than those employed in other fields (Table 3). This result is consistent with those of previous studies.

Burnout is an independent risk factor for coronary heart disease [42] and type 2 diabetes [43]. Similar findings are presented in Table 3. The participants who had at least one CD reported a higher level of WB than those without CD ($\beta = 3.47$, $p < 0.0001$).

The onset of regional neck/shoulder and/or low back pain was associated with an increased risk of burnout [44]. In the present study, NBSP was significantly related to WB ($\beta = 6.30$, $p < 0.0001$). Overall, the increased occurrence frequency of neck and shoulder pain increased WB.

Burnout was strongly associated with alcohol abuse or dependence among American surgeons [45] and was significantly positively associated with higher AU among doctors, nurses, and residents [46]. The present study demonstrated that AUF was significantly associated with work-related burnout in a univariate linear regression (Table 3; M_0: $\beta = 0.07$, $p < 0.0001$). Even after adjusting for other risk factors, we observed that this association was still significant (Table 3; M_1: $\beta = 0.04$, $p < 0.01$). However, this association did not become significant after the addition of an extra adjusted variable, namely, NBSP, in the M_1 model (M_2 model). NBSP fully explained the residual effect of AUF on WB after an adjustment for other risk factors.

Previous studies demonstrated a close relationship between musculoskeletal pain, burnout, and alcohol use. Musculoskeletal pain is associated with the frequency of drinking, and the association between alcohol consumption and pain is curvilinear [47]. For example, moderate alcohol consumption was associated with a decreased risk of disabling chronic back or neck pain [48] and chronic widespread pain [49]. Excessive alcohol use may cause the development of chronic pain by increasing the risk of traumatic injury and deleterious effects on the musculoskeletal system [50]. To determine the causal relationship between AUF, NBSP, and WB, three variables were modeled and the results are presented in Table 5.

The mediation model (Table 5) demonstrated that AUF mediated the relationship between NBSP and WB and that NBSP mediated the relationship between AUF and WB. Some individuals who often reported NBSP used alcohol to cope with pain; however, this strategy worsened their WB due to increased alcohol use (the mediation proportion was only 1.95%). In addition, the individuals who often consumed alcohol often reported NBSP, which further increased WB due to worsening musculoskeletal pain (the mediation proportion reached 27.08%). These relationships formed a vicious circle of WB for medical staff who used alcohol and had musculoskeletal pain.

The present study only surveyed the frequency of alcohol use in the past month and ignored the amount of alcohol intake per day by the participants. This could mean that alcohol's effects on burnout and musculoskeletal pain were weakened. The severity of musculoskeletal pain was also ignored since we could not further explore whether the dose–response relationship between alcohol use and musculoskeletal pain or burnout existed. Notably, our study was conducted during the COVID-19 pandemic. It was reported that over 50% of healthcare professionals reported burnout symptoms during the COVID-19 pandemic, which was mainly caused by contacting patients, supply shortages, and work impacting household activities [51]. However, our study's variables did not include these factors.

5. Conclusions

Work experience, marriage, and parenthood were negatively associated with WB and the frequency of alcohol use. A sleep duration of less than 6 h per day, overtime work, physician medical profession, suffering from CDs, and increased NBSP were positively associated with WB and frequency of alcohol use. Leisure activity with family and friends, regular exercise weekly, and a master's degree or above were negatively associated with WB. Shift work, nurse medical profession, and increased BAP were positively associated with WB.

Alcohol use and NBSP were closely associated, and both were independent risk factors for WB. Mediation models indicated that the individuals who used alcohol to cope with NBSP or those with NBSP who often consumed alcohol had worsened WB due to a vicious circle of musculoskeletal pain and alcohol use. Therefore, medical institutions should positively encourage that staff quit drinking or drink in moderation. In particular, individuals who suffer from neck and shoulder pain should not consider alcohol use to cope with burnout symptoms.

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ORIGINAL ARTICLE

Observational Study

Is burnout a mediating factor between sharps injury and work-related factors or musculoskeletal pain?

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Author contributions: Chen YH and Yeh CJ conceived and designed this manuscript; Jong GP and Yeh CJ analyzed and interpreted the data of this study; Chen YH wrote the original draft; Jong GP and Yeh CJ reviewed and edited the manuscript; Jong GP and Yeh CJ also share equal contribution; all authors were contributed to drafting and/or revising the article; and all authors approved the final version to be published.

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Abstract

BACKGROUND

Burnout, musculoskeletal pain, and sharps injuries (SIs) affect medical workers.

AIM

To establish a model between SIs, burnout, and the risk factors to assess the extent to which burnout affects SIs.

METHODS

This questionnaire was used for an observational and cross-sectional study, which was based on members at a hospital affiliated with a medical university in Taichung, Taiwan, in 2020. The valid responses constituted 68.5% (1734 of 2531). The items were drawn from the Nordic Musculoskeletal Questionnaire and Copenhagen burnout inventory and concerned work experience, occupational category, presence of chronic diseases, sleep duration, overtime work, and work schedule. Factor analysis, chi-square test, Fisher exact test, Multiple linear, logistic regression and Sobel test were conducted. The present analyses were performed using SAS Enterprise Guide 6.1 software (SAS Institute Inc., Cary, NC, United States), and significance was set at $P < 0.05$.

RESULTS

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Personal and work-related burnout ranks, sex, work experience ranks, occupational groups, drinking in the past month, sleep duration per day, presence of chronic diseases, overtime work ranks, and work schedule were associated with SIs. Frequent upper limb and lower limb pain (pain occurring every day or once a week) determined to be related to SIs. High personal burnout (> Q3) and high work-related burnout (> Q3) mediated the relationship between SIs and frequent lower limb pain. Similarly, frequent lower limb pain mediated the relationship of SIs with high personal and high work-related burnout. High personal and high work-related burnout mediated the relationships of SIs with overtime work and irregular shift work. The mediating model provides strong evidence of an association between mental health and SIs.

CONCLUSION

Burnout was determined to contribute to SIs occurrence; specifically, it mediated the relationships of SIs with frequent musculoskeletal pain, overtime work, and irregular shift work.

Key Words: Personal burnout; Work-related burnout; Sharps injuries; Musculoskeletal pain; Mediating factor; Overtime work

Core Tip: Burnout affects approximately half of all nurses, physicians, and other clinicians. Sharps injuries, which frequently occur among health care workers, constitute a critical problem. Our study found burnout was determined to contribute to sharps injuries occurrence; specifically, it mediated the relationships of sharps injuries with frequent musculoskeletal pain, overtime work, and irregular shift work. Results from the present study suggest that if the problem of burnout is ignored, training or safe operation may not be sufficient to effectively prevent work-related injuries. To the best of our knowledge, this finding has never been reported.

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INTRODUCTION

In May 2018, burnout was recognized as an "occupational phenomenon" in the International Classification of Diseases, 11th Revision (ICD-11) of the World Health Organization. Burnout is a state of physical, emotional, and mental exhaustion that results from long-term involvement in work situations that are emotionally demanding[1]. The specific definition of burnout in the ICD-11 is "a syndrome conceptualized as resulting from chronic workplace stress that has not been successfully managed."

Burnout is responsible for high physician turnover and reduced clinical hours, which cause total losses of approximately 4.6 billion dollars in the United States each year[2]. Moreover, burnout affects approximately half of all nurses, physicians, and other clinicians[3]. Studies on resident physicians and nurses have indicated that most cases of burnout are personal or work-related. Studies have noted that work-related burnout (WB) and personal burnout (PB) occur in 30% and 50% of individuals with burnout, respectively[4]. Notably, burnout also affects the patient-related quality of care[5]. The numerous reasons for the development of burnout include basic demographic characteristics such as sex[4,6] and age[7]; occupational factors such as work experience (WE)[8], overtime (OT) work[9], and shift work[10]; lifestyle habits such as sleep duration (SLD)[10,11] and exercise[11]; and health status (*e.g.*, the presence of chronic diseases)[12].

In the United States, 13% of the workforce experience losses in productivity stemming from a painful physical condition, amounting to an estimated US$61.2 billion in pain-related lost productive time each year[13]. Musculoskeletal (MS) in the lower back, shoulders, and neck are most commonly reported[14]. In addition, myofascial pain syndromes from trigger points are among the main causes of MS pain due to traumatic/micro traumatic events (often secondary to occupational postures/attitudes/activities)[15].

The United States Centers for Disease Control and Prevention defines sharp injuries (SI) as an exposure event (blood/body fluid exposure) that occurs when a needle or other sharp object penetrates the skin. SI frequently occurs among health care workers and constitutes a critical infective problem upon contamination of the sharp object. As one study noted, 0.42 hepatitis B infections, 0.05 to 1.30 hepatitis C infections, and 0.04 to 0.32 human immunodeficiency virus (HIV) infections develop per 100 cases of SI per year. The literature review conducted in that study revealed that SIs led to mean costs of €1966 if the source patient was HIV positive and had coinfections of hepatitis B and hepatitis C[16]. SI occurrence has been reported to be associated with occupational factors such as WE[17], work hours[18], and shift work schedules[19] as well as demographic characteristics such as sex[20] and age[21]. Moreover, one article asserted that the experience of SIs was related to the mental health of health care workers[22]. Therefore, the relationship between burnout level (as measured using a routine questionnaire) and SI deserves scholarly attention with regard to the prevention of work-related injuries among medical personnel. In the present study, a model of causal relationships between SI, burnout, and work-related risk factors was established to assess the extent to which burnout affects SI. This investigation serves as a basis on which the impact of mental health on occupational injuries can be further explored in the future. Specifically, the present study examined the relationship between mental health and occupational injuries, with burnout and SI as agent variables.

MATERIALS AND METHODS

This questionnaire was used for an observational and cross-sectional study, which was based on members at a hospital affiliated with a medical university in Taichung, Taiwan, in 2020. Of the 2531 individuals to whom the questionnaire was sent, 1838 (72.6%) completed the questionnaire. After exclusion for missing data, 1734 questionnaires (68.5%) were determined to be valid.

The participants' WE (years) and occupational category were provided by the occupational safety department of the hospital. On the questionnaire, the participants were asked whether they had a listed chronic disease (CD), with the selection of one or more diseases classified as a "yes" response. The participants were also asked whether they had experienced a SI in the past year. In response to the question on smoking in the past month, "never" or "have quit smoking" were classified as "no." As for drinking in the preceding month, answers of "seldom" or "every day" were classified as "yes," whereas "never" was classified as "no." SLD was classified as < 5, 5–6, 6–7, 7–8, or > 8 h. The participants were asked whether they exercised at least once a day, at least once a week, at least once a month, less than once a month, or never. Possible responses to the question on OT work were the following: seldom, fewer than 45 h per month, 45–80 h per month, and more than 80 h per month. The responses were classified as seldom, < 45 h per month, and > 45 h per month accordingly. As for work schedule, the options given were day shift work, night shift work, irregular shift work, and regular shift work.

This study adopted the Nordic MS Questionnaire (NMQ) modified and translated by the Taiwan Institute of Occupational Safety and Health[23]. The NMQ, which is used in the investigation of the site and frequency of MS pain, was developed in a project funded by the Nordic Council of Ministers. The NMQ has acceptable reliability [23] and has been applied in a wide range of occupational groups, including nurses [24]. Items on the NMQ include questions on the presence of pain attributable to work-related factors in the preceding year and on the pain sites, the options for which were the neck (N1), left shoulder (N2), right shoulder (N3), upper back (N4), waist or lower back (N5), left elbow (N6), right elbow (N7), left wrist (N8), right wrist (N9), left hip/thigh/buttock (N10), right hip/thigh/buttock (N11), left knee (N12), right knee (N13), left ankle (N14), and right ankle (N15). If a participant answered "yes" to the question on the experience of work-related pain over the past year, they were instructed to indicate its frequency: every day, once a week, once a month, or once

every half year. Pain occurring every day or once a week was defined as frequent MS (FMS) pain and was scored as 1. Pain occurring once a month or once every half year was scored as 0.

In the present study, factor analysis was conducted on the NMQ results to determine the underlying variables that explained most of the questionnaire. According to the principle proposed by Hair *et al*[25], factors that should be retained have feature vector values exceeding 1. Through varimax rotation, the standardized scoring coefficients constituted new factor loadings and were defined as new factors according to the corresponding significance of the factor loadings.

The Copenhagen burnout inventory (CBI), which comprises three scales assessing PB, WB, and client-related burnout, has extremely high internal reliability and low nonresponse rate[26]. The present study used the Chinese version of CBI, which has proven to be a reliable and valid tool for assessment of burnout problems[27]; thus, it was used to evaluate burnout in the present study, with a focus on PB and WB. The first six items, which concern PB, are as follows: C1: "How often do you feel tired?" C2: "How often are you physically exhausted?" C3: "How often are you emotionally exhausted?" C4: "How often do you think 'I can't take it anymore'?" C5: "How often do you feel worn out?" C6: "How often do you feel weak and susceptible to illness?"

Items 7–13, which concern WB, are as follows: C7: "Is your work emotionally exhausting?" C8: "Do you feel burnt out because of your work?" C9: "Does your work frustrate you?" C10: "Do you feel worn out at the end of the working day?" C11: "Are you exhausted in the morning at the thought of another day at work?" C12: "Do you feel that every working hour is tiring for you?" C13: "Do you have enough energy for family and friends during leisure time?"

The response options-"always", "often", "sometimes", "seldom", and "never/almost never"-are scored as 100, 75, 50, 25, and 0 points, respectively, except for item C13, which is inverse scored (*i.e.*, the responses are scored as 0, 25, 50, 75, and 100 points, respectively). Levels of PB and WB are represented by the mean of the total PB and WB scores (the sum of scores on items C1–C6 and items C7–C13), respectively.

