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► To cite this version:

Frédéric Dutheil, Julien S. Baker, Martial Mermillod, Mélanie de Cesare, Alexia Vidal, et al.. Shift work, and particularly permanent night shifts, promote dyslipidaemia: A systematic review and meta-analysis. *Atherosclerosis*, 2020, 313, pp.156-169. 10.1016/j.atherosclerosis.2020.08.015 . hal-03031098

HAL Id: hal-03031098

<https://hal.science/hal-03031098>

Submitted on 17 Oct 2022

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Shift work, and particularly permanent night shifts, promote dyslipidaemia: A systematic review and meta-analysis

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Abstract

Background and aims: Shift work is common worldwide and linked to deleterious cardiovascular effects that might be underlined by dyslipidemia. The aim of this systematic review and meta-analysis is to determine the impact of shiftwork on dyslipidemia.

Methods: Searching in PubMed, Cochrane Library, Science Direct and Embase databases without language restriction on 15 February, 2020, included studies that describe blood lipids levels or a risk measure in shift workers compared with fixed-day workers (controls). Differences by study-level characteristics were estimated using stratified meta-analysis by type of shift work, and meta-regression to examine relations between dyslipidemia and demographic, lifestyle and work characteristics. Estimates were pooled using random-effect meta-analysis.

Results: We included a total of 66 articles, representing 197,063 workers. Shift work globally increased the levels of triglycerides (overall SMD = 0.09; 95CI 0.05 to 0.13; $p < 0.001$), and globally decreased the levels of c-HDL (-0.08; 95CI -0.12 to -0.03; $p = 0.001$). Permanent night shift workers were an at-risk type of shift for dyslipidemia with significantly higher blood levels of total cholesterol (0.22; 95CI 0.01 to 0.42; $p = 0.043$) and triglycerides (0.18; 0.03 to 0.33; $p = 0.017$), and significantly lower blood levels of c-HDL (-0.16; 95CI -0.32 to 0.00; $p = 0.05$). Permanent night shift workers were more at-risk for total cholesterol than rotating 3*8 shift workers (Coefficient 0.22; 95CI 0.01 to 0.42; $p = 0.038$) and rotating 2*12 shift workers (0.24; 0.02 to 0.46; $p = 0.037$), and more at-risk for triglycerides than rotating day shift workers (0.21; 95CI 0.03 to 0.38; $p = 0.023$). Results were non-significant for c-LDL, nor depending on type of shifts.

Conclusions: Shift work, and particularly permanent night shift, is associated with dyslipidaemia via elevated total cholesterol and triglycerides, and reduced HDL-cholesterol.

Our current study provides a practical and valuable strengthening of the evidence-base required for preventive health initiatives and workplace reform.

Key words: dyslipidemia – blood lipids level – cholesterol – shift work – night shift – cardiovascular disease – metabolic disease – preventive medicine – work conditions.

Introduction

Shift work that involves night time, is common, accounting for approximately 20% of the work force.[1] Although definitions vary slightly across sources, shift work can be defined as employment in any work schedule that is not a regular daytime schedule.[2] The full spectrum of shift work comprises regular evening or night schedules, rotating shifts, split shifts, on-call or casual shifts, irregular schedules, and other non-day schedules.[2] Unfortunately, shift work is linked to several health problems [3–5], including deleterious effects on the cardiovascular and metabolic systems.[6–13] For instance, shift workers appear to be at increased risk for coronary heart disease,[7,11–13] stroke,[6] insulin resistance,[7,8] and metabolic syndrome.[9,10] Lipid profiles are directly linked to the risk of cardiovascular diseases.[14,15] Specifically, in shift workers, both reduced high-density lipoprotein (HDL)-cholesterol and elevated blood LDL and triglycerides may represent an increased risk of cardiovascular diseases.[9] Indeed, it is reasonable to expect that shift work may influence lipid metabolism, particularly deleterious for the health of workers.[16] Some cross-sectional and longitudinal studies have concluded that shift work may increase dyslipidemia.[17–19] However, results are conflicting, with some studies not supporting a link between shiftwork and dyslipidemia.[20–24] Moreover, most of the previous studies did not take into account the confounding factors such key demographic, lifestyle, workplace and shift work characteristics.

Therefore, the primary objective of this study was to conduct a systematic review and meta-analysis to determine the impact of shift work on dyslipidemia. Secondary objectives were to determine if one type of shift work would be particularly deleterious on dyslipidemia, and to examine relations between dyslipidemia and demographic, lifestyle and work characteristics.

Materials and methods

Literature search

A systematic search of all observational epidemiological studies about shift work and lipid metabolism was conducted. The following databases were searched on 15 February, 2020: PubMed, Embase, Cochrane Library, and ScienceDirect. The following relevant mesh terms/keywords were used: “night work” OR “nightwork” OR “shift work” OR “shiftwork” AND “lipids” OR “metabolism” OR “blood” OR "LDL" OR "HDL" OR "cholesterol" OR "triglycerides" (details of search strategy is presented in Supplementary Data 1). The search was not limited to specific years and no language restrictions applied. The studies included in the meta-analysis had to describe blood lipids levels or a risk measure i.e. odds ratio (OR), hazard ratio (HR) or relative risk (RR) in shift workers compared with fixed-day workers (controls). Studies could be cross-sectional, cohort studies or case-study designs. Reference lists of all publications meeting the inclusion criteria, as well as from putative reviews, were manually searched to identify any further studies missed through electronic searching. The search strategy is described in Figure 1. Three authors (Mélanie De Cesare, Alexia Vidal and Valentin Navel) conducted separately all literature searches and collated the abstracts. Four authors (Mélanie De Cesare, Alexia Vidal, Valentin Navel and Frédéric Dutheil) separately reviewed the abstracts and based on the selection criteria decided the suitability of the articles for inclusion. A fourth author (Geraldine Naughton) was asked to review the article where consensus on suitability was not met. Then, all authors reviewed the eligible articles. We followed the PRISMA guidelines (Supplementary Data 2) and we registered our search protocol (PROSPERO identification CRD42020168531).

Data collection

The data collected included first author's name, publication year, country, study design, aims and outcomes of included articles, sample size, mean age, sex, occupation / type of work, type of shift work (permanent night shift, rotating shift work, schedules), length of service, body mass index, smoking, alcohol, physical activity, blood lipid levels and risk measurements for total-, HDL-, LDL-cholesterol, and triglycerides.

Outcomes

The primary outcome was the effects of shift work on blood lipid profiles. Secondary outcomes were the risk of dyslipidaemia according to the type of shift work and the association between blood lipid profiles and covariates.

Quality of assessment

Although not designed to quantify the integrity of studies,[25] the “STrengthening the Reporting of OBservational studies in Epidemiology” (STROBE) criteria were used for checking the quality of reporting.[26] The 22 items identified in the STROBE criteria were evaluated for a maximal score of 34 for each study. The methodological quality of the studies was further evaluated by three authors (Frédéric Dutheil, Mélanie De Cesare and Valentin Navel) using the Newcastle-Ottawa Quality Assessment Scale (NOS) model.[27] The following 9 items were assessed in all cohort studies: 4 items on selection bias (representativeness of the exposed and non-exposed cohort, ascertainment of expose), 2 items on comparability bias (design and analysis) and 3 items on outcome bias (assessment of outcome, longer and adequacy of follow-up). Similar items were used to evaluate case control studies. Each item was assigned a judgment of “Yes”, “No”, “Can’t say”, or “Not applicable”.

Disagreements were addressed by obtaining a consensus with a third author (Bruno Pereira) (Supplementary Data 3 and 4).

Statistical analysis

Statistical analyses were conducted using Comprehensive Meta-analysis software (version 2, Biostat Corporation) and Stata software (version 13, StataCorp, College Station, US).[28–34] Characteristics of the work and workers are summarized for each study sample and reported as mean \pm standard-deviation (SD) and number (%) for continuous and categorical variables respectively. For rigor, effect sizes were defined as standard mean differences (SMD) of blood lipid levels or a measure of risk (i.e. odds ratio, hazard ratio, or relative risk). First, we conducted meta-analyses on blood lipids levels (total cholesterol, triglycerides, HDL-cholesterol, LDL-cholesterol). Standard difference in means between groups (SMD, difference between means divided by the pooled standard deviation, with a correction for small sample bias) and 95% confidence interval (95%CI) were estimated using DerSimonian and Laird random-effects models (assuming that the true effect estimates varied among studies).[35] A SMD is defined as a unitless measure of the effects of shift work on blood lipids levels centered at zero if the blood lipids levels in shift workers are not different from fixed day workers. A positive SMD denoted higher blood lipid levels in shift workers than in fixed day workers. A scale for SMD has been suggested with 0.8 reflecting a large effect, 0.5 a moderate effect, and 0.2 a small effect.[35] *p* values less than 0.05 were considered statistically significant. Then, we conducted meta-analyses on risks (i.e. odds ratio, hazard ratio, or relative risk) for dyslipidemia in shift workers compared with fixed-day workers. We stratified these meta-analyses on the type of shift work. Statistical heterogeneity between results was assessed by examining forest plots, confidence intervals, and using I^2 , which is the most common metric for measuring the magnitude of between-study heterogeneity and is

easily interpretable. I^2 values range between 0% and 100% and are typically considered low for heterogeneity scores of <25%, modest for 25–50%, and high for >50%. For example, a significant heterogeneity may be due to the variability between the characteristics of the studies, such as those of the workers (age, sex, etc), the type of shift work or the occupation. Publication bias was taken into consideration and funnel plots were compiled, with sensitivity analysis excluding studies not evenly distributed around the base of the funnel. We also computed sensitivity analyses depending on the type of risks. When possible (sufficient sample size), meta-regressions were proposed to study the relation between blood lipids levels and characteristics of workers (e.g. age, sex, smoking, alcohol, physical activity) and other working characteristics (e.g. duration of exposure to shift work, type of occupation). Results were expressed as regression coefficients and 95% CI.

Results

An initial search produced 5689 possible articles (Figure 1). We identified 66 eligible articles [7–10,16,17,21–24,36–91] including 41 cross-sectional studies,[7–10,17,21,23,37,38,40,42,47–50,54,55,58–62,66–69,71,72,75,76,78,80–84,86,87,89–91] 24 prospective or retrospective cohort studies[16,22,24,36,39,43–46,51–53,56,57,63–65,70,73,74,77,79,85,88] and 1 case-control study.[41] Overall, these studies included a total of 80,254 shift workers and 116,809 day workers (Table 1). All articles were written in English, except two in French,[42,70] one in Spanish[52] and one in Italian.[44]

More details on quality of articles (Supplementary Data 3 and 4), population of workers (sample size, gender, age, body mass index, smoking and alcohol status, physical activity), occupational characteristics (type of work, type of shift work and length of service), bloods

lipids (levels and risk of dyslipidemia), study designs, geographic zones, follow-up, aims and outcomes of included articles are described in Table 1 and Supplementary Data 5.

Results

Meta-analysis of total cholesterol for each type of shift works

We included 43 studies.[7,10,16,17,21–24,36,38–43,46,48–50,52,55,60,63–66,68–70,72–76,78–82,85,86,90,91] The overall SMD was 0.01 (95CI -0.03 to 0.04, $p = 0.638$) with an important heterogeneity ($I^2 = 73.0\%$) (Figure 2 and Supplementary Data 6). Among the 43 included studies, 4 studies reported permanent night shift,[39,41,69,82] 23 reported rotating 3*8 shift,[16,21–24,36,42,46,48,50,52,55,60,63–66,69,70,73,76,80,85] 10 reported rotating 2*12 shift,[10,24,40,60,72,74,78,86,90,91] 2 reported rotating day shift,[36,55] and 9 were unspecified.[7,17,38,43,49,68,75,79,81] Only permanent night shift workers had increased blood level of total cholesterol (SMD = 0.22; 95CI 0.01 to 0.42; $p = 0.043$; $I^2 = 60.3\%$) (Supplementary Data 6). Meta-regressions demonstrated that permanent night shift workers had higher blood levels of total cholesterol than rotating 3*8 shift workers (Coefficient 0.22; 95CI 0.01 to 0.42; $p = 0.038$), rotating 2*12 shift workers (0.24; 0.02 to 0.46; $p = 0.037$), and unspecified shift workers (0.23; 0.01 to 0.46; $p = 0.049$). We did not retrieve any significant results on the others socio-demographical parameters and between type of shift works (Figure 3 and 4).

