In 18th century, people who had to work during the night were called antipodes, indicating their opposite way of living compared to the rest of the population. Nowadays, the 24-hour economy, ongoing globalization and technological developments have led to the fact that about 19% of the workforce has to work during the night, and 17% is involved in work schedules with permanent or rotating shifts. In the airline industry, an even higher percentage of employees are exposed to a variety of irregular working hours or time zone crossings. In general, it has been shown that on the short-term, irregular working hours can lead to fatigue, sleep loss, and digestive disturbances. More chronic health effects include gastrointestinal, reproductive, metabolic and cardiovascular disorders. The first goal of this thesis therefore was to better determine the health effects of exposure to irregular working hours among employees in the airline industry. The second objective was to reduce the impact of exposure to irregular working hours, by developing and evaluating a mobile health intervention aimed at reducing fatigue, and improving health-related behaviour.
Irregular working hours in the airline industry Work schedule related health outcomes and possibilities for prevention

Alwin van Drongelen
The study presented in this thesis was conducted at the EMGO+ Institute for Health and Care Research, Department of Public and Occupational Health of the VU University Medical Center. The EMGO+ Institute participates in the Netherlands School of Primary Care Research (CaRe), which was acknowledged in 2005 by the Royal Netherlands Academy of Arts and Sciences (KNAW).

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Irregular working hours in the airline industry Work schedule related health outcomes and possibilities for prevention

ACADEMISCH PROEFSCHRIFT

ter verkrijging van de graad Doctor aan de Vrije Universiteit Amsterdam, op gezag van de rector magnificus prof.dr. F.A. van der Duyn Schouten, in het openbaar te verdedigen ten overstaan van de promotiecommissie van de Faculteit der Geneeskunde op vrijdag 6 februari 2015 om 11.45 uur in de aula van de universiteit, De Boelelaan 1105

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Chapter 1

General introduction
IRREGULAR WORKING HOURS & HEALTH

Rise of the antipodes

In 1703, Bernardino Ramazzini wrote in his book on occupational diseases about the extraordinary job of bakers, who had to work during the night and sleep during the day. Antipodes, he called them, indicating their opposite way of living compared to the rest of the population (1,2). In the ages that followed, work outside the traditional dawn to dusk barrier was quickly introduced to other types of jobs as well. The growth of large cities, the industrial revolution, and the invention of artificial light provided strong motivation for entrepreneurs to expand their economic activities around the clock (3). During the second half of the 20th century, the 24-hour economy gradually made its appearance. Companies and institutions in transportation, telecommunication, healthcare, retail, security, and aviation, went to meet the growing global demand for service at any time of the day, caused by developments in technology (such as computers and internet), economy (such as growth of the service economy), and demography (such as the increase of two earners) (3). Consequently, nowadays, less than 25% of the workforce still works in a five days a week work schedule (4). The other 75% of the workers are involved in atypical schedules, including extended working hours, on-call shifts, and work during weekends (4,5). In addition, recent surveys in Europe and the US found that Ramazzini’s antipodes are all among us nowadays; about 19% of the workers has to work during the night, and 17% is involved in schedules with permanent or rotating shifts (6,7). This means that in the Netherlands, an estimated total of 1.1 million people work during the night on a regular basis.

Health effects

The 2010 European Survey on Working Conditions showed that employees with atypical work schedules are likely to report that their work affects their health (6). This feeling is supported by the scientific literature on shift work, referring to all sorts of irregular working hours during the (early) morning, evening and night (8). Acute effects of these irregular working hours include fatigue, sleep loss, and digestive disturbances (9). Although researchers debate about whether or not there is a causal relation, chronic effects comprise gastrointestinal, reproductive, metabolic and cardiovascular disorders (2,10-12). In addition, work schedules that rotate between day and night work have been identified as a probable risk for cancer by the International Agency on Research on Cancer (IARC) (13). Furthermore, it has been found that irregular working hours interfere with social life and affect the work-family balance, which can result in psychosocial problems, and social marginalization (4,14).

The health problems above can increase the demand on the healthcare system and lead to high costs for the society. For the employer, the health effects of irregular working hours can lead to a loss of productivity due to increased sickness absence of the involved employees (15,16). Sickness absence is widely used as health indicator in occupational health research because it is seen as a
precursor of health deterioration and work disability (17,18). However, although studied quite often, the association between exposure to irregular working hours and sickness absence is not clear (19-23).

The biological clock, sleep, and performance

Biological rhythms align our body functions with the environment. The periods of these rhythms vary from less than a second (e.g. firing of neurons) to close to a month (e.g. menstrual cycle). Because of the adaptation to the daily rotation of the earth and its accompanying light/dark cycle, the most common rhythms repeat approximately every 24 hours (24,25). Within the human body, these circadian rhythms (circa=approximately, die=day) regulate multiple body systems (e.g. temperature, alertness, and hormone production), coordinated by the biological clock, which is situated in the suprachiasmatic nuclei (SCN) of the hypothalamus. Although circadian rhythms are generated endogenously, they are aligned by exogenous factors, ensuring synchronization with the environment (24,25). Sunlight, received through the eye, is the most important time cue for the biological clock, directing us to sleep at night and to be active during the daytime. Other cues, such as physical exercise, social activities, and nutrition, have a synchronizing effect that is much weaker (2,25,26).

The increased health risk of workers exposed to irregular working hours is predominantly ascribed to disturbance of the biological clock (circadian disruption) (24,25). Rotating between day and night shifts and travelling across time zones can both lead to a disturbance of the normal sleep/wake pattern and accompanying body functions. The biological clock attempts to adjust to the new sleep/wake pattern, but rarely reaches full adaptation because of its ability to adjust about 1.5 hour per day (27). Moreover, because peripheral organs have a rhythm of their own that can have another readjustment speed, the human body is not only out of phase with its environment, but it is internally desynchronized as well. These consequences induce digestive problems, fatigue, and sleep loss (4,24,26). The latter two, fatigue and sleep loss, are the most prominent effects of being exposed to irregular working hours, and vary depending on duty hours, work schedules, the number of time zones crossed, and individual tolerance (27-29). In addition, sleep can be disturbed as a result of noise or light, or because of domestic and social responsibilities during the nonconventional sleeping times (27). The effects of sleep loss accumulate over time; several weeks with less than 6 hours of sleep may yield levels of fatigue that mimic total sleep deprivation (28). This can have detrimental effects on human performance and decision making, and might result in an increased number of errors and accidents (25,30,31).
RISK FACTORS AND PREVENTION

Health-related risk factors

Work schedule characteristics can contribute to the health impact of exposure to irregular working hours (4,32). It is generally thought that exposure to light during the night causes most circadian disruption and subsequent suppression of the sleep inducing hormone melatonin (24,33). Therefore, guidelines have been proposed to minimize circadian disruption, and the accompanying sleep deficits and health complaints (34-36). In rotating work schedules, these guidelines include reducing the number of consecutive night shifts, a late start of the morning shift to prevent preceding sleep loss, and a rapid, forward rotation of shifts (morning shift>afternoon shift>night shift). In aviation, the guidelines for the work schedules of flight crew include the use of computerized scheduling tools that take into account circadian disruption and sleep regulation of the individual (36).

Individual variation in tolerance to working with irregular working hours has been found to influence the health impact of irregular working hours as well. While some employees drop out soon because of for instance sleep loss and fatigue, others continue working with irregular working hours throughout their whole career, without developing any health problems (37,38). These tolerance differences might be associated with individual characteristics, such as age. On the one hand, it becomes more difficult for older people to adjust to circadian and sleep disturbances, inducing more problems related to the irregular working hours (39-41). On the other hand, whereas younger employees are able to adjust to changing working hours better, older colleagues have more experience how to cope with the alternating schedules, and tend to show an increased resistance to disturbed sleep (2,8,37,42). The found adjustment problems of older employees might be associated with becoming more of a morning type with increasing age (39,40,43,44). The human preference for the timing of sleep and wake (chronotype) differs between individuals; people tend to be either morning types (larks) or evening types (owls) (9,45). Evening types seem to have a higher tolerance for night work and circadian disruption, and their sleep-wake behaviour seems less rigid than that of morning types. Morning types on the other hand tend to have fewer problems with working in the early morning (42).

Personality traits, such as flexibility, extraversion and self-esteem, have been found to be associated with increased tolerance to irregular working hours as well, but the predictive value of these traits is relatively low (41,42). In addition, males tend to have a higher tolerance to irregular working hours, although differences between the sexes might be explained by social rather than biological pathways (41,42). Compared to men, women may experience less social support and bear most of the responsibilities at home (46-48). Employees who receive support from their family and friends, and employees who have less domestic obligations, have been found to tolerate irregular working hours better (14,37).
It has also been stated that health behaviour and lifestyle should be considered as determinants of tolerance to irregular working hours (41). Good physical fitness and proper sleeping habits (i.e. sleeping in a quiet, dark room), for instance, have been found to have beneficial effects on fatigue, performance, and recovery mechanisms (49). In addition, healthy sleeping and eating habits might decrease the risk for metabolic disorders (e.g. diabetes, overweight) of employees involved in irregular working hours (50,51). Therefore, effective coping and commitment to adapt the daily habits to changing work schedules seem to be important determinants of tolerance as well (4,41).

In summary, the health effects of irregular working hours seem to arise from a combination of work-related and individual factors, including work schedule characteristics and working conditions; familial and social responsibilities;
personal characteristics; lifestyle and behaviour (52). The possible working mechanisms are shown in a theoretical model (Figure 1), which is loosely based on the Workload Model (53,54) and the Standard Shiftwork Index model (55). The model shows that given a certain working situation, exposure to irregular working hours disrupts the circadian rhythm and the sleep/wake pattern, leading to sleep loss and fatigue. However, other work-related factors, such as physiological and psychosocial workload, can have an influence on these effects as well. Whether these short-term effects result in long-term health effects, also depends on factors outside the working situation (family life, social activities) and the capacity of the worker to cope with their irregular working hours. This workers’ capacity is determined by individual characteristics, coping strategies, physical and mental fitness, and lifestyle and behaviour.

Possibilities for research and prevention

To be able to better determine the health effects of exposure to irregular working hours, an IARC working group advised researchers to include all current and past work schedule information in their studies (e.g. the amount of work during the night, and the direction and speed of rotation of the shifts) (56,57). Since it is difficult for employees to recall this information, company databases could be a more reliable source to provide such data, especially because companies store information about individual work schedules for longer periods of time. In addition, companies’ human resource records comprise information about demographic and job characteristics, while health-related information, such as the number of sickness absence days and occupational accidents, is available at occupational health services or insurance companies. Therefore, linking these sources of information would create an optimal basis for longitudinal research, answering relevant questions from both scientific and societal point of view.

Since the found associations between work-related and individual factors and the health effects of irregular working hours are either weak or unclear, further research is necessary to better understand which mechanisms affect the health of employees involved (8,41,52). An extensive company database would enable the investigation of associations between specific work schedule characteristics and health-related outcomes, taking into account objective data on work-related and individual factors. With the outcomes of such analyses, it might be possible to develop effective interventions, helping employees to cope with their irregular work schedules. This is especially important because there will be a further increase in the mean age of employees in the upcoming years (58). In the meantime, the economic crisis has caused a stagnation in employment flow, since employees hold on to their job for a longer period of time, despite possible health complaints (59). To preserve the health and wellbeing of the aging workforce who is exposed to irregular working hours, evidence-based guidelines are necessary, taking into account criteria for scheduling and individual characteristics (58).
THIS THESIS

Study population

Within the airline industry, the percentage of employees involved in irregular working hours is high. Airplanes fly to worldwide destinations 24 hours a day, exposing the flight crew members to a variety of irregular working hours and multiple time zone crossings. Although a recent joint cohort analysis showed that flight crew members are relatively healthy, which results in a low overall mortality compared to the general population, fatigue and sleep disturbances are common phenomena among both cockpit and cabin crew (60,61). In addition to the flight crew members, the airline industry employs a large number of ground staff employees (e.g. baggage handlers, cleaning personnel, technicians, ramp agents, customer service agents, and flight dispatchers) who are necessary to support the 24-hour flight operation and are exposed to all kinds of irregular working hours as well.

In order to analyze the occupational health risks of irregular working hours in both flight crew and ground staff employees, the Monitoring Occupational Health Risks in Employees (MORE) cohort was set up. The MORE cohort is a five-year historic cohort consisting of all workers employed at an internationally operating airline company at January 1, 2010. The cohort data comprised all human resource records of the employees since January 1, 2005, combined with sickness absence and occupational accident data, which was provided by the occupational health service of the airline company.

To investigate the possibilities to increase the tolerance, coping strategies, and health outcomes of employees involved in irregular working hours, an additional group of employees was recruited in 2012. This group of airline pilots helped to evaluate the health effects of an intervention consisting of easy obtainable, tailored advice (MORE Energy).

Aims

This thesis addresses the following objectives:
1. To investigate the associations between cumulative exposure to irregular working hours within the airline industry, and adverse health effects such as sickness absence and occupational accidents.
2. To develop and evaluate an intervention aimed at reducing fatigue, and improving the health of airline pilots who are involved in irregular working hours and time zone crossings.

Outline

The thesis is divided into three sections. First, the current status of the scientific literature regarding the association between exposure to irregular working hours and health outcomes is summarized in two systematic reviews. The first
systematic review focuses on the association between exposure to shift work and body weight change (Chapter 2). The second review reports about the association between exposure to shift work and sickness absence (Chapter 3).

In the second section, data of the MORE cohort was analyzed. Chapter 4 describes a study that involves the ground staff employees of the MORE cohort, analyzing the association between cumulative exposure to different types of shift schedules, night shifts, and sickness absence. In Chapter 5, the association between cumulative exposure to flight schedules and sickness absence among flight crew members is described. Finally, the association between flight schedule exposure and occupational accidents among cabin crew members is presented (Chapter 6).

The third section of this thesis focuses on the development and evaluation of an mHealth intervention (MORE Energy) that aims to reduce fatigue and improve health of airline pilots. Chapter 7 describes the development of the intervention consisting of tailored advice on exposure to daylight, sleep, physical activity, and nutrition, provided through a mobile application and a website. Chapter 8 presents the process evaluation of the MORE Energy intervention, which was performed to get more insight in the strengths and weaknesses of the implementation, and to facilitate the interpretation of the results. In Chapter 9, the results of the randomized controlled trial, evaluating the intervention among the included airline pilots on outcome variables, such as perceived fatigue, need for recovery, sleep quality, nutritional behaviour, physical activity, and sickness absence, are presented.

In the final chapter (Chapter 10) the main findings of this thesis are summarized and explained. Methodological issues are considered, and implications for practice and further research are discussed.
REFERENCES

Chapter 2

The effects of shift work on body weight change - a systematic review of longitudinal studies

Alwin van Drongelen
Cécile R.L. Boot
Suzanne L. Merkus
Tjabe Smid
Allard J. van der Beek

ABSTRACT

**Objective** This systematic review aims to summarise the available evidence and thereby elucidate the effects of shift work which includes night work, on body weight change.

**Methods** A systematic search strategy on longitudinal studies was performed. Articles were included following strict inclusion criteria, methodological quality was assessed by a standardised quality checklist. The results were summarised using a levels of evidence synthesis.

**Results** The search strategy resulted in eight articles that met the inclusion criteria. Five of them were considered as high quality and three as low quality studies. Seven studies presented crude results for an association between shift work exposure and change in body weight; five high quality and two low quality studies. There was strong evidence for a crude relationship between shift work and body weight increase. Five studies presented weight related outcomes adjusted for potentially relevant confounders (age, gender, bodyweight at baseline and physical activity). Two studies found a significant difference between groups in the same direction. Consequently, the evidence for a for these confounders adjusted relationship between shift work exposure and body weight was considered to be insufficient.

**Conclusion** Strong evidence for a crude association between shift work exposure and body weight increase was found. In order to further clarify the underlying mechanisms, more and better high quality studies about this subject are necessary.
INTRODUCTION

Due to the 24/7 economy, the number of jobs including shift work and irregular working hours has increased substantially during the last decades. Up to an estimated 20% of the European workers are thought to be exposed to shift work schedules that include time spent working at night (1). A recent report of the European Working Conditions Survey (2) indicates that this proportion has stabilised during the last 10 years. In the Netherlands, more than 20% of the working population reports that they work in shifts while approximately 50% reports occasional work during the evening or night (3). An overview article by Costa (4) stated that only 24% of the workforce still has a regular daytime, Monday to Friday working week.

A large amount of research has been published concerning the health effects of shift work. This research shows that, although the pathways are unclear, shift schedules including nightly hours are probably related to gastrointestinal and cardiovascular diseases (1,5-9). Further, this kind of work is thought to be associated with an increased risk for several types of cancer (10-13).

Shift work including night work has also been found to be associated with diabetes and metabolic disturbances, but the evidence is not conclusive (6,14,15). However, recent longitudinal studies showed significantly increased risks for the metabolic syndrome in shift and night health care workers (16,17). Still, the underlying mechanisms for the onset of metabolic health problems as a result of shift work are not clear yet. Possible mediators are reduced sleep and physical activity, changed eating habits and patterns, and an altered circadian rhythm (18-20). Weight gain, overweight or obesity might be the mediating factor between shift work and metabolic disturbances, which can eventually result in diabetes or cardiovascular diseases (1,5).