The categorical variables were subjected to the chi-square test or Fisher exact test. Significance in the differences among the means of continuous variables was determined using the *t* test or one-way ANOVA. Multiple linear or logistic regression was conducted to control the interference of potential risk factors in the association between the independent variables (IVs) and the dependent variable (DV)-specifically, to determine whether adjustments to variables significantly affected IV–DV associations. Mediation effects were analyzed on the basis of the strategy proposed by Baron and Kenny[28] in which: (1) The IV significantly affects the mediator (first-stage effect); (2) The IV significantly affects the DV in the absence of the mediator; (3) The mediator has a significant unique effect on the DV (second-stage effect); and (4) The effect of the IV on the DV weakens upon addition of the mediator to the model. A method for mediation suitable for a combination of categorical and continuous variables, developed by Iacobucci[29], was used; the (formula 1) are as follows.

$$\hat{Y} = b_{01} + cX$$

$$\hat{M} = b_{02} + aX$$

$$\hat{Y} = b_{03} + c'X + bM$$

$$Z_a = \hat{a}/\widehat{S_a}$$

$$Z_b = \hat{b}/\widehat{S_b}$$

Where *X* is an IV; *Y* is a DV; *M* is the adjusted variable (*i.e.*, the mediating factor) in a simple mediation model; *a* is a logistic/Linear regression coefficient of *X* against *M* when *M* and *X* are a DV and IV, respectively; *b* is the logistic/Linear regression coefficient of *M* against *Y* in a simple mediation model; *c* is the logistic/Linear regression coefficient of *X* against *Y*; and *c*' is the logistic/Linear regression coefficient of *X* against *Y* with *M* as the adjusting variable. The standard errors of *a* and *b* are represented by s_a and s_b, respectively.

The original formula of the Sobel test was rederived into formula 2.

$$Z_{mediation}\,(Z_m) = \frac{\frac{a}{s_a}\times\frac{b}{s_b}}{\sqrt{{Z_a}^2+{Z_b}^2+1}}$$

Results exceeding |1.96| and |2.57| (for a two-tailed test) are significant at α = 0.05 and α = 0.01, respectively. The present analyses were performed using SAS Enterprise Guide 6.1 software (SAS Institute Inc., Cary, NC, United States), and significance was set at $P < 0.05$.

RESULTS

As shown in Table 1, the mean PB and WB scores were 36.69 ± 17.59 and 34.19 ± 16.29, respectively. SI incidence was 8.42%. Q1, Q2, and Q3 represented the lower quartile, median, and upper quartile, respectively. The highest proportions of SIs (12.55% and 12.42%) corresponded to PB and WB (rank > Q3 for both), respectively. Differences in SI occurrence were significant among the PB or WB ranks. Women reported higher PB and WB than men (37.39 *vs* 33.64 and 34.89 *vs* 31.13, respectively; $P < 0.01$ for both), but SIs were more common in men (13.85% *vs* 7.17%; $P < 0.01$). Regarding WE, ranks > Q2 and ≤ Q3 corresponded to the highest PB level (mean = 38.94 ± 17.60), whereas a rank > Q3 corresponded to the lowest WB level (mean = 31.36 ± 15.46). Moreover, ranks > Q1 and ≤ Q2 with regard to WE corresponded to the highest proportion of SI occurrence (12.21%). Significant differences in the proportion of SI occurrence and in the levels of PB and WB were noted among occupational groups, with nurses experiencing the highest PB and WB (41.22 and 39.33). Notably, SIs occurred most commonly among physicians (15.86%). Levels of PB (mean = 39.51) and WB (mean = 36.17) were significantly higher in participants who reported drinking during the preceding month, as was SI occurrence (11.41%). SLD was significantly associated with PB level, WB level, and SI occurrence. The highest PB and WB (mean scores = 48.52 and 41.82, respectively) were observed in the participants who reported sleeping ≤ 5 h per night, as was the highest SI occurrence (14.52%). The participants who exercised daily reported significantly lower PB and WB (mean scores = 31.27 and 28.84, respectively) than those who exercised less frequently, but no significant difference in SI occurrence was noted. Compared with those without such conditions, the participants with CD had significantly higher levels of PB and WB (mean scores = 38.69 and 35.43, respectively) and were more likely to have sustained an SI (10.53%). Burnout levels and SI occurrence differed significantly according to the monthly number of OT hours. Specifically, the participants who worked > 45 h per month had the highest PB and WB (mean scores = 48.51 and 43.73, respectively). These individuals were also the most likely to have sustained an SI (16.98%). Burnout levels and SI occurrence also differed significantly with work schedule. Specifically, the participants who worked irregular shifts reported the highest PB and WB (mean scores = 43.54 and 40.90, respectively) as well as the highest SI occurrence (13.45%).

Table 2 presents information on the sites and occurrence of MS pain experienced over the 12 mo as well as the sites and proportion of MS pain that occurred at least once a week (*i.e.*, FMS pain). Because the eigenvalues of factors 1 and 2 exceeded 1, these factors were retained. Although the eigenvalue of factor 3 was lower than 1, it was retained for the maximum explaining questionnaire. The factor loadings were converted into standardized scoring coefficients through varimax rotation. The relatively large factor loading values in bold for factors 1, 2, and 3 correspond to pain in the upper trunk, lower limbs, and upper limbs, respectively. Frequent upper torso pain (FUTP) occurred in the neck, both shoulders, and upper back, and its standardized coefficient was defined as FUTP. As for frequent lower limb pain (FLLP), sites included both hip/thigh/buttocks, both knees, and both ankles, and its standardized coefficient was defined as FLLP. Frequent upper limb pain (FULP) occurred in both elbows and both wrists, and its standardized coefficient was defined as FULP. The explained variation in FUTP, FLLP, and FULP was 73.86%, 23.11%, and 8.67%, respectively. This indicated that the participants experienced upper trunk pain most frequently, followed by lower limb and upper limb pain. Although FULP had the smallest explained variation of the three, it was retained because the present study was focused on the relationship between SI and upper limb pain.

Table 3 shows that the participants who had experienced an SI in the preceding year had significantly higher FLLP and FULP scores than those who had not, but no significant differences were noted for the FUTP score. In short, FLLP and FULP were identified as risk factors for SIs.

Because of the extremely high proportion of SIs corresponding to PB or WB ranks > Q3 (Table 1), PB rank was reclassified as PB > Q3 and PB ≤ Q3, and WB rank was reclassified as WB > Q3 and WB ≤ Q3. PB > Q3 and WB > Q3 corresponded to high PB level (HPBL) and high WB level (HWBL), respectively. Similarly, the participants who worked irregular shifts had significantly higher PB and WB scores; therefore, the work schedule was reclassified as irregular work shifts (IRWS) and other work schedules. Moreover, because SIs were only reported by nine participants who worked > 45 h of OT per month, OT work was reclassified as an experience of OT (EOT) work and seldom worked OT.

Table 1 Descriptive statistics concerning the results of the Copenhagen burn inventory and occurrence of sharps injuries (*n* = 1734)

Characters	*n*	PB score	WB score	SI
		mean ± SD	mean ± SD	Subject (%)
SI in past one year	1734	36.69 ± 17.59	34.19 ± 16.29	146 (8.42)
PB ranks				[1,b]
> Q3	542	56.93 ± 12.20	-	68 (12.55)
> Q2 and ≤ Q3	482	37.22 ± 3.31	-	30 (6.22)
> Q1 and ≤ Q2	394	27.08 ± 2.09	-	29 (7.36)
≤ Q1	316	13.12 ± 6.79	-	19 (6.01)
WB ranks				[1,b]
> Q3	451	-	54.66 ± 9.45	56 (12.42)
> Q2 and ≤ Q3	572	-	36.70 ± 4.03	39 (6.82)
> Q1 and ≤ Q2	344	-	26.61 ± 1.78	25 (7.27)
≤ Q1	367	-	12.20 ± 7.27	26 (7.08)
Sex		[b]	[b]	[2,b]
Male	325	33.64 ± 16.48	31.13 ± 15.28	45 (13.85)
Female	1409	37.39 ± 17.77	34.89 ± 16.44	101 (7.17)
WE ranks		[b]	[b]	[1,b]
≤ Q1	375	36.23 ± 17.73	34.72 ± 17.37	34 (9.07)
> Q1 and ≤ Q2	434	37.29 ± 17.98	35.12 ± 16.10	53 (12.21)
> Q2 and ≤ Q3	487	38.94 ± 17.60	35.48 ± 16.06	38 (7.80)
> Q3	438	34.07 ± 16.73[c]	31.36 ± 15.46	21 (4.79)
Occupation groups		[c]	[c]	[1,b]
Doctors	145	37.10 ± 17.37	34.11 ± 16.78	23 (15.86)
Nurses	627	41.22 ± 17.27	39.33 ± 15.55	55 (8.77)
Others	962	33.67 ± 17.20	30.84 ± 15.82[c]	68 (7.07)
Right-handed				
Yes	1663	36.89 ± 17.64	34.31 ± 16.31	142 (8.54)
No	71	31.87 ± 15.62	31.34 ± 15.48	4 (5.63)
Drinking in past month		[c]	[b]	[2,b]
Yes	561	39.51 ± 17.05	36.17 ± 16.03	64 (11.41)
No	1173	35.34 ± 17.69	33.24 ± 16.33	82 (6.99)
Smoking in past month				
Yes	12	31.60 ± 16.80	25.89 ± 17.04	2 (16.67)
No	1722	36.72 ± 17.60	34.24 ± 16.27	144 (8.36)
SLD (per day) ranks		[c]	[c]	[1,a]
≤ 5 h	62	48.52 ± 20.62	41.82 ± 17.57	9 (14.52)
> 5 and ≤ 6 h	566	41.04 ± 17.91	38.26 ± 16.47	54 (9.54)
> 6 and ≤ 7 h	771	34.91 ± 16.38	32.35 ± 15.40	66 (8.56)
> 7 h	335	31.23 ± 16.47	29.89 ± 15.80	17 (5.07)
Exercise per day		[b]	[c]	
Yes	133	31.27 ± 18.88	28.84 ± 17.87	11 (8.27)
No	1601	37.14 ± 17.41	34.63 ± 16.08	135 (8.43)

Suffering chronic disease		[b]	[a]	[2,a]
Yes	608	38.69 ± 17.95	35.43 ± 16.70	64 (10.53)
No	1126	35.61 ± 17.31	33.51 ± 16.02	82 (7.28)
OT work ranks		[c]	[c]	[1,b]
> 45 h / mo	53	48.51 ± 19.78	43.73 ± 18.34	9 (16.98)
< 45 h / m	481	41.32 ± 17.21	39.27 ± 15.82	58 (12.06)
Seldom	1200	34.31 ± 17.07[c]	31.73 ± 15.75	79 (6.58)
Work schedule classes		[c]	[c]	[1,b]
Irregular shift	223	43.54 ± 18.63	40.90 ± 16.91	30 (13.45)
Regular shift	204	37.89 ± 17.15	35.19 ± 15.19	25 (12.25)
Night	204	37.77 ± 18.14	37.45 ± 16.26	17 (8.33)
Day	1103	34.88 ± 16.99	32.04 ± 15.89	74 (6.71)

[1]Chi-square test.
[2]Fisher exact test.
[a]$P < 0.05$.
[b]$P < 0.01$.
[c]$P < 0.0001$. OT: Over time; PB: Personal burnout; SD: Standard deviation; SI: Sharp injuries; SLD: Sleep duration; WB: Work-related burnout.

Table 2 Sites of musculoskeletal pain and factor analysis of the Nordic musculoskeletal questionnaire, *n* (%)

Pain site	Pain past 12 months	FMS pain	Factor loadings		
	Subjects	Subjects	Factor 1: Upper torso	Factor 2: Lower limb	Factor 3: Upper limb
Neck	636 (36.68)	405 (23.36)	0.29	-0.04	-0.05
Left shoulder	370 (21.34)	234 (13.49)	0.27	-0.06	-0.03
Right shoulder	444 (25.61)	283 (16.32)	0.29	-0.05	-0.02
Upper back	327 (18.86)	210 (12.11)	0.19	0	0.01
Waist or lower back	529 (35.01)	300 (17.30)	0.12	0.02	0
Left elbow	65 (3.75)	35 (2.02)	-0.03	-0.02	0.25
Right elbow	126 (7.27)	81 (4.67)	-0.01	-0.04	0.27
Left wrist	103 (5.94)	67 (3.86)	-0.03	0	0.24
Right wrist	205 (11.82)	110 (6.34)	-0.02	-0.04	0.31
Left hip/thigh/buttock	70 (4.04)	48 (2.77)	-0.04	0.19	0.04
Right hip/thigh/buttock	70 (4.04)	45 (2.60)	-0.04	0.19	0.05
Left knee	95 (5.48)	51 (2.94)	0.04	0.2	-0.09
Right knee	88 (5.08)	51 (2.94)	0.02	0.29	-0.11
Left ankle	42 (2.42)	31 (1.79)	-0.06	0.23	0
Right ankle	51(2.94)	39 (2.25)	-0.05	0.21	0
Eigenvalues			4.02	1.26	0.47
Explained variation (%)			73.86	23.11	8.67

The relatively large factor loading values were marked in bold for corresponding to musculoskeletal pain sites.

Figure 1 shows the mediation effect of burnout in the association between SIs and the risk factors. The value of *c* must be statistically significant and greater than that of *c*′. Moreover, the values of *a* and *b* must be statistically significant. In addition, $a \times b$ and c-c' must differ significantly and be able to be tested by calculating the $Z_{mediation}$ value (Z_m). HPBL partially mediated the relationships of SI with FLLP ($Z_m = 2.84$),

Table 3 Differences in frequent musculoskeletal pain scores between participants who had and had not experienced an sharps injury in the preceding year

FMS pain score	With SIs in past year	Without SIs in past year	*P* value
	mean ± SD	mean ± SD	
FUTP	0.11 ± 0.97	-0.01 ± 0.86	
FLLP	0.24 ± 1.17	-0.02 ± 0.78	[b]
FULP	0.16 ± 0.96	-0.02 ± 0.70	[a]

[a]$P < 0.05$.