Meta-analysis of triglycerides for each type of shift works

We included 48 studies.[10,17,21–23,36–43,46–60,62,66–71,73–84,86] Shift work globally increased the levels of triglycerides (overall SMD 0.09; 95CI 0.05 to 0.13; $p < 0.001$) with an important heterogeneity ($I^2 = 80.3\%$) (Figure 2 and Supplementary Data 7). Among the 48 included studies, seven reported permanent night shift,[39,41,58,67,69,71,82] 21 reported

rotating 3*8 shift,[21,23,36,42,46–48,50,52–55,59,60,66,69,70,73,76,77,80] eleven reported rotating 2*12 shift,[10,40,51,56,57,60,74,78,83,86,91] four reported rotating day shift,[36,53–55] and 12 were unspecified.[17,37,38,43,49,62,67,68,75,79,81,84] We found significantly increased blood levels of triglycerides among permanent night shift workers (0.18; 0.03 to 0.33; $p = 0.017$; $I^2 = 73.8\%$), rotating 3*8 shift workers (0.09; 0.03 to 0.16; $p = 0.004$; $I^2 = 73.6\%$), rotating 2*12 shift workers (0.07; 0.01 to 0.13; $p = 0.017$; $I^2 = 31.6\%$), and non-specified shift workers (0.11; 0.03 to 0.18; $p = 0.004$; $I^2 = 80.9\%$) (Supplementary Data 7). Meta-regressions demonstrated that permanent night shift workers had a higher blood levels of triglycerides than rotating day shift workers (Coefficient = 0.21; 95CI 0.03 to 0.38; $p = 0.023$). We did not retrieve any significant results on the other socio-demographical parameters and between types of shift works (Figure 3 and 4).

Meta-analysis of LDL cholesterol for each type of shift works

Among the 31 studies reporting LDL cholesterol,[7,10,17,38,40,43,48,49,51,52,54,55,62,65–70,74,76–82,84–86,91] permanent night shift was reported in 3 studies,[67,69,82] rotating 3*8 shift in 12 studies,[47,52,54,55,65,66,69,70,76,77,80,85] rotating 2*12 shift in 7 studies,[10,40,51,74,78,86,91] rotating day shift in 2 studies,[53,55] and unspecified in 11 studies (Figure 2 and Supplementary Data 8).[7,17,38,43,49,62,67,68,79,81,84] Meta-analysis, globally and stratified by type of shift works, as well as meta-regressions, did not retrieve any significant results (Figure 3 and 4).

Meta-analysis of HDL cholesterol for each type of shift works

We included 46 studies.[10,17,23,24,37,38,40,41,43,45,47–59,62,65–71,73–86,91] The overall SMD was -0.08 (95CI -0.12 to -0.03; $p = 0.001$) with an important heterogeneity ($I^2 = 85.9\%$) (Figure 2 and Supplementary Data 9). Among the 46 included studies, 6 studies

reported permanent night shift,[41,58,67,69,71,82] 19 reported rotating 3*8 shift,[23,24,47,48,50,52–55,59,65,66,69,70,73,76,77,80,85] 11 reported rotating 2*12 shift,[10,24,40,51,56,57,74,78,83,86,91] 3 reported rotating day shift,[53–55] and 13 were unspecified.[17,37,38,43,45,49,62,67,68,75,79,81,84] We found a significantly lower blood level of c-HDL among permanent night shift workers (SMD = -0.16; 95CI -0.32 to 0.00; $p = 0.05$; $I^2 = 72.3\%$), rotating 3*8 shift workers (-0.10; 95CI -0.17 to -0.02; $p = 0.018$; $I^2 = 78.8\%$), and non-specified shift workers (-0.08; 95CI -0.15 to -0.01; $p = 0.027$; $I^2 = 81.7\%$). We also found a significantly higher blood level of c-HDL among rotating day shift workers (0.18; 95CI 0.04 to 0.31; $p = 0.010$; $I^2 = 80.4\%$) (Supplementary Data 9). Meta-regressions demonstrated that permanent night shift workers (Coefficient = -0.32; 95CI -0.57 to -0.07; $p = 0.014$), rotating 3*8 shift workers (-0.26; 95CI -0.47 to -0.04; $p = 0.019$), and rotating 2*12 shift workers (-0.24; 95CI -0.47 to -0.02; $p = 0.034$) had lower blood levels of c-HDL than rotating day shift workers. We also showed that rotating day shift workers had higher blood levels of c-HDL than non-specified shift workers (0.24; 95CI 0.03 to 0.47; $p = 0.028$). We showed a negative role of regular physical activity on blood levels of c-HDL in condition of shift work (-0.01; 95CI -0.01 to 0.00; $p = 0.007$). We did not retrieve any significant results on the other socio-demographical parameters (Figure 3 and 4).

Meta-analyses of odds ratio for each type of lipid related risk

We included 3 studies reporting Odds Ratio (OR) for high total cholesterol (Supplementary Data 10),[17,38,89] 7 studies reporting OR for high triglyceride (Supplementary Data 11),[8,9,17,38,61,87,88] 2 studies reporting OR for high c-LDL (Supplementary Data 12),[17,89] and 6 studies reporting OR for low c-HDL (Supplementary Data 13).[8,9,17,38,44,87] Shift work exposure increased the risk of high triglyceride levels by

12% (ES = 1.12; 95CI 1.01 to 1.23; $p < 0.001$; $I^2=55.2\%$) without significance for total cholesterol, c-LDL, and c-HDL. Insufficient data did not permit meta-regression.

Discussion

This current meta-analysis presents a broad comprehensive review of the associations between shift work and dyslipidaemia in 197,063 workers. The main finding was that shift work induced dyslipidaemia with elevated triglycerides, elevated total, and decreased HDL-cholesterol. More specifically, permanent night shifts were the most deleterious type of shift work on dyslipidemia; with elevated triglycerides, elevated total cholesterol, and decreased HDL-cholesterol. Results from meta-regressions confirmed the more negative impact of permanent night shifts than other types of shift work.

Shift work and dyslipidemia

Some potential biological mechanisms may explain the link between shift work and dyslipidemia. First, long-term exposure to shift work might disturb the normal circadian rhythm and generate an imbalance in lipid metabolism.[92] Melatonin is an important mediator of circadian rhythms. Production of melatonin is supported by darkness but inhibited by light at night, so night work can inhibit the secretion of melatonin. Animal studies showed that decreased secretion of melatonin was associated with dyslipidemia, such as an elevated blood level of triglyceride.[93] Alternatively, workers may consume meals at unusual times; the desynchronization of food intake and internal metabolic rhythm may also affect the energy balance and weight regulation.[94] It has been shown that nocturnal food intake (in particular those rich in carbohydrate) might aggravate metabolic disturbances of triglyceride and lipid levels.[51,95] Another potential mechanism may lie in the capacity of shift work to decrease sleep duration and quality, which may have an adverse impact on psychological and physical

health.[96] Short sleep duration is associated with an increased risk of obesity,[97] type 2 diabetes,[98] cardiovascular outcomes[99] and all-cause mortality,[100] with a dose response relationship between short sleep duration (less than six hours) and mortality.[101] Restricting sleep duration over just one week resulted in significant reduction in insulin sensitivity in middle aged and older men.[102] Prolonged exposure to disturbed sleep may therefore have profound consequences on the metabolic health of shift workers. Interestingly, we showed that shift work is mainly deleterious on triglycerides and c-HDL, but not c-LDL. The literature already reported that night shifts may have a slight protective effect on c-LDL.[103] Even if it has been hypothesized a possible selection bias of healthy workers who might undergo night shift,[103] we want to acknowledge the important gap in the literature surrounding the physiology of the absence of influence of shift work on c-LDL.

The deleterious effect of permanent night shift

We demonstrated that permanent night shifts might be the worst schedule for workers in terms of dyslipidemia. The shift work is commonly regarded as the work outside regular day time, with working time during normally sleeping periods.[104] Putative explanations might be that, most often, permanent night shift workers keep a desynchronized circadian rhythm, with awakening during normal sleeping periods.[105] This desynchronized circadian rhythm might affect sleep quality involving chronic disrupted sleep.[106,107] Indeed, day sleeps have typically been found to be considerably shorter than normal night sleeps, because of multiple reasons including increased environmental noise, light levels, and conflicting social, domestic and family demands.[108] The circadian system is impacted by sleep disturbance, and contribute to the regulation of metabolism and energy expenditure.[104] Desynchronization between the central (brain) and peripheral (outside of brain, such as digestive system and adipose tissue) clocks by altered food intake and diet composition can

lead to the development of metabolic syndrome and obesity.[109,110] Many studies describe peripheral appetite regulation with circadian secretion of ghrelin, an orexigenic hormone secreted by stomachal tissue, and leptin, an anorexigenic hormone secreted by adipose tissue.[111,112] Permanent night shift workers present a disrupted control of ghrelin and leptin, associated with behavioral changes in diet, sleep and increased adiposity and related metabolic alterations.[109,110] It has been showed that ghrelin secretion was related to pituitary gland and pulsatile neuroendocrine secretion from the hypothalamus to modify sleep-wake pattern by increasing wakefulness and to decrease the duration of deep sleeping periods.[113,114] Thus, all these changes in the circadian clock are associated with temporal alteration in feeding behavior and increased weight gain, explaining the high proportion of obesity in night shift workers.[115] It seems also salient to note that night shift work is positively associated with abnormal eating patterns and BMI.[116,117] Then, dyslipidemia could be an epiphenomenon of snacking. Moreover, animal studies suggest that circadian disruption alters hepatic clock gene expression, bile acid metabolism and lipid homeostasis to contribute to dyslipidemia.[118]

Socio-demographic characteristics of workers

Despite we found no link between dyslipidemia and occupational settings, age, sex, marital status, smoking or drinking, physical activity, or obesity, the literature is abundant. We stratified our results by types of shift work to identify at-risk shifting for dyslipidemia without focusing on type of occupation, because of heterogeneity between included studies. However, occupational setting, particularly the manual work, is known to be a socioeconomic factor increasing dyslipidemia, hypertension, obesity and diabetes.[119–121] In our study, the proportion of women and elderly workers exposed to shift work remained low, with most studies including only men between 30 and 45 years, precluding further analyses.

Nevertheless, older individuals and men are at-risk populations for dyslipidemia, particularly in post-industrialised countries.[122,123] Despite an important social determinant of health,[124] marital status, seems to not influence the risk of dyslipidemia with contradictory and inconclusive results.[125,126] In our meta-analysis, smoking and alcohol intake were not linked to dyslipidaemia. However, smoking promotes dyslipidaemia by worsening the control of lipid metabolism.[127,128] Similarly, the link between misuse of alcohol and dyslipidemia is well established, with yet contradictory results for regular low doses.[129–131] Contrary to our results, physical activity might be protective on HDL levels. During the past decades, there was cumulative evidence concerning the impact of regular physical activity on plasma lipoprotein metabolism and, finally, reducing the incidence of cardiovascular diseases.[132]

Limitations

Several limitations in our review should be mentioned. Our meta-analysis inherited the limitations of the 66 individual studies of which it was composed and therefore is subjected to the bias of included studies. Even if a recent meta-analysis demonstrated associations between short sleep duration and cardiometabolic risk,[101] this is the first meta-analysis to systematically quantify the strength of associations between shift work and dyslipidemia. Despite our stratification by type of shift work (permanent night shift, 3*8, 2*12, rotating day shift), there is heterogeneity within each subgroup regarding schedule and rhythm of night shift. Moreover, although the shift work is relatively objective and specific, it was not clearly defined in some published studies, which might have affected the precision of the results. There is also heterogeneity in reporting blood lipid levels between studies, and different cut-off for dyslipidemia for studies reporting odds ratio or hazard ratio. Moreover, odds ratio and hazard ratio were adjusted on different variables between studies, precluding robust conclusions. Most studies have a cross-sectional design. Therefore, the associations between

shift work and dyslipidemia risk might be underestimated by the potential healthy worker survival effect in the cross-sectional studies.[133] Even if methodological quality of the included studies was evaluated by subjective assessments (STROBE and NOS), overall methodological quality was reasonably good without major comparability bias between exposed and non-exposed groups, with a large volume of data available and consistency for the main outcomes of interest. We also want to acknowledge that we were not able to increase the number of studies with c-LDL using the formula of Friedewald ($LDL = \text{total cholesterol} - (\text{triglycerides}/5 + HDL)$),[134] as we did not have access to raw data. Finally, few studies reported duration of exposure to shift work, precluding the analysis of a possible dose-response relation. Generalizability of our results may also suffer from the limited number of studies from Africa and South America. For the future, it would be interesting to investigate more prospective and interventional studies to explore the underlying mechanisms and putative preventive strategy.

Conclusions

Shift work, and particularly permanent night shift, is associated with dyslipidaemia via elevated triglycerides, elevated total cholesterol, and reduced HDL-cholesterol. Given the increasing prevalence of shift work worldwide and the heavy economic burden of cardiovascular diseases that may be promoted by dyslipidemia in shift workers, our current study provides a practical and valuable strengthening of the evidence-base required for preventive health initiatives and workplace reform. When shift work is unavoidable, permanent night shifts should be removed from schedules and at least replaced by rotating shifts, preferentially in two schedules; one during the day and one at night. Further studies should investigate economic benefits of removing permanent night shifts, both in terms of healthcare and for factories.