Overweight and obesity are major health care problems for current society. As an indirect result of the population getting heavier, health care costs are thought to be increasing. Estimations vary from 1 to 7% of the total health care cost in the developed world, and the amount of indirect costs due to loss of productivity and disability pensions might be even higher (21). It has been shown that overweight and obesity lead to an elevated risk of some forms of cancer, cardiovascular and digestive diseases, diabetes mellitus, sleep apnoea, and osteoarthritis (22,23). In a large cohort study for example, Colditz et al. (24) showed that body mass index (BMI) is a main predictor for the onset of diabetes. In a recent review it was found that due to obesity, the all cause mortality is increased by approximately 20% (25).

In recent years, several studies have investigated the association between shift work and weight gain, overweight or obesity (26-31). Several of them demonstrated a significant relation between working in shifts and body weight or obesity (26-29), while some others did not (30,31). Most of these studies, however, had a cross-sectional design and thereby failed to determine a clear
causal relationship between shift work and body weight change. Longitudinal research would be able to give more insight in the working mechanisms of this relationship and results could be used in efficient worksite prevention. This could eventually lead to a reduced risk for various kinds of diseases and a smaller burden on health care costs.

Up to date, no systematic review has been published about the effects of shift work on body weight. This review aims to summarise the available evidence and thereby elucidate the relationship between exposure to shift work, which includes night work, and body weight change. A systematic literature search, selection and quality assessment has been performed. In order to be able to find indications for causality, only longitudinal studies are included.

METHOD

Search Strategy

The literature search aimed to identify relevant peer-reviewed studies providing information about change in body weight as a consequence of shift work.

The review was based on publications retrieved by a computerised search of the following databases: Medline, Embase, Cochrane library, and PsycINFO. The databases were searched for published articles up to June 18, 2010. The search terms included were: work schedule tolerance (Mesh), shift work, night work, irregular working hours, body weights and measures (Mesh), body weight changes (Mesh), BMI and body mass. After inclusion of the articles based on the selection criteria below, references were checked for additional articles.

The full Medline search strategy can be seen in Appendix 1, the search strategies for the other databases were based on this strategy.

Selection Criteria

The retrieved abstracts were checked on the following criteria:

1. The study was a full text, peer reviewed article in written English, Dutch, German, French, Spanish or Italian.
2. The study compared a group of shift workers with a control group of day workers. Working at night (12am-6am) was part of the shift work exposure.
3. The study had a longitudinal design; either prospective or retrospective.
4. The outcome included: body weight, BMI, waist to hip ratio or waist circumference. At least two measurements of the outcome were provided or the difference between outcome measurements was presented.
5. The study presented the association between shift work and day work and an outcome related to body weight, or this association could be calculated by the authors.

Two reviewers (AvD and CB) read all the abstracts independently. If no abstract
was available or if it was not clear whether the article should be included based on
the title or abstract, the full text article was read. Articles were included if they
met all five inclusion criteria. If consensus between the two reviewers could not
be reached, a third reviewer made a final decision.

Quality assessment

Differences in methodological quality across studies indicate that the results
of some studies are more likely to be affected by bias than others, making it
important to take the quality of a study into account. Two reviewers (AvD and
SM) independently assessed the quality of each included study.

A standardised checklist of predefined criteria was used, which was a modified
version of the checklists by Hayden et al. (32) and Van der Windt et al. (33) (Table
1). Each item was scored as positive (+) or negative (-, potential bias). If the paper
provided insufficient information on the specific item, the item was scored with a
question mark (?), don’t know). If an item was not applicable, it was scored as not
applicable (NA).

Disagreements between the reviewers on individual items were identified and
solved during a consensus meeting. Subsequently, the first author of each included
article with a quality item that had scored a question mark was contacted in order
to provide the author an opportunity to clarify that quality item of their article.

Eventually, for each study, a total quality score was calculated by counting the
number of items that were rated positively. This number was divided by the
total number of applicable items of the study. Based on this total score, a study
was classified as either a high or low quality study. A study was classified as
high quality if a study scored positively on at least 51% of the applicable items
in the quality assessment list; otherwise, a study was classified as low quality.
High quality studies were considered to have an overall low risk of bias, while the
low quality studies have a high risk of bias. This is in accordance with previously
published systematic reviews (21,33-35).

Data extraction

Details about the following elements were extracted and tabulated from the
publications: study population, sample size, response rate, study design, follow-
up duration, exposure, controlled confounders, outcome measurement, results
without adjustment for confounders, results with adjustment for confounders,
and overall conclusion.

The associations between exposure to shift work and body weight outcome were
presented as the mean differences in outcome between baseline and follow-up. If
possible, the 95% confidence intervals (CI) were calculated and presented as well.

The first author of the included article was contacted to provide additional
information if calculation of the adjusted mean difference or p-value was not
possible.

Table 1. Checklist of methodological quality based on Hayden et al. (32) and van der Windt et al. (33).

<table>
<thead>
<tr>
<th>Study objective</th>
<th>1 Positive if a specific, clearly stated objective is described.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study population</td>
<td>2 Positive if the main features of the study population are clearly described (sampling frame and distribution of the study population by age and gender).</td>
</tr>
<tr>
<td></td>
<td>3 Positive if the inclusion and exclusion criteria are clearly described.</td>
</tr>
<tr>
<td></td>
<td>4 Positive if the participation rate is ≥ 80%, or if it is lower, the non-response is not selective (data presented).</td>
</tr>
<tr>
<td></td>
<td>5 Positive if the response rate (proportion completing the study and providing outcome data) is ≥ 80% or if the non-response is not selective (data presented).</td>
</tr>
<tr>
<td></td>
<td>6 Positive if information (potential confounders and outcomes) is presented about the population lost to follow-up.</td>
</tr>
<tr>
<td>Exposure assessment</td>
<td>7 Positive if the characteristics of shift work are clearly described (type of work and shift schedules).</td>
</tr>
<tr>
<td></td>
<td>8 Positive if data are collected and presented about occupational exposure in the past and during the follow-up period.</td>
</tr>
<tr>
<td>Confounder assessment</td>
<td>9 Positive if the most important confounders (age, gender, body weight at baseline, physical activity) are measured and used in the analysis for body weight outcome.</td>
</tr>
<tr>
<td></td>
<td>10 Positive if confounders are measured the same for all participants using standardised methods of acceptable quality.</td>
</tr>
<tr>
<td>Outcome assessment</td>
<td>11 Positive if body weight is measured the same for all participants using a standardised method of physical examination.</td>
</tr>
<tr>
<td></td>
<td>12 Positive if data were collected for ≥ 1 year.</td>
</tr>
<tr>
<td>Analysis and data presentation</td>
<td>13 Positive if the appropriate statistical model is used to evaluate the data.</td>
</tr>
<tr>
<td></td>
<td>14 Positive if mean differences in body weight outcome are presented or can be calculated (including 95% CI).</td>
</tr>
</tbody>
</table>

Analysis

Results of the studies were analysed and where possible, a statistical meta-analysis was performed. To gain insight in factors interfering with the relationship between shift work and body weight change, crude and adjusted results were analysed separately.

To summarise the results and thereby draw conclusions about the relationship, a levels of evidence synthesis was used. This synthesis took into account the methodological quality and the outcomes of the selected studies. It was applied to both the crude and adjusted weight related outcomes of the studies.
The three levels used were based on Hoogendoorn et al. (34) and Sacket et al. (36):

*Strong evidence*: consistent findings in multiple high quality cohort studies.  
*Moderate evidence*: consistent findings in one high quality cohort study and in one or more low quality cohort studies.  
*Insufficient evidence*: only one study available or inconsistent findings in multiple cohort studies.

Findings were considered consistent if at least 75% of the selected cohort studies showed significant (p<0.05) results in the same direction.

**RESULTS**

**Study selection**

The results of the selection procedure are presented in Figure 1. The search strategy resulted in 1,047 citations (571 PubMed, 291 Embase, 160 Cochrane, and 25 PsychINFO). After excluding the doublings, 839 titles and abstracts were examined. Out of these, 65 full texts were selected for further investigation. Seven articles met all inclusion criteria. The references of these articles were checked and this resulted in one additional article. The percentage agreement between the two reviewers was 95%. Initial disagreement about three of the 65 studies (resulting in a Cohen’s $\kappa$ of 0.86) was resolved in a consensus meeting.

The most frequent reason for exclusion was the fact that the studies did not measure a change in body weight or another appropriate outcome. Many studies did measure body weight or BMI multiple times, but only used the baseline measurement as a confounder or covariate for their specific outcome. Therefore, change in weight outcome was not presented or it could not be calculated.
Methodological quality assessment

The outcome of the quality assessment is presented in Table 2. The scoring of the quality items by the two reviewers resulted in an initial agreement of 75% (Cohen’s κ of 0.56). All disagreements were resolved in a consensus meeting between the two reviewers.

Two out of six authors replied to our invitation to clarify the methodological quality of their article. As a result, two unclear items (?) were changed into positive (+). Eventually, five out of eight articles were considered high quality studies.
Table 2. Results of the methodological quality assessment.

<table>
<thead>
<tr>
<th>Study</th>
<th>Methodological items</th>
<th>Total score</th>
<th>Total %</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suwazono et al. (37)</td>
<td>+ + + + + +* - -</td>
<td>11/14</td>
<td>79%</td>
<td>high</td>
</tr>
<tr>
<td>Morikawa et al. (38)</td>
<td>+ ? - ? + - + + + - + +</td>
<td>9/14</td>
<td>64%</td>
<td>high</td>
</tr>
<tr>
<td>Niedhammer et al. (39)</td>
<td>+ + - - + + + - + + ?</td>
<td>9/14</td>
<td>64%</td>
<td>high</td>
</tr>
<tr>
<td>Geliebter et al. (43)</td>
<td>+ + + + NA NA</td>
<td>7/12</td>
<td>58%</td>
<td>high</td>
</tr>
<tr>
<td>van Amelsvoort et al. (40)</td>
<td>+ + + - - + + + +</td>
<td>8/14</td>
<td>57%</td>
<td>high</td>
</tr>
<tr>
<td>Copertaro et al. (41)</td>
<td>+ + ? ? ? + + + ? + +</td>
<td>7/14</td>
<td>50%</td>
<td>low</td>
</tr>
<tr>
<td>Hannerz et al. (42)</td>
<td>- + + + - - - + - + +</td>
<td>7/14</td>
<td>50%</td>
<td>low</td>
</tr>
<tr>
<td>Romon et al. (44)</td>
<td>+ + - - NA NA</td>
<td>4/12</td>
<td>33%</td>
<td>low</td>
</tr>
</tbody>
</table>

+ Positive score on quality item
- Negative score on quality item
? Unclear or insufficient information
NA Item is Not Applicable
* Item changed into “+” due to supplied information by the author

Study characteristics

Large differences existed between the studies. Especially the kind of shift work exposure, population, sample size, and duration of follow-up differed substantially. For this reason no overall meta-analysis was performed on the outcome data. The characteristics of the eight studies included in this review are presented in Table 3.

Study design

Six studies had a prospective design (37-42) and two retrospective studies were included (43,44). The follow-up periods of the prospective studies ranged from 12 months (40) up to 14 years (37). In the retrospective studies, data were obtained from the start of the participants’ employment in the job (43,44).

Population

Four studies reported findings from a population of nurses (39-41,43). Besides nurses, Geliebter et al. (43) included security personnel as well, while van Amelsvoort et al. (40) included a mixture of nurses and factory personnel. Three studies reported about male factory personnel only (37,38,44). Hannerz et al. (42) used a random nationwide sample. In this study, a male sample from the Central Population Register of Denmark was studied and participants with poor self-rated health at baseline were excluded.

The number of participants in the selected studies ranged from 55 (41) to 7,254 (37).
Suwazono et al. (37) did not report a drop out rate for the 14 years of follow-up, while Copertaro et al. (41) did not report any loss to follow-up during 18 months. van Amelsvoort et al. (40) retained 70% of their initial sample after 12 months. Morikawa et al. (38) lost 16% during 10 years. Hannerz et al. (42) lost 18% to follow-up in five years, while Niedhammer et al. (39) lost 5% in 1985, and 16% in 1990.

**Exposure**
The authors of the selected studies used different definitions for shift, night and day work. A summary of the exposure characteristics is presented in Table 4.

The working hours of the experimental groups in some studies consisted of three different shifts (morning, evening, and night) with a continuous (covering the whole week) rotating system (37,41). However, other studies included participants with both two and three-shift systems (38), participants exposed to both continuous and non-continuous (covering only week days) systems (44), and to counterclockwise shift systems (38,40). Further, some studies included nurses with permanent night (39,43) or evening (43) work. The exposure in these two latter studies shows the profound differences between studies because another study excluded all participants with fixed, permanent night work (37).

Differences in day work definitions were present as well. The control group of three studies worked between approximately 7am and 5.30pm (42-44). Other studies did not give any specifications of the day working hours (37,38,40), while participants in the control group of some other studies worked in morning or evening shifts themselves (Table 4) (39,41).

**Outcome measurement**
Different outcome measures for body weight change were used. Several studies measured body weight and calculated it in kilograms of body weight change (39,43,44). Others obtained body weight and body height and converted this into BMI and BMI change (37,38,42). Copertaro et al. (41) reported a change in mean waist circumference. Van Amelsvoort et al. (40) was the only study that, in addition to change in body weight and BMI, presented waist to hip ratio as well.

Secondly, there was a difference in the way the outcome was measured. In six out of eight studies, qualified people (e.g. physicians) measured the body weight related outcomes (37-41,44). Two studies based their outcomes on self-reported body weight changes provided by the participants (42,43).

**Confounding**
The different studies measured a wide variety of potential confounders. These confounders however, were not always used in the analyses to adjust the body weight related outcomes (Table 3).

**Outcomes**
The unadjusted and adjusted results on body weight related outcome of the
eight included articles are presented in Table 5. Two articles provided sufficient information about the outcome (42,44), while mean values could be calculated in two other studies (38,43). Four first authors were contacted by email and asked to provide additional data for adjusted mean difference or p-value calculation. One author did not respond (41), another author did, but could not reproduce the data (39). Van Amelsvoort (40) provided data about the adjusted difference in several outcomes between groups. Suwazono (37) provided data about the mean percentual BMI change for both groups. However, the author reported that due to job schedule type changes, this mean change was only available for a one year period from baseline (while the follow-up period of the study was 14 years).

**Associations between shift work and body weight change, crude results**

Seven out of the eight studies presented crude, non-adjusted, outcomes of type of work and body weight change: five high and two low quality studies. The five high quality studies (37-40,43) did find a significant difference between the groups. Morikawa et al. (37) and Suwazono et al. (38) found more body weight related change for shift workers in a male Japanese population, while Niedhammer et al. (39) and Geliebter et al. (43) reported similar results for male and female nurses in France and the US, respectively. Van Amelsvoort et al. (40) however, found significant results in the other direction. The two low quality studies (41,44) did not find any significant difference in body weight related outcome between groups.

Because multiple high quality studies provided consistent (four out of five studies; 80%) findings, it is concluded that there is strong evidence for a crude relationship between shift work and body weight change.

**Associations between shift work and body weight change, adjusted for potentially relevant confounders**

Six out of eight articles presented body weight related outcomes adjusted for potential confounders, five high quality studies and one low quality study. The high quality study of Geliebter et al. (43) found a significant difference in body weight change between late shift and day shift nurses, while adjusting for age, years in shift work, and smoking status. The potentially relevant confounders gender, body weight at baseline, and physical activity were not taken into account and therefore, the study was not considered in the analysis.

The other studies showed varying results. Hannerz et al. (42) found no significant difference in their Danish male sample. Niedhammer et al. (39) did not find a significant effect of night work on body weight change in a nurses population. The two high quality studies among male Japanese workers did find a significant effect. Morikawa et al. (38) found a difference in BMI increase between shift workers and day workers after a follow-up of 10 years. Suwazono et al. (37) showed a significantly higher BMI increase after one year for shift workers compared to day workers. Again, the study of van Amelsvoort et al. (40) found results in the other direction. The shift workers showed a loss in weight outcome after adjustment, which was significantly different from the day workers.
Because two out of four high quality studies (50%) found a significant difference in the same direction, the results are considered to be inconsistent. Subsequently, if the low quality study of Hannerz et al. (42) is included, only 40% (two out of five) of the studies show results in the same direction. Therefore moderate evidence was rejected as well, and it is concluded that there is insufficient evidence for an adjusted relationship between shift work and body weight change.
Table 3. Study characteristics.

<table>
<thead>
<tr>
<th>Study</th>
<th>Qual. score</th>
<th>Study population</th>
<th>Sample size</th>
<th>Response rate</th>
<th>Study design</th>
<th>Follow up time</th>
<th>Exposure</th>
<th>Controlled confounders</th>
<th>Outcome measurement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suwazono et al. (37)</td>
<td>79%</td>
<td>Japanese male workers at a steel company</td>
<td>n=7,254</td>
<td>None reported</td>
<td>Prospective study on the effect of shift work on weight gain</td>
<td>14 years</td>
<td>Day shifts: no hours reported</td>
<td>Age, BMI measured during the study, drinking, smoking and regular exercise</td>
<td>BMI obtained by annual health examination was calculated into the percentage BMI increase relative to BMI at job entry</td>
</tr>
<tr>
<td>Morikawa et al. (38)</td>
<td>64%</td>
<td>Japanese male blue collar workers at a sash and zipper factory</td>
<td>n=1,144</td>
<td>84%</td>
<td>Prospective study on the effects of shiftwork on changes in metabolic disturbance parameters</td>
<td>10 years</td>
<td>Day work: no specifications presented. Shift work: various systems</td>
<td>Age, BMI, smoking, alcohol consumption and leisure time physical activity at baseline</td>
<td>Change in BMI, calculated after obtaining weight and height at the beginning and end of the study</td>
</tr>
<tr>
<td>Niedhammer et al. (39)</td>
<td>64%</td>
<td>French female nurses</td>
<td>1985: n=363</td>
<td>1985: 89%</td>
<td>Prospective study on the relationship between night work, overweight and weight gain</td>
<td>5 years</td>
<td>Day work: permanent or alternating day and evening work</td>
<td>Age, BMI at baseline, births during the 5 year period, smoking and sports activities</td>
<td>Weight gain measured by a physician each 5 years. (plus a correlation coefficient between exposure to night work and weight gain)</td>
</tr>
<tr>
<td>Geliebter et al. (43)</td>
<td>58%</td>
<td>US male and female nurses, aid nurses, and security personnel</td>
<td>n=85</td>
<td>None reported</td>
<td>Retrospective measurement of weight gain during day and night work</td>
<td>None</td>
<td>Day shift: 8am to 4pm Late shift: 4pm to 12am or 12am to 8am</td>
<td>Age, years on the shift, smoking status</td>
<td>Self reported weight change since the start of their current job type</td>
</tr>
</tbody>
</table>

BMI=body mass index. NA=not available.
Table 3. Study characteristics (continued).