[b]$P < 0.01$. FMS: Frequent musculoskeletal; FUTP: Frequent upper torso pain; Sis: Sharps injuries.

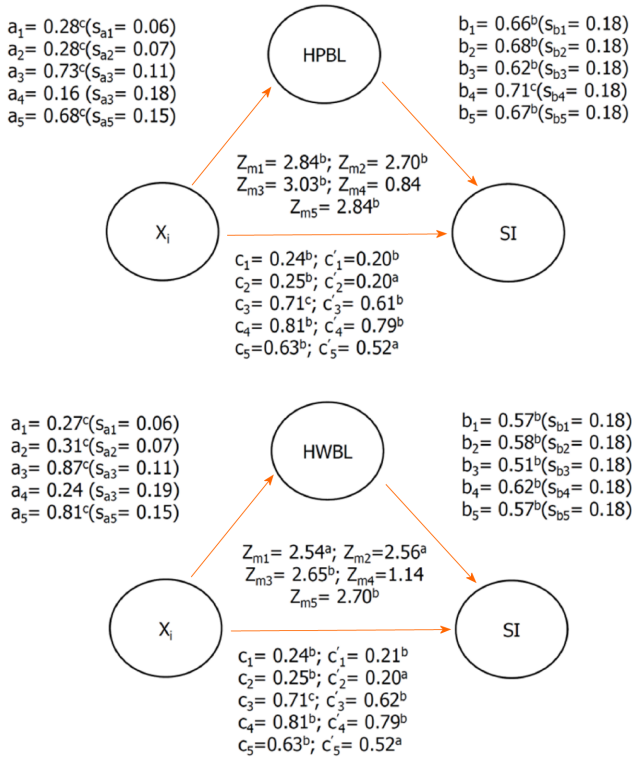

Figure 1 Mediation effects of high personal burnout level/high work-related burnout level in the association between sharps injuries and X_i. $^aP < 0.05$, $^bP < 0.01$, $^cP < 0.0001$. $_1$: Frequent lower limb pain; $_2$: Frequent upper limb pain; $_3$: Experience of overtime *vs* seldom worked overtime; $_4$: Doctors *vs* Nurses and others; $_5$: Irregular work shifts *vs* other work schedules; *ai*: The logistic regression coefficient of risk factors for the association between sharps injurie (SI) and risk factors; s_{ai}: The standard error of a_i; b_i: The logistic regression coefficient of burnout as an adjusted variable with regard to the association between SI and X_i; s_{bi}: The standard error of b_i. SI: Sharps injurie; HPBL: High personal burnout level; HWBL: High work-related burnout level.

FULP (Z_m = 2.70), EOT work (Z_m = 3.03), and IRWS (Z_m = 2.84). HWBL partially mediated the relationships of SI with FLLP (Z_m = 2.54), FULP (Z_m = 2.56), EOT work (Z_m = 2.65), and IRWS (Z_m = 2.70). A strong relationship between FMS pain and burnout was observed, but whether FMS pain also mediated the relationship between SI and burnout remains to be determined. Figure 2 shows FLLP significantly mediated the relationships of SI with HPBL (Z_m = 2.44) and HWBL (Z_m = 2.40). By contrast, the mediating effect of FULP was not significant. Neither FLLP nor FULP mediated the relationships of SI with EOT work, being a physician, and IRWS.

From the analytical results (Table 1-3, Figure 1 and 2), the following inferences can be made: an increase in the frequency of limb pain was closely correlated with an increase in SI incidence, and an increase in burnout level caused by an increase in the frequency of limb pain increased SI occurrence. The participants with HPBL accounted for a higher proportion of the SIs that occurred, and the increase in FLLP caused by HPBL also raised the proportion of SI occurrence. The participants with EOT work were more likely to sustain an SI, as were the participants experiencing serious burnout caused by OT work, which would increase the rate of SI occurrence. Similarly,

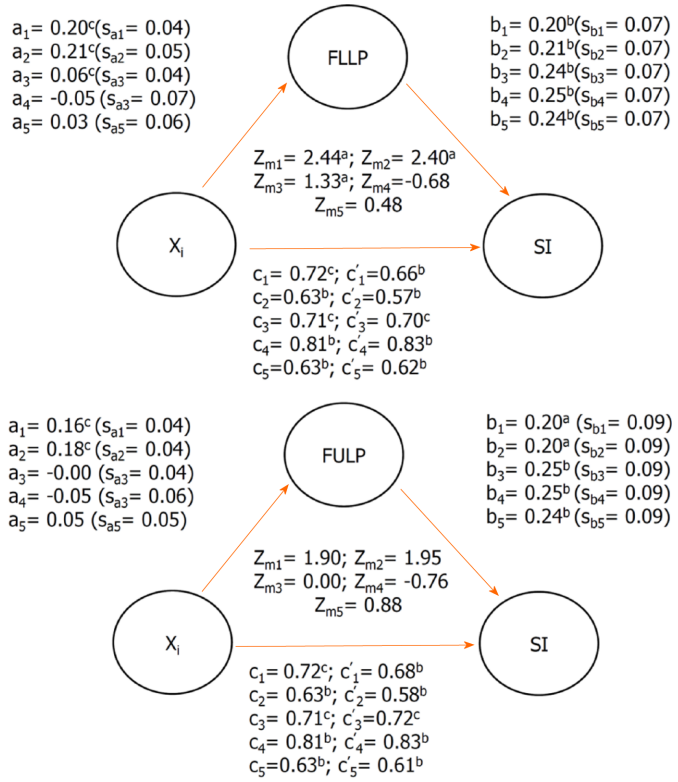

Figure 2 Mediation effects of frequent lower limb pain/frequent upper limb pain in the association between sharps injuries and X_i. $^aP <$ 0.05, $^bP < 0.01$, $^cP < 0.0001$. $_1$: High personal burnout level; $_2$: High work-related burnout level; $_3$: Experience of overtime *vs* seldom worked overtime; $_4$: Doctors *vs* Nurses and others; $_5$: Irregular work shifts *vs* other work schedules; a_i: The logistic regression coefficient of risk factors for the association between sharps injuries (SI) and risk factors; s_{ai}: The standard error of a_i; b_i: The logistic regression coefficient of burnout as an adjusted variable with regard to the association between SI and X_i; s_{bi}: The standard error of b_i. SI: Sharps injurie; FLLP: Frequent lower limb pain; FULP: Frequent upper limb pain.

the participants with IRWS were also more likely to sustain an SI, as were the participants experiencing serious burnout caused by IRWS, which would increase the rate of SI occurrence.

Constructed on the basis of the results presented in Figure 1 and 2 is a simple mediation model that indicates the existence of direct or mediating relationships between SI and FLLP, HPBL/HWBL, and EOT work or IRWS. HPBL and HWBL mediated the SI–FLLP relationship. Similarly, FLLP was a mediating factor in the relationships of SI with HPBL and HWBL. Furthermore, HPBL and HWBL mediated the relationships of SI with EOT work and IRWS.

DISCUSSION

In line with reports that both PB and WB levels are significantly higher among female resident physicians[4] and that male nurses experience burnout syndrome less commonly than female nurses[6], the women in the present sample reported significantly higher PB and WB than the men (Table 1). Regarding SIs, a study indicated that male health workers were 10 times more likely to sustain an SI than were female health workers[30]. The men in the present study were more likely to sustain SIs than the women (13.85% *vs* 7.17%).

Studies have reported that nurses and clinicians working OT are more likely to experience burnout[9]. In one study, an increase in weekly work hours increased the occurrence of SIs among nurses[31]. As shown in Table 1, a dose–response relationship between SI and OT work (> 45, < 45 h, or seldom) was observed. Similar results were noted for relationships of PB and WB with OT. Specifically, more OT work hours increased SI occurrence and the mean levels of PB and WB, and PB and WB was positively associated with SIs. These results suggest that OT work was related to PB and WB level as well as to SI occurrence. PB and WB may contribute critically to the relationship between SI and OT work; this possibility warrants further investigation. As shown in Figure 1, PB and WB partially mediated the relationship between SI and

EOT work; the effects were significant. These results suggest that EOT work affected SI directly or indirectly (through an unknown path). Studies have noted that increased OT was significantly associated with impairments in attention, executive function[32], and stress response[33]. Whether OT work affects SI incidence through these factors remains to be determined.

One study noted that burnout syndrome was more common among nurses working irregular shifts than among those working regular shifts[6]. In the same vein, studies have observed that working regular shifts exerted protective effects against Sis[19,21]. Consistent with results from other studies, in the present study, the highest mean PB and WB was reported by participants working irregular shifts (Table 1). As shown in Figure 1, PB and WB also partially mediated the relationship between SI and irregular shifts, indicating that irregular shifts may have affected SI through burnout in some participants; in others, irregular shifts may have exerted direct effects on SI through other routes.

A large study conducted in the Netherlands on MS pain occurring over 12 mo reported that lower back pain occurred the most frequently (43.9%), followed by shoulder pain (30.3%) and neck pain (31.4%)[14]. In line with these results, the corresponding occurrence of low back pain, shoulder pain, and neck pain in the present study was 35.01%, 46.95%, and 36.68%, respectively (Table 2). A study on seven occupational groups in Norway reported a significant association between burnout and MS pain[34]. In the present study, the frequency of limb pain (lower or upper) was positively associated with HPBL and HWBL (a = 0.28, P < 0.0001; a = 0.28, P < 0.0001; Figure 1). A cross-sectional study on burnout and occupational accidents in which the Maslach Burnout Inventory (MBI) questionnaire was administered to employees in the occupational medicine department of a hospital reported that each one-unit increase in the burnout score corresponded to a 9% increase in the risk of injury[35]. In a study on Chinese nurses in which the MBI questionnaire was again used, emotional exhaustion was positively associated with SI occurrence[36]. Regarding the present results obtained from the CBI, SI occurrence differed significantly in PB (P < 0.01) and WB ranks (P < 0.01) (Table 1). As shown in Figure 2, HPBL (c = 0.72, P < 0.001) and HWBL (c = 0.63, P < 0.01) were positively associated with SI occurrence. The present results are consistent with those from other studies that used the MBI. However, in an extension of the literature, we further explored the causal relationships between SI, work-related risk factors, and burnout through the analysis of mediating effects. As shown in Figure 2, FLLP also mediated the relationships of SI with HPBL and HWBL, indicating that FLLP and HPBL or HWBL form a vicious circle with SI (Figure 3). These findings serve as a valuable reference for SI prevention. To test for significance, we used the Z_m formula developed by Iacobucci[29], which can effectively test for mediating effects in samples exceeding 300 when X, Y, and M are categorical variables. The present sample size of 1734 more than meets this requirement. Therefore, the Z_m formula was suitable.

WE, drinking in the preceding year, SLD, exercise, and CD, variables adjusted in the model, were identified as risk factors for SI and burnout. The significant association of these variables with SI and burnout is supported by results from other studies. For example, studies have indicated that individuals with less WE are at a higher risk of sustaining SIs[17], and the report of burnout was significantly positively associated with higher alcohol consumption[37]. Moreover, PB has been demonstrated to be significantly associated with impaired sleep quality[11], and reductions in SLD increase the risk of occupational injury[38]. University students or nurses who engage in physical activity or exercise have been noted to report significantly lower levels of PB and fatigue[11], and individuals with burnout appear to be more susceptible to physical illness than those without burnout[39]. Therefore, the adjustment of these variables was both necessary and appropriate for reducing the impacts of possible confounders on the SI model.

The burnout mediation model regarding SI and occupational risk factors (*e.g.*, OT work, irregular shift, and MS pain) provides strong evidence of an association between mental health and SIs. The literature mostly examines the relationship between SI and the work process or the use of protective equipment; deeper psychological factors are seldom explored. The relationship between SIs and work-related injuries not induced by burnout warrants further investigation. A study on 112 workers in metal melting industries reported no significant association between occupational burnout and unsafe actions[40]. Despite the small sample size in that study, results from both that study and the present study suggest that if the problem of burnout is ignored, training or safe operation may not be sufficient to effectively prevent work-related injuries. Therefore, to mitigate the problem of work-related injuries, institutions should take effective countermeasures to alleviate burnout among medical personnel.

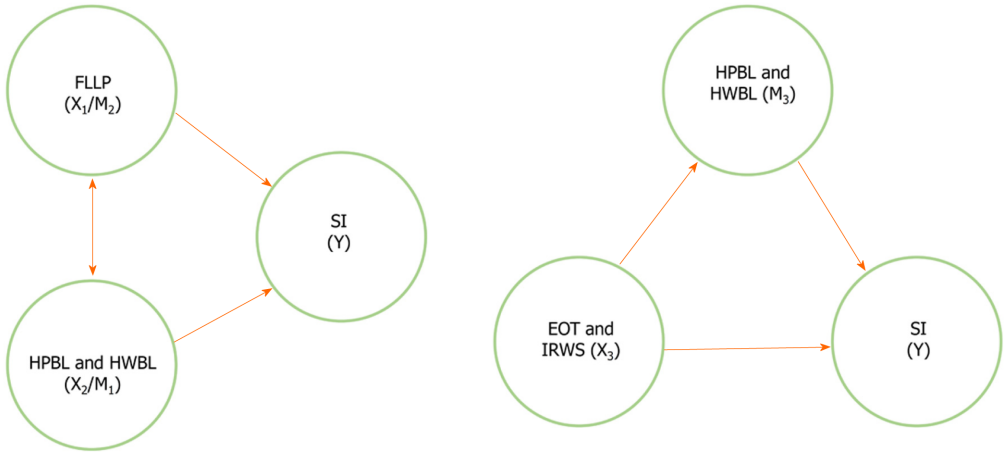

Figure 3 Simple mediation model for burnout and frequent lower limb pain. X_i and Y are the independent and dependent variables, respectively, whereas M_i is the mediating factor of sharps injuries (Y) and X_i. FLLP: Frequent lower limb pain; HPBL: High personal burnout level; HWBL: High work-related burnout level; EOT: The experience of overtime (work); IRWS: Irregular work shifts.