Conflict of interest

The authors declared they do not have anything to disclose regarding conflict of interest with respect to this manuscript.

Acknowledgements

We thank Kathryn Duncan, librarian of the Australian Catholic University, and Nathalie Piñol-Domenech for her help in the collection of full texts of articles.

References

- [1] H.A. Kolstad, Nightshift work and risk of breast cancer and other cancers--a critical review of the epidemiologic evidence, *Scand J Work Environ Health*. 34 (2008) 5–22. <https://doi.org/10.5271/sjweh.1194>.
- [2] M.V. Vyas, A.X. Garg, A.V. Iansavichus, J. Costella, A. Donner, L.E. Laugsand, I. Janszky, M. Mrkobrada, G. Parraga, D.G. Hackam, Shift work and vascular events: systematic review and meta-analysis, *BMJ*. 345 (2012) e4800–e4800. <https://doi.org/10.1136/bmj.e4800>.
- [3] X. Lin, W. Chen, F. Wei, M. Ying, W. Wei, X. Xie, Night-shift work increases morbidity of breast cancer and all-cause mortality: a meta-analysis of 16 prospective cohort studies, *Sleep Med*. 16 (2015) 1381–1387. <https://doi.org/10.1016/j.sleep.2015.02.543>.
- [4] S. Ijaz, J. Verbeek, A. Seidler, M.-L. Lindbohm, A. Ojajärvi, N. Orsini, G. Costa, K. Neuvonen, Night-shift work and breast cancer--a systematic review and meta-analysis, *Scand J Work Environ Health*. 39 (2013) 431–447. <https://doi.org/10.5271/sjweh.3371>.
- [5] D. Rao, H. Yu, Y. Bai, X. Zheng, L. Xie, Does night-shift work increase the risk of prostate cancer? a systematic review and meta-analysis, *Onco Targets Ther*. 8 (2015) 2817–2826. <https://doi.org/10.2147/OTT.S89769>.
- [6] J. Hermansson, K. Gillander Gådin, B. Karlsson, B. Lindahl, B. Stegmayr, A. Knutsson, Ischemic stroke and shift work, *Scand J Work Environ Health*. 33 (2007) 435–439. <https://doi.org/10.5271/sjweh.1165>.
- [7] C.M. Haupt, D. Alte, M. Dörr, D.M. Robinson, S.B. Felix, U. John, H. Völzke, The relation of exposure to shift work with atherosclerosis and myocardial infarction in a

- general population, *Atherosclerosis*. 201 (2008) 205–211. <https://doi.org/10.1016/j.atherosclerosis.2007.12.059>.
- [8] B.H. Karlsson, A.K. Knutsson, B.O. Lindahl, L.S. Alfredsson, Metabolic disturbances in male workers with rotating three-shift work. Results of the WOLF study, *International Archives of Occupational and Environmental Health*. 76 (2003) 424–430. <https://doi.org/10.1007/s00420-003-0440-y>.
- [9] B. Karlsson, A. Knutsson, B. Lindahl, Is there an association between shift work and having a metabolic syndrome? Results from a population based study of 27,485 people, *Occup Environ Med*. 58 (2001) 747–752. <https://doi.org/10.1136/oem.58.11.747>.
- [10] S. Sookoian, C. Gemma, T. Fernández Gianotti, A. Burgueño, A. Alvarez, C.D. González, C.J. Pirola, Effects of rotating shift work on biomarkers of metabolic syndrome and inflammation, *J Intern Med*. 261 (2007) 285–292. <https://doi.org/10.1111/j.1365-2796.2007.01766.x>.
- [11] Y. Fujino, H. Iso, A. Tamakoshi, Y. Inaba, A. Koizumi, T. Kubo, T. Yoshimura, Japanese Collaborative Cohort Study Group, A prospective cohort study of shift work and risk of ischemic heart disease in Japanese male workers, *Am. J. Epidemiol.* 164 (2006) 128–135. <https://doi.org/10.1093/aje/kwj185>.
- [12] A. Knutsson, T. Akerstedt, B.G. Jonsson, K. Orth-Gomer, Increased risk of ischaemic heart disease in shift workers, *Lancet*. 2 (1986) 89–92. [https://doi.org/10.1016/s0140-6736\(86\)91619-3](https://doi.org/10.1016/s0140-6736(86)91619-3).
- [13] A. Knutsson, J. Hallquist, C. Reuterwall, T. Theorell, T. Akerstedt, Shiftwork and myocardial infarction: a case-control study, *Occup Environ Med*. 56 (1999) 46–50. <https://doi.org/10.1136/oem.56.1.46>.
- [14] S. Nagasawa, T. Okamura, H. Iso, A. Tamakoshi, M. Yamada, M. Watanabe, Y. Murakami, K. Miura, H. Ueshima, Evidence for Cardiovascular Prevention from Observational Cohorts in Japan (EPOCH-JAPAN) Research Group, Relation between serum total cholesterol level and cardiovascular disease stratified by sex and age group: a pooled analysis of 65 594 individuals from 10 cohort studies in Japan, *J Am Heart Assoc*. 1 (2012) e001974. <https://doi.org/10.1161/JAHA.112.001974>.
- [15] V.M. Maher, B.G. Brown, S.M. Marcovina, L.A. Hillger, X.Q. Zhao, J.J. Albers, Effects of lowering elevated LDL cholesterol on the cardiovascular risk of lipoprotein(a), *JAMA*. 274 (1995) 1771–1774.
- [16] M. Dochi, Y. Suwazono, K. Sakata, Y. Okubo, M. Oishi, K. Tanaka, E. Kobayashi, K. Nogawa, Shift work is a risk factor for increased total cholesterol level: a 14-year prospective cohort study in 6886 male workers, *Occupational and Environmental Medicine*. 66 (2009) 592–597. <https://doi.org/10.1136/oem.2008.042176>.
- [17] M. Ghiasvand, R. Heshmat, R. Golpira, V. Haghpanah, A. Soleimani, P. Shoushtarizadeh, S. Tavangar, B. Larijani, Shift working and risk of lipid disorders: A cross-sectional study, *Lipids Health Dis*. 5 (2006) 9. <https://doi.org/10.1186/1476-511X-5-9>.
- [18] M. Ha, J. Park, Shiftwork and metabolic risk factors of cardiovascular disease, *J Occup Health*. 47 (2005) 89–95. <https://doi.org/10.1539/joh.47.89>.
- [19] T. Theorell, T. Akerstedt, Day and night work: changes in cholesterol, uric acid, glucose and potassium in serum and in circadian patterns of urinary catecholamine excretion. A longitudinal cross-over study of railway workers, *Acta Med Scand*. 200 (1976) 47–53. <https://doi.org/10.1111/j.0954-6820.1976.tb08194.x>.
- [20] R.G. Bursey, A cardiovascular study of shift workers with respect to coronary artery disease risk factor prevalence, *J Soc Occup Med*. 40 (1990) 65–67.

- [21] A. Knutsson, T. Akerstedt, B.G. Jonsson, Prevalence of risk factors for coronary artery disease among day and shift workers., *Scand J Work Environ Health*. 14 (1988) 317–321. <https://doi.org/10.5271/sjweh.1913>.
- [22] Y. Morikawa, H. Nakagawa, K. Miura, Y. Soyama, M. Ishizaki, T. Kido, Y. Naruse, Y. Suwazono, K. Nogawa, Effect of shift work on body mass index and metabolic parameters, *Scand J Work Environ Health*. 33 (2007) 45–50. <https://doi.org/10.5271/sjweh.1063>.
- [23] M. Romon, M.C. Nuttens, C. Fievet, P. Pot, J.M. Bard, D. Furon, J.C. Fruchart, Increased triglyceride levels in shift workers, *Am. J. Med.* 93 (1992) 259–262. [https://doi.org/10.1016/0002-9343\(92\)90230-9](https://doi.org/10.1016/0002-9343(92)90230-9).
- [24] L. Tenkanen, T. Sjöblom, R. Kalimo, T. Alikoski, M. Härmä, Shift work, occupation and coronary heart disease over 6 years of follow-up in the Helsinki Heart Study, *Scand J Work Environ Health*. 23 (1997) 257–265. <https://doi.org/10.5271/sjweh.218>.
- [25] B.R. da Costa, M. Cevallos, D.G. Altman, A.W.S. Rutjes, M. Egger, Uses and misuses of the STROBE statement: bibliographic study, *BMJ Open*. 1 (2011) e000048. <https://doi.org/10.1136/bmjopen-2010-000048>.
- [26] J.P. Vandenbroucke, E. von Elm, D.G. Altman, P.C. Gøtzsche, C.D. Mulrow, S.J. Pocock, C. Poole, J.J. Schlesselman, M. Egger, STROBE initiative, Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration, *Ann. Intern. Med.* 147 (2007) W163-194. <https://doi.org/10.7326/0003-4819-147-8-200710160-00010-w1>.
- [27] G.A. Wells, B. Shea, D. O’Connell, J. Peterson, V. Welch, M. Losos, P. Tugwell, The Newcastle–Ottawa Scale (NOS) for Assessing the Quality of Nonrandomised Studies in Meta-Analyses, (2014). Available online: www.ohri.ca/programs/clinical_epidemiology/oxford.asp.
- [28] M. Ollier, A. Chamoux, G. Naughton, B. Pereira, F. Dutheil, Chest CT scan screening for lung cancer in asbestos occupational exposure: a systematic review and meta-analysis, *Chest*. 145 (2014) 1339–1346. <https://doi.org/10.1378/chest.13-2181>.
- [29] C. Lanhers, B. Pereira, G. Naughton, M. Trousselard, F.-X. Lesage, F. Dutheil, Creatine Supplementation and Lower Limb Strength Performance: A Systematic Review and Meta-Analyses, *Sports Med.* 45 (2015) 1285–1294. <https://doi.org/10.1007/s40279-015-0337-4>.
- [30] C. Lanhers, B. Pereira, G. Naughton, M. Trousselard, F.-X. Lesage, F. Dutheil, Creatine Supplementation and Upper Limb Strength Performance: A Systematic Review and Meta-Analysis, *Sports Med.* 47 (2017) 163–173. <https://doi.org/10.1007/s40279-016-0571-4>.
- [31] C. Benoist d’Azy, B. Pereira, F. Chiambaretta, F. Dutheil, Oxidative and Anti-Oxidative Stress Markers in Chronic Glaucoma: A Systematic Review and Meta-Analysis, *PLoS ONE*. 11 (2016) e0166915. <https://doi.org/10.1371/journal.pone.0166915>.
- [32] C. Benoist d’Azy, B. Pereira, G. Naughton, F. Chiambaretta, F. Dutheil, Antibiotrophylaxis in Prevention of Endophthalmitis in Intravitreal Injection: A Systematic Review and Meta-Analysis, *PLoS ONE*. 11 (2016) e0156431. <https://doi.org/10.1371/journal.pone.0156431>.
- [33] R. Courtin, B. Pereira, G. Naughton, A. Chamoux, F. Chiambaretta, C. Lanhers, F. Dutheil, Prevalence of dry eye disease in visual display terminal workers: a systematic review and meta-analysis, *BMJ Open*. 6 (2016) e009675. <https://doi.org/10.1136/bmjopen-2015-009675>.
- [34] V. Navel, A. Mulliez, C. Benoist d’Azy, J.S. Baker, J. Malecaze, F. Chiambaretta, F. Dutheil, Efficacy of treatments for Demodex blepharitis: A systematic review and