<table>
<thead>
<tr>
<th>Study</th>
<th>Qual. score</th>
<th>Study population</th>
<th>Sample size</th>
<th>Response rate</th>
<th>Study design</th>
<th>Follow up time</th>
<th>Exposure</th>
<th>Controlled confounders</th>
<th>Outcome measurement</th>
</tr>
</thead>
<tbody>
<tr>
<td>van Amelsvoort et al. (40)</td>
<td>57%</td>
<td>Mix of nurses, workers at a incinerator plant and other employees</td>
<td>n=264 105 day-workers 159 shift-workers</td>
<td>65%</td>
<td>Prospective study on the impact of one year shift work on cardiovascular disease risk factors</td>
<td>1 year</td>
<td>Day work: no specifications presented</td>
<td>Shift work: working in an alternating work schedule, including nights</td>
<td>Age, gender, BMI at baseline, physical sporting activity and physical activity during leisure time. Data obtained after contacting the first author</td>
</tr>
<tr>
<td>Coper- taro et al. (41)</td>
<td>50%</td>
<td>Italian female and male nurses</td>
<td>n=58 30 rotating shifts 28 daytime shifts</td>
<td>None reported</td>
<td>Prospective measurement of predictors for cardiovascular disease</td>
<td>18 months (four measurements)</td>
<td>Day shifts: 8am-14pm or 14pm-22pm Rotating shifts: starting at 6am, 14pm or 22pm</td>
<td>NA</td>
<td>Waist circumference (cm) measured by medics</td>
</tr>
<tr>
<td>Hannerz et al. (42)</td>
<td>50%</td>
<td>Random male sample from the Central Population Register of Denmark</td>
<td>n=1,980 379 irregular working 1601 regular working</td>
<td>76%</td>
<td>Prospective study on work factors related with changes in BMI</td>
<td>5 years (two measurements)</td>
<td>NA</td>
<td>Age, cohabiting, smoking, baseline bmi, work hours/week, cold work environment, hot work environment, physical activity at work, decision authority, psychological demands, possibilities to communicate with colleagues, conflicts at work, job insecurity</td>
<td>Self reported height and weight was calculated into ΔBMI</td>
</tr>
<tr>
<td>Romon et al. (44)</td>
<td>33%</td>
<td>French male factory workers</td>
<td>n=84 273 rotating shift 475 rotating shift 20 day shift</td>
<td>None reported</td>
<td>Retrospective dietary survey of annual weight gain</td>
<td>None</td>
<td>Day shifts: permanent day work between 7.30am and 17.30pm Rotation shifts: shift work starting at 5am, 13pm or 21pm.</td>
<td>None. Groups were matched on age, socio-professional level and seniority</td>
<td>Annual weight gain in kg/year since the start of the shift type. Obtained by occupation health service records</td>
</tr>
</tbody>
</table>

BMI=body mass index. NA=not available.
<table>
<thead>
<tr>
<th>Study</th>
<th>Qual. score</th>
<th>Shift system</th>
<th>Schedule</th>
<th>Continuity</th>
<th>Rotation</th>
<th>Shifts</th>
<th>Working time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suwazono et al. (37)</td>
<td>79%</td>
<td>four team/three-shift system</td>
<td>five days on, two off, five evenings on, one off, five nights on, two off</td>
<td>continuous</td>
<td>clockwise</td>
<td>no info</td>
<td>no information presented</td>
</tr>
<tr>
<td>Morikawa et al. (38)</td>
<td>64%</td>
<td>two-shift or three-shift system</td>
<td>five on, two off and three or four on, one off (three-shift)</td>
<td>continuous and non-continuous</td>
<td>counterclockwise (three-shift)</td>
<td>no info</td>
<td>no information presented</td>
</tr>
<tr>
<td>Niedhammer et al. (39)</td>
<td>64%</td>
<td>three-shift or permanent night</td>
<td>several kinds</td>
<td>no information presented</td>
<td>clockwise</td>
<td>permanent day or morning and evening shifts</td>
<td>9am-17pm or 6am-14pm and 13pm-21pm</td>
</tr>
<tr>
<td>Giebeler et al. (43)</td>
<td>58%</td>
<td>permanent night or evening shift</td>
<td>fixed</td>
<td>no information presented</td>
<td>none</td>
<td>none</td>
<td>8am-4pm</td>
</tr>
<tr>
<td>van Amelsvoort et al. (40)</td>
<td>57%</td>
<td>all kinds of exposure:</td>
<td>32% fast clockwise schedule (at most three consecutive night shifts)</td>
<td>no information presented</td>
<td>no info</td>
<td>no information presented</td>
<td></td>
</tr>
<tr>
<td>Copertaro et al. (41)</td>
<td>50%</td>
<td>three-shift system</td>
<td>one morning, one evening, one night, two off</td>
<td>continuous</td>
<td>clockwise</td>
<td>morning and afternoon</td>
<td>8am-14pm and 14pm-22pm</td>
</tr>
<tr>
<td>Hannerz et al. (42)</td>
<td>50%</td>
<td></td>
<td>various irregular working hours</td>
<td></td>
<td></td>
<td>permanent day duty</td>
<td></td>
</tr>
<tr>
<td>Romon et al. (44)</td>
<td>33%</td>
<td>three-shift system</td>
<td>five on, two off (slow) or three on, one off (fast)</td>
<td>continuous and non-continuous</td>
<td>no information presented</td>
<td>none</td>
<td>8 hours between 7.30am-17.30pm</td>
</tr>
</tbody>
</table>
Table 5. Study results.

<table>
<thead>
<tr>
<th>Study</th>
<th>Qual. score</th>
<th>Crude</th>
<th>Adjusted</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suwazono et al.</td>
<td>79%</td>
<td>Provided data by the first author. %BMI change after one year from baseline: shift ΔBMI 0.56%(0.44% - 0.69%)95%CI day ΔBMI 0.31%(0.21% - 0.42%)95%CI</td>
<td>Provided data by the first author. %BMI change after one year from baseline: shift ΔBMI 0.63%(0.44% - 0.82%)95%CI day ΔBMI 0.40%(0.24% - 0.56%)95% CI</td>
<td>Shiftworkers had a significant higher increase in BMI after one year from baseline compared to dayworkers. No differences in results between adjusted and non-adjusted analysis.</td>
</tr>
<tr>
<td>Morikawa et al.</td>
<td>64%</td>
<td>Mean BMI change for shift-shift workers was 0.88 (se 0.07) Mean BMI change for day-day workers was 0.63(se 0.06). p= 0.002, calculated mean difference 0.25 (se 0.08)</td>
<td>Mean BMI change for shift-shift workers was 0.89 (se 0.07) Mean BMI change for day-day workers was 0.62(se 0.06) p= 0.001, calculated mean difference 0.83 (se 0.25)</td>
<td>There was a significant higher BMI change in shift-shift workers after 10 years of follow-up compared to the day-day workers.</td>
</tr>
<tr>
<td>Niedhammer et al.</td>
<td>64%</td>
<td>1985. Mean weight change for current night workers was 0.3kg, for current day workers 0.6kg. NS</td>
<td>1985. Correlation coefficient: -0.0 (NS)</td>
<td>1985. No significant difference in weight gain between groups after 5 years. Both crude and adjusted analyses.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1990. Mean weight change for night workers was 2.2kg, for day workers 1.3kg. Significant difference but no p-value reported</td>
<td>1990. Correlation coefficient: 0.8 (0.08) NS</td>
<td>1990. A significant crude difference in weight gain between groups after 5 years.</td>
</tr>
<tr>
<td>Geliebter et al.</td>
<td>58%</td>
<td>Late shift weight gain since start of current job type = 4.3kg Day shift weight gain = 0.9kg p=0.02, calculated mean difference is 3.4 (se 1.43)</td>
<td>Late shift weight gain = 4.4kg Day shift weight gain = 0.7kg p=0.008, calculated mean difference is 3.7 (se 1.36)</td>
<td>Significant more reported weight change in late shift workers compared to day shift workers. Both crude and adjusted analyses.</td>
</tr>
</tbody>
</table>

BMI=body mass index. 95% CI=95% confidence interval. se=standard error. NS=not significant. sd=standard deviation. NA=not available.
<table>
<thead>
<tr>
<th>Study</th>
<th>Qual. score</th>
<th>Crude</th>
<th>Adjusted</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>van Amelsvoort et al (40)</td>
<td>57%</td>
<td>Mean weight change shift work: -0.98 kg, Mean weight change day work: 0.43 kg, p=0.003. Mean difference 1.41 kg (se 0.47)</td>
<td>Calculated mean difference 1.41 kg (se 0.47)</td>
<td>Significant crude difference between groups in weight and BMI change. Shift workers lost weight and BMI. Day workers gained weight and BMI.</td>
</tr>
<tr>
<td>Data provided by the first author:</td>
<td>Mean weight change shift work: -1.02 kg, Mean weight change day work: 0.28 kg, p=0.007. Mean difference 1.30 kg (se 0.48)</td>
<td>Calculated mean difference 1.30 kg (se 0.48)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Significant crude difference between groups in weight and BMI change. Shift workers lost weight and BMI. Day workers gained weight and BMI.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean BMI change shift work: -0.31 kg, Mean BMI change day work: 0.13 kg, p=0.004. Calculated mean difference 0.44 kg (se 0.15)</td>
<td>Calculated mean difference 0.44 kg (se 0.15)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean BMI change shift work: -0.33 kg, Mean BMI change day work: 0.07 kg, p=0.011. Mean difference 0.40 kg (se 0.16)</td>
<td>Calculated mean difference 0.40 kg (se 0.16)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean waist to hip ratio change shift work: -0.0093, Mean change day work: -0.0052, p=0.3. Calculated mean difference 0.0041 (se 0.0042)</td>
<td>Calculated mean difference 0.0041 (se 0.0042)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean waist to hip ratio change shift work: -0.0102, Mean change day work: -0.0053, p=0.256. Mean difference 0.0049 (se 0.0043)</td>
<td>Calculated mean difference 0.0049 (se 0.0043)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Copertaro et al. (41)</td>
<td>50%</td>
<td>NA</td>
<td>NA</td>
<td>No adjusted difference found between groups.</td>
</tr>
<tr>
<td>Data provided by the first author:</td>
<td>Rotating nurses' circumference changed from 95.8 cm (sd 9.1) to 95.7 cm (sd 9.2), Mean difference of -0.1 in 18 months. No p-value reported</td>
<td>Mean difference of -0.1 in 18 months. No p-value reported</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hannerz et al. (42)</td>
<td>50%</td>
<td>NA</td>
<td>NA</td>
<td>No adjusted difference found between groups.</td>
</tr>
<tr>
<td>Data provided by the first author:</td>
<td>ΔBMI of -0.05 (-.024, 0.15) 95%CI compared to the group without irregular working hours. p=0.6382</td>
<td>ΔBMI of -0.05 (-.024, 0.15) 95%CI compared to the group without irregular working hours. p=0.6382</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Romon et al. (44)</td>
<td>33%</td>
<td>NA</td>
<td>NA</td>
<td>No significant crude difference in annual weight gain between groups.</td>
</tr>
<tr>
<td>Data provided by the first author:</td>
<td>Annual weight gain in: 3 day rotating shifts: 0.73kg (sd 0.30). 5 day rotating shifts: 0.89kg (sd 0.32). Day shifts: 1.02kg (sd 0.54).</td>
<td>Annual weight gain in: 3 day rotating shifts: 0.73kg (sd 0.30). 5 day rotating shifts: 0.89kg (sd 0.32). Day shifts: 1.02kg (sd 0.54).</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

BMI = body mass index. 95% CI = 95% confidence interval. se = standard error. NS = not significant. sd = standard deviation. NA = not available.
DISCUSSION

The present paper is the first systematic review of the scientific literature to investigate the association between exposure to shift work which includes night work, and body weight change. The included studies show that there is strong evidence for a crude relationship between longitudinal exposure to shift work and body weight outcomes. Additionally, it is concluded that there is insufficient evidence for a relation between shift work exposure and body weight change when confounders are taken into account.

The results of this review have to be interpreted with caution because of the limited number of studies, the methodological quality of the studies, and the heterogeneity between the included studies. The small amount of eligible studies was rather surprising regarding the large amount of shift work related literature that has been published. A majority of the articles had to be excluded because, as a result of different study objectives, the relevant outcome data was not presented. The available body weight data of their studies might have altered our results though. Eventually, only five out of eight included studies could be used to investigate the adjusted relation between shift work exposure and body weight change. If the three remaining studies would have made adjustments for potentially relevant confounders, other conclusions might have been drawn for this relation.

One of those potential confounders is physical activity during leisure time. This kind of physical fitness is an important factor influencing body weight gain, it might improve individual tolerance to shift work (19,45,46) and has a positive effect on sleep amount and quality, leading to a reduction in metabolic disturbances (19,47). Shift work literature generally states that employees involved in shift work become physically less active, have less time to participate in (organised, social) sporting activities and find it difficult to stay physically fit (46). Consequently, if this is true, than physical activity would be an intermediate factor rather than a confounder. In this review however, none of the included studies analysed physical activity as an intermediate factor. Moreover, they did not analyse physical activity as an individual confounder, but adjusted their results together with the other confounders (37-40). Hence, another analysis of the role of physical activity may give more insight in the relation between shift work and body weight gain.

Of course, the lack of thorough analysis mentioned above holds true for other factors as well. Factors as age and gender should be analysed for possible effect modifying effects. Moreover, longitudinal studies are most suitable to examine if variables as smoking, energy intake, and physical activity during work, which are routinely included in shift work studies, should be treated as intermediate factors.

Further, to summarize the results of the studies included, a levels of evidence synthesis, which is often used for reviews concerning studies with a longitudinal
design, was applied. Due to this synthesis, the low quality studies were disregarded when multiple high quality studies were available. Because of this, the quality assessment and the chosen distinction between high and low quality studies are very influential. In the present study similar weight was given to all quality items. This resulted in the situation that a study could be considered as high quality although shift work exposure was vaguely assessed, no confounders had been used, or weight change was retrospectively self-reported. It is arguable if this kind of weight allocation is correct.

Another important issue in this review is the fact that when comparing the scores on the quality criteria of the different studies (Table 2), profound reasons for possible selection bias can be observed. Only four out of eight articles had a clear description of their in- and exclusion criteria and yet three studies had a non-selective non-response or a participation rate of at least 80%. Additionally, during follow-up, in some studies the response rate did not reach 80% or there was no response rate presented at all. Selection into shift work may be associated with better adaptability and fewer adverse health effects. This leaves the most suitable, healthy people in the job (healthy worker effect), thereby underestimating the real effect of shift work exposure (5,45).

This review studied the effect of shift work which included night work because working during nights alters the circadian rhythm, which could lead to adverse health effects via several pathways (1,5-9). However, two studies were included which partly used participants who were not exposed to the working hours defined as being night work (12am-6am). Geliebter et al. (43) used fixed evening workers (27 out of the 49 late shift participants) and 27.5% of the participants in the study of Morikawa et al. (38) were on a two-shift system, which normally does not involve night shifts. It is arguable if these numbers have over- or underestimated the association found in these studies, but they at least blurred the association this review was looking for.

Lack of a complete description of exposure might have underestimated the results as well. Only three studies presented information about shift work exposure before the beginning of the study (38,39,41). Further, during the follow-up period, the exact exposure was not entirely clear either. Although it was adequately described in the retrospective (43,44) and the short-term follow-up studies (37,40,41), the other studies only assessed the shift work exposure at baseline and at the end of the follow-up, which implies that it cannot be ruled out that the workers might have changed type of (shift) work several times during this period (38,39,42). Moreover, large differences between studies in follow-up duration were observed. Only two studies reported sufficient follow-up periods, 10 (38) and 14 years (37) respectively, to expect real effects of the shift work exposure. Although Suwazono et al. (37) and van Amelsvoort et al. (40) found significant differences in body weight gain between groups after one year, larger effects and effects in a similar direction might have been found if all studies would have used longer periods of follow-up.
Findings compared to other reviews

Earlier reviews that have addressed the problem of shift work and body weight change did not come to the same conclusion. In a narrative review published in 2003, Knutsson (6) stated that the evidence for the impact of shift work on body weight is inconsistent, and the evidence for a relation with metabolic factors of diabetes is inconclusive. In a recent review, Antunes et al. (48) merely stated that shift work plays a role in increasing BMI.

