

Impact of shift work on irritable bowel syndrome and functional dyspepsia

A meta-analysis

Nian Wang, PhD^a, Xinghuang Liu, PhD^b, Weixiang Ye, MD^a, Zhaohong Shi, PhD^a, Tao Bai, PhD^{b,*}

Abstract

Background: The possible association between shift work with irritable bowel syndrome (IBS) and functional dyspepsia (FD) remains controversial. The purpose of the study is to conduct a meta-analysis to explore the potential association between shift work with IBS/FD.

Methods: We searched relevant observational studies on Medline (PubMed) and Embase until June 30, 2021. Two different investigators extracted data and assessed the quality of each study independently. The meta-analysis was used to evaluate the pooled odds risk (OR) between shift work and IBS/FD.

Results: Eight studies were included ultimately. Shift workers were more likely to suffer from IBS. The OR of shift work was 1.81 (95% confidence interval 1.42; 2.32) with low heterogeneity ($P < .05$, $I^2 = 0\%$) for IBS. However, no evidence of the association was observed between shift work and the risk of FD. The OR of shift work was 0.87 (95% confidence interval 0.62; 1.23) ($P > .05$) for FD.

Conclusions: There was a positive association between shift work and IBS. The prevalence of IBS was 81% higher among shift workers than among non-shift workers. Shift work was probably a risk factor for IBS. The low heterogeneity supports the reliability of the results. However, there was no significant association between shift work and FD. The strength of the evidence was limited and further prospective cohort studies were needed.

Abbreviations: CI = confidence interval, FD = functional dyspepsia, FGIDs = functional gastrointestinal disorders, IBS = irritable bowel syndrome, OR = odds risk.

Keywords: functional dyspepsia, irritable bowel syndrome, meta-analysis, observational study, shift work

1. Introduction

Functional gastrointestinal disorders (FGIDs) are characterized by upper and lower symptoms with no definite organic or biochemical abnormalities. Irritable bowel syndrome (IBS) and functional dyspepsia (FD) are the most common among FGIDs and have received more attention for affecting the quality of life and social functioning. For example, IBS affects 7% to 16% of Americans^[1] and the overall prevalence of dyspepsia was 21%.^[2] Alteration in motility, immunity, visceral sensitivity, intestinal barrier integrity, and psychological factors have been

proved vital mechanisms in IBS.^[3–5] However, the correlation between lifestyle and IBS/FD remains insufficient.

In daily life, shift work is quite common. This is partly because some occupations have to keep people on the job 24 hours a day (such as medical staff), and partly because enterprises have to improve production efficiency. Rotating shift forms include morning shift/night shift/rotating shift, periodic shift, and irregular shift. Over the past few decades, increasing attention and researches have pointed to the possible negative health effects of shift work. Shift work has been proved to increase the risk of cardiovascular disease and metabolic disorders.^[6,7]

This study was supported by the National Administration of Traditional Chinese Medicine: 2019 project of building evidence based practice capacity for TCM (Nos. ZZ13-042-2 and 2019XZZX-XH006).

Patient consent for publication is not required.

The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are publicly available.

^aDivision of Gastroenterology, Wuhan No. 1 Hospital, 215 Zhongshan Road, Wuhan, China, ^bDivision of Gastroenterology, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, 1277 Jiefang Road, Wuhan, China.

*Correspondence: Tao Bai, Division of Gastroenterology, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, 1277 Jiefang Road, Wuhan 430000, China (e-mail: drbaitao@126.com).

Copyright © 2022 the Author(s). Published by Wolters Kluwer Health, Inc.

This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial License 4.0 (CCBY-NC), where it is permissible to download, share, remix, transform, and buildup the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

How to cite this article: Wang N, Liu X, Ye W, Shi Z, Bai T. Impact of shift work on irritable bowel syndrome and functional dyspepsia: a meta-analysis. *Medicine* 2022;101:25(e29211).

Received: 12 March 2022 / Received in final form: 14 March 2022 / Accepted: 17 March 2022

<http://dx.doi.org/10.1097/MD.00000000000029211>

Some researchers believed that medical students in the overnight call were not associated with the development of IBS.^[8] But Borko Nojkov et al confirmed that shift work contributed to the development of IBS. The association between shift work and IBS/FD is controversial. Therefore, we conducted a meta-analysis of published observational studies to review epidemiological evidence on the association between shift work and IBS/FD.