This study was performed in the context of the coronavirus disease 2019 pandemic, which may have been more demanding on medical personnel than the non-pandemic period. Therefore, a similar study that assesses the regular work conditions and exposure of health care workers during the non-pandemic period should be replicated and compared with the result of the pandemic period.

CONCLUSION

Burnout was determined to contribute to SI occurrence; specifically, it mediated the relationships of SI with FUTP, FLLP, EOT, and IRWS. FLLP also mediated the relationship between SI and burnout, forming a vicious circle of burnout and FLLP that further increased the frequency of SIs. To the best of our knowledge, this finding has never been reported. The present findings serve as a reference for the management of mental health and the prevention of SIs among medical personnel worldwide.

ARTICLE HIGHLIGHTS

Research background

Burnout affects approximately half of all nurses, physicians, and other clinicians. Sharps injuries, which frequently occur among health care workers, constitute a critical problem in the hospital.

Research motivation

Studies conducted in many countries revealed the relationship between burnout level (as measured using a routine questionnaire) and sharps injury deserves scholarly attention with regard to the prevention of work-related injuries among medical personnel. However, studies assessing the extent to which burnout affects sharps injuries are scarce.

Research objectives

To be established a model between sharps injuries, burnout, and the risk factors to assess the extent to which burnout affects sharps injuries.

Research methods

A questionnaire was used for an observational and cross-sectional study, which was based on members at a hospital affiliated with a medical university in Taichung, Taiwan, in 2020. The valid responses constituted 68.5% (1734 of 2531). The items were drawn from the Nordic Musculoskeletal Questionnaire and Copenhagen burnout inventory and concerning work experience, occupational category, presence of chronic diseases, sleep duration, overtime work, and work schedule. Factor analysis, chi-

square test, Fisher exact test, multiple linear, logistic regression, and Sobel test were conducted.

Research results

Our study found burnout was determined to contribute to sharps injuries occurrence; specifically, it mediated the relationships of sharps injuries with frequent musculoskeletal pain, overtime work, and irregular shift work.

Research conclusions

Burnout was determined to contribute to SIs occurrence; specifically, it mediated the relationships of sharps injuries with frequent musculoskeletal pain, overtime work, and irregular shift work.

Research perspectives

A similar study that assesses the regular work conditions and exposure of health care workers during the non-pandemic period should be replicated and compared with the result of the pandemic period.

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ORIGINAL ARTICLE

Observational Study

Association of overtime work and obesity with needle stick and sharp injuries in medical practice

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Author contributions: Chen YH and Yeh CJ conceived and designed this manuscript; Jong GP and Yeh CJ analyzed and interpreted the data of this study; Chen YH wrote the original draft; Jong GP and Yeh CJ reviewed and edited the manuscript; Jong GP and Yeh CJ also share equal contribution; all authors were contributed to drafting and/or revising the article, and all authors approved the final version to be published.

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Abstract

BACKGROUND

Needle stick and sharps injuries (NSIs) may cause infections among medical personnel. Obesity and overtime work among medical personnel increase the incidence of work injuries.

AIM

To investigate whether overtime work and obesity increase the risk of NSIs.

METHODS

This cross-sectional study used the data of 847 hospital personnel, including 104 doctors, 613 nurses, 67 medical laboratory scientists, 54 specialist technicians, and nine surgical assistants. Of them, 29 participants notified the hospital of having at least one NSI in 2017. The data collected included age, overtime work, body mass index, medical specialty such as doctor or nurse, and professional grade such as attending physician or resident. The χ^2 and Fisher's exact tests were used to compare categorical variables. Multiple logistic regression analysis and the Sobel test were used to assess the risk of NSIs.

RESULTS

Overtime work, body weight, and medical specialty were significantly associated with NSIs ($P < 0.05$). After adjustment for risk factors, heavy overtime work was an independent risk factor for NSIs, and healthy body weight and nursing specialty were independent protective factors against NSIs. After adjustment for risk factors, medical personnel with healthy body weight has half as many NSIs as

and revised according to the STROBE statement.

Country/Territory of origin: Taiwan

Specialty type: Public, environmental and occupational health

Provenance and peer review: Unsolicited article; Externally peer reviewed.

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those with unhealthy body weight; the proportion of NSIs in doctors with healthy body weight was 0.2 times that in doctors with unhealthy body weight; the proportion of injuries among residents was 17.3 times higher than that among attending physicians; the proportion of injuries among junior nurses was 3.9 times higher than that among experienced nurses; the proportion of injuries among nurses with heavy overtime work was 6.6 times higher than that among nurses with mild overtime work; and the proportion of injuries among residents was 19.5 times higher than that among junior nurses. Heavy overtime work mediated the association of medical specialty with NSIs.

CONCLUSION
In addition to promoting the use of safety needles and providing infection control education, managers should review overtime schedules, and medical personnel should be encouraged to maintain a healthy weight.

Key Words: Medical staff; Needle stick and sharps injuries; Overtime work; Healthy body weight; Obesity

Core tip: Needle stick and sharp injuries (NSIs) are complex multifactorial processes that are commonly observed in physical, psychological, and environmental fields. Therefore, preventing NSIs in medical personnel remains a critical health issue. To reduce the risk of NSIs, other factors affecting their incidence, such as medical specialty and body weight, should be analyzed. We investigated whether overtime and obesity increase the risk of NSIs. We also aimed to provide insights into the development of more effective prevention plans for NSIs. To the best of our knowledge, these findings have never been reported.

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INTRODUCTION

Needlestick and sharp injuries (NSIs) carry the risk of various infections, such as hepatitis B, hepatitis C, and human immunodeficiency virus (HIV) infections[1,2]. In 2000, occupational exposure to percutaneous injuries caused by medical personnel resulted in 16000 cases of hepatitis C, 66000 cases of hepatitis B, and 1000 cases of HIV worldwide[3]. The mean number of NSIs per 100 occupied beds per year was 4.8–7.6 from 2009 to 2011 in Japan[4]. Poor organizational climate and high workloads are associated with NSIs and near-misses in nurses[5]; however, the incidence of NSIs remains higher among doctors, commonly due to stress or overwork, followed by careless attitude[6]. This careless attitude can be effectively reduced by providing preventive education[7-10] and supplying protective equipment for procedures such as intravenous access or blood draws[5]. Some occupational factors, such as long working hours and overtime, can increase the risk of NSIs among medical personnel [11,12]; the risk of work-related injuries due to overtime has also been observed in other occupations[13]. According to the Survey of Occupational Injuries and Illnesses compiled by the United States Department of Labor, overtime work increased the injury hazard rate by 61%. In particular, the injury hazard rate was increased by 37% and 23% for work that lasted more than 12 h daily and 60 h, respectively, per week [13]. To ensure that medical services are promptly delivered, medical personnel routinely extend their working hours in cases of personnel shortage or sudden spikes in demand at the medical site. In Taiwanese hospitals, medical personnel working overtime mainly comprise doctors, 40% of whom work more than 60 h per week. In particular, 97% and 83% of doctors in medical centers and regional hospitals, respectively, work overtime[14].

Obesity has been significantly associated with diseases such as type 2 diabetes, cardiovascular diseases, and several forms of cancer[15] and occupational injuries[16]. Occupational injuries caused by obesity generally comprise sprains, strains, lower limb injuries, and falls[17]. However, a study found no significant relationship between obesity and contact with sharp material agents without adjusting for medical specialty and overtime work[16]. Male health workers were found to be 10 times more likely than female health workers to encounter NSIs[18]. Furthermore, low work experience was associated with high NSI incidence among nurses[9], and resident doctors (RDs) have a higher incidence of NSIs than do attending physicians (APs)[19]. NSI incidence among doctors differed from that among nurses[7], and RDs had a higher incidence than APs and nurses[19].

NSIs are complex multifactorial processes that are related to physical, psychological and environmental fields. Therefore, preventing NSIs in medical personnel remains a critical health issue. To further reduce the risk of NSIs, other factors affecting NSI incidence should be analyzed, such as medical specialty and body weight (BW), and an effective prevention plan should be developed accordingly.

MATERIALS AND METHODS

This cross-sectional study used data regarding doctors, nurses, and medical laboratory scientists working in Chung Shan Medical University Hospital, Taichung, Taiwan, recorded during 2017. The following data were collected: sex, age, height, weight, intensity of overtime work, medical specialty (doctor, nurse, medical laboratory scientist, specialist, or surgical assistant), professional level (AP or RD for doctors and N, N1, N2, N3 or N4 for nurses based on The Guidelines of Nursing Clinical Ladder System Program in Hospital). In this study, nurses with the professional level of N, which represents < 1 year of clinical work, were categorized as junior nurses (JNs) and nurses with higher levels were categorized as experienced nurses. We defined a medical laboratory scientist as a professional technician (excluding pathology laboratory personnel), a specialized technician as a specialist nurse in some medical specialty, and a surgical assistant as a person who assists a doctor in performing a surgical operation.

This study included 847 participants (104 doctors, 613 nurses, 67 medical laboratory scientists, 54 specialist technicians, and nine surgical assistants). Among them, 29 notified the hospital of having at least one NSI in 2017; NSIs were recorded by the hospital's occupational safety and health department. In this study, the aforementioned data were analyzed after depersonalization. Body weight was classified according to the definition of overweight or obesity by the Health Promotion Administration, Ministry of Health and Welfare. Specifically, body mass index (BMI) between 18.5 and 24.0 was considered a healthy BW (HBW), and any other BMI outside this range was considered an unhealthy BW (UHBW). Overtime work was classified according to the workload levels in the *Guidelines for Prevention of Diseases Caused by Abnormal Workloads (Second Edition)* from the Occupational Safety and Health Administration, Ministry of Labor. Specifically, extra work (both overtime and non-overtime) was categorized as slight (< 45 h/mo), moderate (45–80 h/mo), and heavy (> 80 h/mo) overtime work, respectively.

All statistical analyses were conducted using SAS v6.1 (SAS Institute, Cary, NC, United States). In addition, the χ^2 and Fisher's exact tests were used to compare categorical variables. Multiple logistic regression analysis was used to analyze the correlation of NSI with the study's main variables. The mediation effect was determined using the following approach proposed by Baron and Kenny (1986)[20]: (1) The independent variable (IV) significantly affects the mediator (first-stage effect); (2) The IV significantly affects the dependent variable (DV) in the absence of the mediator; (3) The mediator has a significant unique effect on the DV (second-stage effect); and (4) The effect of the IV on the DV decreases upon the addition of the mediator to the model. Finally, the Sobel test[21] was conducted to determine the significance of this mediation effect, for which the sample size was required to be at least 200[22]. Before performing the Sobel test, if the IV, mediator, or DV was not continuous, the logistic regression coefficient was standardized: X is an independent variable, Y is a dependent variable and M is an adjusting variable (mediating factor) in a simple mediating model. a is the unary logistic regression coefficient of X against M when M is the dependent variable and X is the independent variable. b is the logistic regression coefficient of M against Y in a simple mediating model. c is the unary logistic regression coefficient of X against Y, and c' is the logistic regression coefficient

of X against Y with M as the adjusting variable. Moreover, S_a and S_a were the standard errors of a and b, respectively. Mediation analysis for categorical variables was conducted following the method recommended by Iacobucci (2012)[23].

$$\hat{Y} = b_{01} + cX$$

$$\hat{M} = b_{02} + aX$$

$$\hat{Y} = b_{03} + c'X + bM$$

$$Z_a = \hat{a}/\widehat{S_a}$$

$$Z_b = \hat{b}/\widehat{S_b}$$

The original Sobel test formula was modified as follows:

$$Z_{mediation} = \frac{\frac{a}{s_a} \times \frac{b}{s_b}}{\sqrt{Z_a{}^2 + Z_b{}^2 + 1}}$$

It was considered significant at the α = 0.05 Level if its value exceeded |1.96| (for a two-tailed test with α = 0.05). In this study, statistical significance was indicated by $P < 0.05$.

This study was approved by Institutional Review Board of Chung Shan Medical University Hospital on December 2, 2019 (CSMUH No: CS19137).

RESULTS

Table 1 presents the participant characteristics, including sex, body weight, and level of overtime work. If the χ^2 test's assumptions were violated, Fisher's exact test was performed. Medical personnel were classified as doctors, nurses, and others (which included medical laboratory scientists, specialist nurses, and surgical assistants). Different types of medical personnel differed significantly in terms of NSI, sex, age, and moderate or heavy overtime (Table 1). Among them, the proportion of NSIs was the highest among doctors (7.7%). Furthermore, our cohort had an exceptionally low proportion of male nurses, with 95.9% of nurses being female; by contrast, the proportion of female doctors was lower (26.9%). Among the medical specialties, nurses were the youngest, with a mean age of 33.6 years. Moreover, no significant differences were observed in HBW between the three groups. The proportions of moderate and heavy overtime work among doctors (29.8% and 16.3%, respectively) were significantly higher than those among nurses and others.

Among doctors, APs and RDs differed significantly in terms of NSIs, sex, age, and moderate and heavy overtime, but not in terms of HBW. The proportion of NSIs among RDs (21.2%) was considerably higher than that among APs (21.2% *vs* 1.4%, $P < 0.01$). The significant difference in age between RDs and APs was expected due to the training system (45.5 *vs* 31.0, $P < 0.0001$). The proportion of moderate overtime was higher among APs than RDs (31.0% *vs* 27.3%, $P < 0.01$) but that of heavy overtime was considerably higher among RDs than APs (33.3% *vs* 8.5%, $P < 0.01$).