In these reviews, both longitudinal and cross-sectional data were used to explain the findings, no differentiation was made between crude and adjusted associations, and the methods used were non-systematic. Moreover, they did not perform a methodological quality assessment and did not use a levels of evidence synthesis.

Explanation of the findings

Our findings are in accordance with shift work literature, which claims that shift work exposure can lead to unhealthy behaviour and to subsequent disturbances in gastrointestinal and psychophysiological functioning causing body weight gain and obesity (9,26,38).

The review presented here found insufficient evidence for an adjusted relation between shift work exposure and body weight gain. However, two Japanese studies adjusted for health behaviour and still found a relation between shift work and body weight gain (37,38). Although they did not measure food intake, the studies explain their results by claiming that the timing and amount of food intake is involved. However, two recent reviews state that total energy intake seems not to be affected by shift work, although meal frequency is irregular and reduced, and that high-energy snacking seems to be increased (19,49). Therefore, it seems that food intake itself cannot fully explain possible body weight gain as a result of shift work. It has become clear though, that irregular meal pattern and time of day intake could contribute to negative consequences in metabolism (20) because of the relation between circadian rhythm and food intake (19).

During daytime, when individuals normally eat, the human body promotes glucose metabolism and fat storage, while during the night, glucose sparing and fat metabolism is promoted. As a result, shift workers show a lowered glucose and lipid tolerance following the change from day to night working (50). Other studies reported about increased leptin and blood lipid concentrations, higher low-density lipoprotein levels and a decreased glucose tolerance and insulin sensitivity as a result of nocturnal eating (48,51-55). These factors are all considered as risk factors for body weight gain and the onset of the metabolic syndrome, type 2 diabetes, and cardiovascular diseases (19,53,56). Interestingly, Sopowoski et al. (57) found that men have higher and longer elevated triacylglycerol levels compared to women in response to eating at night. These findings could mean that women have lower risk to gain weight as a result of night work compared to
men. This might be a part of the explanation for the results shown in this review; two all male, high quality studies did find an adjusted association between weight gain and shift work exposure while this was not found in female nurses studies.

Implications for further research

This review found strong evidence for a crude relationship between shift work which includes night work and body weight gain. Although recent literature suggests that shift work itself, due to nocturnal eating and alterations in circadian rhythm, could lead to body weight gain, insufficient evidence was found in the results of the included studies of this review. In order to clarify this further, more and better research should be conducted. With the resulting data, stronger conclusions about the risk factors of shift work for body weight gain can be drawn. Furthermore, this can shed more light on the involvement of shift work exposure on the onset of metabolic disturbances, diabetes type 2, and cardiovascular diseases. Shift work researchers should consider publishing more data about body weight outcomes in the future, even if it is not their primary outcome.

Further, to be able to compare the different aspects of shift work systems and their health consequences better, exposure has to be assessed more properly (12,58). The shift exposure assessment should encompass at least the following modalities: the type of shift work, the schedule, the number of different shifts (morning, evening, night) per month or year, and the cumulative numbers of years in shift work. Ideally, the information about the type and schedule of shift work should include the amount of night work, the rest periods, the rotating type, and direction of rotation. The information should make clear whether the schedule is continuous (includes weekends) or discontinuous as well. Eventually, all this information should be summarised into an “integrated exposure” variable by, for instance, summing the products of the shifts worked and the number of years worked on this particular schedule (58).

The chosen control group is important as well. In general, the control group should be day workers, composed of people who are quite similar to shift workers (58). Often, the chosen control group works during the day and evening. This can be seen in the studies by Niedhammer et al. (39) and Copertaro et al. (41) as well, and might have altered the results found. Further, when the control group consists of a group of day workers, they often tend to differ from shift workers socially, economically and in personality factors. This should be measured and used in the analysis.

Different aspects of shift work systems can cause circadian disruption. This disruption might lead to detrimental health effects, as for example, body weight gain. Tolerance to shift work might be an important factor with regards to the development of detrimental health effects. Shift work tolerance is a complex phenomenon with large interindividual differences in the speed of (re)adapting to circadian disruption (12,45,59). Costa (45) claims that short-term adjustment (circadian adjustment and sleeping) and long term adjustment (personal factors,
working circumstances, social circumstances) to shift work are related to different factors. Therefore, in future studies, the relation between exposure and body weight change should be conducted with large cohorts of newly employed shift workers and these cohorts should be followed for an extensive period of time. Importantly, potentially relevant confounders, intermediate factors, and effect modifiers should be appropriately and objectively measured, and adequately used in the analysis. For instance, health habits, like physical activity, should be considered as a possible intermediate factor, and should be analysed like that as well. Further, these factors should be measured objectively because imprecise measures of health habits have shown to increase the likelihood of false null findings (26).

CONCLUSION

This review shows that there seems to be an association between exposure to shift work which includes night work, and body weight increase. If the results of the studies are adjusted for potentially relevant confounders (gender, age, body weight at baseline and physical activity), insufficient evidence remains. In order to further clarify the underlying mechanisms, shift work studies should present more body weight related outcomes. More importantly, better high quality studies about this subject are necessary.

Acknowledgement

The authors would like to thank David Bruinveld, Hynek Hlobil, Ilse Jansma, and Carina Ligthart for their support during the writing of this article.
REFERENCES

APPENDIX 1

Search strategy for Medline:

Search #1 AND #2 AND #3 NOT #4

#1 Shift work

“Work Schedule Tolerance”(Mesh) OR “Personnel Staffing and Scheduling”(Mesh) OR shiftwork(tiab) OR “shift-work”(tiab) OR nightwork(tiab) OR “irregular working”(tiab) OR “rotate shift”(tiab) OR “rotate shifts”(tiab) OR “Workload”(Mesh) OR workload(tiab) OR ((night(tiab) OR shift(tiab)) AND work(tiab)) OR (“Circadian Rhythm”(Mesh) OR “Sleep Disorders, Circadian Rhythm”(Mesh) OR “Biological Clocks”(Mesh) OR “Sleep-Wake Schedule”(tw) OR “sleep-wake cycle”(tiab) OR “circadian rhythm”(tiab) OR Nyctohemeral(tiab) OR diurnal(tiab)) AND (Work(mh) OR work(tiab) OR labour(tiab) OR labor(tiab) OR “Workplace”(Mesh) OR “Occupations”(Mesh) OR occupation*(tiab) OR vocation*(tiab)) OR “Workplace/psychology”(Mesh)

#2 Overweight/ weight gain

“Overnutrition”(Mesh) OR “Body Weights and Measures”(Mesh) OR “obese”(tiab) OR “obesit”*(tiab) OR “overweight”(tiab) OR “Body Mass”(tiab) OR BMI(tiab) OR “Body Weight Changes”(Mesh)

#3 Study type

“Cohort Studies”(Mesh) OR cohort(tiab) OR research design(mh:noexp) OR comparative study(pt) OR evaluation studies(pt) OR control(tw) OR control*(tw) OR prospective*(tw) OR volunteer*(tw) OR longitudinal(tiab) OR retrospective(tiab) OR “Case-Control Studies”(Mesh)

#4 Publication types filter

NOT (“addresses”(Publication Type) OR “biography”(Publication Type) OR “comment”(Publication Type) OR “directory”(Publication Type) OR “editorial”(Publication Type) OR “festschrift”(Publication Type) OR “interview”(Publication Type) OR “lectures”(Publication Type) OR “legal case”(Publication Type) OR “legislation”(Publication Type) OR “letter”(Publication Type) OR “news”(Publication Type) OR “newspaper article”(Publication Type) OR “patient education handout”(Publication Type) OR “popular works”(Publication Type) OR “congresses”(Publication Type) OR “consensus development conference”(Publication Type) OR “consensus development conference, nih”(Publication Type) OR “practice guideline”(Publication Type))
Chapter 3

The association between shift work and sick leave: a systematic review

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Alwin van Drongelen
Kari Anne Holte
Merete Labriola
Thomas Lund
Willem van Mechelen
Allard J. van der Beek

*Occupational and Environmental Medicine*
*2012;69(10):701-12*
ABSTRACT

Objectives This systematic review aimed to determine whether an association exists between shift work and sick leave.

Methods A systematic literature review was conducted on observational studies. Six databases were searched. Two reviewers independently selected relevant articles and appraised methodological quality. Data extraction was performed independently by review couples. Articles were categorised according to shift work characteristics and summarised using a levels of evidence synthesis.

Results The search strategy yielded 1,207 references, of which 24 studies met the inclusion criteria. Nine studies were appraised as high quality and used in the levels of evidence synthesis. Two high quality longitudinal studies found a positive association between fixed evening shifts and longer sick leave for female health care workers. The evidence was assessed as strong. Evidence was inconclusive for rotating shifts, shift work including nights, for fixed night work, and for 8-hour and 12-hour shifts.

Conclusions Evidence was found for an association between evening work and sick leave in female health care workers. This finding implies that the association between shift work and sick leave might be schedule and population specific. To study the association further, more high quality studies are necessary that assess and adjust for detailed shift work exposure.
INTRODUCTION

Within various industries and business sectors, continuous production processes and services are needed to facilitate the demands of a 24-hour economy and increased globalisation. The health care sector, too, works around the clock, monitoring patients in need of care. This necessitates the availability of staff outside regular working hours on both evening and night shifts. It is estimated that 17% of the European workforce works in shifts (1).

Shift work has been associated with negative consequences for the employee. These include impacts on health and psychosocial well-being, such as work-family conflict (2), increased fatigue (3), problems with adapting and re-adapting to night work (4), and an increased risk for cardiovascular disease (5), gastrointestinal problems (6,7), and cancer (8).

Sick leave is a widely used outcome within occupational health research (9), due to its predictive value of medically certified sick spells of >7 days for all-cause mortality (10,11). Sick leave is defined as “absence from work that is attributed to sickness by the employee and accepted as such by the employer” (12). However, sick leave may also reflect a variety of social, economic, and psychological processes that need not be associated with an underlying illness (13).

The financial costs related to sick leave are high for the employer as well as for society (14). These include sick leave benefits and salary costs of the absentee as well as salary costs of replacement staff, costs associated with lost productivity, and reduced quality of services (12,14). Long-term sick leave is seen to contribute disproportionately to these costs, while it makes up only a small fraction of the absence episodes (14). For the employee, long-term sick leave is associated with a lower probability to return to work (15,16), leading to financial deprivation as well as social isolation through exclusion from the job market (13).

It is unknown whether shift work is associated with sick leave. Determining whether such an association exists can contribute to the theoretical understanding of health and psychosocial consequences of shift work. Additionally, if any such association exists, it will be clear whether interventions are necessary to improve shift workers’ health and to alleviate the economic burden and social isolation associated with sick leave.

A number of reviews have been undertaken to study shift work in relation to various outcomes, such as general health outcomes (6,17-19), safety outcomes (20), and work-family balance (21). However, to date, no review has been conducted that has specifically studied the association between shift work and sick leave. Thus, this review aims to establish whether an association exists between shift work and sick leave.
Chapter 3 | The association between shift work and sick leave

METHODS

A systematic review was conducted to summarise the evidence for a possible association between shift work and sick leave. For the purpose of this review, shift work was defined as regular employment outside the hours 6am–6pm (22), in schedules that include evening and/or night shifts. The definition encompasses three important assumptions: 1) repetitive and regular exposure to shift work contributes to negative effects (23,24), 2) early morning work is regarded as shift work, and 3) inclusion of evening and/or night shifts ensures that a substantial amount of time is regularly spent outside standard working hours.

Search methods

Sources
Medline, CINAHL, and PsycINFO were searched using EBSCOhost. EMBASE, Web of Science, and NIOSHTIC-2 were searched using their internet interfaces. The electronic databases were searched from inception to 21st of April 2010 for peer-reviewed articles. Additionally, references of relevant articles were hand-searched.

Search strategy
The search strategy was developed by the first author in conjunction with a search specialist affiliated with the VU University Medical Center in Amsterdam, The Netherlands. The Mesh Browser (Medline), EMTREE (EMBASE) and Major Subject Headings (PsycINFO) were consulted to retrieve useful search terms. Key terms included: work schedule tolerance (Mesh), personnel staffing and scheduling (Mesh), work rest cycles (Major Subject Heading), shift work, nightshift, compressed weeks, irregulars working hours; and absenteeism (Mesh), sick leave (Mesh), and absence duration. The Boolean operators AND & OR, as well as the proximity operator NEAR, were incorporated into the search terms. See Appendix 2 for the full Medline search strategy, the search strategies for the other databases were based on this.

Selection process
Articles eligible for inclusion in the review were assessed with a selection table in which reasons for in-/exclusion could be indicated. One exclusion criterion was enough to exclude the study from the review. Eligibility for inclusion was restricted to the following criteria:

Language & literature: peer-reviewed, full text articles written in English, Norwegian, Danish, Swedish, German, French, or Dutch.
Design: observational studies: cross-sectional, case-control, and prospective or retrospective cohort studies.
Exposure: shift work in both traditional (8-hour) and compressed (10 to 12-hour) style.
Control group: day workers with working hours between 6am–6pm on week days.
Outcome: sick leave due to illness, not due to accidents.

Data analysis: for reasons of transparency and validity, the data analysis techniques had to be reported. Further, a comparison had to have been made between the shift work and control groups.

Results: for reasons of accuracy and precision, numerical results of the comparison between the shift work and control groups had to be given, together with the 95% CI or level of significance. If the latter had not been done, data should have been provided in order for the review team to perform the calculations.

Two levels of screening were used. In the first level, titles and abstracts found in the search databases were screened for eligibility. This was done independently by two reviewers (SLM & AvD). In the second level, the full text articles were evaluated that were deemed eligible for inclusion in the first level, or for which insufficient information was available to determine eligibility. In a consensus meeting agreement was reached on the full text selections. Where agreement could not be reached eligibility was settled by an arbitrator (KAH). If a full text article was written in a language foreign to reviewer AvD, then a third reviewer was asked to assess eligibility (ML). Inter-rater agreement was calculated for the full text selections using Cohen’s Kappa coefficient.

Methodological quality assessment

Issues of selection bias, information bias and confounding were systematically appraised with a standardised checklist modified from other systematic reviews (25-27). A checklist was made for each study design: cross-sectional, prospective or retrospective cohort, and case-control. See Table 1 for an overview of the items.

Two reviewers independently assessed the methodological quality of the studies (SLM & AvD). Items were scored positive (+) if sufficient information was given in the original article; items were scored negative (-) if the item was not considered. Items were scored non-applicable (NA) if the item did not apply to the article. If insufficient information was given, the item was scored ‘do not know’ (?). A consensus meeting was held to reach agreement on the quality items. If agreement could not be reached, the quality of an item was decided by arbitration (KAH). When an item was scored ‘do not know’, the authors of the articles were contacted and asked to elaborate on the items.

Quality scores were assigned to each article by dividing the number of positive items by the total number of applicable items. High quality studies scored over 50% and additionally reported adjusted outcomes. Low quality studies scored 50% or lower and/or only reported crude outcomes (28-30). When at least two high quality studies were available for each analysis, the low quality studies were excluded from analysis (28).
Table 1: Standardised checklist for the assessment of methodological quality for cross-sectional (CS), case-control (CC), and prospective or retrospective cohort (PRC) studies modified from van der Windt et al. (25), Hayden et al. (26), and van Drongelen et al. (27).

<table>
<thead>
<tr>
<th>Study objective</th>
<th>CS, CC, PRC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study objective</td>
<td>CS, CC, PRC</td>
</tr>
<tr>
<td>1. Positive if a specific, clearly stated objective is described</td>
<td>CS, CC, PRC</td>
</tr>
<tr>
<td>Study population</td>
<td>CS, CC, PRC</td>
</tr>
<tr>
<td>2. Positive if the main features of the study population are described (sampling frame and distribution of the population by age and sex)</td>
<td>CS, CC, PRC</td>
</tr>
<tr>
<td>3. Positive if the participation rate is equal to or more than 80% or if participation rate is 60%–80% and non-response is not selective (data presented)</td>
<td>CS, CC, PRC</td>
</tr>
<tr>
<td>3A. Positive if the participation rate at main moment of follow up is equal to or more than 80% or if the non-response is not selective (data presented)</td>
<td>PRC</td>
</tr>
<tr>
<td>3A. Positive if cases and controls were drawn from the same population and a clear definition of cases and controls was stated</td>
<td>CC</td>
</tr>
<tr>
<td>3B. Positive if contrast between cases and controls are big enough (controls should not be on sick leave at the time of study, nor should they have been on sick leave within 6 months prior to inclusion in the study)</td>
<td>CC</td>
</tr>
<tr>
<td>Exposure assessment: shift work</td>
<td>CS, CC, PRC</td>
</tr>
<tr>
<td>4. Positive if data are collected and presented about shift work (starting/ending times of shifts and rotating/fixed schedule)</td>
<td>CS, CC, PRC</td>
</tr>
<tr>
<td>5. Method for measuring shift work: company records or personal recall during the past 3 months (+), personal recall only for a duration longer than 3 months (-)</td>
<td>CS, CC, PRC</td>
</tr>
<tr>
<td>Exposure assessment: compressed weeks</td>
<td>CS, CC, PRC</td>
</tr>
<tr>
<td>6. Positive if data are collected and presented about compressed weeks (number of working hours &amp; number of consecutive days)</td>
<td>CS, CC, PRC</td>
</tr>
<tr>
<td>7. Method for measuring compressed weeks: company records or personal recall during the past 3 months (+), personal recall only for a duration longer than 3 months (-)</td>
<td>CS, CC, PRC</td>
</tr>
<tr>
<td>Outcome assessment</td>
<td>CS, CC, PRC</td>
</tr>
<tr>
<td>8. Method for assessing sick leave: company records or personal recall over the past 3 months (+), personal recall only for a duration longer than 3 months (-)</td>
<td>CS, CC, PRC</td>
</tr>
<tr>
<td>8A. Positive if data were collected for 1 year or longer</td>
<td>PRC</td>
</tr>
<tr>
<td>8A. Positive if exposure is measured in an identical manner in cases and controls</td>
<td>CC</td>
</tr>
<tr>
<td>Confounding assessment</td>
<td>CS, CC, PRC</td>
</tr>
<tr>
<td>9. Positive if data are collected and presented about occupational exposure to irregular working hours in the past</td>
<td>CS, CC, PRC</td>
</tr>
<tr>
<td>10. Positive if the most important confounders (age, health status) are measured and used in the analysis</td>
<td>CS, CC, PRC</td>
</tr>
<tr>
<td>11. Positive if data are collected and presented about the history of sick leave</td>
<td>CS, CC, PRC</td>
</tr>
<tr>
<td>12. Positive if confounders are measured the same for all participants using standardised methods of acceptable quality (company records or personal recall over the past 3 months)</td>
<td>CS, CC, PRC</td>
</tr>
<tr>
<td>12A Positive if incident cases are used (prospective enrolment)</td>
<td>CC</td>
</tr>
</tbody>
</table>
Table 1: Standardised checklist for the assessment of methodological quality for cross-sectional (CS), case-control (CC), and prospective or retrospective cohort (PRC) studies modified from van der Windt et al. (25), Hayden et al. (26), and van Drongelen et al. (27) (continued).