2. Materials and methods

2.1. Search strategy and selection criteria

In accordance with the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines, we searched published studies through Medline (PubMed) and Embase from inception to June 30, 2021. We identified all pertinent literature that associate between shift work and FGIDs, including FD and IBS. We used (“dyspepsia” or “IBS” or “irritable bowel syndrome”) and (“shift work” or “rotating shift work” or “night shift work” or “work at night” or “irregular work schedule”) as retrieval strategy. The diagnosis of IBS/FD in all included literatures was referred to Rome II criteria and Rome III criteria.^[9,10] The cases included in the literature belong to the secondary study and no patient privacy involved, so ethical approval was waived.

Studies were identified based on predefined inclusion criteria: the study was designed as a case-control or cohort study or cross-sectional study; the exposure of interest was shift work, the outcome was morbidity IBS/FD, 95% confidence interval (CI) or sufficient information to report win odds risk (OR) or relative risk (RR) for calculation. In addition, non-human studies, clinical trials, reviews, letters, duplicate literature, and studies that examined other associations were excluded. Subsequently, 2 investigators (Nian Wang and Xinghuang Liu) independently reviewed eligible articles by titles and abstracts and then by full texts. Any discrepancy between the 2 investigators was solved by a discussion with the senior investigator (Dr Tao Bai).

2.2. Data extraction and quality assessment

We extracted the following data from each eligible article: name of the first author, publication year, country, study design, data sources, subject number, age, diagnose of IBS/FD, the definition of shift work, the proportion of females, confounder adjusted and OR/relative risk/hazard ratio (95% CI). The Agency for Healthcare Research and Quality^[11] was applied to evaluate the cross-sectional studies. The Agency for Healthcare Research and Quality has an 11-item checklist. If it was answered “YES”, the item scored “1”; “NO” or “UNCLEAR” would be scored “0”. A score of more than 7 is considered as high quality, a score of 4 to 6 as moderate-quality, while a score of less than 4 as low quality. Any disagreements were resolved by consensus.

2.3. Data synthesis and meta-analysis

In this meta-analysis, all statistical analyses were performed with R 3.6.0 (Stata Corporation, TX). The OR value and 95% CI of each study were combined to obtain the combined OR value and 95% CI. $P < .05$ was regarded as a significance level. The heterogeneity among the studies was assessed by I^2 statistics. If the result of the heterogeneity test was $I^2 > 50\%$, the random-effects model was applied. Otherwise, the fixed-effects model

was used. Subgroup analysis was conducted to explore the potential influence of variables on pooled effects (such as origin country). Sensitivity analysis was conducted to evaluate the potential effect of the results. All statistical methods were predetermined.

3. Results

3.1. Literature characteristic and quality evaluation

A total of 69 items were retrieved. Of these, 23 articles were excluded because they were reviews, not English, non-human studies, or duplicate literature. After evaluating the full texts of the remaining articles that may be relevant for this meta-analysis, 38 of 46 were excluded for no association or no relevant data. In total, 8 studies were included. The detailed flowchart of the selection process on eligible studies was shown in flow diagram. Table 1 summarizes the 8 pieces of literature that met the inclusion criteria. All the included literature could be attributed to cross-sectional studies. Data were obtained from single-center studies and the questionnaire was taken from medical staff. The sample size ranged from 51 to 468. Shift schedules were classified as rotating shift, day shift, and night shift. In the 8 articles included, 4 articles covered both IBS and FD. Six studies used Rome III criteria to define IBS/FD and the 2 used Rome II criteria. As for the definition of shift work, 4 studies used self-reported, 1 study used overnight call requirements, 1 study was determined by researchers, 1 study used the record, and 1 study did not mention. The proportion of females in the 2 studies was 100%. The result of the quality assessment was presented in Table 2. Among the 8 articles, 7 were of high quality, 1 was of medium quality.