Nurses of different professional grades (N1–N4) differed significantly in terms of age ($P < 0.0001$) and moderate overtime ($P < 0.05$). Nurses with the professional level of N had the highest proportion of NSIs (6.2%). Age increased with the professional grade, which was expected due to the nursing clinical ladder system. Among nurses, nurses with the professional level of N had the highest proportion of moderate overtime work (32.6%), but the proportion of heavy overtime work was not the highest in this group (4.7%).

As presented in Table 2, the proportion of NSIs in participants with HBW was 0.5 times [odds ratio (OR) = 0.5, $P < 0.05$] that in participants with UHBW in the M_1 model of all participants. The proportion of NSIs in doctors with HBW was 0.2 times (OR = 0.2, $P < 0.05$) that in doctors with UHBW in the M_2 model of doctors. In addition, the proportion of NSIs in nurses with HBW was 0.5 times that in nurses with UHBW, but the difference was not significant.

Table 2 presents a clear effect of heavy overtime work on NSIs: medical personnel with heavy overtime work were 4.3–5.7 times more likely to experience an NSI than those with mild overtime work, and the difference was significant. Similarly, NSIs occurred 5.4 times more proportion in doctors with heavy overtime work (OR = 5.4, $P < 0.05$) than in those with slight overtime work; however, this effect could be

Table 1 Characteristics of study participants according to their medical specialty and professional grade

Variable	Total*n*	NSIs			Female			Age		HBW			Moderate OT			Heavy OT		
		n	%	*P*[1]	*n*	%	*P*[1]	mean ± SD	*P*[2]	*n*[3]	%	*P*[1]	*n*	%	*P*	*n*	%	*P*[1]
Profession groups																		
Doctors	104	8	7.7	[a]	28	26.9	[c]	40.9 ± 10.4	[c]	53	51.0	NS	31	29.8	[b]	17	16.3	[c]
Nurses	613	16	2.6		588	95.9		33.6 ± 8.3		354	57.8		147	24.0		28	4.6	
Others	130	5	3.9		95	73.1		40.6 ± 7.1		64	49.2		15	11.5		0	0.0	
Profession grade (doctor)																		
AP	71	1	1.4	[b]	14	19.7	[a]	45.5 ± 9.3	[c]	33	46.5	NS	22	31.0	[b]	6	8.5	[b]
RD	33	7	21.2		14	42.4		31.0 ± 2.9		20	60.6		9	27.3		11	33.3	
Profession grade (nurse)																		
N	129	8	6.2	[3]	119	92.2	NS	25.3 ± 3.3	[c]	78	60.5	NS	42	32.6	[a]	6	4.7	NS
N1	134	1	0.8		128	95.5		29.0 ± 4.9[b]		70	52.2		35	26.1		3	2.2	
N2	145	3	2.1		140	96.6		34.6 ± 6.7		84	57.9		24	16.6		9	6.2	
N3	143	4	2.8		140	97.9		40.5 ± 6.5		86	60.1		29	20.3		6	4.2	
N4	62	0	0		61	98.4		42.3 ± 4.8		36	58.1		17	27.4		4	6.5	

[a]$P < 0.05$.
[b]$P < 0.01$.
[c]$P < 0.0001$.
NS: Not significant.
[1]Chi-square test or Fisher's exact test.
[2]Moderate overtime work is 45–80 h/mo, and heavy overtime work is > 80 h/mo.
[3]Overweight/Obesity.
OT: Overtime; NSIs: Needle stick and sharps injuries.

explained by the other effects such as HBW (OR = 0.2, $P < 0.05$) and RDs (OR = 17.3, $P < 0.05$). Although nurses with heavy overtime work experienced more NSIs (OR = 3.7 and 3.8) than others, the difference was not significant.

Doctors experienced more NSIs incidence than other types of medical personnel, but the difference was nonsignificant (OR = 1.3–2.1, $P > 0.05$). After adjustment for other variables (M_1 model), the nurse specialty was identified as an independent protective factor for NSIs (OR = 0.3, $P < 0.05$). Among doctors, regardless of whether adjustments were made for other variables, being an RD was an independent risk factor for NSIs (OR = 18.9, $P < 0.01$ and OR = 17.3, $P < 0.05$). Similarly, among nurses, being a JN was also an independent risk factor for NSIs regardless of whether adjustments were made for variables (both OR = 3.9, $P < 0.01$).

Consequently, RDs and JNs were added to the logistic regression model in Table 3 for further exploring the relationships of BW and overtime work with NSI in professional experience. HBW was a protective factor against NSI occurred regardless of whether adjustments were made for variables (M_0, M_1, and M_2). However, after adjustment for HBW and RD effects, the effect of heavy overtime work was no longer significant (M_2, OR = 1.9, $P > 0.05$). The proportion of NSIs among RDs was 4.1 times (M_1, OR = 4.1, $P < 0.05$) higher than that among JNs without adjustment for variables; this increased to 19.5 times (M_2, OR = 19.5, $P < 0.05$) after adjustment for sex, age, overtime work, and body weight. Therefore, UHBW was determined to be an independent risk factor for NSIs in RDs and JNs.

Table 4 presents the results of multiple logistic regressions after adjusting for age for NSI because experienced nurses have a wider age distribution. The results indicated that the proportion of NSIs among nurses with heavy overtime work was 6.6 times (OR = 6.6, $P < 0.05$) higher than that among nurses with mild overtime work, and the difference was significant. However, the proportion of NSIs in nurses with HBW was 1.2 times (M_1, OR = 1.2, $P > 0.05$) that of nurses with UHBW, but the difference was not significant.

Table 5 illustrates the significant mediation effects ($Z_m = 2.5$, $P < 0.05$) of heavy overtime work on the relationship between NSIs and doctors. No mediation effects were noted for the other five combinations.

Table 2 Main effects on needle stick and sharps injuries in different models for all participants

Main effect		ORs of NSIs for All participants				ORs of NSIs for doctors				ORs of NSIs for nurses			
		N	*n*	M_0	M_1	*N*	*n*	M_0	M_2	*N*	*n*	M_0	M_2
Body weight level	HBW	471	11	0.5[NS]	0.5[a]	53	2	0.3	0.2[a]	354	7	0.6	0.5
	UHBW	376	18	1.0	1.0	51	6	1.0	1.0	259	9	1.0	1.0
OT work	Heavy	45	6	5.7[b]	4.3[a]	17	4	5.4[a]	2.0	28	2	3.7	3.8
	Moderate	193	7	1.4	1.2	31	1	0.6	0.5	147	5	1.7	1.4
	Mild	609	16	1.0	1.0	56	3	1.0	1.0	438	9	1.0	1.0
Type of medical personnel	Doctors	104	8	2.1	1.3	-	-	-	-	-	-	-	-
	Nurses	613	16	0.7	0.3[a]	-	-	-	-	-	-	-	-
	Others	130	5	1.0	1.0	-	-	-	-	-	-	-	-
Professional grade (Doctors)	RD	-	-	-	-	33	7	18.9[b]	17.3[a]	-	-	-	-
	AP	-	-	-	-	71	1	1.0	1.0	-	-	-	-
Professional grade (Nurses)	Junior	-	-	-	-	-	-	-	-	129	8	3.9[b]	3.9[b]
	experiencing	-	-	-	-	-	-	-	-	484	8	1.0	1.0

[a]$P < 0.05$.
[b]$P < 0.01$.
[c]$P < 0.0001$.
NS: Not significant.
Odds ratio = 1.0 indicates the reference; ORs: Odds ratios; *N*: Participants; *n*: Participants for needle stick and sharps injuries; M_0: Model only including main effect; M_1: Model adjusted for sex, age, overtime work, and medical specialty; M_2: Model adjusted for sex (only doctors), overtime work, professional grade, and body weight; HBW: Healthy body weight; UHBW: Unhealthy body weight; OT: Overtime; NSIs: Needle stick and sharps injuries.

Table 3 Main effects on needle stick and sharps injuries in various models for resident doctors and junior nurses

Main effect		*N*	ORs for NSIs			
			n	M_0	M_1	M_2
Body weight level	HBW	95	3	0.1[b]	0.1[b]	0.1[b]
	UHBW	52	12	1.0	1.0	1.0
OT work	Heavy	13	4	4.5[a]	4.5[a]	1.9
	Moderate	46	5	1.6	1.6	1.7
	Mild	88	6	1.0	1.0	1.0
Professional subfield	RD	26	7	4.1[a]	12.7[b]	19.5[a]
	JN	121	8	1.0	1.0	1.0

[a]$P < 0.05$.
[b]$P < 0.001$.
Odds ratio = 1.0 indicates the reference. ORs: Odds ratios; *N*: Participants; *n*: Participants for needle stick and sharps injuries; M_0: Model only including the main effect; M_1: Model adjusted for sex and age; M_2: Model adjusted for sex, age, and main effects; RD: Resident doctor; JN: Junior nurse; HBW: Healthy body weight; UHBW: Unhealthy body weight; OT: Overtime; NSIs: Needle stick and sharps injuries.

DISCUSSION

A cross-sectional study evaluating NSI incidence among 29 doctors and 51 nurses demonstrated that the proportion of NSIs among nurses was 0.2 times that among doctors[6]. A study including NSI data from 2002 to 2007 in a university hospital in Pakistan demonstrated that the number of NSIs has higher in junior doctors than in nurses[7]. The differences between doctors and nurses may stem from differences in their work patterns or attitudes. For example, doctors often experience NSIs during wound irrigation, sutures, incisions, handling body fluids, and tissue sample

Table 4 Main effects on needle stick and sharps injuries for experienced nurses

Main effect		Participants	ORs for NSIs		
			n	M_0	M_1
Body weight level	HBW	276	5	1.3	1.2
	UHBW	208	3	1.0	1.0
OT work	Heavy	22	2	7.0[a]	6.6[a]
	Moderate	105	1	0.7	0.7
	Mild	357	5	1.0	1.0

[a]*P* <0.05.

Odds ratio = 1.0 indicates the reference. ORs: Odds ratios; HBW: Healthy body weight; OT: Overtime; NSIs: Needle stick and sharps injuries; *n*: Participants for needle stick and sharps injuries; M_0: Model only including the main effect; M_1: Model adjusted for age, sex, body weight, and overtime work.

Table 5 Mediation effect of heavy overtime work and healthy body weight for needle stick and sharps injuries and the main effect

IV	Mediator factor												
	Heavy OT work[4]							HBW[5]					
	c	c'	a	s_a	b	s_b	Z_m	c'	a	s_a	b	s_b	Z_m
All participants													
Doctors[1]	1.1[a]	0.8	1.6[c]	0.3	1.4[b]	0.5	2.5*	1.0[a]	-0.2	0.2	-0.7[NS]	0.4	0.8
Doctors effect													
RD[2]	2.9[b]	2.6[a]	1.7[b]	0.6	1.1	0.8	1.2	3.3[b]	0.6	0.4	-1.8[a]	0.9	-1.1
Nurse effect													
JN[3]	1.4[b]	1.4[b]	0	0.5	1.2	0.8	0	1.4[b]	0.1	0.2	-0.6	0.5	-0.4

[a]*P* < 0.05.
[b]*P* < 0.01.
[c]*P* < 0.0001.
NS: Not significant.
[1]Reference variable includes nurses and others.
[2]Reference variable is Aps.
[3]Reference variable is experienced nurses.
[4]Reference variable includes moderate overtime and slight overtime.
[5]Reference variable is unhealthy body weight.
IV: Independent variable; RD: Resident doctor; JN: Junior nurse; HBW: Healthy body weight.

collection. By contrast, for nurses, injuries often occur during injections, intravenous infusions, heparin cap sealing, intravenous connections, and venous or arterial blood collection[24]. In addition, some studies have determined that the NSI risk is affected by education and work experience[9,10,25] among nurses and by stress and carelessness[6] among doctors. Consistent with this finding, our study indicated that doctors experienced more NSIs than nurses did (7.7% *vs* 2.6%). In addition, nurses who intensively contact patients were the protective factor of NSIs (OR = 0.3, $P < 0.05$). Our analysis revealed that the proportion of NSIs 4.1 times (OR = 4.1, $P < 0.05$) higher among RDs than among JNs; this increased to 19.5 times after adjusting for age and overtime work. Therefore, the NSI risk among RDs may be more serious than expected and has often been ignored in the past.

A cross-sectional survey of staff physicians, RDs, staff dentists, nurses, and laboratory technicians illustrated that RDs were significantly associated with NSIs; NSIs were three times more common among RDs than among APs[19]. The present data indicate a difference of 17.3 times between RDs and APs (21.2% *vs* 1.4%), which was markedly higher than in past studies. This may be because the numbers of NSIs among APs were low ($n = 1$), which may have led to the overestimation of this result. Nevertheless, the risk of NSIs among RDs was higher than that among other types of

medical personnel; for example this risk was 19.5 times higher in RDs than that in JNs.

Nurses with less work experience have a higher risk of NSIs[5,9]; in particular, nursing work experience of < 5 years was associated with significantly more NSIs than nursing work experience of > 5 years[5,11]. Consistent with these results, our study demonstrated that JNs have a higher risk of NSIs (OR = 3.9, P < 0.001) than experienced nurses after adjustment for other variables.

A cohort study including 11 728 employees revealed that claims costs were 7–11 times higher among those with BMI ≥ 40 compared with those within the recommended weight range[26]. A prospective cohort study of nearly 70 000 public sector employees demonstrated that, compared with employees whose BMI was in the healthy range, overweight or obese employees had an 11%–62% excess risk of occupational injury[16]. In addition, a study involving 7690 employees aged 18–65 years of an aluminum manufacturing company in the USA revealed that the proportion of injuries of participants with overweight or obesity was 1.3–2.2 times higher than those with normal weight[27]. The present results were in agreement with these findings and revealed that the proportion of NSIs among medical personnel with HBW was 0.5 times (OR = 0.5, P < 0.05) that among medical personnel with UHBW. Although we observed a relationship between NSIs and BW, the present study structure and data collected was insufficient to illustrate how BW affects NSIs. However, studies have demonstrated that fatigue increases the risk of NSIs among nurses and medical interns [28,29], and studies on grip strength have identified that, all things being equal, young people with obesity use more energy, have reduced endurance, and have accelerated power loss compared with nonobese young people. However, these obesity-related differences were not observed in the older age group[30]. These studies may explain the positive correlation between obesity and NSIs; obese people are more likely to use their poorer muscle strength improperly and be more prone to fatigue when performing clinical tasks, thus increasing their risk of NSIs.