<table>
<thead>
<tr>
<th>Analysis and data presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>13. Positive if measures of association are presented (OR/RR), including 95% CIs and numbers in the analysis (totals)</td>
</tr>
<tr>
<td>14. Positive if the number of cases in the multivariate analysis is at least 10 times the number of independent variables in the analysis (final model)</td>
</tr>
<tr>
<td>15. Positive if the appropriate statistical model is used</td>
</tr>
<tr>
<td>14A Positive if a logistic regression model is used in the case of an unmatched case-control study and a conditional logistic regression model in the case of a matched case-control study</td>
</tr>
</tbody>
</table>

Evidence synthesis

To summarise the results on the relationship between shift work and sick leave, a levels of evidence synthesis was performed. This was based on the methodological quality, study design, and the consistency of the study outcomes. The following criteria were based on Ariëns et al. (31):

*Strong evidence*: consistent findings in multiple high-quality cohort or case-control studies.

*Moderate evidence*: consistent findings in one high-quality cohort or case-control study and multiple high-quality cross-sectional studies.

*Some evidence*: findings of one cohort or case-control study or consistent findings in multiple cross-sectional studies, of which at least one study was of high quality.

*Inconclusive evidence*: all other cases (consistent findings in multiple low-quality cross-sectional studies, or inconsistent findings in multiple studies).

The study outcomes were first inspected for statistical significance ($p<0.05$). In the case of no statistical significance, it was checked whether the effect estimates were meaningful, defined as RR/OR/HR > 1.4 or < 0.71. The meaningful cut-off point 1.4 was based on the upper range for significant effect estimates of work-related predictors for sick leave (32,33). The cut-off point 0.71 is the inverse of 1.4. Findings were considered to be consistent if ≥75% of the studies showed significant or meaningful results, as previously defined, in the same direction.

Data extraction

A reviewer couple independently extracted data from each article with help of a data extraction table. One reviewer (SLM) extracted data from all included articles, while ML, TL, KAH, and AvD formed a review couple with SLM for individual articles. ML and TL extracted data from 10 and 11 articles, respectively. TL was a co-author of an additional two articles included in the review; therefore KAH performed the data extraction from those articles. One article was written in a language that was foreign to ML, TL and KAH, and therefore AvD performed the data extraction from that article.
The following details were extracted from the articles: language, country, study design, population characteristics, sample size, participation rate (all designs), participation rate at main moment of follow up (cohort design), working times and shift characteristics, outcome assessment, confounders measured, analysis technique used, and adjusted results.

RESULTS

Search

An overview of the references found in the different databases and the selection process is given in Figure 1. The search strategy yielded a total of 1,576 references. After removing the duplicates, 1,207 titles and abstracts were screened for eligibility. From these, 183 full text articles were retrieved and further examined. This resulted in 24 articles that met the inclusion criteria.

Reader couple SLM & ML assessed one full text article for eligibility, and agreed on exclusion. Reader couple SLM & AvD examined the remaining 182 full text articles. This resulted in an 80% agreement, with a Cohen’s Kappa value of 0.52, indicating a fair inter-rater agreement (34). The main reasons for exclusion were a lack of reporting analysis techniques and numerical results.

Methodological quality assessment

The outcome of the methodological quality assessment is given in Table 2. The inter-rater agreement for the quality assessment was 81%, resulting in a Cohen’s Kappa of 0.70, reflecting good agreement between the two reviewers (34).

Methodological quality was appraised as high for nine of the 24 studies. The majority of all included studies received positive scores on items describing the study objectives and the study population (items 1&2), as well as the
appropriateness of analyses (items 15&15A). In addition, when confounders were measured, this was done with tools of acceptable quality (item 12). However, it can be seen that confounding variables that are specific to the possible association between shift work and sick leave, were seldom measured or used in the analyses (items 9,10 & 11).

Study characteristics

Of the 24 included studies, 13 originated in Europe, six were conducted in North America, four were performed in Asia, and one was a cross-country study. Twenty-three studies specified the sex of the participants: 12 studies included both male and female workers, five studies included only male participants and six studies included only female workers. A variety of populations were studied, including nurses and health care workers, general working populations, chemical industry workers, and law enforcement.

Statistical pooling

There was wide variation in outcome measures, study designs and shift schedules, making statistical pooling of the results not possible. Therefore, the results were summarised qualitatively.

Study quality and design

From the 24 studies that reported on the difference between shift work and day work, nine studies were assessed as high quality. These nine high quality studies were included in the levels of evidence synthesis. Four of the nine studies had a longitudinal design: two were prospective cohort studies (A1,A2), and two were case-control studies (A3,A4). The remaining five had a cross-sectional design (A5-A9). See Table 3 for the study characteristics, see Table 4 for shift schedules assessed, and see Table 5 for the outcomes and conclusions of the high quality studies.
Table 2: Methodological quality appraisal of the studies.

<table>
<thead>
<tr>
<th>Study References</th>
<th>Methodological items</th>
<th>Score</th>
<th>Adjusted analysis</th>
<th>Quality</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>3A</td>
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<tr>
<td><strong>Prospective/retrospective cohort studies</strong></td>
<td></td>
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<tr>
<td>Tüchsen et al. (A1)</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Tüchsen et al. (A2)</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
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<tr>
<td>Angerbach et al. (A11)</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
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<tr>
<td><strong>Case-control studies</strong></td>
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<tr>
<td>Kleiven et al. (A3)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Bourbonnais et al. (A4)</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
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<tr>
<td><strong>Cross-sectional studies</strong></td>
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<tr>
<td>Higashi et al. (A5)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Niedhammer et al. (A6)</td>
<td>+</td>
<td>+</td>
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</tr>
<tr>
<td>Böckerman &amp; Laukkanen (A7)</td>
<td>+</td>
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<tr>
<td>Ohayon et al. (A8)</td>
<td>+</td>
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<tr>
<td>Eyal et al. (A9)</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Chan et al. (A10)</td>
<td>+</td>
<td>+</td>
<td>NA</td>
<td>NA</td>
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<tr>
<td>Koller (A12)</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Smith et al. (A13)</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Colligan &amp; Frockt (A14)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
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<tr>
<td>Drake et al. (A15)</td>
<td>+</td>
<td>-</td>
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<tr>
<td>Chee et al. (A16)</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>NA</td>
</tr>
<tr>
<td>Lambert et al. (A17)</td>
<td>+</td>
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</tbody>
</table>

a Item changed from “?” after information was retrieved from the authors
b Item changed from “?” after a copy of the questionnaire found on the internet
c Not able to establish contact with the corresponding author
### Table 2: Methodological quality appraisal of the studies (continued).

<table>
<thead>
<tr>
<th>Study References</th>
<th>Methodological items</th>
<th>Score (%)</th>
<th>Adjusted analysis</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adjusted analysis</strong></td>
<td><strong>1</strong></td>
<td><strong>2</strong></td>
<td><strong>3</strong></td>
<td><strong>3A</strong></td>
</tr>
<tr>
<td>Olsen &amp; Dahl (A18)</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Jamal &amp; Baba (A19)</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Sveinsdottir (A20)</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Demerouti et al. (A21)</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Aguirre &amp; Foret (A22)</td>
<td>+</td>
<td>+</td>
<td>?c</td>
<td>-</td>
</tr>
<tr>
<td>Drago &amp; Wooden (A23)</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Fawer &amp; Lob (A24)</td>
<td>-</td>
<td>-</td>
<td>+</td>
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</tbody>
</table>

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b Item changed from “?” after a copy of the questionnaire found on the internet  
c Not able to establish contact with the corresponding author
Table 3: Study characteristics of the high quality studies.

<table>
<thead>
<tr>
<th>Study</th>
<th>Quality score</th>
<th>Study population</th>
<th>Sex</th>
<th>Sample size</th>
<th>Participation rate (%)</th>
<th>Exposure shift workers</th>
<th>Recall / register period</th>
<th>Outcome measures</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prospective cohort studies</strong></td>
<td></td>
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</tbody>
</table>
| Tüchsen et al. (A1) | 67%           | Danish carers of the elderly: social, nursing home, home care and health care assistants/ helpers | Female   | N=5,627: 1,231 evening; 405 night; 748 shifts 3243 day | 79%                    | Fixed evening, fixed night, rotating shifts                  | Register: 52 weeks       | 1) Incidence of sick leave spells of ≥2 weeks  
2) Incidence of sick leave spells of ≥8 weeks |
| Tüchsen et al. (A2) | 67%           | Danish working population, random sample               | Shift workers: 49% male Day workers: 52% male | N=5,017: 1,008 shift workers; 4,009 day | 75%                    | Irregular working hours                                     | Register: 78 weeks       | 1) Proportion sick leave spells lasting ≥2 weeks  
2) Proportion sick leave spells lasting ≥8 weeks |
| **Case-control studies** |               |                                                        |          |                                          |                        |                                                             |                          |                                                        |
| Kleiven et al. (A3) | 76%           | Norwegian chemical plant workers                       | Cases: 91.8% male Referents: 91.5% male | Cases/references: N=3,580/7,582 | NA – Data retrieved from registers | Three-shift system                                           | Register: 10 years       | Sick spells > 3 days                                    |
| Bourbonnais et al. (A4) | 59%           | Canadian nurses with sick leave diagnosed “most likely to be related to workload” | Female   | Cases/references: N=184/1,165 Schedules: 42/240 evening; 32/154 night; 46/268 shifts, 24/162 unknown; 40/341 day | NA – Data retrieved from registers | Fixed evening, fixed night, and rotating shifts             | Register: 3 years 5 months | Sick spells ≥6 days for full-time workers, ≥8 days for part-time workers |
Table 3: Study characteristics of the high quality studies (continued).

<table>
<thead>
<tr>
<th>Study</th>
<th>Quality score</th>
<th>Study population</th>
<th>Sex</th>
<th>Sample size</th>
<th>Participation rate (%)</th>
<th>Exposure shift workers</th>
<th>Recall / register period</th>
<th>Outcome measures</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tr>
<tr>
<td>Cross-sectional studies</td>
<td></td>
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</tr>
</tbody>
</table>
| Higashi et al. (A5) | 67% | Japanese chemical fibre & textile workers in production, maintenance and service departments | Male | N=26,324; 13,472 three-shifts; 12,852 day | NA – Data retrieved from registers | Three-shift system | Register: 1 year | 1) % Spells/man/year  
2) % Number of lost work days/total normal potential work days |
| Niedhammer et al. (A6) | 62% | French workers, random sample from voluntarily participating occupational physicians | 58% male | N=24,486; 3,206 shifts excluding nights; 1,111 nights; 1,256 shifts including nights; 18,913 day | 97% | Shift work without nights, fixed night, shift work including nights | Recall: 12 months | Proportion workers who had at least 1 sick leave spell of >8 days |
| Böckerman & Laukkanen (A7) | 54% | Finnish workers from all sectors of the economy: mostly blue-collar workers | 58% male | N= 725; 297 shift/period workers, 428 not shift/period workers | 69% | Shift and period work as one group | Recall: 12 months | Proportion workers with ≥2 sick leave days |
| Ohayon et al. (A8) | 54% | French psychiatric hospital staff: medical, maintenance, social services & administrative staff | Two-shift: 21% male; Fixed/rotating nights: 40% male Fixed day: 32% male | N= 817; 323 two-shift; 52 fixed/rotating night; 442 day | 41% | Two-shift system, fixed/rotating nights | Recall: 12 months | Proportion workers who had at least 1 sick day |
| Eyal et al. (A9) | 54% | Israeli shift workers in a company - industry unknown | Male | N= 519; 250 shift workers; 269 white-collar workers | NA - Data retrieved from registers | Shift work | Register: 12 months | ≥ 20 accumulated days of registered absence |
### Table 4: Overview over the shift schedules for the high quality studies.

<table>
<thead>
<tr>
<th>Study</th>
<th>Quality score</th>
<th>Exposure shift workers</th>
<th>Continuity (incl/excl weekends)</th>
<th>Rotation</th>
<th>Shift work experience</th>
<th>Exposure day workers</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prospective cohort studies</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tüchsen et al. (A1)</td>
<td>67%</td>
<td>1) Fixed evening 2) Fixed night 3) Rotating shifts: intermittent day/evening, intermittent evening/night, intermittent day/evening/night. Evening work usually between 14:00-23:00.</td>
<td>Not given</td>
<td>Fixed and rotating (speed/direction not given)</td>
<td>Not given</td>
<td>Day work</td>
</tr>
<tr>
<td>Tüchsen et al. (A2)</td>
<td>67%</td>
<td>Irregular working hours: two-shift system, fixed evening shifts, three-shift system, and fixed nights</td>
<td>Not given</td>
<td>Fixed and rotating</td>
<td>Not given</td>
<td>Average person years at risk: Men: 1.32 person years; Women: 1.28 person years</td>
</tr>
<tr>
<td><strong>Case-control studies</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Kleiven et al. (A3)</td>
<td>76%</td>
<td>Three-shift system: slowly rotating between day/evening/night</td>
<td>Not given</td>
<td>Rotating (speed/direction not given)</td>
<td>Not given</td>
<td>Day work</td>
</tr>
<tr>
<td>Bourbonnais et al. (A4)</td>
<td>59%</td>
<td>&quot;Evening, night, shift&quot;: assumed fixed evening, fixed night, and rotating shift schedules</td>
<td>Not given</td>
<td>Fixed and rotating (speed/direction not given)</td>
<td>Not given</td>
<td>M ± sd seniority in hospital: Cases: 10.9 ± 5.0 years; Controls 10.3 ± 5.0 years (p = 0.097) M ± sd seniority last position: Cases: 45.3 ± 42.1 months; Controls: 43.6 ± 42.5 months (p = 0.601)</td>
</tr>
</tbody>
</table>

M=mean. sd=standard deviation
Table 4: Overview over the shift schedules for the high quality studies (continued).

<table>
<thead>
<tr>
<th>Study</th>
<th>Quality score</th>
<th>Exposure shift workers</th>
<th>Continuity (incl/excl weekends)</th>
<th>Rotation</th>
<th>Shift work experience</th>
<th>Exposure day workers</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cross-sectional studies</strong></td>
<td></td>
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</tr>
<tr>
<td>Higashi et al. (A5)</td>
<td>67%</td>
<td>Three-shift system: rotated between starting times: 6am, 2pm, and 10pm</td>
<td>Continuous</td>
<td>Rotating (speed/direction not given)</td>
<td>Not given</td>
<td>Not given</td>
</tr>
</tbody>
</table>
| Niedhammer et al. (A6)                     | 62%           | 1) Shift work without nights  
2) Night work  
3) Shift work including nights | Not given                       | Fixed and rotating (speed/direction not given) | Not given                              | Day work                               |
| Böckerman & Laukkanen (A7)                 | 54%           | Shift and period work as one group (definition used: hours worked not limited to the usual daily/weekly hours) | Not given                       | Not given                              | Not given                              | Non-shift and non-period workers       |
| Ohayon et al. (A8)                         | 54%           | 1) Two-shift system: rotated mainly between morning/evening shifts (6.30am-2.30pm/1.30pm-21.30pm)  
2) Fixed/rotating night: either fixed night time or rotating between day/evening/night | Not given                       | Fixed and rotating (speed/direction not given) | Not given                              | Daytime (8am – 9am to 4pm – 5pm)       |
| Eyal et al. (A9)                           | 54%           | Shift work                                                                              | Not given                       | Not given                              | Not given                              | Day work – white collar workers        |

M=mean, sd=standard deviation
Table 5. Outcomes and conclusions for the high quality studies.