3.2. Overall meta-analysis of the association between IBS and shift work

When IBS was used as an outcome, the 8 studies were analyzed to seek whether the association was positive or negative. The heterogeneity test showed that I^2 was 0 and the fixed effect model was selected. The OR and 95% CI of 8 studies were quantitatively combined, and the pooled OR and 95% CI was 1.81 (1.42; 2.32) (Fig. 1). It suggested that shift workers had an 81% increase in the prevalence or incidence of IBS compared with non-shift workers. We conducted subgroup analysis to explore the sources of heterogeneity and influence by region (Europe, America, and Asia). The pooled OR were 1.76 (95% CI 1.2; 2.58) and 1.81 (95% CI 1.42; 2.32), respectively (Fig. 2). This subgroup analysis had no statistical significance for heterogeneity. Sensitivity analysis was performed to test the robustness of our study findings. The pooled OR was 1.81 (95% CI 1.42; 2.32) after excluding studies without adjusting covariates (Fig. 3). The sensitivity analysis indicated that shift work obviously increased the risk of IBS.

3.3. Overall meta-analysis of the association between FD and shift work

When FD was used as an outcome, the pooled OR was 0.87 (95% CI 0.62; 1.23) (Fig. 4). The results showed that there was no significant correlation between shift work and FD. The pooled OR was 0.87 (95% CI 0.62; 1.23) and there was no statistical significance. Due to the limited number of included literature, no publication bias test was performed.

Table 1

Information of included studies.

Study	Rogers et al	Zhou et al	Lu et al	Wells et al	Nojkov et al	Koh et al	Kim et al	Wang
Publication year	2021	2021	2006	2012	2010	2014	2013	2008
Country	USA	China	Singapore	UK	USA	Korea	Korea	China
Study design	Cross-sectional	Cross-sectional	Cross-sectional	Cross-sectional	Cross-sectional	Cross-sectional	Cross-sectional	Cross-sectional
Data sources	Single center; questionnaire research of nurses	Single center; questionnaire research of nurses	Single center; questionnaire research of nurses	Single center; questionnaire research of medical studies	Single center; questionnaire research of nurses	Single center; questionnaire research of nurses	Single center; questionnaire research of nurses	Single center; questionnaire research of nurses
Subject number	Day shift: 24; Night shift: 27	Total: 468	Regular hours: 60; Rotating shift: 58	Preclinical medical students: 110; Clerkship medical students: 118	Permanent day shift worker: 214; Rotating shift worker: 75	Day shift workers: 98; Rotating shift workers: 203	Rotating shift: 147; Day work: 64	Rotating shift: 157; Day shift: 128
Age (yrs)	21–59 years old (mean 32.9±10.0)	22–55 years old (mean 31.4±8.4)	20–60 years old (median: 29)	20–36 years old (mean: 25.0±2.1)	None	With FGIDs: 23.3–33 Without FGIDs: 36–23	21–53 years old (mean 32.3±7.8)	Mean 30.4±7.9 years old
Diagnose of IBS/FD	Rome III criteria	Rome III criteria	Rome II criteria	Rome III criteria	Rome III criteria	Rome III criteria	Rome III criteria	Rome II criteria
Definition of shift work	Not mentioned	Self-reported	Self-reported	Overnight call requirements	Self-reported	Self-reported	By the researchers	Record
Proportion of female	96%	Not mentioned	100%	47.7%	89.6%	96.7%	Not mentioned	100%
Confounder adjusted	None	Age, work schedule, night pain, and psychological factors	None	None	Age, gender, and sleep quality	Age, BMI, marriage, drinking, work experience, college graduate, poor sleep quality, psychosocial alarm	Disease, basic demographic factors, and factors that reflect the life style	None
OR/RR/HR (95% CI)	IBS: OR–1.67 [0.45, 6.41]	IBS: OR–1.88 [1.03, 2.49]; FD: OR–0.76 [0.42, 1.21]	IBS: OR–1.90 [0.72, 5.21]	IBS: OR–1.20 [0.60, 2.41]	IBS: OR–2.14 [1.14, 3.03]	IBS: OR–1.32 [0.47, 3.74]; FD: OR–0.71 [0.29, 1.70]	IBS: OR–2.36 [1.01, 5.47]; FD: OR–0.98 [0.46, 2.09]	IBS: OR–1.67 [0.65, 4.67]; FD: OR–1.50 [0.72, 3.21]

CI = confidence interval, FD = functional dyspepsia, FGIDs = functional gastrointestinal disorders, HR = hazard ratio, IBS = irritable bowel syndrome, OR = odds risk, RR = relative risk.

Table 2
The quality assessment for the included articles.

