## Background

The World health organization estimates that the death toll due to heart disease and stroke will be 23.3 million in 2030 (Mathers, 2006). Most cardiovascular incidence is found in 80% of low and middle income earners occurring equally in men and women (WHO, 2011). Estimated risk age of cardiovascular disease occurrence range from 25years and above (WHO-NCD, 2011). Some notable risk factors of cardiovascular disease are tobacco use, physical inactivity, high cholesterol, diabetes, obesity, unhealthy diet and harmful use of alcohol. Most cardiovascular risk factors are preventable or modifiable through changes in lifestyle (Groenevald, 2008). With increased surge in technology and modernization there has been increased need for a 24hour working schedule to maintain, enhance productivity and efficiency in service delivery. Presently, cardiovascular disease has been associated to occupational factors as a risk. Amongst it is shift work.

Shift work has notably been known to cause disruption within the circadian rhythm. Circadian rhythm is the series of physiology and behaviour changes the body undergoes during rest/activity and fast/ feeding that is influenced by the light reception during the day of the 24hour circadian cycle (Morris, 2012). The stress resulting from shift work disrupts the physiological rhythms which cause a slow change in the body wake and sleep circle, this induces strain on the shift worker that potentially affects his working efficiency, physical and psychological wellbeing, family life and social life. This influence can be acting separately or in combination to influence the magnitude of effects in the individual (Colquhoun and Rutenfranz 1980). Morris et al 2012 provides detailed biological progress of changes in circadian rhythm due to the change in light reception, sleep-wake release of body chemicals to modulate the body on its ready to do activity. The release and suppression of the various chemical compounds has been speculated to be the main cause of death relating to the peak time of occurrence of death recorded. This invariably suggests that shift work effect is basically due to the alteration in time of the release and suppression of chemicals responsible for maintenance of the body circadian rhythm. But cardiovascular disease association to shift work has been questioned due to varying methods, population, definition of shift work and vascular or coronary events (Wang, 2011). This has called for concerns by researchers to establish the link and help in ensuring facts about it, so that policies to reduce shift work induced cardiovascular events will be implemented.

A work schedule done by any person that includes hours beyond daytime is called a shift worker. While a work schedule which frequently includes working hours of 2200 and 0600 are regarded as night work and the person in such activity is a night worker (Knutsson, 1999). Shift work includes work done aside the regular working hours 0900- 1700 (William, 2008). Shift work would therefore be all working hours done within the 1800 and 0800 that involves the relief of the previous worker on duty by another. Any work schedule that involves night and rotating shift are regarded as shift work. International Labor Organization (ILO) defines shift work as a working time for workers in which they are made to succeed or relief one another at their place of work.

Recently, systematic reviews have been giving information’s on the relationship between shift work and cardiovascular disease. Various articles have mentioned that the exposure to shift work has its effect on the shift worker when its duration of exposure exceeds 5years. Some argue that the effect is more in the first three years of exposure. It was also observed that rotation in various forms of shift schedules has been the cause of unhealthy factor to the shift worker but others say this was not observed in their research work. Other articles mentioned that the longer the hours spent on or frequency of doing shift work is a causal factor to the health of the shift worker. In further research shift work was found to be unhealthy for the shift worker but other researches did not agree so. Some articles has also mentioned that the rate of hospitalization due to occupation and sick leave from work obtained was more for shift workers due to their working pattern Alfredsson, 1985 but same was not observed when Taylor, 1972 carried out its research on the absenteeism of shift and day workers cases. For example, the epidemiological evidence of a causal relation between shift work and ischemic heart disease by Frost, 2009 examined the exposure in years in shift work to fatal, non-fatal incidence and combination of fatal with nonfatal incidence outcomes. And the relationship of work and its risk to cardiovascular disease was examined by Hwang, 2012.

## Why it is important to do this overview

There are a couple of Systematic Reviews but none properly models the exposure according to the various hypotheses. The most recent systematic review study of Vyas, 2012 was able to focus on cardiovascular events (coronary disease, coronary events and mortality, ischemic stroke, myocardial infarction, cerebrovascular and all cardiovascular mortality); a complete identification of relevant studies, using quantitative synthesis through conventional meta-analytical techniques and use of validated tool to assess the quality of all included studies was done. It was able to provide in-depth analysis of methodological strong studies, adjusting for socioeconomic status effects, comparing of association of risk to different types of vascular events as well the different shift work schedules.

But the problem in the study was that;

There was no clear definition of the exposure to shift work.

There was no formulated hypothesis based on the exposures to shift work.

Reanalysing the formulated hypotheses based on the exposure to shift work would show the association to cardiovascular events.

## Objectives

We are going to formulate proper hypotheses, re-model the exposure to shift work and analyse the hypotheses formulated.

## Methods

## Criteria for considering reviews for inclusion

We are going to use other systematic reviews to find plausible hypotheses based on PECO. We are going to use studies which clearly define the exposure to shift work with outcome of cardiovascular events. We are going to analyse the hypotheses. And all data excluded will be based on data not indicating shift work and cardiovascular effect. Data extracted will be tabulated and classified based on the formulated hypotheses and exposure of the participants.

## Primary Outcome cont’d

## We will include self-reported cardiovascular event, hospital records, national census records and national registry for death.