A strong dose–response effect was noted between work hours and hazard rate[13], and working hours before injury will increase significantly compared to the past[31]. The positive trend between work hours and NSIs was observed in medical personnel: nurses with work hours of > 8 h/d[11] or > 40 h/wk[8] had higher risk of NSIs than those working < 8 h/d or < 40 h/wk. Our study found that the proportion of NSIs in participants with heavy overtime work was 4.3 times (OR = 4.3, P < 0.05) that in those with mild overtime work, but moderate overtime work effect (OR = 1.2, P > 0.05) was not significant; therefore, only heavy overtime work increased the risk of NSIs. Heavy overtime work was a risk factor for NSIs among doctors (OR = 5.4, P < 0.05) without adjustment for any variable, but this relationship was not significant when adjustments were made for sex, overtime work, professional grade, and BW; this was probably due to the higher proportion of heavy overtime work in RDs (33.3%) than in APs (8.5%). A dose–response effect was also noted between overtime work and NSIs for nurses, but it was not significant. However, experienced nurses engaged in heavy overtime work had 6.6 times (OR = 6.6, P < 0.05) more NSIs than those engaged in mild overtime work (Table 4); the effect of moderate overtime work on NSIs was not significant. Therefore, even among experienced nurses, only heavy overtime work affected the risk of NSIs. The proportion of NSIs was related to overtime work, but this relationship was not significant among nurses (Table 2); however, the association between NSIs and overtime work (OR = 6.6–7.0, P < 0.05) was significant among experienced nurses (Table 4). In addition, the mediation analysis (Table 5) demonstrated that heavy overtime work mediated (Z_m = 2.5, P < 0.05) the relationship between NSIs and medical specialty, confirming the impact of heavy overtime work on NSI. However, heavy overtime work and HBW were not mediation factors for the relationship between NSIs and experience level for doctors or nurses, indicating that low experience among medical personnel might itself be the cause of NSIs. A study indicated that the incidence of NSIs among first-year RDs was higher than expected—more than 60% during the first 6 mo[32]—implying that education and training may influence the risk of NSIs. Burnout also increases the risk of occupational accidents and its sequelae[33], and it was also a factor influencing NSIs among nurses [34]. Burnout decreases with an increase in professional experience[35]; this may also explain by burnout why RDs experience higher NSIs incidence than Aps. Future studies should comprehensively assess the burnout level of participants.

Because this study only collected data from one hospital, its findings are limited by the data collection method, sample size, as well as the hospital's environmental facilities, education, and training systems. In addition, because the number of reported NSIs was low, slight variations in the sample could have considerable influence on the conclusions. Moreover, factors such as hospital employees' work patterns, workload, burnout level, work stress, and willingness to report occupational injuries were not

considered in this study. These factors should be incorporated in the questionnaire design of future studies to further control for and discuss these effects on NSI risk. Although our results regarding NSI risk were consistent with those of past studies, this study compared the NSI risk between doctors and nurses, which has been rarely discussed in the literature. The findings can guide NSI prevention strategies in the medical practice.

CONCLUSION

This study revealed that heavy overtime work and low professional experience were associated with an increased NSI risk, particularly among RDs. Moreover, the present data indicated that HBW may reduce the risk of NSIs, which has rarely been evaluated in other studies. Maintaining an HBW had a protective effect against NSI for RDs and JNs. Therefore, in addition to promoting the use of safety needles and strengthening education and training related to infection control, the overtime schedule of medical personnel should be regularly reviewed; long work hours and excessive overtime should be avoided. Furthermore, strategies aimed at promoting the maintenance of HBW among employees should be implemented, which could further reduce NSI incidence.

ARTICLE HIGHLIGHTS

Research background

Needle stick and sharp injuries (NSIs) may cause infections among medical personnel. Obesity and overtime work among medical personnel increase the incidence of work injuries.

Research motivation

The associations of overtime work and obesity with NSIs are unclear.

Research objectives

The study aimed to investigate whether overtime work and obesity increase the risk of NSIs.

Research methods

This cross-sectional study used the data of 847 hospital personnel, including 104 doctors, 613 nurses, 67 medical laboratory scientists, 54 specialist technicians, and nine surgical assistants. Of them, 29 participants notified the hospital of having at least one NSI in 2017. The χ^2 and Fisher's exact tests were used to compare categorical variables. Multiple logistic regression analysis and the Sobel test were used to assess the risk of NSIs.

Research results

Overtime work, body weight (BW), and medical specialty were significantly associated with NSIs. After adjustment for risk factors, heavy overtime work was an independent risk factor for NSIs, and healthy BW (HBW) and nursing specialty were independent protective factors against NSIs. Also, after adjustment for risk factors, medical personnel with HBW had half as many NSIs as those with unhealthy BW (UHBW); the proportion of NSIs in doctors with HBW was 0.2 times that in doctors with UHBW; the proportion of injuries among residents was 17.3 times higher than that among attending physicians; the proportion of injuries among junior nurses was 3.9 times higher than that among experienced nurses; the proportion of injuries among nurses with heavy overtime work was 6.6 times higher than that among nurses with mild overtime work; and the proportion of injuries among residents was 19.5 times higher than that among junior nurses. Heavy overtime work mediated the association of medical specialty with NSIs.

Research conclusions

Heavy overtime work and low professional experience were associated with an increased NSI risk, particularly among resident doctors. Maintaining HBW had a protective effect against NSI for resident doctors and junior nurses.

Research perspectives

In addition to promoting the use of safety needles and providing infection control education, managers should review overtime schedules, and medical personnel should be encouraged to maintain an HBW.

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Sodium-glucose co-transporter-2 inhibitors reduce the risk of new-onset stroke in patients with type 2 diabetes: A population-based cohort study

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Background: Epidemiological evidence suggests the association of diabetes with an increased risk of stroke. Clinical studies have investigated the effects of sodium-glucose co-transporter-2 (SGLT2) inhibitors on new-onset stroke (NOS), but the results are inconsistent.

Objectives: To determine the association between the use of SGLT2 inhibitors and NOS in patients with type 2 diabetes mellitus (DM).

Methods: We conducted a retrospective longitudinal cohort study based on the Taiwan Health Insurance Review and Assessment Service database (2016–2019). The primary outcome of the assessment was the risk of incident stroke by estimating hazard ratios (HRs) and 95% confidence intervals (CIs). Multiple Cox regression was applied to estimate the adjusted HR of NOS. Subgroup analysis was also conducted.

Results: Among the 232,101 eligible patients with type 2 DM aged ≥ 20 years, SGLT2-inhibitor users were compared with non-SGLT2-inhibitor users based on age, sex, and the duration of type 2 DM matching at a ratio of 1:2. The event rate per 10 000 person-months was 9.20 (95% CI 8.95 to 9.45) for SGLT2-inhibitor users and 10.5(10.3–10.6) for non-SGLT2-inhibitor users. There was a decreased risk of NOS for SGLT2-inhibitor users (adjusted HR 0.85, 95% CI 0.82–0.88) compared with non-SGLT2-inhibitor users. Results for the propensity score-matched analyses showed similar results (adjusted HR 0.87, 95% CI 0.84–0.91 for both SGLT2-inhibitor users and non-SGLT2-inhibitor users).

Conclusion: The risk of developing NOS was lower in patients with SGLT2-inhibitor users than in non-SGLT2-inhibitor users. The decreased risk of NOS in patients with type 2 DM was greater among patients with concurrent use of statins, biguanides, thiazolidinediones, and glucagon-like peptide-1 receptor agonists. We, therefore, suggest that the long-term use of SGLT2 inhibitors may help reduce the incidence of NOS in patients with type 2 DM.

KEYWORDS

new-onset stroke, SGLT2 inhibitor, type 2 DM, concurrent medication, ischemic stroke, hemorrhagic stroke

Introduction

The global incidence and prevalence of type 2 diabetes mellitus (DM) have increased over the past two decades and caused much health burden across the world (1, 2). Past studies have demonstrated that type 2 DM is associated with an elevated risk of stroke (3, 4). Stroke in patients with type 2 DM has a poor prognosis, which is marked by worse mortality outcomes relative to that in several other diabetes-related comorbidities, including coronary heart diseases (4). It affects approximately 40% of patients with ischemic stroke who had been diagnosed with diabetes in the United States (5). A study reported that controlling glucose levels with intensive diabetes therapy could reduce the risk of stroke by 57% (6).

Sodium-glucose co-transporter-2 (SGLT2) inhibitors are used in patients with type 2 DM as glucose-lowering therapies targeting SGLT2 (7, 8). Although these drugs are primarily indicated for diabetes, several studies have examined their use in the primary and secondary prevention of stroke (9, 10). Animal studies have demonstrated a neuroprotective effect of SGLT2 inhibitors, which play an important role in antioxidant, anti-inflammatory, and anti-apoptotic mechanisms (11–13). SGLT2 inhibitors also improve the endothelial function, prevent remodeling, and exert a protective effect on the neurovascular unit and the blood–brain barrier, which can be promising in stroke therapy (14). However, the results of previous studies are inconsistent in a clinical setting (15–17). Therefore, the objective of the present study was to evaluate the risk of new-onset stroke (NOS) associated with the prescription of SGLT2 inhibitors in a nationwide cohort study of patients with type 2 DM in Taiwan.

Materials and methods

Study design

This is a retrospective study conducted on a population-based cohort using data from the insurance claims provided by the Taiwanese Bureau of National Health Insurance (TBNHI) from January 2004 to December 2019. This database contains anonymized longitudinal medical records that store the claims' information forms in two tables: a visit table and a prescription table. The visit tables contain the patient's identification numbers, sex, age, three diagnostic codes for outpatient and five for inpatient visits, medications, drug doses, medical expenditures, and hospital and physician information. The prescription table contains the quantity and expenditure for all administered drugs, operations, and treatments undertaken.

Patients included in this study were of age at least 20 years, with a newly diagnosed case of type 2 DM with or without prescribed SGLT2 inhibitors between May 2016 and December 2019. SGLT2-inhibitor users were defined as patients who received at least an SGLT2 inhibitor prescription for 180 days during the study period. In contrast, non-SGLT2 inhibitor users were patients who did not receive an SGLT2 inhibitor prescription throughout the study period.

Study population

The study population comprised patients with type 2 DM (ICD-10-CM, E11) who were admitted to the hospital or visited the hospital as an outpatient between May 1, 2016 and December 31, 2019. At least one of the following enrollment criteria was required to be met for inclusion in this study: (1) two or more outpatient visits within 6 months, (2) all antidiabetic drugs were continuously prescribed to the patients for >6 months during the follow-up period, or (3) one or more inpatient admissions with a diagnosis of type 2 DM. The primary endpoint was the development of stroke, which was defined by the time a stroke (ICD-10-CM codes I60, I61, I62, I63, I65, I66, I67.84, G45, G46) code first appeared in the inpatient or outpatient claim records. Comorbidities related to stroke were defined according to the ICD-10-CM code and included coronary heart disease (ICD-10-CM code I20–I25), hypertension (ICD-10-CM code I10), hyperlipidemia (ICD-9-CM code E78.1–E78.5), chronic kidney disease (ICD-10-CM code N18), chronic liver disease (ICD-10-CM code K71, K75, K76), chronic obstructive pulmonary disease (ICD-10-CM code J44), atrial fibrillation and flutter (ICD-10-CM code I48), and rheumatoid arthritis (ICD-9-CM code M05). Patients who fulfilled any of the following criteria

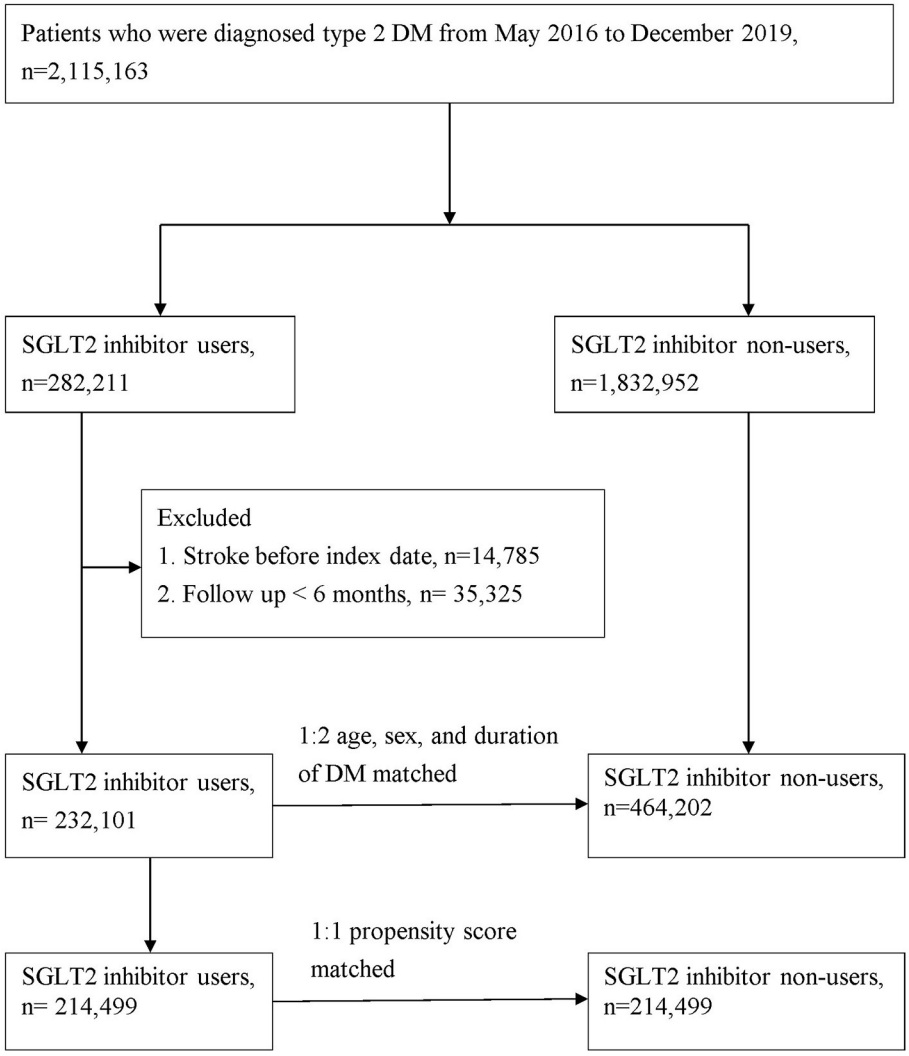

FIGURE 1
Patient flow chart.

were excluded from the study: (1) prior history of stroke before May 1, 2016 and (2) patient age of <20 years. Considering the differences in the baseline characteristics and stroke risk between the SGLT2-inhibitor users and non-SGLT2-inhibitor users, we applied age-, sex-, and type 2 DM duration matching at a ratio of 1:2 for patients with type 2 DM with and without SGLT2 inhibitor use. Finally, the study group comprised 232,101 participants with type 2 DM who were SGLT2 inhibitor users, and the control group included 464,202 randomly selected participants with type 2 DM who were non-SGLT2-inhibitor users (Figure 1). We also conducted propensity score matching with age, sex, duration of type 2 DM, comorbidities, and drug index date at a ratio of 1:1 for sensitivity analysis in patients with type 2 DM with and without the use of an SGLT2 inhibitor (Figure 1).