- meta-analysis, *The Ocular Surface*. (2019) S1542012419300655. <https://doi.org/10.1016/j.jtos.2019.06.004>.
- [35] R. DerSimonian, N. Laird, Meta-analysis in clinical trials, *Control Clin Trials*. 7 (1986) 177–188.
- [36] H. Akbari, R. Mirzaei, T. Nasrabadi, M. Gholami-Fesharaki, Evaluation of the Effect of Shift Work on Serum Cholesterol and Triglyceride Levels, *Iran Red Crescent Med J*. 17 (2015). <https://doi.org/10.5812/ircmj.18723>.
- [37] E. Alefishat, R. Abu Farha, Is Shift Work Associated with Lipid Disturbances and Increased Insulin Resistance?, *Metabolic Syndrome and Related Disorders*. 13 (2015) 400–405. <https://doi.org/10.1089/met.2015.0052>.
- [38] H. Asare-Anane, A. Abdul-Latif, E.K. Ofori, M. Abdul-Rahman, S.D. Amanquah, Shift work and the risk of cardiovascular disease among workers in cocoa processing company, Tema, *BMC Res Notes*. 8 (2015) 798. <https://doi.org/10.1186/s13104-015-1750-3>.
- [39] N. Biggi, D. Consonni, V. Galluzzo, M. Sogliani, G. Costa, Metabolic Syndrome in Permanent Night Workers, *Chronobiology International*. 25 (2008) 443–454. <https://doi.org/10.1080/07420520802114193>.
- [40] A. Burgueño, C. Gemma, T.F. Gianotti, S. Sookoian, C.J. Pirola, Increased levels of resistin in rotating shift workers: A potential mediator of cardiovascular risk associated with circadian misalignment, *Atherosclerosis*. 210 (2010) 625–629. <https://doi.org/10.1016/j.atherosclerosis.2009.12.032>.
- [41] T. Caciari, G. Tomei, S. De Sio, A. Capozzella, M.P. Schifano, L. Trovè, T. Casale, C. Cardella, F. Tomei, M.V. Rosati, Evaluation of some cardiovascular risk parameters in health professionals exposed to night work, *Ann Ig*. 25 (2013) 23–30. <https://doi.org/10.7416/ai.2013.1903>.
- [42] S. Chatti, F. Debbabi, A. Ben Abdelaziz, R. Harbaoui, H. Ghannem, N. Mrizak, Facteurs de risque cardiovasculaire chez les travailleurs postés d’une centrale de production d’électricité au centre tunisien, *Annales de Cardiologie et d’Angéiologie*. 59 (2010) 190–195. <https://doi.org/10.1016/j.ancard.2009.07.002>.
- [43] C.-C. Chen, L.-J. Shiu, Y.-L. Li, K.-Y. Tung, K.-Y. Chan, C.-J. Yeh, S.-C. Chen, R.-H. Wong, Shift Work and Arteriosclerosis Risk in Professional Bus Drivers, *Annals of Epidemiology*. 20 (2010) 60–66. <https://doi.org/10.1016/j.annepidem.2009.07.093>.
- [44] A. Copertaro, M. Barbaresi, M. Bracci, Lavoro a turni e rischio cardiometabolico., *Recenti Progressi in Medicina*. 100 (2009) 502–507.
- [45] D. De Bacquer, M. Van Risseghem, E. Clays, F. Kittel, G. De Backer, L. Braeckman, Rotating shift work and the metabolic syndrome: a prospective study, *International Journal of Epidemiology*. 38 (2009) 848–854. <https://doi.org/10.1093/ije/dyn360>.
- [46] T. Ellingsen, A. Bener, A.A. Gehani, Study of shift work and risk of coronary events, *Journal of the Royal Society for the Promotion of Health*. 127 (2007) 265–267. <https://doi.org/10.1177/1466424007083702>.
- [47] Y. Esquirol, V. Bongard, J. Ferrieres, H. Verdier, B. Perret, Shiftwork and Higher Pancreatic Secretion: Early Detection of an Intermediate State of Insulin Resistance?, *Chronobiology International*. 29 (2012) 1258–1266. <https://doi.org/10.3109/07420528.2012.719959>.
- [48] Y. Esquirol, V. Bongard, L. Mabile, B. Jonnier, J. Soulat, B. Perret, Shift Work and Metabolic Syndrome: Respective Impacts of Job Strain, Physical Activity, and Dietary Rhythms, *Chronobiology International*. 26 (2009) 544–559. <https://doi.org/10.1080/07420520902821176>.
- [49] Y. Guo, Y. Rong, X. Huang, H. Lai, X. Luo, Z. Zhang, Y. Liu, M. He, T. Wu, W. Chen, Shift Work and the Relationship with Metabolic Syndrome in Chinese Aged

- Workers, PLoS ONE. 10 (2015) e0120632. <https://doi.org/10.1371/journal.pone.0120632>.
- [50] A. Hamta, A. Kazemnejad, M. Gholami-Fesharaki, M. Rowzati, Simultaneous effect of shift work on blood pressure and lipid profile: a path analysis, *International Journal of Occupational Safety and Ergonomics*. 24 (2018) 68–72. <https://doi.org/10.1080/10803548.2017.1314139>.
- [51] G. Jermendy, J. Nádas, I. Hegyi, I. Vasas, T. Hidvégi, Assessment of cardiometabolic risk among shift workers in Hungary, *Health Qual Life Outcomes*. 10 (2012) 18. <https://doi.org/10.1186/1477-7525-10-18>.
- [52] M.J. Jesús Fernández Rodríguez, I. Bautista Castaño, L. Bello Luján, L. Hernandez Bethencourt, Valoración nutricional de trabajadores sanitarios expuestos a turnicidad en Canarias, *Nutricion Hospitalaria*. 19 (2004) 286–291.
- [53] T. Kawada, T. Otsuka, Effect of Shift Work on the Development of Metabolic Syndrome After 3 Years in Japanese Male Workers, *Archives of Environmental & Occupational Health*. 69 (2014) 55–61. <https://doi.org/10.1080/19338244.2012.732123>.
- [54] T. Kawada, T. Otsuka, H. Inagaki, Y. Wakayama, M. Katsumata, Q. Li, Y.-J. Li, A cross-sectional study on the shift work and metabolic syndrome in Japanese male workers, *The Aging Male*. 13 (2010) 174–178. <https://doi.org/10.3109/13685530903536692>.
- [55] M.A.-C. Lennernäs, L. Hambraus, T. Åkerstedt, Nutrient intake in day workers and shift workers, *Work & Stress*. 8 (1994) 332–342. <https://doi.org/10.1080/02678379408256540>.
- [56] Y.C. Lin, I.-C. Hsieh, P.-C. Chen, Utilizing the metabolic syndrome component count in workers' health surveillance: An example of day-time vs. day-night rotating shift workers, *Int J Occup Med Environ Health*. 28 (2015) 675–688. <https://doi.org/10.13075/ijomeh.1896.00335>.
- [57] Y.-C. Lin, T.-J. Hsiao, P.-C. Chen, Persistent Rotating Shift-Work Exposure Accelerates Development of Metabolic Syndrome among Middle-Aged Female Employees: A Five-Year Follow-Up, *Chronobiology International*. 26 (2009) 740–755. <https://doi.org/10.1080/07420520902929029>.
- [58] I. Mohebbi, K. Shateri, M. Seyedmohammadzad, The relationship between working schedule patterns and the markers of the metabolic syndrome: Comparison of shift workers with day workers, *International Journal of Occupational Medicine and Environmental Health*. 25 (2012). <https://doi.org/10.2478/s13382-012-0051-5>.
- [59] K. Murata, E. Yano, T. Shinozaki, Impact of shift work on cardiovascular functions in a 10-year follow-up study, *Scand J Work Environ Health*. 25 (1999) 272–277. <https://doi.org/10.5271/sjweh.434>.
- [60] K. Nakamura, S. Shimai, S. Kikuchi, K. Tominaga, H. Takahashi, M. Tanaka, S. Nakano, Y. Motohashi, H. Nakadaira, M. Yamamoto, Shift work and risk factors for coronary heart disease in Japanese blue-collar workers: serum lipids and anthropometric characteristics, *Occup Med (Lond)*. 47 (1997) 142–146. <https://doi.org/10.1093/occmed/47.3.142>.
- [61] A.M. Pimenta, G. Kac, R.R.C.E. Souza, L.M. de B.A. Ferreira, S.M. de F. Silqueira, Night-shift work and cardiovascular risk among employees of a public university, *Rev Assoc Med Bras* (1992). 58 (2012) 168–177.
- [62] S. Puttonen, M. Kivimäki, M. Elovainio, L. Pulkki-Råback, M. Hintsanen, J. Vahtera, R. Telama, M. Juonala, J.S.A. Viikari, O.T. Raitakari, L. Keltikangas-Järvinen, Shift work in young adults and carotid artery intima-media thickness: The Cardiovascular Risk in Young Finns study, *Atherosclerosis*. 205 (2009) 608–613. <https://doi.org/10.1016/j.atherosclerosis.2009.01.016>.

- [63] Y. Suwazono, M. Dochi, M. Oishi, K. Tanaka, E. Kobayashi, K. Sakata, Shift Work and Impaired Glucose Metabolism: A 14-Year Cohort Study on 7104 Male Workers, *Chronobiology International*. 26 (2009) 926–941. <https://doi.org/10.1080/07420520903044422>.
- [64] M. Uetani, K. Sakata, M. Oishi, K. Tanaka, S. Nakada, K. Nogawa, Y. Suwazono, The Influence of Being Overweight on the Relationship Between Shift Work and Increased Total Cholesterol Level, *Annals of Epidemiology*. 21 (2011) 327–335. <https://doi.org/10.1016/j.annepidem.2011.01.001>.
- [65] L.G.P.M. van Amelsvoort, E.G. Schouten, F.J. Kok, Impact of One Year of Shift Work on Cardiovascular Disease Risk Factors, *Journal of Occupational and Environmental Medicine*. 46 (2004) 699–706. <https://doi.org/10.1097/01.jom.0000131794.83723.45>.
- [66] H.H. Ye, J.U. Jeong, M.J. Jeon, J. Sakong, The Association between Shift Work and the Metabolic Syndrome in Female Workers, *Ann Occup Environ Med*. 25 (2013) 33. <https://doi.org/10.1186/2052-4374-25-33>.
- [67] H. Amano, Y. Fukuda, T. Yokoo, K. Yamaoka, Interleukin-6 Level among Shift and Night Workers in Japan: Cross-Sectional Analysis of the J-HOPE Study, *J Atheroscler Thromb*. 25 (2018) 1206–1214. <https://doi.org/10.5551/jat.42036>.
- [68] M. Aslam, A.A. Siddiqui, G. Sandeep, S.V. Madhu, High prevalence of obesity among nursing personnel working in tertiary care hospital, *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*. 12 (2018) 313–316. <https://doi.org/10.1016/j.dsx.2017.12.014>.
- [69] L.E. Charles, J.K. Gu, C.A. Tinney-Zara, D. Fekedulegn, C.C. Ma, P. Baughman, T.A. Hartley, M.E. Andrew, J.M. Violanti, C.M. Burchfiel, Separate and Joint Associations of Shift Work and Sleep Quality with Lipids, Safety and Health at Work. 7 (2016) 111–119. <https://doi.org/10.1016/j.shaw.2015.11.007>.
- [70] N. Copin, G. Gusto, S. Vol, S. Rollier, O. Lantieri, G. Lasfargues, J. Tichet, Perturbation du métabolisme lipidique chez des travailleurs postés consultants de centres d'examen de santé, *La Presse Médicale*. 45 (2016) e145–e156. <https://doi.org/10.1016/j.lpm.2015.12.014>.
- [71] R.A. Farha, E. Alefishat, Shift Work and the Risk of Cardiovascular Diseases and Metabolic Syndrome Among Jordanian Employees, *Oman Med J*. 33 (2018) 235–242. <https://doi.org/10.5001/omj.2018.43>.
- [72] R.H. Gowda, G.M. Sukumar, S.H. Gowda, Association between metabolic risk, oxidative stress and rotating shift work in a tertiary health care facility, *Clinical Epidemiology and Global Health*. (2019) S2213398418302756. <https://doi.org/10.1016/j.cegh.2019.01.002>.
- [73] G. Hulsege, H.S.J. Picavet, A.J. van der Beek, W.M.M. Verschuren, J.W. Twisk, K.I. Proper, Shift work, chronotype and the risk of cardiometabolic risk factors, *Eur J Public Health*. 29 (2019) 128–134. <https://doi.org/10.1093/eurpub/cky092>.
- [74] J.H. Joo, D.W. Lee, D.-W. Choi, E.-C. Park, Association between night work and dyslipidemia in South Korean men and women: a cross-sectional study, *Lipids Health Dis*. 18 (2019) 75. <https://doi.org/10.1186/s12944-019-1020-9>.
- [75] C. Jung, S.H. Jung, B. Lee, D. Choi, B. Kim, C. Kim, S. Kang, J. Mok, Differential Impact of Sleep Duration on Fasting Plasma Glucose Level According to Work Timing, *Archives of Medical Research*. 49 (2018) 51–57. <https://doi.org/10.1016/j.arcmed.2018.03.005>.
- [76] W. Kang, W.-J. Park, K.-H. Jang, S.-H. Kim, D.-H. Gwon, H.-M. Lim, J.-S. Ahn, J.-D. Moon, Coronary artery atherosclerosis associated with shift work in chemical plant workers by using coronary CT angiography, *Occup Environ Med*. 73 (2016) 501–505. <https://doi.org/10.1136/oemed-2015-103118>.