<table>
<thead>
<tr>
<th>Study</th>
<th>Quality Score</th>
<th>Analysis</th>
<th>Confounder used in analysis</th>
<th>Adjusted outcomes</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prospective cohort studies</strong></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Tüchsen et al. (A1)</td>
<td>67%</td>
<td>Poisson regression model</td>
<td>Age, education, BMI, smoking status, leisure time physical activity, general health, psychosocial and physical work environment factors</td>
<td>Model 1:</td>
<td>Fixed evening workers had a significantly increased risk for taking a ≥2-week and a ≥8-week sick leave spell in model 1. When additionally adjusting for work environment factors (model 2), the increased risk was still evident for ≥2-week sick leave spells, but not for ≥8-week sick leave spells.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Model 2: adjusted for all variables</td>
<td>Model 2:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>≥2wks</td>
<td>RR (95% CI):</td>
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</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Fixed night:</td>
<td>1.03 (0.80-1.32)</td>
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<tr>
<td></td>
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<td></td>
<td>Fixed evening:</td>
<td>1.31 (1.13-1.5)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Rotating shifts:</td>
<td>0.97 (0.80-1.18)</td>
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<td></td>
<td></td>
<td></td>
<td>≥8wks</td>
<td>RR (95% CI):</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Fixed night:</td>
<td>1.17 (0.84-1.62)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Fixed evening:</td>
<td>1.26 (1.03-1.55)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Rotating shifts:</td>
<td>0.91 (0.69-1.20)</td>
<td></td>
</tr>
<tr>
<td>Tüchsen et al. (A2)</td>
<td>67%</td>
<td>Cox proportional hazards model</td>
<td>Age, sex, children, education, work sector, establishment size, replacement policy, full-time work, overtime, 3 day sick leave without certificate rule</td>
<td>Model 1:</td>
<td>After adjusting for age, only shift working men showed a significantly increased risk for taking a ≥8-week sick leave spell in a year. In model 2 this association was ameliorated.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Model 2: adjusted for all variables</td>
<td>Model 2:</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>≥2wks</td>
<td>HR (95% CI):</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Men:</td>
<td>0.94 (0.74-1.19)</td>
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<td></td>
<td></td>
<td></td>
<td>Women:</td>
<td>1.20 (0.96-1.50)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>≥8wks</td>
<td>HR (95% CI):</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Men:</td>
<td>1.43 (1.01-2.04)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Women:</td>
<td>1.35 (0.98-1.84)</td>
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<tr>
<td><strong>Case-control studies</strong></td>
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<tr>
<td>Kleiven et al. (A3)</td>
<td>76%</td>
<td>Logistic regression, stratification</td>
<td>Age, sex, seniority</td>
<td>OR (95% CI):</td>
<td>No significant difference was found between three-shift workers and day workers for taking sick spells lasting ≥3 days.</td>
</tr>
<tr>
<td></td>
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<td>Minor mental illness: 1.04 (0.64-1.70)</td>
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<td>Gastrointestinal diseases: 1.02 (0.64 -1.63)</td>
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<td>Coronary heart disease: 0.75 (0.42-1.31)</td>
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<td>Musculoskeletal disease: 1.14 (0.92 -1.40)</td>
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<td></td>
<td>Neoplasm: 0.75 (0.29 -1.94)</td>
<td></td>
</tr>
<tr>
<td>Bourbonnais et al. (A4)</td>
<td>59%</td>
<td>Chi square tests, multiple logistic regression</td>
<td>Duration of stay, nurse-patient ratio, job title, interaction between nurse-patient ratio and job title, job classification</td>
<td>Proportion ≥1 sick leave spells of ≥6-8 days: OR (95% CI):</td>
<td>Working night and evening shifts significantly increased the odds for sick leave, rotating shifts showed a meaningful increased odds.</td>
</tr>
<tr>
<td></td>
<td></td>
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<td></td>
<td>Night shifts: 1.96 (1.14-3.36)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Evening shifts: 1.67 (1.02-2.75)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Rotating shifts: 1.43 (0.88-2.31)</td>
<td></td>
</tr>
</tbody>
</table>

BMI=body mass index. wks=weeks. OR=odds ratio. HR=hazard ratio. RR=relative risk. 95% CI=95% confidence interval.
Table 5. Outcomes and conclusions for the high quality studies (continued).

<table>
<thead>
<tr>
<th>Study</th>
<th>Quality Score</th>
<th>Analysis</th>
<th>Confounder used in analysis</th>
<th>Adjusted outcomes</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Higashi et al. (A5)</td>
<td>67%</td>
<td>Mantel-Haenszel test</td>
<td>Age</td>
<td>Shift vs. day: 1) % Spells/man/year: 25.1 vs. 33.1 (p&lt;0.01), 2) % Lost days/working days: 0.83 vs. 1.04 (NS)</td>
<td>Three-shift workers had a significantly lower percentage of sick leave spells than day workers, but not % lost workdays</td>
</tr>
<tr>
<td>Niedhammer et al. (A6)</td>
<td>62%</td>
<td>Logistic regression</td>
<td>Age, decision latitude, psychological demands, social support, bullying, aggression from public, occupation, work status, work hours, and physical-, ergonomic-, biological-, and chemical exposure</td>
<td>Men: OR (95% CI) Fixed night: 1.11 (0.89-1.38) Shift excluding nights: 1.26 (1.09-1.45) Shift including nights: 1.24 (1.04-1.49) Women: OR (95% CI) Fixed night: 1.07 (0.79-1.45) Shift excluding nights: 1.03 (0.86-1.23) Shift including nights: 1.29 (0.91-1.83)</td>
<td>Men working shifts including nights, as well as shifts excluding nights, showed a significantly increased odds for taking sick leave. No associations were found for women.</td>
</tr>
<tr>
<td>Böckerman &amp; Laukkanen (A7)</td>
<td>54%</td>
<td>Logistic regression</td>
<td>Sex, work sector, education, children at home, company size, replacement, work hours, match in work hours, sick leave policy</td>
<td>Marginal effect: 0.075 (p=0.045)</td>
<td>Participation in shift or period work significantly increases the prevalence of sickness absenteeism by 8%.</td>
</tr>
<tr>
<td>Ohayon et al. (A8)</td>
<td>54%</td>
<td>Chi square, logistic regression</td>
<td>Age, sex, profession, children at home, daytime sleepiness, sleep duration, circadian rhythm disorders, obstructive sleep apnoea syndrome, insomnia disorder</td>
<td>Proportion workers at least 1 sick day: Two-shift: OR 2.6 (p&lt;0.05) (95% CI not reported) Fixed/rotating night: no numerical results given</td>
<td>Two-shift workers had a significantly increased OR for sick leave than day workers. No difference was found between night time/rotating shifts and day workers.</td>
</tr>
<tr>
<td>Eyal et al. (A9)</td>
<td>54%</td>
<td>Relative risk</td>
<td>Age</td>
<td>RR to take ≥20 days sick leave: 1.3 (p&lt;0.05)</td>
<td>Blue-collar shift workers had a significantly increased RR for sick leave.</td>
</tr>
</tbody>
</table>

BMI=body mass index. wks=weeks. OR=odds ratio. HR=hazard ratio. RR=relative risk. 95% CI=95% confidence interval.
Summary of findings

The effect estimates for an association between shift work and sick leave varied amongst the included studies from protective (OR 0.75 - ns) to an increased risk for sick leave (OR 2.6 – p<0.05). One out of the four high quality studies with a longitudinal design reported a significant increase in sick leave due to night and evening work, and a meaningful increase for rotating shift work (A4), while one study found a significant increased effect for evening workers only (A1).

It is concluded that the findings are inconsistent (two out of four), and that there is inconclusive evidence for an association between sick leave and shift work. Including the high quality cross-sectional studies, of which four showed an increased risk for sick leave (A6,A7,A8,A9), would not have changed the consistency of the review findings (six out of nine studies with a positive association).

From Table 4 it is clear that various shift schedules were included in the different studies. Shift schedules could have different effects on sick leave; therefore a subdivision according to schedule characteristics was made. Six out of nine high quality studies described the shift schedules sufficiently to be able to group them into a category.

Evening work
Four high quality studies reported on shift work excluding nights, ie evening work: one prospective cohort study (A1), one case-control study (A4), and two cross-sectional studies (A6, A8). Tüchsen et al. (A1) found that fixed evening workers had a significantly increased RR for sick leave spells of ≥2 weeks. Bourbonnais et al. (A4) found a significantly increased OR for fixed evening shifts to take sick leave for ≥6-8 days. Niedhammer et al. (A6) found a significantly increased odds for male shift workers who did not work nights to take sick leave spells for >8 days, while this was not found for women. Ohayon et al. (A8) found a significantly increased OR for two-shift workers to take >1 day sick leave in the 12 months preceding the study.

It is concluded that the findings in the studies are consistent (three out of four) for an association between shift work excluding nights and sick leave. Two of the studies had a longitudinal design with findings in the same direction for fixed evening work among a female health care population. Therefore, the evidence was assessed as strong for an increased risk for sick leave with fixed evening work.

Night work
Five high quality studies reported on the association between shift work including night work and sick leave. Of these studies one had a prospective cohort design (A1), two had a case-control design (A3,A4) and two had a cross-sectional design (A5,A6). Tüchsen et al. (A1) did not find a significant association between fixed night work or schedules that could include night work and sick leave. Kleiven et al. (A3) did not find a significant association between working in three-shifts...
and taking sick leave spells >3 days. Bourbonnais et al. (A4) found a significantly increased odds for taking sick leave spells for ≥6-8 days for fixed night workers. Niedhammer et al. (A6) did not find a significant association between fixed night work and sick leave. They did find a significantly increased odds for men working shifts including nights to take sick leave spells for >8 days, with similar effect estimates for women. Higashi et al. (A5) found that three-shift workers had a significantly lower percentage of sick leave spells than day workers, but no significant difference was found for percentage lost days. When considering meaningful results, only Bourbonnais et al. (A4) found an increased meaningful result for rotating shift workers.

The findings from the studies were inconsistent. This applies to the studies with a longitudinal as well as a cross-sectional design. In total, two studies did not find an association between shift work including nights and sick leave; one study found a significantly increased odds for fixed night work, and a meaningful increase for rotating night work; one study found a significantly increased odds for men; and one study found a significantly lower sick leave. Furthermore, one study found an increased odds for sick spells but not for days lost. It is concluded that the evidence for an association between shift work including nights and sick leave was inconclusive.

Fixed shifts
Three studies focussed on fixed evening and/or night shifts: one prospective cohort study (A1), one case-control (A4), and one cross-sectional study (A6). As stated before, Tüchsen et al. (A1) and Bourbonnais et al. (A4) found significantly increased risks for fixed evening workers to take sick leave. Bourbonnais et al. (A4) found a significantly increased OR for fixed night shift workers to take sick leave. Tüchsen et al. (A1) and Niedhammer et al. (A6) did not find an association between fixed night shifts and sick leave.

In summary, two studies reported on fixed evening shifts, and three reported on fixed night shifts. The findings were inconsistent. The same two studies that were described under the heading ‘evening work’ found an association between fixed evening shifts and sick leave. One study found an association between fixed night shifts and sick leave, while two did not find the latter association. It was concluded, as before, that there was strong evidence for an association between fixed evening work and sick leave. It is further concluded that there was inconclusive evidence for an association between fixed night shifts and sick leave.

Rotating shifts
Six high quality studies assessed shift work in a rotating schedule: one prospective cohort study (A1), two case-control studies (A3,A4), and three cross-sectional studies (A5,A6,A8). Tüchsen et al. (A1), Kleiven et al. (A3), found no significant association between rotating shift work and sick leave. Bourbonnais et al. (A4) found a meaningful increased risk for rotating shifts on sick leave. Higashi et al. (A5) found that rotating shift workers had a significantly lower risk for percentage sick spells, but not for percentage sick days. Niedhammer et al. (A6) found a
significantly increased odds for male rotating shift workers to take sick leave. Ohayon et al. (A8) found that rotating two-shift workers showed a significantly increased odds for sick leave compared to day workers.

It is concluded that the study findings are inconsistent and that there is inconclusive evidence for an association between rotating shift work and sick leave. Two studies with a longitudinal design found no association between rotating shift work and sick leave, while one found a meaningful increased risk. Two cross-sectional studies reported an increased odds for sick leave, while one reported a risk reduction.

**Shift duration**

Four high quality studies reported on traditional 8-hour shift work in comparison with day work. One had a prospective cohort design (A1), one had a case-control design (A3), and two had a cross-sectional design (A5,A8).

Tüchsen et al. (A1) found a significantly increased risk for 8-hour fixed evening shift workers to take sick leave, but they did not find an association for 8-hour rotating schedules. Kleiven et al. (A3) did not find an association between 8-hour shifts and sick leave. Higashi et al. (A5) found a significantly lower risk for rotating three-shift workers to take sick leave spells, but they did not find the association for individual sick days. Ohayon et al. (A8) found a significantly increased risk for two-shift workers to take sick leave, but not for rotating or night shift workers. The findings for 8-hour shifts were inconsistent; there is inconclusive evidence for an association between 8-hour shift work and sick leave.

Two low quality studies (A10,A11) reported on 12-hour shifts in comparison with day work. They both had a cross-sectional design and did not report adjusted outcomes. It was therefore concluded that there is inconclusive evidence for the association between 12-hour shifts and sick leave.

**DISCUSSION**

The review found strong evidence for a positive association between fixed evening work and sick leave among female health care workers. Evidence was assessed as inconclusive for the following associations with sick leave: rotating shifts, shift work including nights, fixed night shifts, as well as 8-hour and 12-hour shifts.

**Strengths and limitations of the review**

A strength of the current review is the addition of the criterion ‘reporting adjusted outcomes’ to the high quality scores. The quality assessment form used in this review was based on previous systematic reviews where all items were weighed equally (25-27). Weighing selection bias, information bias, and confounding equally, assumes that the biases are equally important in influencing the study outcomes and can therefore overestimate the quality of the studies. Adding an important criterion to the quality score can adjust for this overestimation. The most often assessed quality item in systematic reviews is ‘adjustment for
confounding’ (35), and therefore this was used as the additional quality criterion.

An additional strength of the review was the modification of the levels of evidence from an earlier review by Ariëns et al. (31). The moderate level of evidence was revised from “consistent findings in multiple cohort or case-control studies, of which only one study was of high quality”, to “consistent findings in one high quality cohort or case-control study and multiple high quality cross-sectional studies”. The version by Ariëns et al. (31) was based on the assumption that longitudinal study designs increase the validity of evidence for an association between two variables when compared to cross-sectional studies. As the validity of a study depends more on the quality of the study than on its design, the levels of evidence were adapted to increase the weight of high quality cross-sectional studies over low quality longitudinal studies.

The levels of evidence synthesis in this review was based on significant and/or meaningful effect estimates; both approaches have strengths and limitations. The strength of significant findings is their valid effect estimates in 95% of similar studies when repeated, yet the effect warrants discussion as to whether the size is important. The strength of including non-significant meaningful effects is not missing studies that can contribute to the building of evidence. However, use of arbitrary cut-off points, as done in previous reviews (36,37), questions the legitimacy of the meaningfulness. In the current review, on the contrary, the cut-off points were based on effect estimates found in the sick leave literature (32,33). Caution should be applied in using meaningful estimates, as they are only valid in studies with overall high quality yet low sample sizes. For instance, Bourbonnais et al. (A4) found a non-significant association between rotating shifts and sick leave. Use of a meaningful estimate was plausible, reasoning that in this high quality study a larger sample would narrow the confidence interval and make the association significant. This changed the conclusion from a strong level of evidence for no association between rotating shifts and sick leave, to inconclusive evidence for this association. This warrants further research into the topic.

**Strengths and limitations of the studies**

The included studies often lacked detailed information on schedule characteristics, whereby the differentiations were not clear-cut, making it difficult to interpret the schedule characteristics’ effects on sick leave. Additionally, three included studies appraised as high quality did not specify or differentiate between schedule characteristics (A2,A7,A9), and could not be used in the detailed analysis. Reducing the number of studies in the analysis lowers the chance to detect moderate or strong evidence for associations, which means that if the studies had included schedule characteristics this could have led to different conclusions of this review.

In the scientific literature there is little agreement on definition, measurement methods and reporting units of sick leave (9). This was reflected in the included studies. The definition of sick leave was not given in some studies (A6,A8), while in other studies it was defined (A7), or categorised according to diagnosis
Chapter 3 | The association between shift work and sick leave

(A3,A5). Various reporting units were used: average number of sick leave (spells) per group, proportions of sick leave (A6,A7), and sick leave for time at risk (A1). As sick leave is regarded to mirror a variety of factors, such as health (14,15), and psychosocial processes (14), a uniform sick leave outcome could increase the understanding of the processes that underlies sick leave.

Possible explanations of the findings

In the nine studies that reported adjusted results, differences existed in the size of the adjusted effect estimates. A source of between-study variance could lie in the different confounders that were adjusted for. Adjusting for confounders is important in sick leave research due to the multifactorial causes of sick leave (14). Adjustment leads to a more precise effect estimate for the association between shift work and sick leave, with important confounders being age, shift work experience, work environmental factors as well as health indicators. Six of the nine high quality articles adjusted for work environmental factors or proxies thereof (A1,A2,A4,A6,A7,A8), however only two articles adjusted for health indicators (A1,A8), and none adjusted for shift work experience. Adjustment for psychosocial and physical work environment factors could have led to lower effect estimates for shifts excluding night work (A1,A4,A6), than when no adjustment was made for these factors (A8). Adjusting for work environmental factors could also explain the lower effect estimates found for fixed night shifts (A1,A6), than when adjusting for proxies of work environment factors (A4). The two articles that adjusted for health indicators varied to such an extent that it cannot be stated which effect the adjustment had on the size of the effect estimates.