Statistical analysis

Data were presented as valid percentages and the mean values with a standard deviation. Differences in the demographic data and clinical characteristics between SGLT2-inhibitor users and non-SGLT2-inhibitor users were examined using a *t*-test for continuous variables, whereas Chi-square tests were performed for categorical variables. The Cox proportional hazard regression model was applied to compare the risk of developing study events between the SGLT2 inhibitor group and the non-SGLT2 inhibitor group. Adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated after adjusting for important risk factors toward developing the study events, including age, sex, concurrent medication, and comorbidities. The risk of study outcomes over time for the

TABLE 1 Baseline characteristics of all patients.

Characteristics		2:1 sex, age matching			1:1 Propensity score matching		
		Non- SGLT2 ($n = 464,202$)	SGLT2 ($n = 232,101$)	*P*	Non-SGLT2 ($n = 214,499$)	SGLT2 ($n = 214,499$)	ASD
Sex				1.0000			0.00177
Female		204,534 (44.06%)	102,267 (44.06%)		94,518 (44.06%)	94,707 (44.15%)	
Male		259,668 (55.94%)	129,834 (55.94%)		119,981 (55.94%)	119,792 (55.85%)	
Age				1.0000			0.00000
<50		114,804 (24.73%)	57,402 (24.73%)		53,466 (24.93%)	53,131 (24.77%)	
51–60		138,494 (29.83%)	69,247 (29.83%)		64,132 (29.90%)	64,128 (29.90%)	
61–70		142,538 (30.71%)	71,269 (30.71%)		66,008 (30.77%)	65,896 (30.72%)	
>70		68,366 (14.73%)	34,183 (14.73%)		30,893 (14.4%)	31,344 (14.61%)	
Years (Mean ± SD)		58.34 ± 12.21	58.34 ± 12.21	1.0000	58.44 ± 11.89	58.29 ± 12.23	
DM history				<0.0001			0.02967
<=2 years		133,455 (28.75%)	59,608 (25.68%)		54,688 (25.50%)	55,752 (25.99%)	
3-4 years		243,394 (52.43%)	126,088 (54.32%)		115,391 (53.80%)	115,875 (54.02%)	
≥5 years		87,353 (18.82%)	46,405 (19.99%)		44,420 (20.71%)	42,872 (19.99%)	
Comorbidities							
dv11	Hypertension	250,659 (54%)	139,336 (60.03%)	<0.0001	128,819 (60.06%)	12,738 5(59.39%)	0.01363
dv13	Coronary artery disease	51,129 (11.01%)	41,448 (17.86%)	<0.0001	33,966 (15.84%)	35,030 (16.33%)	0.01350
dv14	Hyperlipidemia	257,784 (55.53%)	153,956 (66.33%)	<0.0001	142,463 (66.42%)	140,575 (65.54%)	0.01858
dv19	Chronic kidney disease	104,962 (22.61%)	59,599 (25.68%)	<0.0001	57,593 (26.85%)	54,907 (25.60%)	0.02847
dv20	Chronic liver disease	50,928 (10.97%)	26,537 (11.43%)	<0.0001	24,725 (11.53%)	24,501 (11.42%)	0.00328
dv66	COPD	15,910 (3.43%)	8,446 (3.64%)	<0.0001	7,301 (3.40%)	7,631 (3.56%)	0.00839
dv29	Atrial fibrillation and flutter	4,902 (1.06%)	3,824 (1.65%)	<0.0001	3,087 (1.44%)	3,149 (1.47%)	0.00242
	Rheumatoid arthritis	3,188 (0.69%)	1,285 (0.55%)	0.01696	1,168 (0.54%)	1,202 (0.56%)	0.00214
Concurrent medication							
Dr1	NSAIDs	263,337 (56.73%)	133,108 (57.35%)	<0.0001	122,355 (57.04%)	122,768 (57.23%)	0.00389
Dr2	Corticosteroids	88,850 (19.14%)	45,398 (19.56%)	<0.0001	41,286 (19.25%)	41,608 (19.40%)	0.00380
Dr3	PPIs	35,647 (7.68%)	18,410 (7.93%)	0.0002	16,619 (7.75%)	16,739 (7.80%)	0.00209
Dr4	H2-receptor antagonists	120,629 (25.99%)	61,091 (26.32%)	0.0027	55,435 (25.84%)	56,109 (26.16%)	0.00716
Dr5	Aspirins	92,245 (19.87%)	63,518 (27.37%)	<0.0001	55,176 (25.72%)	55,748 (25.99%)	0.00609
Dr25	Statins	240,244 (51.75%)	162,084 (69.83%)	<0.0001	147,212 (68.63%)	146,131 (68.13%)	0.01084
Dr13	Biguanides	242,784 (52.3%)	151,068 (65.09%)	<0.0001	134,691 (62.79%)	136,345 (63.56%)	0.01599
Dr14	Sulfonylureas	155,979 (33.6%)	101,140 (43.58%)	<0.0001	91,743 (42.77%)	90,022 (41.97%)	0.01624
Dr15	Alpha glucosidase inhibitors	45,540 (9.81%)	43,008 (18.53%)	<0.0001	34,432 (16.05%)	35,391 (16.50%)	0.01211
Dr16	Thiazolidinediones	43,754 (9.43%)	41,938 (18.07%)	<0.0001	34,607 (16.13%)	34,857 (16.25%)	0.00316
Dr17	DPP4 inhibitors	99,152 (21.36%)	93,734 (40.39%)	<0.0001	80,445 (37.50%)	79,384 (37.01%)	0.01023
Dr18	Insulins	71,925 (15.49%)	57,020 (24.57%)	<0.0001	48,358 (22.54%)	48,840 (22.77%)	0.00537
Dr26	GLP-1 receptor agonists	5,101 (1.1%)	4,244 (1.83%)	<0.0001	3,763 (1.75%)	3,665 (1.71%)	0.00350

COPD, chronic obstructive pulmonary disease; DPP4, Dipeptidyl peptidase 4; GLP-1, Glucagon-like peptide-1; NSAID, Non-steroid anti-inflammatory drug; PPI, proton pump inhibitor; ASD, absolute standardized difference; PSM, propensity score matching; SD, standard deviation.

SGLT2 inhibitor group compared with the non-SGLT2 inhibitor group was determined by survival analysis using the Kaplan–Meier method.

We also conducted a sensitivity analysis to test the robustness of our primary findings. Initially, a propensity score was calculated for each patient to minimize confounding by indication, when patients with other risk factors between the SGLT2 inhibitor user group and non-SGLT2 inhibitor user group. Then, the propensity score matching (1:1) and absolute standardized difference (ASD) were performed to estimate the difference between the two groups. An ASD of <0.10 implied a negligible

TABLE 2 Incidence rate of stroke.

	2:1 sex age matching		1:1 Propensity score matching	
	Non- SGLT2	SGLT2	Non- SGLT2	SGLT2
N	464,202	232,101	214,499	214,499
Follow up person months	11,135,130	5,634,359	5,177,840	5,191,193
New case	11,701	5,186	5,328	4,678
Incidence rate*(95% C.I.)	10.50 (10.30–10.60)	9.20 (8.95–9.45)	10.20 (10.00–10.50)	9.01 (8.75–9.27)
Crude Relative risk (95% C.I.)	Reference	0.88 (0.85–0.91)	Reference	0.88 (0.84–0.91)
Adjusted HR* (95% C.I.)†	Reference	0.85 (0.82–0.88)	Reference	0.87 (0.84–0.91)

*Incidence rate, per 10,000 person-months. †adjusted hazard ratio, the covariates including duration of DM history, sex, age, co-morbidities, and medication at baseline.

difference in the potential confounders between the two groups.

In addition, we conducted subgroup analyses stratified by sex, age, duration of type 2 DM, presence of comorbidities, and concurrent medication at baseline for the primary outcomes of NOS. Statistical significance was considered at $P < 0.05$. All statistical calculations were performed using the statistical analysis software, version 9.3 (SAS Institute, Inc., Cary, NC, USA).

Results

Study population and baseline characteristics

A total of 696,303 patients were enrolled in the present study, with the SGLT2-inhibitor user group consisting of 232,101 individuals from the NHIRD who were diagnosed with type 2 DM from May 2016 through December 2019. This group was compared with 464,202 control patients who were non-SGLT2-inhibitor users at a 1:2 ratio (Figure 1). There were more men (55.94%) than women (44.06%) in this study. At the baseline, patients receiving SGLT2 inhibitor had more comorbidities, except for rheumatoid arthritis, and they used more concurrent medication than those not receiving SGLT2 inhibitor (Table 1).

Analysis of the main TBNHI cohort

During the follow-up, 5,186 and 11,701 NOSs events were recorded in the SGLT2-inhibitor user and non-SGLT2-inhibitor user groups, respectively. The event rate was 9.20 per 10 000 person-months (95% CI 8.95–9.45) for SGLT2-inhibitor users when compared with 10.50 (95% CI 10.30–10.60) for non-SGLT2-inhibitor users. There was a significantly lower the incidence rate of NOS after adjusting for the duration of type 2 DM history, sex, age, comorbidities, and concurrent medication among the SGLT2-inhibitor users when compared to that among the non-SGLT2-inhibitor users (adjusted HR: 0.85; 95% CI: 0.82–0.88) (Table 2). The cumulative incidence rate of developing stroke was also lower in the SGLT2-inhibitor users than in the non-SGLT2-inhibitor in the Kaplan–Meier survival analysis ($P < 0.0001$; Figure 2A).

Propensity score-matched analysis

We included 428,998 patients (214,499 in the SGLT2-inhibitor group and 214,499 in the non-SGLT2-inhibitor group) in the propensity score matching, and the baseline characteristics of sex, age, and duration of type 2 DM did not differ (Table 1). At the baseline, the non-SGLT2-inhibitor group had more comorbidities, except for coronary artery disease, chronic obstructive pulmonary disease, atrial fibrillation and flutter, and rheumatoid arthritis than the SGLT2-inhibitor group. However, the SGLT2 inhibitor users used more concurrent medication, except statins, sulfonylureas, dipeptidyl peptidase 4 inhibitors, and glucagon-like peptide-1 receptor agonists than the non-SGLT2 inhibitor users (Table 1).

There were 4,678 and 5,328 NOS events recorded in the SGLT2-inhibitor and non-SGLT2-inhibitor groups, respectively, in the follow-up period. The event rate was 9.01 per 10 000 person-months (95% CI 8.75–9.27) for the SGLT2-inhibitor group compared with 10.20 (95% CI 10.00–10.50) for the non-SGLT2-inhibitor group. The relative risk of NOS after adjusting the duration of type 2 DM history, sex, age, comorbidities, and concurrent medication demonstrated a decreasing risk of incident stroke in the SGLT2 inhibitor group when compared to those in the non-SGLT2-inhibitor group (adjusted HR: 0.87; 95% CI: 0.84–0.91) (Table 2). Similarly, the SGLT2-inhibitor group revealed a significantly lower cumulative incidence rate of developing stroke than the non-SGLT2-inhibitor group as per the Kaplan–Meier survival analysis ($P < 0.0001$, Figure 2B).