- [77] S.-W. Kim, E.-C. Jang, S.-C. Kwon, W. Han, M.-S. Kang, Y.-H. Nam, Y.-J. Lee, Night shift work and inflammatory markers in male workers aged 20–39 in a display manufacturing company, *Ann of Occup and Environ Med.* 28 (2016) 48. <https://doi.org/10.1186/s40557-016-0135-y>.
- [78] K. Kiranmala, M. Aslam, B.K. Mishra, R. Jhamb, S.V. Madhu, Association of postprandial triglyceride responses with insulin resistance among rotational night shift healthcare workers, *Exp Physiol.* 104 (2019) 819–825. <https://doi.org/10.1113/EP087514>.
- [79] B. Loef, D. van Baarle, A.J. van der Beek, P.K. Beekhof, L.W. van Kerkhof, K.I. Proper, The association between exposure to different aspects of shift work and metabolic risk factors in health care workers, and the role of chronotype, *PLoS ONE.* 14 (2019) e0211557. <https://doi.org/10.1371/journal.pone.0211557>.
- [80] Y.-C. Lu, C.-P. Wang, T.-H. Yu, I.-T. Tsai, W.-C. Hung, I.-C. Lu, C.-C. Hsu, W.-H. Tang, J.-Y. Houg, F.-M. Chung, M.-C. Yen Jean, Shift work is associated with metabolic syndrome in male steel workers-the role of resistin and WBC count-related metabolic derangements, *Diabetol Metab Syndr.* 9 (2017) 83. <https://doi.org/10.1186/s13098-017-0283-4>.
- [81] N.S. Mashhadi, S. Saadat, M.R. Afsharmanesh, S. Shirali, Study of association between beverage consumption pattern and lipid profile in shift workers, *Diabetes & Metabolic Syndrome: Clinical Research & Reviews.* 10 (2016) 227–229. <https://doi.org/10.1016/j.dsx.2016.06.011>.
- [82] K. Raspante Cerqueira Teixeira, L.A. de Medeiros, J.A. Mendes, E.R. Vaz, T.M. Cunha, E.P. de Oliveira, N. Penha-Silva, C.A. Crispim, The erythrocyte membrane stability is associated with sleep time and social jetlag in shift workers, *PLoS ONE.* 14 (2019) e0222698. <https://doi.org/10.1371/journal.pone.0222698>.
- [83] J. Ritonja, K.J. Aronson, A.G. Day, J. Korsiak, J. Tranmer, Investigating Cortisol Production and Pattern as Mediators in the Relationship Between Shift Work and Cardiometabolic Risk, *Canadian Journal of Cardiology.* 34 (2018) 683–689. <https://doi.org/10.1016/j.cjca.2018.02.006>.
- [84] J. Ritonja, J. Tranmer, K.J. Aronson, The relationship between night work, chronotype, and cardiometabolic risk factors in female hospital employees, *Chronobiology International.* 36 (2019) 616–628. <https://doi.org/10.1080/07420528.2019.1570247>.
- [85] M. Skogstad, A. Mamen, L.-K. Lunde, B. Ulvestad, D. Matre, H.C.D. Aass, R. Øvstebø, P. Nielsen, K.N. Samuelsen, Ø. Skare, P.A. Sirnes, Shift Work Including Night Work and Long Working Hours in Industrial Plants Increases the Risk of Atherosclerosis, *Int J Environ Res Public Health.* 16 (2019). <https://doi.org/10.3390/ijerph16030521>.
- [86] L. Ye, W. Gu, Y. Chen, X. Li, J. Shi, A. Lv, J. Hu, R. Zhang, R. Liu, J. Hong, J. Wang, Y. Zhang, The impact of shift work on glycemic characteristics assessed by CGM and its association with metabolic indices in non-diabetic subjects, *Acta Diabetol.* (2019). <https://doi.org/10.1007/s00592-019-01372-z>.
- [87] G. Chico-Barba, K. Jiménez-Limas, B. Sánchez-Jiménez, R. Sámano, A.L. Rodríguez-Ventura, R. Castillo-Pérez, M. Tolentino, Burnout and Metabolic Syndrome in Female Nurses: An Observational Study, *IJERPH.* 16 (2019) 1993. <https://doi.org/10.3390/ijerph16111993>.
- [88] O. Itani, Y. Kaneita, M. Tokiya, M. Jike, A. Murata, S. Nakagome, Y. Otsuka, T. Ohida, Short sleep duration, shift work, and actual days taken off work are predictive life-style risk factors for new-onset metabolic syndrome: a seven-year cohort study of 40,000 male workers, *Sleep Medicine.* 39 (2017) 87–94. <https://doi.org/10.1016/j.sleep.2017.07.027>.

- [89] M. Weigl, F. Schmuck, B. Heiden, P. Angerer, A. Müller, Associations of understaffing and cardiovascular health of hospital care providers: A multi-source study, *International Journal of Nursing Studies*. 99 (2019) 103390. <https://doi.org/10.1016/j.ijnurstu.2019.103390>.
- [90] M. Khosravipour, M. Shah Mohammadi, The effects of exposure to night shift work on liver function: A cross-sectional study with emphasis of alkaline phosphatase enzyme, *Chronobiology International*. 37 (2020) 142–145. <https://doi.org/10.1080/07420528.2019.1684936>.
- [91] M. Khosravipour, M. Shahmohammadi, H.V. Athar, The effects of rotating and extended night shift work on the prevalence of metabolic syndrome and its components, *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*. 13 (2019) 3085–3089. <https://doi.org/10.1016/j.dsx.2019.11.006>.
- [92] M. Garaulet, J.A. Madrid, Chronobiology, genetics and metabolic syndrome, *Curr. Opin. Lipidol.* 20 (2009) 127–134. <https://doi.org/10.1097/MOL.0b013e3283292399>.
- [93] D. Corbalán-Tutau, J.A. Madrid, F. Nicolás, M. Garaulet, Daily profile in two circadian markers “melatonin and cortisol” and associations with metabolic syndrome components, *Physiol. Behav.* 123 (2014) 231–235. <https://doi.org/10.1016/j.physbeh.2012.06.005>.
- [94] C. Ekmekcioglu, Y. Touitou, Chronobiological aspects of food intake and metabolism and their relevance on energy balance and weight regulation, *Obes Rev.* 12 (2011) 14–25. <https://doi.org/10.1111/j.1467-789X.2010.00716.x>.
- [95] R. Salgado-Delgado, M. Angeles-Castellanos, N. Saderi, R.M. Buijs, C. Escobar, Food intake during the normal activity phase prevents obesity and circadian desynchrony in a rat model of night work, *Endocrinology*. 151 (2010) 1019–1029. <https://doi.org/10.1210/en.2009-0864>.
- [96] J. Barton, E. Spelten, P. Totterdell, L. Smith, S. Folkard, Is there an optimum number of night shifts? Relationship between sleep, health and well-being, *Work Stress*. 9 (1995) 109–123. <https://doi.org/10.1080/02678379508256545>.
- [97] F.P. Cappuccio, F.M. Taggart, N.-B. Kandala, A. Currie, E. Peile, S. Stranges, M.A. Miller, Meta-analysis of short sleep duration and obesity in children and adults, *Sleep*. 31 (2008) 619–626. <https://doi.org/10.1093/sleep/31.5.619>.
- [98] F.P. Cappuccio, L. D’Elia, P. Strazzullo, M.A. Miller, Quantity and quality of sleep and incidence of type 2 diabetes: a systematic review and meta-analysis, *Diabetes Care*. 33 (2010) 414–420. <https://doi.org/10.2337/dc09-1124>.
- [99] F.P. Cappuccio, D. Cooper, L. D’Elia, P. Strazzullo, M.A. Miller, Sleep duration predicts cardiovascular outcomes: a systematic review and meta-analysis of prospective studies, *Eur. Heart J.* 32 (2011) 1484–1492. <https://doi.org/10.1093/eurheartj/ehr007>.
- [100] F.P. Cappuccio, L. D’Elia, P. Strazzullo, M.A. Miller, Sleep duration and all-cause mortality: a systematic review and meta-analysis of prospective studies, *Sleep*. 33 (2010) 585–592. <https://doi.org/10.1093/sleep/33.5.585>.
- [101] O. Itani, M. Jike, N. Watanabe, Y. Kaneita, Short sleep duration and health outcomes: a systematic review, meta-analysis, and meta-regression, *Sleep Med*. 32 (2017) 246–256. <https://doi.org/10.1016/j.sleep.2016.08.006>.
- [102] O.M. Buxton, M. Pavlova, E.W. Reid, W. Wang, D.C. Simonson, G.K. Adler, Sleep Restriction for 1 Week Reduces Insulin Sensitivity in Healthy Men, *Diabetes*. 59 (2010) 2126–2133. <https://doi.org/10.2337/db09-0699>.
- [103] H. Qiao, Z. Beibei, T. Chong, Z. Tieying, G. Yuzhi, M. Jing, P.M. Davidson, Both frequency and duration of rotating night shifts are associated with metabolic parameters: a cross-sectional study, *Sleep Med*. 71 (2020) 89–96. <https://doi.org/10.1016/j.sleep.2020.02.016>.

- [104] L. Kervezee, A. Kosmadopoulos, D.B. Boivin, Metabolic and cardiovascular consequences of shift work: The role of circadian disruption and sleep disturbances, *Eur. J. Neurosci.* 51 (2020) 396–412. <https://doi.org/10.1111/ejn.14216>.
- [105] C.I. Eastman, Z. Boulos, M. Terman, S.S. Campbell, D.-J. Dijk, A.J. Lewy, Light Treatment for Sleep Disorders: Consensus Report: VI. Shift Work, *J Biol Rhythms.* 10 (1995) 157–164. <https://doi.org/10.1177/074873049501000208>.
- [106] T.H. Monk, D.J. Buysse, B.D. Billy, M.E. Fletcher, K.S. Kennedy, A.E. Begley, J.E. Schlarb, S.R. Beach, Shiftworkers report worse sleep than day workers, even in retirement, *J Sleep Res.* 22 (2013) 201–208. <https://doi.org/10.1111/jsr.12003>.
- [107] N.S. Murali, A. Svatikova, V.K. Somers, Cardiovascular physiology and sleep, *Front. Biosci.* 8 (2003) s636-652. <https://doi.org/10.2741/1105>.
- [108] S. Folkard, J. Barton, Does the ‘forbidden zone’ for sleep onset influence morning shift sleep duration?, *Ergonomics.* 36 (1993) 85–91. <https://doi.org/10.1080/00140139308967858>.
- [109] C.A. Crispim, J. Waterhouse, A.R. Dâmaso, I.Z. Zimberg, H.G. Padilha, L.M. Oyama, S. Tufik, M.T. de Mello, Hormonal appetite control is altered by shift work: a preliminary study, *Metabolism.* 60 (2011) 1726–1735. <https://doi.org/10.1016/j.metabol.2011.04.014>.
- [110] D. Schiavo-Cardozo, M.M.O. Lima, J.C. Pareja, B. Geloneze, Appetite-regulating hormones from the upper gut: disrupted control of xenin and ghrelin in night workers, *Clin Endocrinol.* 79 (2013) 807–811. <https://doi.org/10.1111/cen.12114>.
- [111] S. Becerril, A. Rodríguez, V. Catalán, B. Ramírez, X. Unamuno, P. Portincasa, J. Gómez-Ambrosi, G. Frühbeck, Functional Relationship between Leptin and Nitric Oxide in Metabolism, *Nutrients.* 11 (2019). <https://doi.org/10.3390/nu11092129>.
- [112] A. Tremblay, F. Duthiel, V. Drapeau, L. Metz, B. Lesour, R. Chapier, B. Pereira, J. Verney, J.S. Baker, A. Vinet, G. Walther, P. Obert, D. Courteix, D. Thivel, Long-term effects of high-intensity resistance and endurance exercise on plasma leptin and ghrelin in overweight individuals: the RESOLVE Study, *Appl Physiol Nutr Metab.* 44 (2019) 1172–1179. <https://doi.org/10.1139/apnm-2019-0019>.
- [113] V. Morin, F. Hozer, J.-F. Costemale-Lacoste, The effects of ghrelin on sleep, appetite, and memory, and its possible role in depression: A review of the literature, *L’Encéphale.* 44 (2018) 256–263. <https://doi.org/10.1016/j.encep.2017.10.012>.
- [114] V. Tolle, M.-H. Bassant, P. Zizzari, F. Poindessous-Jazat, C. Tomasetto, J. Epelbaum, M.-T. Bluet-Pajot, Ultradian Rhythmicity of Ghrelin Secretion in Relation with GH, Feeding Behavior, and Sleep-Wake Patterns in Rats, *Endocrinology.* 143 (2002) 1353–1361. <https://doi.org/10.1210/endo.143.4.8712>.
- [115] A. Engin, Circadian Rhythms in Diet-Induced Obesity, *Adv. Exp. Med. Biol.* 960 (2017) 19–52. https://doi.org/10.1007/978-3-319-48382-5_2.
- [116] Z. Samhat, R. Attieh, Y. Sacre, Relationship between night shift work, eating habits and BMI among nurses in Lebanon, *BMC Nurs.* 19 (2020) 25. <https://doi.org/10.1186/s12912-020-00412-2>.
- [117] G. Hulsegge, B. Loef, T. Benda, A.J. van der Beek, K.I. Proper, Shift work and its relation with meal and snack patterns among healthcare workers, *Scand J Work Environ Health.* 46 (2020) 143–151. <https://doi.org/10.5271/sjweh.3829>.
- [118] J.M. Ferrell, J.Y.L. Chiang, Short-term circadian disruption impairs bile acid and lipid homeostasis in mice, *Cell Mol Gastroenterol Hepatol.* 1 (2015) 664–677. <https://doi.org/10.1016/j.jcmgh.2015.08.003>.
- [119] G.B. Petarli, M. Cattafesta, M.M. Sant’Anna, O.M. de P.A. Bezerra, E. Zandonade, L.B. Salaroli, Multimorbidity and complex multimorbidity in Brazilian rural workers, *PLoS ONE.* 14 (2019) e0225416. <https://doi.org/10.1371/journal.pone.0225416>.