AHRQ questionnaire for cross-sectional studies

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Total
Rogers et al	1	1	0	0	1	0	0	0	1	0	0	4
Zhou et al	1	1	0	1	1	0	0	1	1	1	0	7
Lu et al	1	1	1	1	1	0	0	1	1	1	0	8
Wells et al	1	1	1	1	1	0	0	0	1	1	0	7
Nojkov et al	1	1	1	0	1	0	0	1	1	1	0	7
Koh et al	1	1	1	1	1	0	1	1	1	0	0	8
Kim et al	1	1	0	1	1	0	1	1	1	1	0	9
Wang	1	1	1	0	1	0	0	1	1	1	0	7

Q1: Define the source of information (survey, record review).
 Q2: List inclusion and exclusion criteria for exposed and unexposed subjects (cases and controls) or refer to previous and publications.
 Q3: Indicate time period used for identifying patients.
 Q4: Indicate whether or not subjects were consecutive if not population-based.
 Q5: Indicate if evaluators of subjective components of study were masked to other aspects of the status of the participants.
 Q6: Describe any assessments undertaken for quality assurance purpose (e.g., test/retest of primary outcome measurements).
 Q7: Explain any patient exclusions from analysis.
 Q8: Describe how confounding was assessed and/or controlled.
 Q9: If applicable, explain how missing data were handled in the analysis.
 Q10: Summarize patient response rates and completeness of data collection.
 Q11: Clarify what follow-up, if any, was expected and the percentage of patients for which incomplete data or follow-up was obtained.
 AHRQ = Agency for Healthcare Research and Quality.

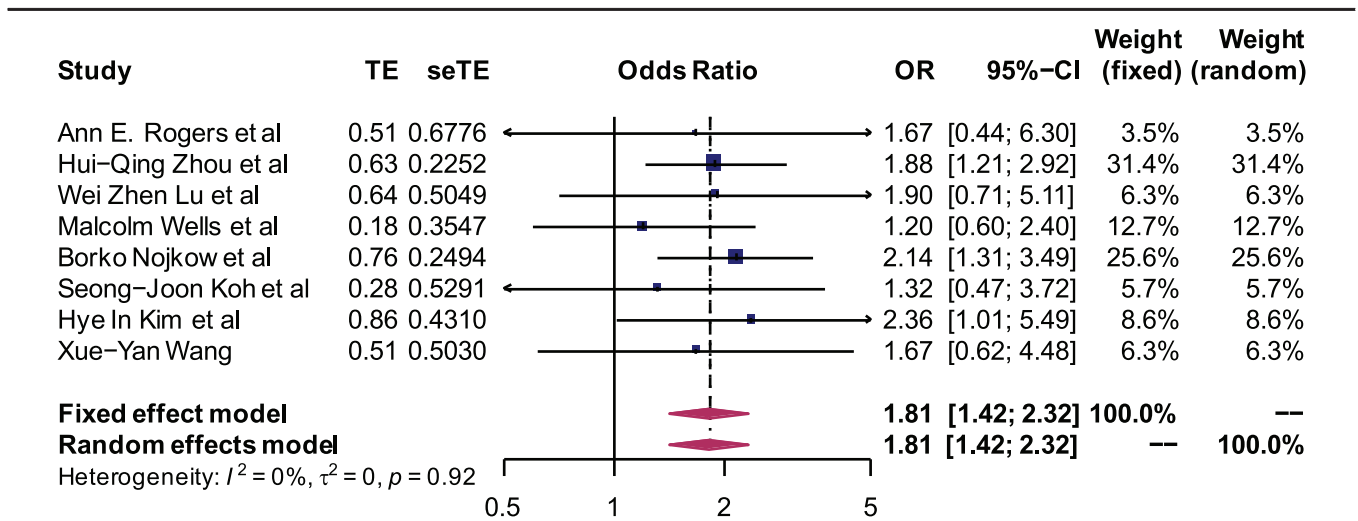


Figure 1. Forest plot of the summary odds risk of IBS risk for shift work. IBS = irritable bowel syndrome.

4. Discussion

This study systematically reviewed the existing epidemiological evidence on the association between shift work and IBS/FD. Systematic review and meta-analysis found that shift work was an independent risk factor for IBS, but not significantly associated with FD.