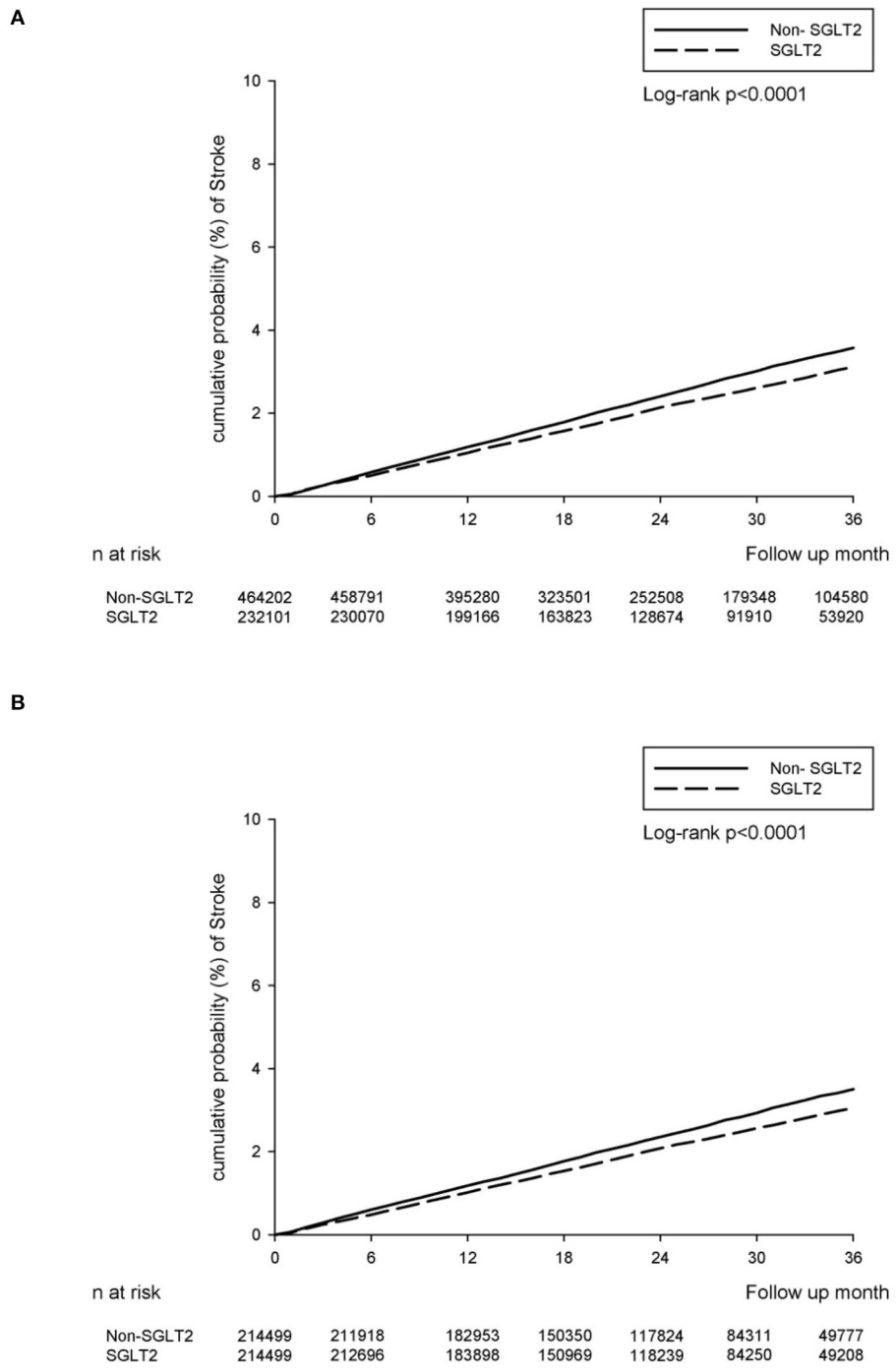

FIGURE 2
The cumulative incidence rate of developing stroke between SGLT2-inhibitor group and non-SGLT2-inhibitor group. **(A)** The main TBNHI Cohort. **(B)** The propensity score-matched cohort.

Subgroup analysis

The results of the subgroup analyses revealed that, after adjusting for the duration of type 2 DM history, sex, age, comorbidities, and concurrent medication were partly consistent with the results of the main analyses (Table 3). The two groups were different in terms of their incidental stroke, with the SGLT2 inhibitor users exhibiting a substantially high risk of NOS with male, an adjusted HR = 1.34 (95% CI: 1.30 to 1.39) than female. Compared with younger patients (aged < 50),

TABLE 3 Multiple Cox regression to estimate the hazard ratio for subgroup analysis.

	aHR (95% CI)	
	2:1 sex, age matching	**1:1 propensity score matching**
Sex		
Female	reference	reference
Male	1.34(1.30–1.39)	1.33(1.27–1.38)
Age		
<50	reference	reference
51–60	1.59(1.51–1.68)	1.51(1.41–1.63)
61–70	2.24(2.13–2.36)	2.17(2.02–2.32)
>70	3.67(3.48–3.88)	3.55(3.31–3.82)
Duration of type 2 DM history		
<=2 years	1.21(1.14–1.28)	1.27(1.11–1.37)
2–4 years	1.16(1.11–1.23)	1.20(1.12–1.28)
>=4 years	reference	reference
Comorbidity(ref: non-comorbidity)		
Hypertension	1.22(1.18–1.26)	1.28(1.23–1.34)
Coronary artery disease	1.02(0.97–1.06)	1.02(0.97–1.07)
Hyperlipidemia	0.77(0.74–0.79)	0.80(0.77–0.83)
Chronic kidney disease	1.17(1.13–1.21)	1.16(1.11–1.21)
Chronic liver disease	0.81(0.77–0.85)	0.79(0.74–0.85)
Malignancy	1.02(0.96–1.08)	1.03(0.95–1.13)
COPD	1.08(1.01–1.16)	1.06(0.97–1.15)
Atrial fibrillation and flutter	1.79(1.64–1.95)	1.82(1.64–2.02)
Rheumatoid Arthritis	1.23(1.04–1.44)	1.15(0.91–1.45)
Medication (reference: non-medication)		
NSAIDs	1.00(0.97–1.04)	1.05(1.01–1.09)
Corticosteroids	1.07(1.03–1.11)	1.08(1.02–1.13)
PPIs	1.19(1.13–1.25)	1.20(1.12–1.28)
H2-receptor antagonists	1.05(1.02–1.09)	1.07(1.02–1.12)
Aspirins	1.53(1.48–1.59)	1.55(1.49–1.62)
Statins	0.84(0.81–0.86)	0.88(0.84–0.92)
Biguanides	0.77(0.75–0.79)	0.85(0.82–0.89)
Sulfonylureas	1.09(1.06–1.13)	1.14(1.10–1.19)
Alpha glucosidase inhibitors	1.03(0.98–1.07)	1.06(1.01–1.12)
Thiazolidinediones	0.89(0.85–0.93)	0.93(0.88–0.98)
DPP4 inhibitors	1.05(1.02–1.09)	1.08(1.03–1.12)
Insulins	1.62(1.56–1.68)	1.67(1.60–1.74)
GLP-1 receptor agonists	0.84(0.71–0.98)	0.77(0.63-y0.93)

COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; DPP4, Dipeptidyl peptidase 4; GLP-1, Glucagon-like peptide-1; NSAID, Non-steroid anti-inflammatory drug; PPI, proton pump inhibitor.

elderly patients exhibited a significantly higher risk of NOS (aHR 1.59, 95% CI 1.51–1.68 for patients aged 50–60; aHR 2.24, 95% CI 2.13–2.36 for patients aged 60–70; aHR 3.67, 95% CI 3.48–3.88 for patients aged > 70). The duration of type 2 DM history were higher in the <=2 or 2–4 years than in the ≥4 years. Patients with hypertension, chronic kidney disease, chronic obstructive pulmonary disease, atrial fibrillation and flutter, and rheumatoid arthritis were also at significantly higher risks of NOS (aHR = 1.22, 1.17, 1.08, 1.79, and 1.23, respectively). However, patients with hyperlipidemia and chronic liver disease have significantly lower risks of NOS (aHR = 0.77, and 0.81, respectively). Similar findings were also noted for concurrent medication of statins (aHR 0.84, 95% CI 0.81–0.86 in the main TBNHI cohort; aHR 0.88, 95% CI 0.84–0.92 in the propensity score matching), biguanides (aHR 0.77, 95% CI 0.75–0.79 in the main TBNHI cohort; aHR 0.85, 95% CI 0.82–0.89 in the propensity score matching), thiazolidinediones (aHR 0.89, 95% CI 0.85–0.93 in the main TBNHI cohort; aHR 0.93, 95% CI 0.88–0.98 in the propensity score matching), and glucagon-like peptide-1 receptor agonists (aHR 0.84, 95% CI 0.71–0.98 in the main TBNHI cohort; aHR 0.77, 95% CI 0.63–0.93 in the propensity score matching). However, an increased risk of NOS was noted for concurrent medication with non-steroid anti-inflammatory drugs (aHR 1.01, 95% CI 0.98–1.05 in the main TBNHI cohort; aHR 1.05, 95% CI 1.01–1.05 in the propensity score matching), corticosteroids (aHR 1.07, 95% CI 1.03–1.11 in the main TBNHI cohort; aHR 1.08, 95% CI 1.02–1.13 in the propensity score matching), proton pump inhibitors (aHR 1.19, 95% CI 1.13–1.25 in the main TBNHI cohort; aHR 1.20, 95% CI 1.12–1.20 in the propensity score matching), H2-receptor antagonists (aHR 1.05, 95% CI 1.02–1.09 in the main TBNHI cohort; aHR 1.07, 95% CI 1.02–1.12 in the propensity score matching), aspirins (aHR 1.53, 95% CI 1.48–1.59 in the main TBNHI cohort; aHR 1.55, 95% CI 1.49–1.62 in the propensity score matching), sulfonylureas (aHR 1.09, 95% CI 1.06–1.13 in the main TBNHI cohort; aHR 1.14, 95% CI 1.10–1.19 in the propensity score matching), alpha-glucosidase inhibitors (aHR 1.03, 95% CI 0.98–1.07 in the main TBNHI cohort; aHR 1.06, 95% CI 1.01–1.12 in the propensity score matching), Dipeptidyl peptidase 4 inhibitors (aHR 1.05, 95% CI 1.02–1.09 in the main TBNHI cohort; aHR 1.08, 95% CI 1.03–1.12 in the propensity score matching), and insulins (aHR 1.62, 95% CI 1.56–1.68 in the main TBNHI cohort; aHR 1.67, 95% CI 1.60–1.74 in the propensity score matching) (Table 3).

Discussion

The present findings suggest that the incidence of NOS was decreased in type 2 DM patients who were SGLT2-inhibitor users compared with those who were not. Sensitivity analysis was also consistent with the main analysis. The subgroups analysis identified the concurrent use of statins, biguanides, thiazolidinediones, and glucagon-like peptide-1 receptor agonists as having a protective effect against developing NOS. However, we observed the increased risk based on whether non-steroid anti-inflammatory drugs, corticosteroids,

proton pump inhibitors, H2-receptor antagonists, aspirins, sulfonylureas, alpha-glucosidase inhibitors, dipeptidyl peptidase 4 inhibitors, and insulins were prescribed for concurrent use with an SGLT2 inhibitor.

Hypertension, type 2 DM, and obesity are identified as the most important risk factors for stroke (18). Several experimental studies reported improvements in these risk factors in diabetic and obese or stroke-prone mice and rats after treatment with SGLT2 inhibitors (11–13, 19). *In vitro* data has shown that the SGLT2 inhibitor significantly increased survival (67%) of spontaneously hypertensive stroke-prone rats when compared with controls (13). The authors observed that SGLT2 inhibitor-treated rats had weight and blood pressure reduction, which could explain the reduced stroke risk and increased survival. However, the effects of SGLT2 inhibitors on stroke prevention were contradictory in different clinical trials. In the Empagliflozin Cardiovascular Outcomes and Mortality in Type 2 Diabetes (EMPA-REG OUTCOME) trial (17), empagliflozin users were found to be associated with an insignificantly increased risk of stroke when compared to empagliflozin non-users (HR, 1.18; 95% CI, 0.89–1.56; $P = 0.26$). On the other hand, canagliflozin users were found to be associated with an insignificantly decreased risk of stroke relative to canagliflozin non-users (HR, 0.87; 95% CI, 0.69–1.09) in the Cardiovascular and Renal Events in Type 2 Diabetes (CANVAS) trial (20). However, several meta-analyses have demonstrated that SGLT2 inhibitors may lower the risk of embolic stroke (9, 21, 22). Their results were the same as ours and they suggested a possible protective effect of SGLT2 inhibitors including different populations and the level of renal functions.

In our study, subgroups analyses demonstrated that the patients' concurrent use of statins, biguanides, thiazolidinediones, and glucagon-like peptide-1 receptor agonists had a protective effect against developing NOS, whereas patients' concurrent use of non-steroid anti-inflammatory drugs, corticosteroids, proton pump inhibitors, H2-receptor antagonists, aspirins, sulfonylureas, alpha-glucosidase inhibitors, dipeptidyl peptidase 4 inhibitors, and insulins showed an increased risk of developing NOS. This result demonstrates that different drugs may play a major role in lowering or increasing the risk of NOS when combined with SGLT2 inhibitors for patients with type 2 DM, which conforms to previous reports (23–27).

Other than antidiabetic effects, SGLT2 inhibitors also promoted natriuresis and osmotic diuresis to lower blood pressure in patients with cardiovascular disease and heart failure (28–30). As evidence of the efficacy of SGLT-2 inhibitors continued to grow, many trails and meta-analysis on these drugs have expanded their prescriptions from diabetes patients only to also include patients with HF without type 2 DM (28–32). Furthermore, the safety and dose-response relationship of SGLT2 inhibitors were recommended in the clinical practice (33–35).

In summary, there is negative association between the use of SGLT2 inhibitors and the risk of NOS in patients with type 2 DM. The decreased risk of NOS in patients with type 2 DM was greater among patients with concurrent use of statins, biguanides, thiazolidinediones, and glucagon-like peptide-1 receptor agonists. Therefore, we suggest that the long-term use of SGLT2 inhibitors may help reduce the incidence of NOS in patients with type 2 DM.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

This study was approved by the Ethics Committee of the Chung Shan Medical University Hospital (CS1-21037). Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

Author contributions

T-KL and M-CC: conceptualization, methodology, formal analysis, and writing–original draft. Y-HC and J-YH: formal analysis and validation. P-LL: formal analysis. T-KL, Y-HC, J-YH, and M-CC: data curation. L-FP and G-PJ: conceptualization, investigation, writing–review and editing, supervision, project administration, and funding acquisition. All authors read the study and approved the manuscript for publication.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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