- [120] L.S. Welch, J. Dement, K. Ringen, K. Cranford, P.S. Quinn, Impact of Secondary Prevention in an Occupational High-Risk Group:, *Journal of Occupational and Environmental Medicine*. 59 (2017) 67–73. <https://doi.org/10.1097/JOM.0000000000000925>.
- [121] M. Inoue, H. Morita, J. Inagaki, N. Harada, Influence of Differences in Their Jobs on Cardiovascular Risk Factors in Male Blue-collar Shift Workers in Their Fifties, *International Journal of Occupational and Environmental Health*. 10 (2004) 313–318. <https://doi.org/10.1179/oeh.2004.10.3.313>.
- [122] E. Gerdt, V. Regitz-Zagrosek, Sex differences in cardiometabolic disorders, *Nat Med*. 25 (2019) 1657–1666. <https://doi.org/10.1038/s41591-019-0643-8>.
- [123] R. Cifkova, J. Pitha, A. Krajcoviechova, E. Kralikova, Is the impact of conventional risk factors the same in men and women? Plea for a more gender-specific approach, *International Journal of Cardiology*. 286 (2019) 214–219. <https://doi.org/10.1016/j.ijcard.2019.01.039>.
- [124] R. Manfredini, A. De Giorgi, R. Tiseo, B. Boari, R. Cappadona, R. Salmi, M. Gallerani, F. Signani, F. Manfredini, D.P. Mikhailidis, F. Fabbian, Marital Status, Cardiovascular Diseases, and Cardiovascular Risk Factors: A Review of the Evidence, *J Womens Health (Larchmt)*. 26 (2017) 624–632. <https://doi.org/10.1089/jwh.2016.6103>.
- [125] Y. Fukuda, A. Hiyoshi, Associations of Household Expenditure and Marital Status With Cardiovascular Risk Factors in Japanese Adults: Analysis of Nationally Representative Surveys, *Journal of Epidemiology*. (2013) 21–27. <https://doi.org/10.2188/jea.JE20120021>.
- [126] G. Buckland, J. Salas-Salvadó, E. Roure, M. Bulló, L. Serra-Majem, Sociodemographic risk factors associated with metabolic syndrome in a Mediterranean population, *Public Health Nutr*. 11 (2008) 1372–1378. <https://doi.org/10.1017/S1368980008003492>.
- [127] K. Saito, H. Sone, [Effect of smoking on diabetes mellitus and dyslipidemia (effect of smoking on glucose and lipid metabolism)], *Nippon Rinsho*. 71 (2013) 443–448.
- [128] J. Shi, Y. Bai, S. Qiu, Y. Li, C. Kou, Y. Tao, Q. Zhen, Y. Gu, Y. Yu, K. Zhang, Y. Cheng, Y. Liu, Classified status of smoking and quitting has different associations with dyslipidemia in residents in northeast China, *Clin. Chim. Acta*. 486 (2018) 209–213. <https://doi.org/10.1016/j.cca.2018.08.001>.
- [129] Z. Shen, S. Munker, C. Wang, L. Xu, H. Ye, H. Chen, G. Xu, H. Zhang, L. Chen, C. Yu, Y. Li, Association between alcohol intake, overweight, and serum lipid levels and the risk analysis associated with the development of dyslipidemia, *Journal of Clinical Lipidology*. 8 (2014) 273–278. <https://doi.org/10.1016/j.jacl.2014.02.003>.
- [130] P. Song, M. Zha, X. Yang, Y. Xu, H. Wang, Z. Fang, X. Yang, W. Xia, C. Zeng, Socioeconomic and geographic variations in the prevalence, awareness, treatment and control of dyslipidemia in middle-aged and older Chinese, *Atherosclerosis*. 282 (2019) 57–66. <https://doi.org/10.1016/j.atherosclerosis.2019.01.005>.
- [131] D.C. Chan, H.P.R. Barrett, G.F. Watts, Dyslipidemia in Visceral Obesity: Mechanisms, Implications, and Therapy, *American Journal of Cardiovascular Drugs*. 4 (2004) 227–246. <https://doi.org/10.2165/00129784-200404040-00004>.
- [132] G. Riccardi, O. Vaccaro, G. Costabile, A.A. Rivellese, How Well Can We Control Dyslipidemias Through Lifestyle Modifications?, *Curr Cardiol Rep*. 18 (2016) 66. <https://doi.org/10.1007/s11886-016-0744-7>.
- [133] H.M. Arrighi, I. Hertz-Picciotto, The evolving concept of the healthy worker survivor effect, *Epidemiology*. 5 (1994) 189–196. <https://doi.org/10.1097/00001648-199403000-00009>.

[134] A. Wolska, A.T. Remaley, Measuring LDL-cholesterol: what is the best way to do it?,
Curr. Opin. Cardiol. 35 (2020) 405–411.
<https://doi.org/10.1097/HCO.0000000000000740>.

Table 1. Characteristics of included studies.

HDL: HDL cholesterol; LDL: LDL cholesterol; TC: total cholesterol; TG: triglycerides

Study	Design	Country	Follow-up (period)	Type of Work	Shift work		Shift Workers			Day Workers			Blood lipids	
					Type of shift	Schedule (hours)	n	Age (mean±SD)	Sex (%men)	n	Age (mean±SD)	Sex (%men)	Samples	Outcomes
Akbari 2014	retrospective cohort	Iran	2002-2011	steel industry	rotating 3*8	7:00-15:00/ 15:00-23:00/ 23:00-7:00	2854	33.6±5.7	100	2557	34.9±5.9	100	TG, TC	levels
					rotating day shift	7:00-15:00/ 15:00-23:00	362	34.8±5.9	100	2557	34.9±5.9	100	TG, TC	levels
Alefisat 2015	cross sectional	Jordan	-	non specified	unspecified	-	82	32.8±8.0	22.4	58	35.1±6.7	57.3	TG, HDL	levels
Amano 2018	cross sectional	Japan	-	non specified	fixed night	-	142	43.2±8.8	39.4	3660	41.9±10.4	69.1	TG, HDL, LDL	levels
					unspecified	-	1276	35.4±12.1	92.0	3660	41.9±10.4	69.1	TG, HDL, LDL	levels
Asare-Anane 2015	cross sectional	Ghana	2013	cocoa industry	unspecified	-	113	42.0±8.2	-	87	40.3±11.5	-	TG, TC, HDL, LDL	levels & OR
Aslam 2018	cross sectional	India	-	nurses	unspecified	-	290	40.5±8.6	0	206	40.5±6.9	0	TG, TC, HDL, LDL, VLDL	levels
Biggi 2008	prospective cohort	Italy	1976-2007	communal employees	fixed night	23:35-5:35	319	44.5	100	157	35.0	100	TG, TC	levels
Burgueno 2009	cross sectional	Argentina	-	factory	rotating 2*12	6:00-18:00/ 18:00-6:00	184	35.5±8.0	100	255	33.7±8.9	100	TG, TC, HDL, LDL	levels
Caciari 2013	case control	Italy	-	health care	fixed night	-	105	49.3±4.7	100	190	49.1±5.1	100	TG, TC, HDL	levels
							58	45.4±4.2	0	62	45.6±5.1	0	TG, TC, HDL	levels
Chatti 2010	cross sectional	Tunisia	-	thermal power plant	rotating 3*8	-	128	38.7±5.8	100	162	39.7±6.9	95.7	TG, TC	levels
Charles 2016	cross sectional	USA	-	police officers	rotating 3*8	4:00-11:59/ 12:00-7:59/ 8:00-3:59	129	41.2±6.6	86.8	141	41.2±6.9	51.8	TG, TC, HDL, LDL	levels
					fixed night	8:00-3:59	90	41.2±6.6	84.4	141	41.2±6.6	51.8	TG, TC, HDL, LDL	levels
Chen 2010	prospective cohort	Taiwan	2004	bus drivers	unspecified	-	36	49.3±4.2	100	49	42.3±9.8	100	TG, TC, HDL, LDL	levels
Chico-Barba 2019	cross sectional	Mexico	2016-2018	nurses	rotating day shift	-	14	-	0	104	-	0	TG, HDL	OR
					fixed night	18:00-6:00	50	-	0	104	-	0	TG, HDL	OR
Copertaro 2009	retrospective cohort	Italy	2008	health care	rotating 3*8	6:00-14:00/ 14:00-22:00/ 22:00-6:00	193	44.3±8.1	34.7	221	43.1±8.7	27.6	HDL	OR
Copin 2015	retrospective cohort	France	1996-2008	non specified	rotating 3*8	-	2766	45.3±7.0	71.8	4764	46.0±7.8	59.9	TG, TC, HDL, LDL	levels
Debacquer 2008	prospective cohort	Belgium	1995-1998	non specified	unspecified	-	309	44.7±4.3	100	1220	43.1±5.1	100	HDL	levels
Dochi 2008	prospective cohort	Japan	1991-2005	steel industry	rotating 3*8	7:00-15:00/ 15:00-23:00/ 23:00-7:00	2807	36.9±9.4	100	4079	36.2±10.7	100	TC	levels
Ellingsen 2007	prospective cohort	Qatar	1972-2003	fertilizer plant	rotating 3*8	-	27	46.1±7.0	100	40	49.3±6.7	100	TG, TC	levels
					rotating 3*8	-	61	46.6±7.3	100	95	46.9±7.7	100	TG, TC	levels
Esquirol 2009	cross sectional	France	2001-2002	chemical plant	rotating 3*8	5:00-13:00/ 13:00-22:00/ 22:00-5:00/ 8:00-17:00	100	46.5±4.4	100	98	48.8±5.3	100	TG, TC, HDL, LDL	levels
Esquirol 2012	cross sectional	France	2001-2002	chemical plant	rotating 3*8	5:00-13:00/ 13:00-22:00/ 22:00-5:00	97	46.5±4.4	100	95	48.9±5.3	100	TG, HDL	levels
Farha 2018	cross sectional	Jordan	2014	health care	fixed night	16:00-7:00	82	32.8±8.0	57.3	58	35.1±6.7	22.4	TG, HDL	levels
Jesus Fernandez Rodriguez 2004	retrospective cohort	Spain	2000-2001	health care	rotating 3*8	-	210	-	33.3	207	-	24.6	TG, TC, HDL, LDL	levels
Gowda 2019	cross sectional	India	2016	health care	rotating 2*12	9:00-16:30/ 20:00-8:00	61	33.0±19.0	46.9	63	38.0±23.0	53.1	TC	levels
Ghiasvand 2006	cross sectional	Iran	-	non specified	unspecified	7:00-18:00	158	46.4±7.7	100	266	38.7±9.8	100	TG, TC, HDL, LDL	levels & OR