Gastrointestinal activity and functions are regulated by circadian rhythms 24 hours a day.^[12] Shift work may contribute to circadian disturbances. Circadian rhythms also remain in the gastrointestinal system, and it regulates gastrointestinal motility, secretion, immunity, and metabolism.^[13] It has been documented that circadian disruption probably alters the gut microbiota, leading to an inflammatory state associated with shift work.^[14] A study had shown that disrupted circadian rhythms in the gut are linked to gastrointestinal disorders such as

constipation and IBS.^[8,15] Melatonin regulates gastrointestinal motility and sensation, such as improving bowel habits and alleviating abdominal pain or bloating in patients with IBS.^[16] Melatonin is influenced by the 24-hour light-dark cycle and is a reliable marker of the circadian rhythm system.^[17] Razavi et al^[18] revealed that night shift workers are exposed to more light than day workers and therefore have lower levels of melatonin in their urine. Low-dose melatonin accelerated intestinal motility, while high-dose did the opposite.^[19,20]

Shift work was associated with an increased risk of adverse mental health outcomes in general, and depressive symptoms in particular.^[21] Resident physicians who were on call more than 6 times a month had significantly poorer sleep quality and higher anxiety and depression scores compared to other colleagues.^[22] It is well known that patients with IBS often have symptoms such

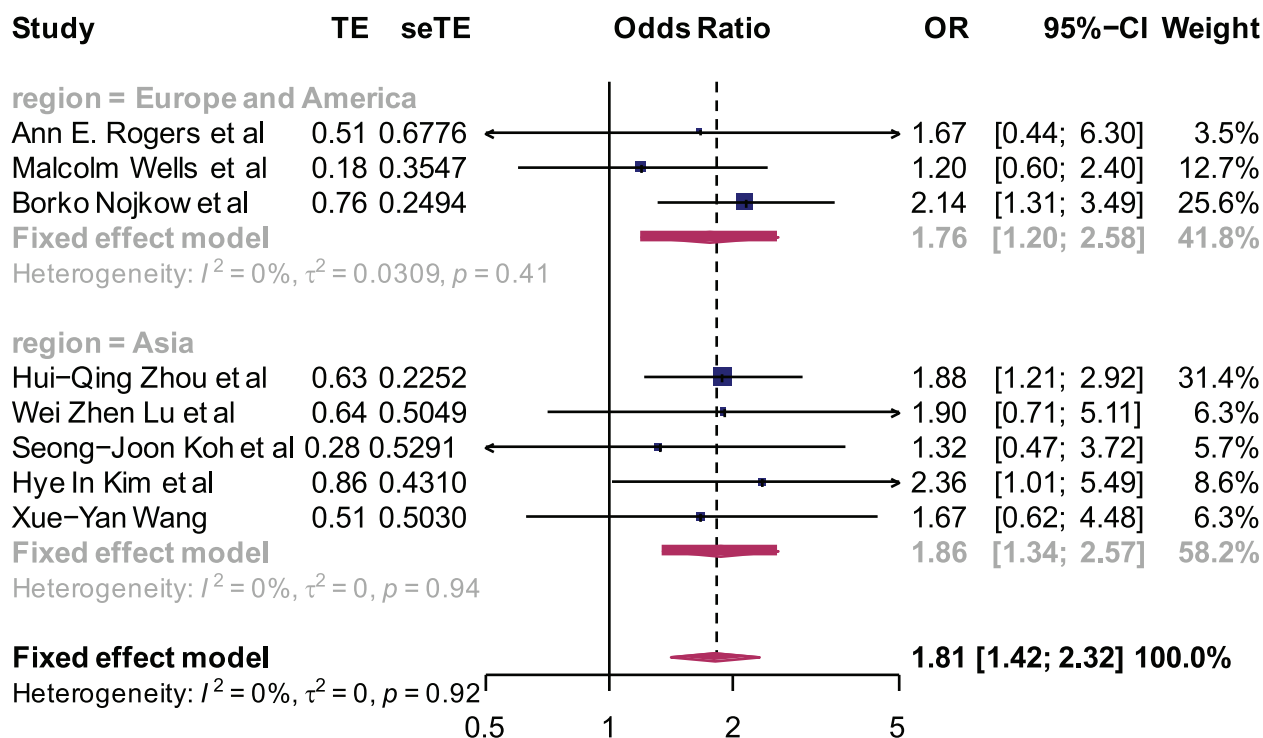


Figure 2. Pooled fixed-effect OR and 95% CI for the association of shift work and IBS by the region. CI = confidence interval, IBS = irritable bowel syndrome, OR = odds risk.