The positive association found between fixed evening shifts and sick leave was based on two studies with similar effect sizes as found in other research for work-related factors (32,33). The relatively low estimates (RR 1.29(A1) and OR 1.67(A4)) are regarded to be a consequence of the multifactorial nature of sick leave. The study outcomes were long-term sick leave spells of ≥2 weeks (A1), and ≥6-8 days (A4), respectively. The predictive value of longer sick leave spells of >3 or >7 days for all-cause mortality (15,16), and disability pensioning (38), suggests that long-term sick leave mirrors an underlying biomedical condition. It could therefore imply that fixed evening work is associated with ill health in female health care workers. Whether this is a causal relation remains unknown.

Possible explanations for the association could not be found in the articles, therefore only hypotheses can be proposed that can be tested further. Firstly, a plausible hypothesis is sick leave as a consequence of repetitive exposure to the same tasks inherent to working fixed shifts. A similar population of female evening workers reported more physical handling task than day workers (39), which in the study by Tüchsen et al. (A1) could have caused musculoskeletal problems and sick leave. Secondly, low management support is associated with sick leave in women (40), and was evident in a similar population (39). Management staff are often less available in evening hours which could explain the low management support. Lastly, it is proposed that willingness to work fixed evenings could be a coping
behaviour: night workers or day workers with existing health problems could transfer to evening work due to the lower overall work load associated with it (39).

Contrary to expectations, the evidence for an association between shift work including nights and sick leave was inconclusive. Current research is focussing on night work as the main contributing factor for ill health (8,41,42), yet this review did not support this hypothesis. Possible differences between studies with regards to the data extracted on population characteristics (sex, country of origin, work sector, confounders) that could explain the varying study outcomes were not found.

A possible explanation could include differences between studies with regards to population characteristics that were not measured, such as shift work experience and health indicators that could lead to the 'healthy worker effect'. It is a common phenomenon in the shift work literature, where shift work tolerant individuals are hypothesised to be relatively healthy and continue working in shifts (selection into shift work), while those who are less tolerant stop working shifts (selection out of shift work) (3). It is possible that the participants of some studies included in this review were relatively healthy individuals, thereby underestimating the association between shift work and sick leave.

Recommendations for future research

The review findings indicate that the existence of an association between shift work and sick leave is schedule specific, due to the strong association found for fixed evening work and inconclusive evidence for other shift types. This indicates that shift work, as a collective phrase, is too broad and that the phrase should be broken down into exposure characteristics and studied accordingly. Surprisingly, a relatively large number of high quality studies (three out of nine) included in the review did not do this. It is therefore recommended to gather more specific information with regards to shift schedule characteristics and use them in the analyses.

Just over a third of the included studies adjusted for confounding, and none adjusted for an important confounder, namely shift work experience. The cumulative effects of exposure to shift work on shift work tolerance and health is hypothesised to have high explanatory value (23,24), but it was often not assessed or reported. Seniority or time at a company, as reported in three articles (A3,A4,A9) are poor proxies for shift work experience. They do not take into account that employees can change between shift work and day work, and thereby might overestimate the exposure to shift work. It is recommended to assess shift work experience in more detail in future studies on shift work and sick leave.
CONCLUSION

Fixed evening work was found to be positively associated with sick leave in female health care workers. This implies that a possible association between shift work and sick leave might be dependent on schedule characteristics as well as population characteristics. Future research should include the assessment of schedule characteristics and exposure to these characteristics over time, when studying the association between shift work and sick leave.

Acknowledgement

The authors would like to acknowledge the contribution of René Otten at the VU Amsterdam Medical Library for his contribution in the development of the search strategy.
REFERENCES

35. Mallen C, Peat G, Croft P. Quality assessment of observational studies is not commonplace in

REFERENCES OF STUDIES INCLUDED IN THE REVIEW

APPENDIX 2

Search strategy for Medline:

Search limits: ‘peer reviewed’ & ‘human’

Mesh and Major Subject Headings:


General word search:

shiftwork OR nightwork OR nightshift OR (shift* N2 work*) OR (shift* N2 system*) OR (shift* N2 schedul*) OR (shift* N2 rotat*) OR (shift* N2 pattern*) OR (night* N2 shift) OR (night* N2 work*) OR (night* N2 schedul*) OR (evening N2 work) OR (evening N2 shift*) OR (morning N2 work) OR (morning N2 shift*) OR (irregular* N2 shift*) OR (irregular* N2 work* N2 hour*) OR (irregular* N2 schedul*) OR (non-standard N2 schedul*) OR (non-standard N2 rotat*) OR (nonstandard N2 schedul*) OR (nonstandard N2 rotat*) OR (work* N2 schedul*) OR (roster*) OR (long N2 work* N2 hour*) OR (hour* N2 long) OR (hour* N2 extend*) OR (long N2 day*) OR (week* N2 work* N2 hour*) OR (hour* N2 12) OR (hour* N2 twelve) OR (hour* N2 80) OR (hour* N2 84) OR (work* N2 week N2 80) OR (work* N2 week N2 84) OR (working N2 time N2 arrangement*) OR (worktime N2 arrangement*) OR (work N2 arrangement*) OR (weekend N2 work*) OR (extend* N2 week*) OR (compress* N2 hour*) OR (compress* N2 week*) AND (long-term N2 sickness N2 absen*) OR (long-term N2 sickness N2 leave*) OR (short-term N2 sickness N2 absen*) OR (short-term N2 sick* N2 leave) OR (temporary N2 sick-leave) OR (sick* N2 absen*) OR (sick* N2 leave) OR (sick* N2 day*) OR (sick* N2 spells*) OR (sick* N2 list*) OR (sick* N2 role) OR (work N2 absen*) OR (absenteeism) OR (days N2 off) OR (absen* N2 spell*) OR (absen* N2 day*) OR (illness N2 day*) OR (illness N2 spell*) OR (illness N2 behavio#r) OR (time N2 return N2 work) OR (duration N2 absence) OR (work N2 loss)
Chapter 4

Cumulative exposure to shift work and sickness absence: associations in a five-year historic cohort

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Hynek Hlobil
Allard J. van der Beek
Tjabe Smid

Submitted
ABSTRACT

Objective To investigate associations between cumulative exposure to shift work and sickness absence among ground staff employees of a large international airline company.

Methods This study is part of the MORE study, a five-year historic cohort. The study population consisted of 7,562 ground staff employees. For each employee, work schedules and sickness absence days during 2005 to 2009 were obtained from company records. For the exposure to different shift schedule types, and exposure to night shifts during 2005 to 2008, the association with long-term sickness absence (>7 consecutive sickness absence days) and the number of sickness absence episodes during 2009, was calculated using logistic and Poisson regression analyses. Socio-demographic variables, work-related variables, job classification variables, and previous sickness absence days were regarded as confounders.

Results After adjusting for previous sickness absence and job classification variables, only the group of employees that switched into working in a three-shift schedule, showed a significantly increased risk for long-term sickness absence (OR=1.31, 95%CI 1.02-1.69). Night shift exposure was not significantly associated with long-term sickness absence. Compared to day work, exposure to shift work was negatively associated with more sickness absence episodes. Employees who were exposed to more than 46 night shifts also showed a lower risk for more sickness absence episodes, compared to employees who were not exposed to night shifts. Subgroup analyses showed that single employees and employees without children had an increased risk for long-term sickness absence when exposed to a two-shift schedule, and when they changed between shift schedule types during the exposure period.

Conclusion Shift work was only associated with future long-term sickness absence when employees started working in a schedule that included nights shifts. Problems adapting to the new shift schedule may have led to sleep problems, fatigue and subsequent sickness absence. Future research should explore the influence of household composition, and take into account both previous sickness absence and psychosocial and physical work factors to obtain a good estimation of the association between shift work and sickness absence.
INTRODUCTION

The current 24-hour economy makes it necessary for employees to work outside the once regular 9 to 5 working hours, in the early morning, evening, and night. Consequently, it has been estimated that almost 20% of the workforce in Europe and the USA works in shift work (1,2). Exposure to shift work has become an important topic in occupational health as it has been associated with negative consequences for the employee. Short-term effects comprise disturbed sleep, increased fatigue (3), and work-family conflict (4). Long-term risks involve cardiovascular disease, gastrointestinal problems (5-9), metabolic disturbances (10-12) and cancer (13,14).

Sickness absence is considered to be a risk factor for health deterioration and mortality (15,16), and can have unfavourable financial consequences for the individual, employer and society (17,18). Work-related risk factors for sickness absence involve both physical (e.g. ergonomic factors, work schedules) and psychosocial (e.g. job strain, social support) characteristics (19-22). In the literature, a distinction is made between short- and long-term sickness absence (21,23). Long-term sickness absence contributes disproportionately to the total sickness absence costs while it accounts for a small fraction of the number of absence episodes. For the employees, long-term sickness absence can be associated with future sickness absence, an increased risk for work disability, and both social and financial problems (17,18,23,24). Short-term sickness absence, on the other hand, can be part of a behavioural pattern, or of a coping strategy to prevent long-term sickness absence (20,25).

To obtain a better understanding of the consequences of shift work, it is necessary to investigate the association between exposure to shift work and both short- and long-term sickness absence. Although shift work in relation to sickness absence has been studied before, its association remains unclear (26-28). Merkus et al. (29) stated that sickness absence should be studied per specific population and shift work schedule. However, it is also possible that it is not the specific schedule, but the cumulative exposure to night shifts that imposes health effects, due to the chronic disruption of the circadian rhythm (30-32).

Therefore, this study aims to investigate the associations between cumulative exposure to different types of shift schedules and cumulative exposure to night shifts on the one hand, and the number of sickness absence episodes and long-term sickness absence on the other, among ground staff employees of a large international airline company.

METHODS

Design

This study used data from the MORE (Monitoring Occupational Health Risks in Employees) cohort. The five-year historic cohort was set up to analyze occupational
health risks of employees of a large airline company and consists of all workers employed at the company at January 1, 2010. The cohort data comprised of sickness absence and human resource records of the employees of the airline company, since January 1, 2005. Individual work schedules were registered for each day of the cohort period. The datasets were combined, anonymized, and coded by an independent occupational physician. According to Dutch law, this study was exempt from Medical Ethical review.

Study population

The study population consisted of ground staff employees of the airline company that were already employed at January 1, 2005. Employees were excluded if they received a disability pension at January 1, 2005, or had more than 365 days of cumulative sickness absence during 2005 to 2008. Furthermore, only employees with complete data on job classification variables at 1-1-2009 were included. In total, 7,652 employees were available for the analyses (Figure 1).

Sickness absence

Sickness absence was defined as registered absence from work due to health reasons. Data was provided by the occupational health service of the airline company. Calendar days of the registered sickness absence episodes were counted as sickness absence days. Partial absence days were considered as full days of sickness absence (21).

The outcome measures were calculated for the period of January 1, 2009 until January 1, 2010.

1. First, the number of sickness absence episodes was calculated for each employee. Each episode was considered to be finished as soon as the employee fully returned to work, for at least one day (33).
2. Next, a dichotomous outcome variable was created to analyse long-term sickness absence in 2009. This variable was defined as at least one episode of more than seven consecutive sickness absence days. Previously, this cut-off has been used to determine medically certified sickness absence, for instance in the Whitehall II cohort (16,34).
Shift schedule exposure

Daily work schedules were analyses for the period 2005 to 2008. For each eligible employee, the number of night shifts (shifts that comprised more than one hour between 00:00 and 06:00) was counted, and categorized into tertiles. Although it has been recommended to assess shift work exposure as extensive as possible (35), the shift work schedules of our study population showed a wide variation in rotation, speed and direction. Therefore, the following basic categories were created:

- Day work (no shifts)
- Two-shift schedule (rotating between morning/day and evening shifts)
- Three-shift schedule (rotating between morning/day, evening, and night shifts)

Subsequently, it was determined in which of these shift schedules the employee had worked during each year of the period 2005 to 2008. With this information, the employees were divided into six different groups, depending on the shift schedule exposure during 2005 to 2008 (Figure 2).
Figure 2. Composition of the different shift type groups.

Covariates

The variables below were regarded as potential confounders and retrieved from the database at January 1, 2009. If the exact value was not available at that date, the proxy at January 1, 2010 was used. Skewed variables were divided into quartiles.

Included socio-demographic variables were age, gender, marital status (married/cohabiting, single, divorced/widow), having children (yes, no), and commuting distance (0 up to 16, 16 up to 24, 24 up to 41, >41 kilometres).

Work-related variables were employment years, mean contract percentage during 2009 (0 up to 50%, 51 up to 80%, 81 up to 99%, and 100%), and working overtime during 2005-2008 (yes, no). By means of the job classification system of the company, all job titles were scored on a continuous scale on the following characteristics: responsibility, knowledge requirements, social interaction, special operational requirements, and aggravated working conditions (36). Due to multicollinearity, only the scores on knowledge requirements (necessary specific knowledge, range 0-90), special operational requirements (required skills, range 0-18), and aggravated working conditions (physiological and physical workload, range 0-22) were used as potential confounders. The variable aggravated working conditions was skewed and therefore divided into quartiles. Finally, the total number of sickness absence days during 2005 to 2008 was calculated, and divided into quartiles (0 up to 26 days, 26 up to 67 days, 67 up to 140 days, ≥ 140 days). This will be referred to as previous sickness absence.

Statistical analyses

Means, standard deviations and frequencies were calculated for the socio-demographic variables, the work schedule variables, the number of sickness absence days and episodes, and long-term sickness absence episodes (>7 days).
The associations of different shift schedule types and cumulative night shift exposure with long-term sickness absence were calculated by performing logistic regression analyses. The associations of the shift schedule types and cumulative night shift exposure with the number of sickness absence episodes were determined using Poisson regression analysis, correcting for overdispersion (37).

For each analysis, three models were composed. First, the crude association was determined. Next, the socio-demographic variables, work-related variables, and previous sickness absence days were added to construct the semi-adjusted model. Finally, the job classification variables were added to create the fully adjusted models.

Interaction terms with age, gender, having children, and marital status were added to the crude model to detect possible effect modification. If the interaction term was statistically significant, subgroup analyses were performed.

A two-tailed significance level of $p<0.05$ was considered to be statistically significant. Statistical analyses were conducted with the Statistical Package for Social Sciences (SPSS) version 20.0.

RESULTS

The socio-demographic, work-related and sickness absence characteristics of the study population are presented in Table 1. The sample consisted of 7,562 employees with an average age of 45.4 years. The majority of the population was male (81.6%), had a fulltime contract (73.9%), and worked in a three-shift schedule during 2005 to 2008 (42.7%). In 2009, on average, the employees reported sick for more than 26 days, with a mean frequency of 1.7 episodes. For 48.6% of the employees at least one sickness absence episode of more than seven days was registered.
Exposure to different shift schedules and sickness absence

The associations between shift schedule exposure and sickness absence are presented in Table 2. In the crude and semi-adjusted models, all shift schedule
groups, except for the group that transferred out of the three-shift schedule, showed an increased risk for long-term sickness absence compared to day workers. After adding the job classification variables to the model, only the group of employees that transferred into a three-shift schedule showed an increased risk for long-term sickness absence (OR = 1.31, 95%CI 1.02-1.69).

In both the semi-adjusted and the fully adjusted model, all shift schedule types had a lower incidence risk ratio (IRR) for the number of sickness absence episodes, compared to the group of employees that worked during the day.

Cumulative night shift exposure and sickness absence

The associations between cumulative night shift exposure and sickness absence are presented in Table 3. In the crude and semi-adjusted models, employees with moderate night shift exposure (up to 110 night shifts between 2005 and 2008) were positively associated with more long-term sickness absence in 2009, compared to employees who had not been exposed to night shifts. After adding the job classification variables, night shift exposure was no longer significantly associated with long-term sickness absence.

In the semi-adjusted model, all employees with night shift exposure showed a significant lower IRR for the number of sickness absence episodes compared to employees who had not been exposed to night shifts. In the fully adjusted model this was only the case for the employees who were exposed to more than 46 night shifts.

Effect modification

The interaction terms having children (p=0.005) and marital status (p=0.027) had a significant effect on the association between shift type and long-term sickness absence (crude model). Otherwise, none of the added interaction terms had a significant effect.

Table 4 presents the results of the subgroup analyses. Employees without children showed to have a higher risk for long-term sickness absence in the fully adjusted model when they worked in a two-shift schedule, transferred into a three-shift schedule, or made another kind of shift schedule transfer. Comparing the three marital status groups, the fully adjusted model showed that married/cohabiting employees in the different shift schedule types did not have a significantly higher risk for long-term sickness absence compared to married/cohabiting day workers. In all models, single employees who worked in a two-shift schedule or made a shift schedule transfer did show significantly higher ORs for long-term sickness absence compared to single day workers. Divorced or widowed employees that transferred into a three-shift schedule after 2005 had an increased risk for long-term sickness absence compared to divorced or widowed day workers.
Table 2. Crude, semi-adjusted, and fully adjusted models for shift schedule types, long-term sickness absence, and sickness absence episodes.