Guo 2015	cross sectional	China	-	motor industry	unspecified	-	9088	-	45.8	1729 4	-	44.1	TG, TC, HDL, LDL	levels
Hamta 2017	cross sectional	Iran	2015	steel industry	rotating 3*8	-	3479	-	100	3060	-	100	TG, TC, HDL	levels
Haupt 2008	cross sectional	Germany	1997-2001	non specified	unspecified	-	698	62.3±9.3	72.7	1812	61.5±10.1	41.9	TC, LDL	levels
Hulsegge 2018	retrospective cohort	Netherlands	2013-2015	non specified	rotating 3*8	-	125	36.2±9.2	65.0	808	39.4±9.0	64.0	TG, TC, HDL	levels
Itani 2017	retrospective cohort	Japan	1999-2006	non specified	unspecified	-	2017 9	-	-	1683 5	-	-	TG	HR
Jermendy 2012	retrospective cohort	Hungary	-	factory	rotating 2*12	-	54	42.2±8.1	100	67	42.5±9.8	100	TG, HDL, LDL	levels
							180	44.5±8.1	0	180	42.9±8.0	0	TG, HDL, LDL	levels
Joo 2019	prospective cohort	South Korea	2013-2016	non specified	rotating 2*12	18:00-0:00/ 0:00-8:00	575	-	34.0	4916	-	48.9	TG, TC, HDL, LDL	levels
Jung 2018	cross sectional	South Korea	-	non specified	unspecified	14:00-0:00/ 21:00-9:00/ 18:00-6:00	1588	-	51.7	7535	-	50.9	TG, TC, HDL	levels
Kang 2016	cross sectional	South Korea	2012-2013	chemical plant	rotating 3*8	7:00-15:00/ 15:00-23:00/ 23:00-7:00	40	45.8±4.7	100	70	47.9±4.4	100	TG, TC, HDL, LDL	levels
Karlsson 2001	cross sectional	Sweden	1992-1997	non specified	unspecified	-	3277	-	100	9719	-	100	TG, HDL	OR
							4632	-	0	9857	-	0	TG, HDL	OR
Karlsson 2003	cross sectional	Sweden	1996-1997	paper manufactory	rotating 3*8	6:00-14:00/ 6:00-18:00/ 14:00-22:00/ 22:00-6:00/ 18:00-6:00	659	44.3	100	665	44.2	100	TG, HDL	OR
Kawada 2010	cross sectional	Japan	2008	car manufactory	rotating day shift	6:30-14:30/ 15:00-23:00	1125	44.6±7.2	100	1700	45.1±7.2	100	TG, HDL, LDL	levels
					rotating 3*8	6:30-14:30/ 14:30-22:30/ 22:30-6:30	182	44.9±7.2	100	1700	45.1±7.2	100	TG, HDL, LDL	levels
Kawada 2013	prospective cohort	Japan	2008	car manufactory	rotating day shift	6:30-14:30/ 15:00-23:00	686	44.3±5.8	100	868	44.4±5.5	100	TG, HDL	levels
					rotating 3*8	6:30-14:30/ 14:30-22:30/ 22:30-6:30	99	44.5±5.2	100	868	44.4±5.5	100	TG, HDL	levels
					rotating day shift	6:30-14:30/ 15:00-23:00	686	47.3±5.8	100	868	47.4±5.5	100	TG, HDL	levels
					rotating 3*8	6:30-14:30/ 14:30-22:30/ 22:30-6:30	99	47.5±5.2	100	868	47.4±5.5	100	TG, HDL	levels
Khosravipour 2019(a)	cross sectional	Iran	2017-2018	petrochemical plant	rotating 2*12	-	997	38.1±5.2	100	578	38.9±5.6	100	TG, TC, HDL, LDL	levels
Khosravipour 2019(b)	cross sectional	Iran	2017-2018	oil refinery industry	rotating 2*12	-	2630	36.4±6.9	100	3848	37.2±7.6	100	TC	levels
Kim 2016	prospective cohort	South Korea	2015	display manufacturing	rotating 3*8	-	86	33.3±3.5	100	112	32.2±4.3	100	TG, HDL, LDL	levels
Kiranmala 2019	cross sectional	India	-	health care	rotating 2*12	-	20	29.7±3.9	60	20	29.7±2.2	60.0	TG, TC, HDL, LDL, VLDL	levels
Knutsson 1988	cross sectional	Sweden	1975-1976	paper manufactory	rotating 3*8	6:00-14:00/ 14:00-22:00/ 22:00-6:00	361	43.2±11.8	100	240	44.8±11.7	100	TG, TC	levels
Lennernas 1994	cross sectional	Sweden	-	cement/insulation manufactory	rotating day shift	5:30-14:00/ 14:00-22:30	34	40.8±7.1	100	44	40.9±6.1	100	TG, TC, HDL, LDL	levels
					rotating 3*8	5:30-14:00/ 14:00-22:30/ 22:30-5:30	25	36.1±7.2	100	44	40.9±6.1	100	TG, TC, HDL, LDL	levels
Lin 2009	prospective cohort	Taiwan	2002	electronic manufactory	rotating 2*12	-	102	31.9±8.2	0	125	31.1±5.8	0	TG, HDL	levels
Lin 2015	retrospective cohort	Taiwan	2002-2007	electronic manufactory	rotating 2*12	7:30-19:30/ 19:30-7:30	565	31.7	79.1	512	33.2	73.2	TG, HDL	levels
Loef 2019	prospective cohort	Netherlands	2016-2017	health care	unspecified	7:30-16:00/ 23:00-7:45/ 15:00-23:00/ 0:00-6:00	503	40.9±12.2	11.9	93	46.8±11.2	16.1	TG, TC, HDL, LDL	levels
Lu 2017	cross sectional	Taiwan	2016	steel industry	rotating 3*8	23:00-7:00/ 15:00-23:00/ 7:00-15:00	870	42.0±8.0	100	862	43.0±8.0	100	TG, TC, HDL, LDL	levels
Mashhadi 2016	cross sectional	Iran	-	airport workers	unspecified	-	17	-	100	24	-	100	TG, TC, HDL,	levels

													LDL	
Mohebbi 2012	cross sectional	Iran	2006-2010	truck drivers	fixed night	21:00-7:00	3039	-	100	3039	-	100	TG, HDL	levels
Morikawa 2007	cohort	Japan	1993-2003	zipper factory	rotating 3*8	8:00-16:30/ 16:30-0:15/ 0:15-8:00/ 6:30- 13:00/13:00-21:00/ 21:00- 6:30	434	33.5±8.6	100	712	36.4±8.2	100	TC	levels
Murata 1999	cross sectional	Japan	1986-1996	electronic manufactory	rotating 3*8	-	117	46.0±7.0	100	63	46±7.0	100	TG, HDL	levels
							130	46.0±7.0	100	58	46±7.0	100	TG, HDL	levels
Nakamura 1997	cross sectional	Japan	1993	industry	rotating 2*12	8:15-18:15/ 22:30-8:15	27	34.8±7.6	100	239	32.7±7.6	100	TG, TC	levels
					rotating 3*8	8:15-15:15/ 15:15-22:30/ 22:30-8:15	33	34.2±6.8	100	239	32.7±7.6	100	TG, TC	levels
Pimenta 2012	cross sectional	Brazil	2010	health care	rotating 2*12	19:00-7:00	81	-	-	130	-	-	TG	OR
Puttonen 2009	cross sectional	Finland	2001	non specified	unspecified	-	712	-	100	515	-	100	TG, HDL, LDL	levels
							831	-	0	668	-	0	TG, HDL, LDL	levels
Raspante Cerqueira Teixeira 2019	cross sectional	Brazil	-	health care	fixed night	-	37	42.4±8.5	100	42	43.4±12.7	100	TG, TC, HDL, LDL	levels
Ritonja 2018	cross sectional	Canada	2011-2014	health care	rotating 2*12	8:00-16:00/ 22:00-8:00	166	38.8±11.5	0	160	44.8±10.0	0	TG, HDL	levels
Ritonja 2019	cross sectional	Canada	2011-2014	health care	unspecified	-	168	39.0±11.6	0	157	44.7±10.0	0	TG, HDL, LDL	levels
Romon 1992	cross sectional	France	1988-1989	nuclear power plant/ chemical plant	rotating 3*8	6:00-14:00/ 14:00-22:00/ 22:00-6:00	71	31.9±10.8	100	70	32.4±10.2	100	TG, TC, HDL	levels
Skogstad 2019	prospective cohort	Norway	-	insulation manufactory	rotating 3*8	7:00-15:00/ 15:00-23:00/ 23:00-7:00	42	40.5±11.0	88.1	29	49.7±8.5	75.9	TC, HDL, LDL	levels
							23	40.0±12.5	95.7	29	49.7±8.5	75.9	TC, HDL, LDL	levels
Sookoian 2007	cross sectional	Argentina	2005	non specified	rotating 2*12	6:00-18:00/ 18:00-6:00	474	36.0±21.8	100	877	34.0±29.6	100	TG, TC, HDL, LDL	levels
Suwazono 2009	prospective cohort	Japan	1991-2005	steel industry	rotating 3*8	7:00-15:00/ 15:00-23:00/ 23:00-7:00	2885	36.8±9.4	100	4219	36.3±10.7	100	TC	levels
Tenkanen 1997	prospective cohort	Finland	1982-1988	industry	rotating 2*12	-	160	51.6	100	511	52.9	100	TC, HDL	levels
					rotating 3*8	-	404	52.6	100	511	52.9	100	TC, HDL	levels
Uetani 2011	prospective cohort	Japan	1991-2005	steel industry	rotating 3*8	7:00-15:00/ 15:00-23:00/ 23:00-7:00	2105	36.2±9.6	100	2977	35.4±10.9	100	CT	levels
							702	38.8±8.3	100	1102	38.2±9.9	100	CT	levels
Van Amelsvoort 2004	prospective cohort	Netherlands	-	non specified	rotating 3*8	-	227	26.8±6.5	55.4	150	24.1±8.2	41.0	CT, HDL, LDL	levels
Weigl 2019	cross sectional	Germany	-	nurses	unspecified	-	227	-	15.0	47	-	15.0	TC, LDL	OR
Ye 2013	cross sectional	South Korea	2012	industry	rotating 3*8	-	183	49.7±8.6	0	71	36.4±12.5	0	TG, TC, HDL, LDL	levels
Ye 2019	cross sectional	China	2016-2017	automotive industry	rotating 2*12	8:00-17:00/ 16:30-4:00	212	33.7±8.0	100	238	34.1±7.5	100	TG, TC, HDL, LDL	levels

Figures legends

Figure 1. Search strategy.

Figure 2. Summary of all meta-analyses on each blood lipid levels and odds ratio.

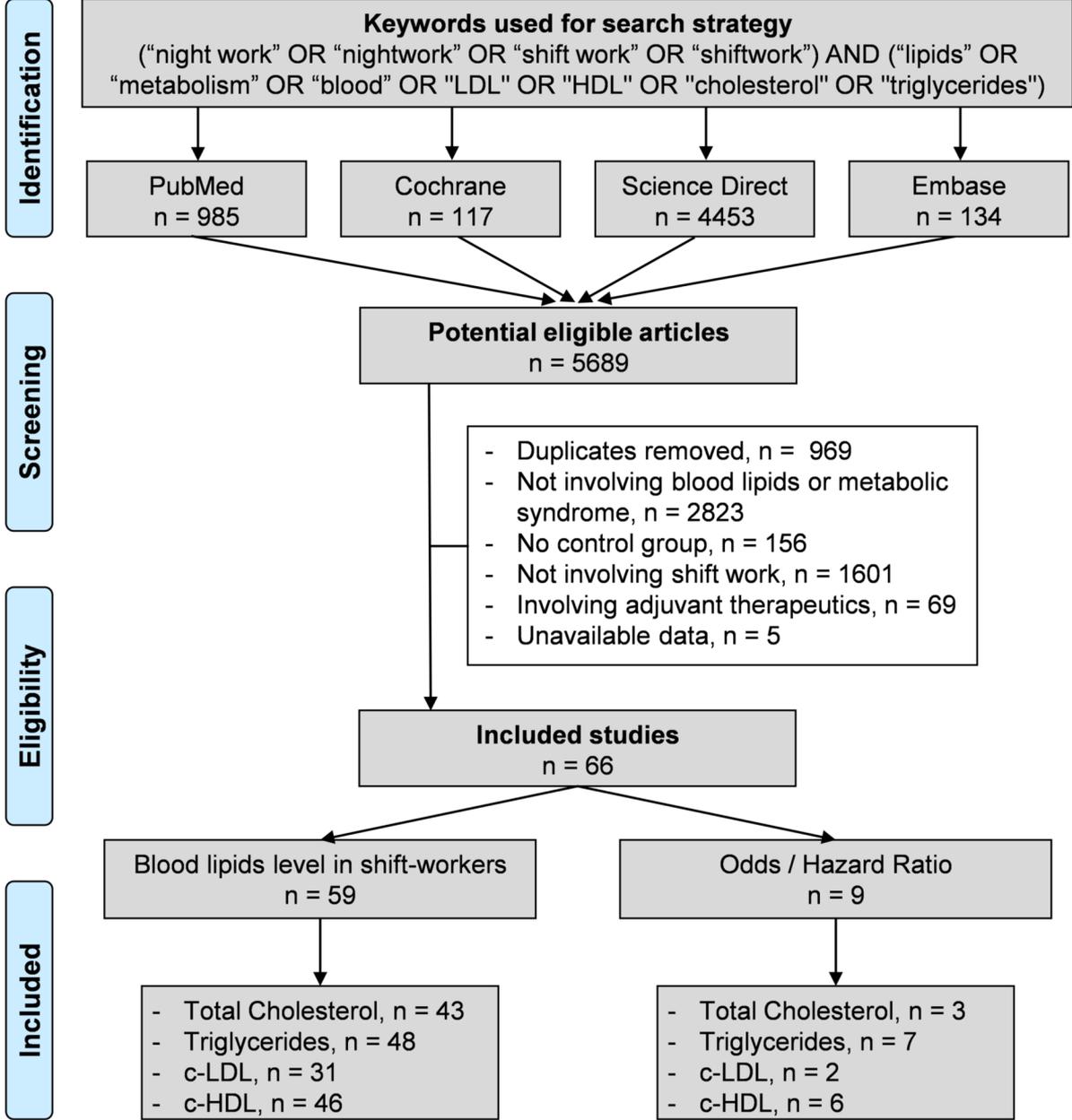
Figure 3. Metaregressions on factors influencing blood lipids levels.