## Search methods for identification of reviews

We will search the following websites and portals for the original articles in the published Vyas 2010 article;

* Cochrane Central Register of Controlled Trials (CENTRAL) (Wiley Online Library);
* MEDLINE (PubMed) (Appendix 1);
* EMBASE (embase.com);
* PsycINFO (ProQuest);
* CINAHL (Cumulative Index to Nursing & Allied Health Literature);
* OSH UPDATE (Occupational Safety and Health Database)
* ClinicalTrials.gov (www.ClinicalTrials.gov) and
* WHO trials portal (www.who.int/ictrp/en/).

## Data collection and analysis

We will formulate PECOs according to the hypotheses generated above and combined studies according to these hypotheses. We will use cardiovascular disease and shift work studies to identify studies which will clearly define the dose or exposure amount to shift work and the outcome or response to be cardiovascular disease. We are going to use Vyas review to locate studies that could answer these hypotheses. We are going to assign a dose to the various exposure categories based on the midpoint of the exposure category in each individual study. We will use these data for a dose-response meta-analysis in Review Manager to calculate an incremental risk ratio and 95% confidence intervals per exposure category. We are going to categorize our exposures into less than 10 years, 10-20 years, and 20-30 years and above 30 years of exposure; less intensive, moderately intensive and highly intensive; rotating shift and permanent shift (night or evening). We will combine studies with similar exposures and outcomes in the same category, and as well the combine risk ratio. We will determine 95% confidence intervals and forest plots with Revman 5.2. We will categorize hypotheses based on disease outcome and as well based on years of exposure (duration) to shift work. Where more than one similar outcome was reported separately we will take the one that best fit our hypothesis. For example if both coronary heart disease and ischemic heart disease were reported we will take only ischemic heart disease. Where more than one job title was specified we will combine to best explain our hypothesis. For example if blue collar and white collar jobs were reported. Where male and female outcomes were reported in the same type of shift we will combine to best explain our hypothesis. We will also categorize all prolonged working hours and lengthen working hours as >40 hours per week.

### Selection of reviews

Two review authors [CP, SK] will independently screen titles and abstracts for inclusion of all the potential studies. We will retrieve the full-text study reports/publication for all citations considered relevant. Two review authors [CP, NS] will independently screen the full-text and identify studies for inclusion, and identify and record reasons for exclusion of ineligible studies. We will resolve any disagreement through discussion or, if required, we will consult a third person [JV]. We will identify and exclude duplicates, collate multiple reports of the same study so that each study rather than each report is the unit of interest in the review.

### Data extraction and management

We will use a piloted data collection form for study characteristics and outcome data. We will extract the following study characteristic

1. Methods: study location, date of study, study design, study setting, total duration of study, withdrawals, and.
2. Participants: N, mean age or age range, gender, severity of health condition, inclusion criteria, and exclusion criteria. diagnostic criteria if applicable,
3. Exposures: description of exposures, duration, intensity, changes in shift work, cumulative dose integrating the various exposures.
4. Outcomes: description of the cardiovascular event and at the duration of exposure.
5. Confounders: description of the confounding factors which were adjusted for in each article.

Two review authors [CP, SK] will independently extract outcome data from included studies. We will make a remark in the table on 'Characteristics of included studies' if outcome data were not reported in a usable way. We will resolve disagreements by consensus or by involving a third person (JV). One review author (CP) will transfer data into the Review Manager (RevMan 2012) file. We will double-check that data are entered correctly. A second review author (NS) will spot-check 20% random studies for accuracy.

### Dealing with missing data

We will contact investigators or study sponsors in order to verify key study characteristics and obtain missing numerical outcome data where possible. Where this is not possible, and the missing data are thought to introduce serious bias, we will explore the impact of including such studies in the overall assessment of results by a sensitivity analysis. If we don't find a full report even after contacting authors we will list such abstract as a study waiting assessment/ classification.

If numerical outcome data are missing, such as SDs or correlation coefficients and they cannot be obtained from the authors, we will calculate them from other available statistics such as P values according to the methods described in the Cochrane Handbook for Systematic Reviews of Interventions ([Higgins 2011](file:///C:\Users\jruo\AppData\Local\Microsoft\Windows\INetCache\Content.Outlook\XXO3TDLW\Higgins%202011)).

### Assessment of heterogeneity

We will assess the clinical homogeneity of the results of included studies based on similarity of populations, exposures, and outcomes. We will consider populations as similar when they are participants 18 years and older who is exposed to shift work for a period of duration. We will use the I2 statistic to measure heterogeneity among the trials in each analysis. If we identify substantial heterogeneity we will report it and explore possible causes by pre-specified subgroup analysis. Moreover, we will quantify the degree of heterogeneity using the I2 statistic, where an I2 value of 25% to 50% indicates a low degree of heterogeneity, 50% to 75% a moderate degree of heterogeneity and more than 75% a high degree of heterogeneity.

## Data synthesis

We will pool data from studies judged to be clinically homogeneous using Review Manager 5.2 software (RevMan 2012). If more than one study provides usable data in any single comparison, we will perform meta-analysis. We will conduct a sensitivity check by using the fixed-effect model to reveal differences in results. We will include a 95% confidence interval (CI) for all estimates.

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## Declarations of interest

This systematic review is the Master's thesis for the Author Nwankwo C Patrick, MSc public health student, University of Eastern Finland. The other two authors Suresh Kumar and Nipun Shrestha are also MSc public health students, University of Eastern Finland. This review is supervised by Jos Verbeek, senior researcher, Cochrane Occupational Safety and Health Review Group, Finnish Institute of Occupational Health, Kuopio, Finland.

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