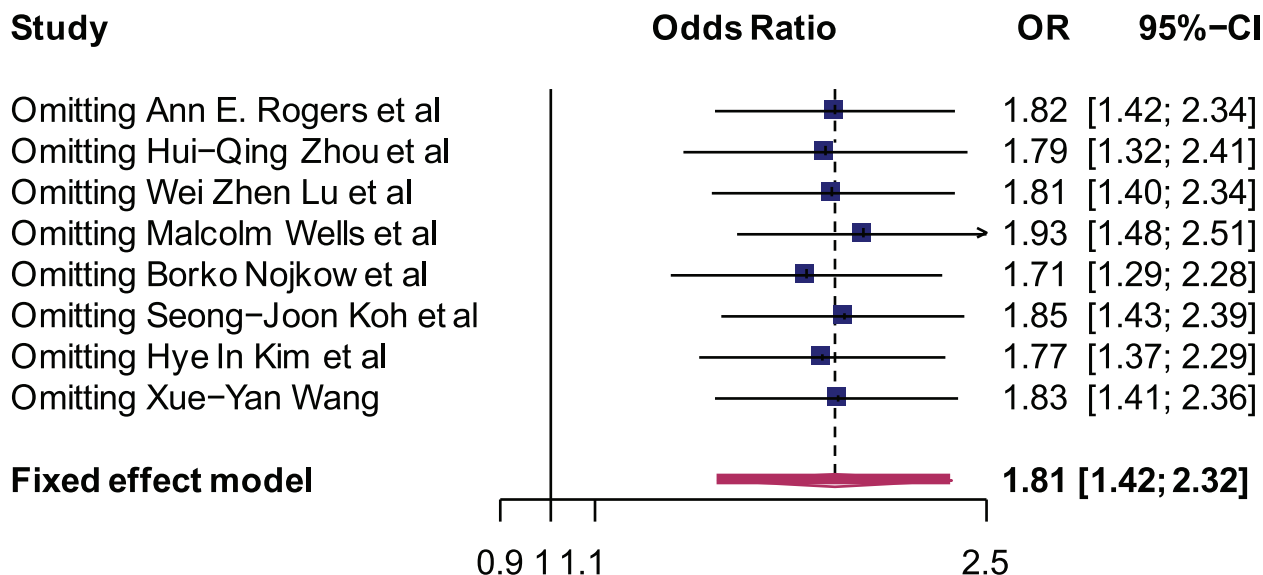


Figure 3. Sensitivity analysis for the cross-sectional studies used IBS as the exposure factor. IBS = irritable bowel syndrome.

as anxiety and depression. This may partly explain the increased incidence of IBS associated with shift work.

This study found no association between FD and shift work. The imbalance between the core circadian physiology and the work schedule is thought to be the main cause of shift work resulting in sleepiness and sleep disruption.^[23] Vege et al^[24] revealed that impaired sleep quality was not associated with FD in the general population. Matsuzaki et al^[25] reported that no independent relationship between FD and sleep disorders after

adjusting for the severity of reflux and bowel symptoms. However, the study on the relationship between FD and shift work has some shortcomings. There were only 4 studies included. The subjects were from the single-center, all of which were nursing-related staff. Therefore, the results of the study need to be further confirmed.

Our study demonstrated that IBS and FD are more common among staff in shift workers than those working the day shift. Shift work is an independent factor for in risk of IBS. Moreover,