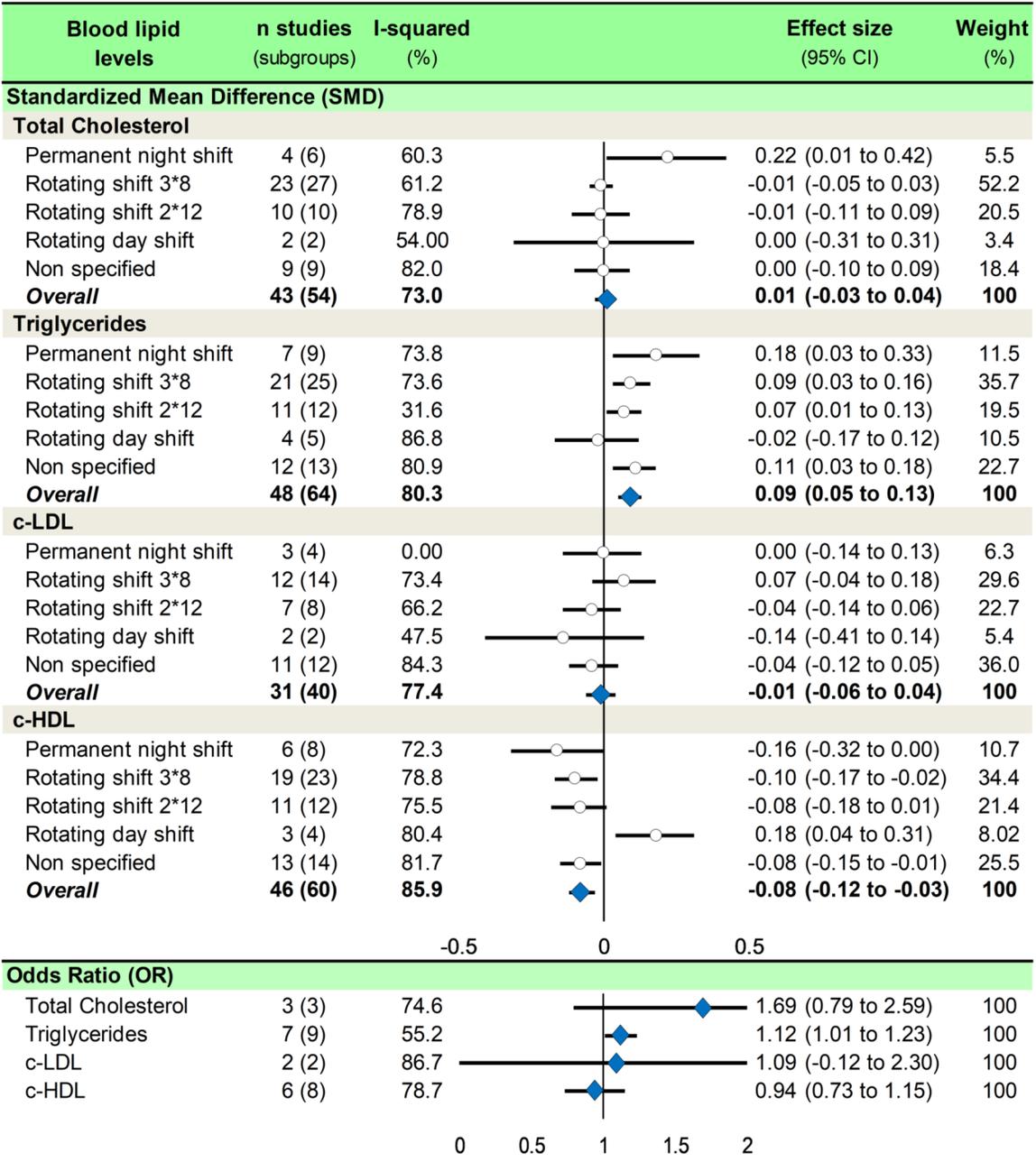
Separate models were used for each variable (* models adjusted on age, sex, physical activity, smoking and drinking)

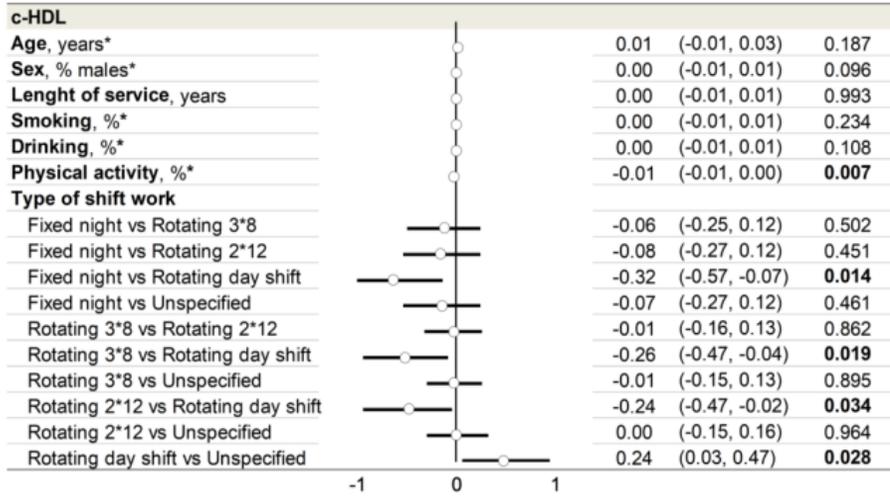
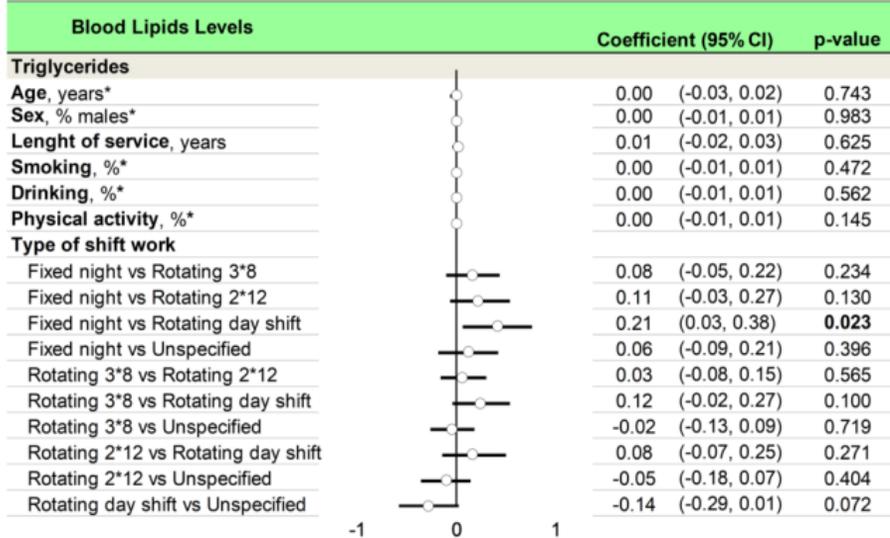
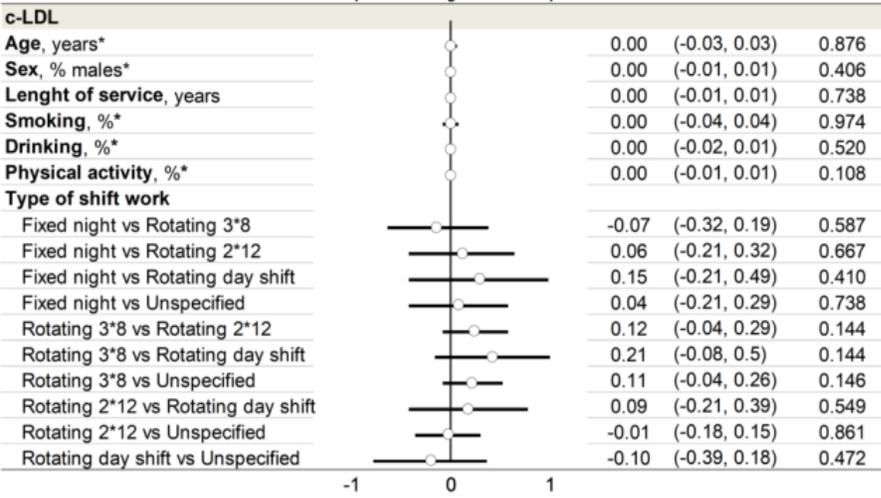
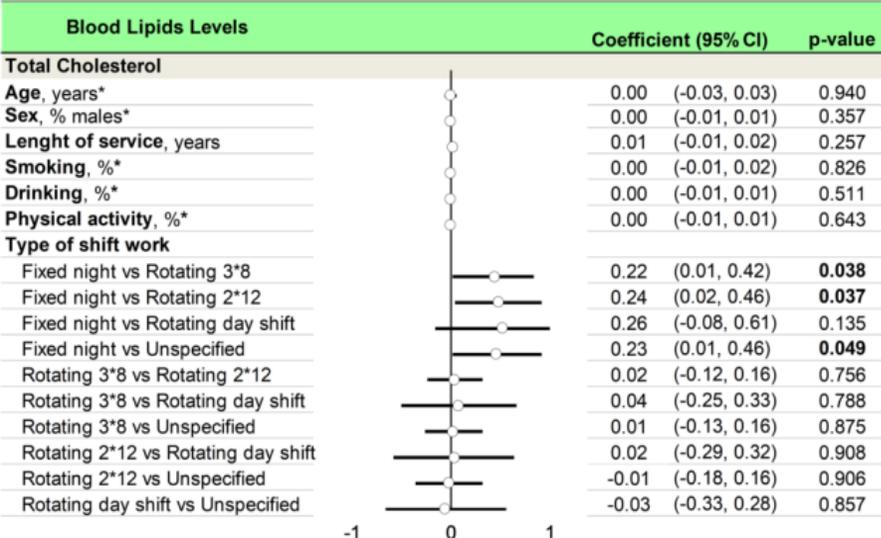
Figure 4. Funnel plots (metafunnel).

SMD: Standardized mean difference; se(SMD): standard error of standardized mean difference

Each dot represents a single study, with its corresponding effect size (x axis) and its associated standard error of the effect estimate (y-axis). Large high-powered studies are placed towards the top, and smaller low-powered studies towards the bottom. The plot should ideally resemble a pyramid or inverted funnel, with scatter due to sampling variation. Studies outside funnel plot are likely to present bias (Sterne JA, Sutton AJ, Ioannidis JP, Terrin N, Jones DR, Lau J, Carpenter J, Rücker G, Harbord RM, Schmid CH, Tetzlaff J, Deeks JJ, Peters J, Macaskill P, Schwarzer G, Duval S, Altman DG, Moher D, Higgins JP. Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. *BMJ*. 2011 Jul 22;343:d4002. doi: 10.1136/bmj.d4002).

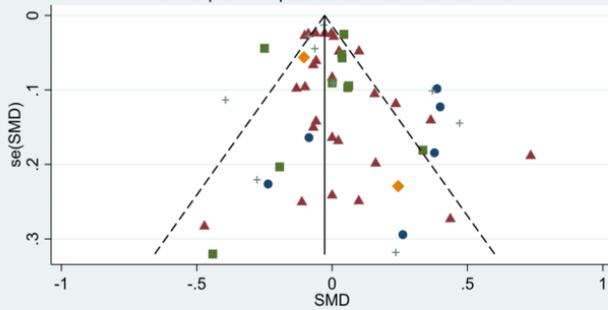






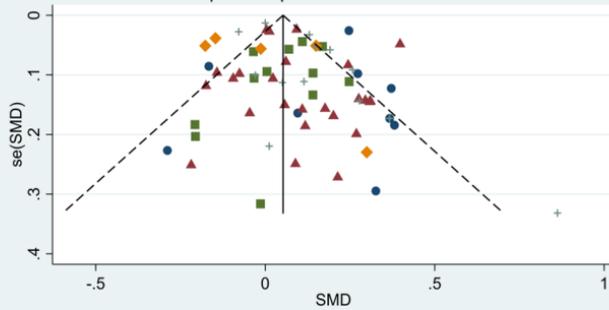
Total Cholesterol

Funnel plot with pseudo 95% confidence limits



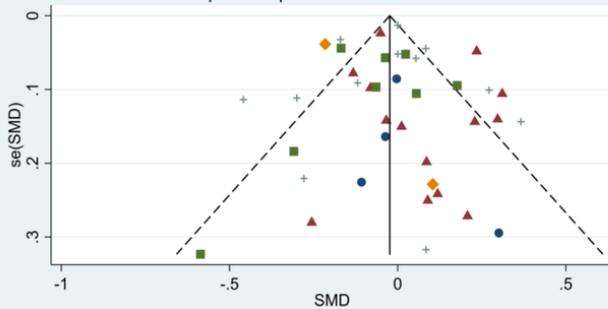
Triglycerides

Funnel plot with pseudo 95% confidence limits



LDL Cholesterol

Funnel plot with pseudo 95% confidence limits



HDL Cholesterol

Funnel plot with pseudo 95% confidence limits