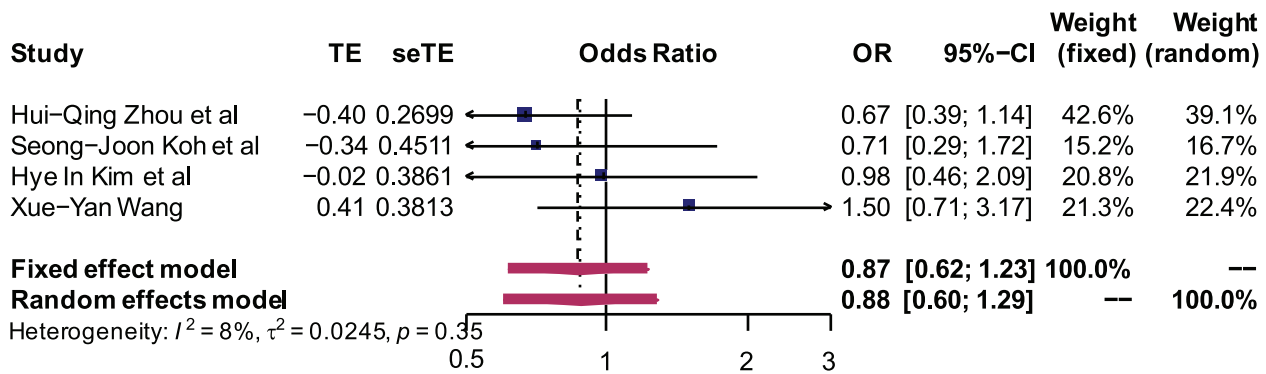


Figure 4. Forest plot of the summary odds risk of FD risk for shift work. FD = functional dyspepsia.

shift work has no significant correlation with FD. There are some limitations in this meta-analysis. Firstly, the definitions of shift work in the included literature were inconsistent. In the included literature, there were about day work and shift work,^[26–29] night work and shift work,^[30] and regular work and shift work.^[31] Secondly, the diagnostic criteria for IBS and FD in the literature are not completely consistent. These may lead to some deviation from the results and conclusions. We have included the currently available cohort studies and performed subgroup analysis. Due to the limited number, the application of the results and conclusions of this study should be considered in combination with other factors.

Author contributions

Tao Bai and Zhaohong Shi were involved in conception and generation of the study protocol and study design. Nian Wang and Xinghuang Liu reviewed the literatures, meta-analysis, as well as have written. Weixiang Ye verified the data. Tao Bai was responsible for resolving disagreements in data selection, synthesis, and assessment. Nian Wang and Xinghuang Liu contributed equally to this study. The manuscript is approved by all authors for publication.

Data curation: Nian Wang.

Formal analysis: Nian Wang.

Writing – original draft: Nian Wang.

References

- [1] Ford AC, Lacy BE, Talley NJ. Irritable bowel syndrome. *N Engl J Med* 2017;26:2566–78.
- [2] Ford AC, Marwaha A, Sood R, Moayyedi P. Global prevalence of, and risk factors for, uninvestigated dyspepsia: a meta-analysis. *Gut* 2015;64:1049–57.
- [3] Arebi N, Gurmany S, Bullas D, Hobson A, Stagg A, Kamm M. Review article: the psychoneuroimmunology of irritable bowel syndrome - an exploration of interactions between psychological, neurological and immunological observations. *Aliment Pharmacol Ther* 2008;28:830–40.
- [4] Lawal A, Kern M, Sidhu H, Hofmann C, Shaker R. Novel evidence for hypersensitivity of visceral sensory neural circuitry in irritable bowel syndrome patients. *Gastroenterology* 2006;130:26–33.
- [5] Lawal A, Kern M, Sidhu H, Hofmann C, F R. Impaired intestinal barrier integrity in the colon of patients with irritable bowel syndrome: involvement of soluble mediators. *Gut* 2009;58:196–201.
- [6] Wang D, Ruan W, Chen Z, Peng Y, Li W. Shift work and risk of cardiovascular disease morbidity and mortality: a dose–response meta-analysis of cohort studies. *Eur J Prev Cardiol* 2018;25:1293–302.
- [7] Gan Y, Yang C, Tong X, et al. Shift work and diabetes mellitus: a meta-analysis of observational studies. *Occup Environ Med* 2014;72:72–8.
- [8] Wells M, Roth L, McWilliam M, Thompson K, Chande N. A cross-sectional study of the association between overnight call and irritable bowel syndrome in medical students. *Can J Gastroenterol* 2012;26:281–4.
- [9] Longstreth GF, Thompson WG, Chey WD, Houghton LA, Mearin F, Spiller RC. Functional bowel disorders. *Gastroenterology* 2006;130:1480–91.
- [10] Thompson WG, Longstreth GF, Drossman DA, et al. Functional bowel disorders and functional abdominal pain. *Gut* 1999;45:II43–7.
- [11] Rostom A, Dubé C, Cranney A, et al. Celiac disease. *Evid Rep Technol Assess (Summ)* 2004;1–6.
- [12] Voigt RM, Forsyth CB, Keshavarzian A. Circadian rhythms: a regulator of gastrointestinal health and dysfunction. *Expert Rev Gastroenterol Hepatol* 2019;13:411–24.
- [13] Bron R, Furness JB. Rhythm of digestion: keeping time in the gastrointestinal tract. *Clin Exp Pharmacol Physiol* 2009;36:1041–8.
- [14] Reynolds AC, Paterson JL, Ferguson SA, Stanley D, Wright KP, Dawson D. The shift work and health research agenda: considering changes in gut microbiota as a pathway linking shift work, sleep loss and circadian misalignment, and metabolic disease. *Sleep Med Rev* 2017;34:3–9.
- [15] Rao SSC, Sadeghi P, Beaty J, Kavlock R. Ambulatory 24-hour colonic manometry in slow-transit constipation. *Am J Gastroenterol* 2004;99:2405–16.
- [16] Esteban-Zubero E, López-Pingarrón L, Alatorre-Jiménez MA, et al. Melatonin's role as a co-adjuvant treatment in colonic diseases: a review. *Life Sci* 2017;170:72–81.
- [17] Hardeland R, Cardinali DP, Srinivasan V, Spence DW, Brown GM, Pandi-Perumal SR. Melatonin—a pleiotropic, orchestrating regulator molecule. *Prog Neurobiol* 2011;93:350–84.
- [18] Razavi P, Devore EE, Bajaj A, et al. Shift work, chronotype, and melatonin rhythm in nurses. *Cancer Epidemiol Biomarkers Prev* 2019;28:1177–86.
- [19] Drago F, Macaudo S, Salehi S. Small doses of melatonin increases intestinal motility in rats. *Dig Dis Sci* 2002;9:1969–74.
- [20] Song GH, Leng PH, Gwee KA, Moochhala SM, Ho KY. Melatonin improves abdominal pain in irritable bowel syndrome patients who have sleep disturbances: a randomised, double blind, placebo controlled study. *Gut* 2005;54:1402–7.
- [21] Torquati L, Mielke GI, Brown WJ, Burton NW, Kolbe-Alexander TL. Shift work and poor mental health: a meta-analysis of longitudinal studies. *Am J Public Health* 2019;109:e13–20.
- [22] Jaradat R, Lahlouh A, Mustafa M. Sleep quality and health related problems of shift work among resident physicians: a cross-sectional study. *Sleep Med* 2020;66:201–6.
- [23] Akerstedt T, Wright KP Jr. Sleep loss and fatigue in shift work and shift work disorder. *Sleep Med Clin* 2009;4:257–71.
- [24] Vege SS, Locke GR 3rd, Weaver AL, Farmer SA, Melton LJ 3rd, Talley NJ. Functional gastrointestinal disorders among people with sleep disturbances: a population-based study. *Mayo Clin Proc* 2004;79:1501–6.
- [25] Matsuzaki J, Suzuki H, Togawa K, et al. Burden of impaired sleep quality on work productivity in functional dyspepsia. *United European Gastroenterol J* 2018;6:398–406.

- [26] Nojkov B, Rubenstein JH, Chey WD, Hoogerwerf WA. The impact of rotating shift work on the prevalence of irritable bowel syndrome in nurses. *Am J Gastroenterol* 2010;105:842–7.
- [27] Koh SJ, Kim M, Oh DY, Kim BG, Lee KL, Kim JW. Psychosocial stress in nurses with shift work schedule is associated with functional gastrointestinal disorders. *J Neurogastroenterol Motil* 2014;4:516–22.
- [28] Kim HI, Jung SA, Choi JY, et al. Impact of shiftwork on irritable bowel syndrome and functional dyspepsia. *J Korean Med Sci* 2013;28:431–7.
- [29] Wang X. Investigation of functional dyspepsia and functional gastrointestinal diseases in shift nurses. *Zhonghua Lao Dong Wei Sheng Zhi Ye Bing Za Zhi* 2008;26:157–60.
- [30] Rogers AE, Hu YJ, Yue Y, et al. Shiftwork, functional bowel symptoms, and the microbiome. *Peer J* 2021;9:e11406.
- [31] Lu WZ, Gwee KA, Ho KY. Functional bowel disorders in rotating shift nurses may be related to sleep disturbances. *Eur J Gastroenterol Hepatol* 2006;18:623.