<table>
<thead>
<tr>
<th>Long-term sickness absence (≥7 days)</th>
<th>crude model</th>
<th>semi-adjusted model</th>
<th>fully adjusted model</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Shift schedule type 2005-2008</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day work</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Two-shift schedule</td>
<td>1.88 (1.63-2.17)*</td>
<td>1.43 (1.22-1.69)*</td>
<td>1.13 (0.94-1.35)</td>
</tr>
<tr>
<td>Three-shift schedule</td>
<td>1.76 (1.50-2.06)*</td>
<td>1.40 (1.17-1.68)*</td>
<td>1.08 (0.89-1.31)</td>
</tr>
<tr>
<td>Transfer out of three-shift</td>
<td>1.23 (0.97-1.54)</td>
<td>1.06 (0.82-1.37)</td>
<td>0.90 (0.69-1.17)</td>
</tr>
<tr>
<td>Transfer into three-shift</td>
<td>2.49 (2.03-3.06)*</td>
<td>1.84 (1.46-2.32)*</td>
<td>1.31 (1.02-1.69)*</td>
</tr>
<tr>
<td>Other kind of transfer</td>
<td>1.59 (1.30-1.94)*</td>
<td>1.33 (1.06-1.67)*</td>
<td>1.06 (0.84-1.35)</td>
</tr>
<tr>
<td><strong>Sickness absence days 2005-2008</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥0 to &lt;26 days</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>≥26 to &lt;67 days</td>
<td>3.06 (2.58-3.62)</td>
<td>2.99 (2.52-3.55)</td>
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</tr>
<tr>
<td>≥67 to &lt;140 days</td>
<td>8.10 (6.80-9.66)</td>
<td>7.45 (6.23-8.90)</td>
<td></td>
</tr>
<tr>
<td>≥140 days</td>
<td>12.53 (10.48-14.99)</td>
<td>11.28 (9.40-13.53)</td>
<td></td>
</tr>
<tr>
<td><strong>Special operational requirements</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.00 (0.99-1.02)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Knowledge requirements</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.98 (0.97-0.98)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Aggravated working conditions</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤4</td>
<td>Reference</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;4 to ≤11</td>
<td>1.14 (0.94-1.37)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;11 to ≤15</td>
<td>1.14 (0.92-1.40)</td>
<td></td>
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</tr>
<tr>
<td>&gt;15</td>
<td>1.21 (0.94-1.55)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

OR=odds ratio. IRR=incidence risk ratio. 95% CI=95% confidence interval. Semi-adjusted model adjusted for age, gender, marital status, having children, commuting distance, employment duration, mean contract percentage, working overtime, and previous sickness absence days. Job classification variables special operational requirements, knowledge requirements, and aggravated working conditions were added to the fully adjusted model. *= p<0.05.
Table 2. Crude, semi-adjusted, and fully adjusted models for shift schedule types, long-term sickness absence, and sickness absence episodes (continued).

<table>
<thead>
<tr>
<th>Sickness absence episodes</th>
<th>crude model</th>
<th>semi-adjusted model</th>
<th>fully adjusted model</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IRR (95% CI)</td>
<td>IRR (95% CI)</td>
<td>IRR (95% CI)</td>
</tr>
<tr>
<td><strong>Shift schedule type 2005-2008</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day work</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Two-shift schedule</td>
<td>0.95 (0.89-1.01)</td>
<td>0.82 (0.77-0.87)</td>
<td>0.82 (0.76-0.88)</td>
</tr>
<tr>
<td>Three-shift schedule</td>
<td>0.95 (0.89-1.02)</td>
<td>0.84 (0.78-0.90)*</td>
<td>0.83 (0.77-0.90)*</td>
</tr>
<tr>
<td>Transfer out of three-shift</td>
<td>0.93 (0.84-1.02)</td>
<td>0.83 (0.75-0.91)*</td>
<td>0.83 (0.75-0.92)*</td>
</tr>
<tr>
<td>Transfer into three-shift</td>
<td>1.05 (0.96-1.14)</td>
<td>0.87 (0.79-0.94)*</td>
<td>0.89 (0.81-0.98)*</td>
</tr>
<tr>
<td>Other kind of transfer</td>
<td>0.97 (0.89-1.06)</td>
<td>0.82 (0.75-0.89)*</td>
<td>0.83 (0.76-0.91)*</td>
</tr>
<tr>
<td><strong>Sickness Absence days 2005-2008</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥0 to &lt;26 days</td>
<td></td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>≥26 to &lt;67 days</td>
<td></td>
<td>2.20 (2.06-2.35)</td>
<td>2.22 (2.08-2.37)</td>
</tr>
<tr>
<td>≥67 to &lt;140 days</td>
<td></td>
<td>3.18 (2.97-3.40)</td>
<td>3.22 (3.01-3.44)</td>
</tr>
<tr>
<td>≥140 days</td>
<td></td>
<td>3.51 (3.28-3.75)</td>
<td>3.57 (3.34-3.82)</td>
</tr>
<tr>
<td><strong>Special operational requirements</strong></td>
<td></td>
<td></td>
<td>1.01 (1.00-1.02)</td>
</tr>
<tr>
<td><strong>Knowledge requirements</strong></td>
<td></td>
<td></td>
<td>1.00 (1.00-1.00)</td>
</tr>
<tr>
<td><strong>Aggravated working conditions</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 4</td>
<td></td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>&gt;4 to ≤11</td>
<td></td>
<td>1.03 (0.96-1.10)</td>
<td></td>
</tr>
<tr>
<td>&gt;11 to ≤15</td>
<td></td>
<td>1.03 (0.95-1.12)</td>
<td></td>
</tr>
<tr>
<td>&gt;15</td>
<td></td>
<td>0.86 (0.78-0.94)</td>
<td></td>
</tr>
</tbody>
</table>

OR=odds ratio. IRR=incidence risk ratio. 95% CI=95% confidence interval. Semi-adjusted model adjusted for age, gender, marital status, having children, commuting distance, employment duration, mean contract percentage, working overtime, and previous sickness absence days. Job classification variables special operational requirements, knowledge requirements, and aggravated working conditions were added to the fully adjusted model. *=p<0.05.
Table 3. Crude, semi-adjusted, and fully adjusted models for night shift exposure, long-term sickness absence, and sickness absence episodes.

<table>
<thead>
<tr>
<th>Long-term sickness absence (&gt;7 days)</th>
<th>crude model</th>
<th>semi-adjusted model</th>
<th>fully adjusted model</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>Number of night shifts 2005-2008</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No night shifts</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Night shifts (1 to ≤46)</td>
<td>1.36 (1.20-1.53)*</td>
<td>1.30 (1.12-1.50)*</td>
<td>1.15 (0.99-1.34)</td>
</tr>
<tr>
<td>Night shifts (47 ≤110)</td>
<td>1.54 (1.36-1.74)*</td>
<td>1.17 (1.01-1.34)*</td>
<td>1.01 (0.87-1.17)</td>
</tr>
<tr>
<td>Night shifts (&gt;110)</td>
<td>1.08 (0.95-1.22)</td>
<td>1.06 (0.92-1.21)</td>
<td>1.05 (0.91-1.21)</td>
</tr>
<tr>
<td>Sickness absence days 2005-2008</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥0 to &lt;26 days</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>≥26 to &lt;67 days</td>
<td>3.08 (2.60-3.65)</td>
<td>2.99 (2.52-3.55)</td>
<td></td>
</tr>
<tr>
<td>≥67 to &lt;140 days</td>
<td>8.11 (6.81-9.66)</td>
<td>7.42 (6.21-8.86)</td>
<td></td>
</tr>
<tr>
<td>≥140 days</td>
<td>12.56 (10.50-15.02)</td>
<td>11.23 (9.36-13.48)</td>
<td></td>
</tr>
<tr>
<td>Special operational requirements</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Knowledge requirements</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤4</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>&gt;4 to ≤11</td>
<td>1.16 (0.97-1.39)</td>
<td>1.18 (0.96-1.45)</td>
<td>1.26 (0.98-1.61)</td>
</tr>
</tbody>
</table>

OR=odds ratio. IRR=incidence risk ratio. 95% CI=95% confidence interval. Semi-adjusted model adjusted for age, gender, marital status, having children, commuting distance, employment duration, mean contract percentage, working overtime, and previous sickness absence days. Job classification variables special operational requirements, knowledge requirements, and aggravated working conditions were added to the fully adjusted model. *=p<0.05.
Table 3. Crude, semi-adjusted, and fully adjusted models for night shift exposure, long-term sickness absence, and sickness absence episodes (continued).

<table>
<thead>
<tr>
<th>Sickness absence episodes</th>
<th>crude model</th>
<th>semi-adjusted model</th>
<th>fully adjusted model</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IRR (95% CI)</td>
<td>IRR (95% CI)</td>
<td>IRR (95% CI)</td>
</tr>
<tr>
<td>Number of night shifts 2005-2008</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No night shifts</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Night shifts (1 to ≤46)</td>
<td>1.03 (0.97-1.08)</td>
<td>0.93 (0.88-0.98)*</td>
<td>0.97 (0.91-1.02)</td>
</tr>
<tr>
<td>Night shifts (47 ≤110)</td>
<td>0.99 (0.94-1.04)</td>
<td>0.87 (0.83-0.92)*</td>
<td>0.91 (0.86-0.96)*</td>
</tr>
<tr>
<td>Night shifts (&gt;110)</td>
<td>0.94 (0.89-0.99)*</td>
<td>0.95 (0.90-1.00)*</td>
<td>0.93 (0.88-0.98)*</td>
</tr>
<tr>
<td>Sickness absence days 2005-2008</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥0 to &lt;26 days</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
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<tr>
<td>≥26 to &lt;67 days</td>
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<tr>
<td>≥67 to &lt;140 days</td>
<td>Reference</td>
<td>Reference</td>
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</tr>
<tr>
<td>≥140 days</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Special operational requirements</td>
<td>1.01 (1.00-1.02)</td>
<td>1.00 (0.99-1.00)</td>
<td></td>
</tr>
<tr>
<td>Knowledge requirements</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aggravated working conditions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 4</td>
<td>Reference</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;4 to ≤11</td>
<td>Reference</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;11 to ≤15</td>
<td>Reference</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;15</td>
<td>Reference</td>
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</tbody>
</table>

OR=odds ratio. IRR=incidence risk ratio. 95% CI=95% confidence interval. Semi-adjusted model adjusted for age, gender, marital status, having children, commuting distance, employment duration, mean contract percentage, working overtime, and previous sickness absence days. Job classification variables special operational requirements, knowledge requirements, and aggravated working conditions were added to the fully adjusted model. *p<0.05.
## Table 4. Crude, semi-adjusted, and fully adjusted models for the subgroup analyses of shift schedule types and long-term sickness absence.

<table>
<thead>
<tr>
<th>Without children (n=2,121)</th>
<th>crude model</th>
<th>semi-adjusted model</th>
<th>fully adjusted model</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td><strong>shifttype 2005-2008</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day work</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Two-shift schedule</td>
<td>2.14 (1.61-2.85)*</td>
<td>1.80 (1.30-2.50)*</td>
<td>1.40 (0.97-2.01)</td>
</tr>
<tr>
<td>Three-shift schedule</td>
<td>2.55 (1.86-3.51)*</td>
<td>2.34 (1.62-3.36)*</td>
<td>1.76 (1.19-2.61)*</td>
</tr>
<tr>
<td>Transfer out of three-shift</td>
<td>1.22 (0.75-1.99)</td>
<td>1.03 (0.60-1.75)</td>
<td>0.89 (0.52-1.55)</td>
</tr>
<tr>
<td>Transfer into three-shift</td>
<td>3.06 (2.07-4.52)*</td>
<td>2.43 (1.55-3.81)*</td>
<td>1.76 (1.08-2.87)*</td>
</tr>
<tr>
<td>Other kind of transfer</td>
<td>2.58 (1.80-3.71)*</td>
<td>2.16 (1.41-3.28)*</td>
<td>1.74 (1.12-2.69)*</td>
</tr>
<tr>
<td>**With children (n=5,441)</td>
<td>crude model</td>
<td>semi-adjusted model</td>
<td>fully adjusted model</td>
</tr>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td><strong>shifttype 2005-2008</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day work</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Two-shift schedule</td>
<td>1.79 (1.52-2.12)*</td>
<td>1.34 (1.10-1.62)*</td>
<td>1.05 (0.85-1.30)</td>
</tr>
<tr>
<td>Three-shift schedule</td>
<td>1.53 (1.27-1.84)*</td>
<td>1.18 (0.96-1.46)</td>
<td>0.91 (0.73-1.14)</td>
</tr>
<tr>
<td>Transfer out of three-shift</td>
<td>1.19 (0.92-1.53)</td>
<td>1.09 (0.81-1.46)</td>
<td>0.90 (0.67-1.22)</td>
</tr>
<tr>
<td>Transfer into three-shift</td>
<td>2.34 (1.83-2.98)*</td>
<td>1.68 (1.28-2.21)*</td>
<td>1.19 (0.88-1.60)</td>
</tr>
<tr>
<td>Other kind of transfer</td>
<td>1.31 (1.03-1.67)*</td>
<td>1.09 (0.83-1.43)</td>
<td>0.85 (0.63-1.13)</td>
</tr>
<tr>
<td>**Married/cohabiting (n= 5,667)</td>
<td>crude model</td>
<td>semi-adjusted model</td>
<td>fully adjusted model</td>
</tr>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td><strong>shifttype 2005-2008</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day work</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Two-shift schedule</td>
<td>1.84 (1.56-2.17)*</td>
<td>1.38 (1.14-1.68)*</td>
<td>1.10 (0.89-1.35)</td>
</tr>
<tr>
<td>Three-shift schedule</td>
<td>1.60 (1.33-1.92)*</td>
<td>1.27 (1.03-1.57)*</td>
<td>0.99 (0.79-1.24)</td>
</tr>
<tr>
<td>Transfer out of three-shift</td>
<td>1.17 (0.90-1.53)</td>
<td>1.04 (0.78-1.39)</td>
<td>0.88 (0.65-1.18)</td>
</tr>
<tr>
<td>Transfer into three-shift</td>
<td>2.27 (1.79-2.89)*</td>
<td>1.67 (1.28-2.19)*</td>
<td>1.18 (0.88-1.58)</td>
</tr>
<tr>
<td>Other kind of transfer</td>
<td>1.38 (1.09-1.75)*</td>
<td>1.17 (0.89-1.53)</td>
<td>0.93 (0.70-1.23)</td>
</tr>
</tbody>
</table>

OR=odds ratio. IRR=incidence risk ratio. 95% CI=95% confidence interval. Semi-adjusted model adjusted for age, gender, marital status, having children, commuting distance, employment duration, mean contract percentage, working overtime, and previous sickness absence days. Job classification variables special operational requirements, knowledge requirements, and aggravated working conditions were added to the fully adjusted model. *=p<0.05.
### Table 4. Crude, semi-adjusted, and fully adjusted models for the subgroup analyses of shift schedule types and long-term sickness absence (continued).

<table>
<thead>
<tr>
<th></th>
<th>Single (n= 1,355)</th>
<th>Divorced/widow (n= 540)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>crude model</td>
<td>semi-adjusted model</td>
</tr>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
</tr>
</tbody>
</table>
| OR=odds ratio. IRR=incidence risk ratio. 95% CI=95% confidence interval. Semi-adjusted model adjusted for age, gender, marital status, having children, commuting distance, employment duration, mean contract percentage, working overtime, and previous sickness absence days. Job classification variables special operational requirements, knowledge requirements, and aggravated working conditions were added to the fully adjusted model. *=p<0.05.

#### Shift type 2005-2008

<table>
<thead>
<tr>
<th></th>
<th>Day work</th>
<th>Two-shift schedule</th>
<th>Three-shift schedule</th>
<th>Transfer out of three-shift</th>
<th>Transfer into three-shift</th>
<th>Other kind of transfer</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Single (n= 1,355)</strong></td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td><strong>OR (95% CI)</strong></td>
<td>2.23 (1.56-3.19)*</td>
<td>1.90 (1.26-2.89)*</td>
<td>1.36 (0.86-2.17)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>OR (95% CI)</strong></td>
<td>3.18 (2.15-4.72)*</td>
<td>2.66 (1.67-4.23)*</td>
<td>1.82 (1.10-3.01)*</td>
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<td></td>
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</tr>
<tr>
<td><strong>OR (95% CI)</strong></td>
<td>1.64 (0.90-3.00)</td>
<td>1.22 (0.62-2.39)</td>
<td>1.03 (0.51-2.05)</td>
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<td></td>
</tr>
<tr>
<td><strong>OR (95% CI)</strong></td>
<td>3.23 (2.00-5.21)*</td>
<td>2.45 (1.41-4.27)*</td>
<td>1.66 (0.90-3.03)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>OR (95% CI)</strong></td>
<td>2.75 (1.75-4.32)*</td>
<td>2.29 (1.35-3.90)*</td>
<td>1.84 (1.06-3.18)*</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Day work</th>
<th>Two-shift schedule</th>
<th>Three-shift schedule</th>
<th>Transfer out of three-shift</th>
<th>Transfer into three-shift</th>
<th>Other kind of transfer</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Divorced/widow (n= 540)</strong></td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td><strong>OR (95% CI)</strong></td>
<td>1.73 (1.04-2.86)*</td>
<td>1.43 (0.80-2.57)</td>
<td>1.20 (0.63-2.27)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td><strong>OR (95% CI)</strong></td>
<td>1.25 (0.73-2.14)</td>
<td>1.21 (0.66-2.23)</td>
<td>1.00 (0.52-1.96)</td>
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</tr>
<tr>
<td><strong>OR (95% CI)</strong></td>
<td>0.97 (0.42-2.28)</td>
<td>1.01 (0.38-2.66)</td>
<td>0.89 (0.32-2.45)</td>
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</tr>
<tr>
<td><strong>OR (95% CI)</strong></td>
<td>5.97 (2.23-15.97)*</td>
<td>4.90 (1.61-14.94)*</td>
<td>3.96 (1.24-12.69)*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>OR (95% CI)</strong></td>
<td>1.59 (0.76-3.30)</td>
<td>1.39 (0.60-3.25)</td>
<td>1.05 (0.43-2.56)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
DISCUSSION

The results of this study showed that shift work or exposure to night shifts did not result in an increased risk for sickness absence when job classification variables were taken into account. Only the group of employees that changed into shift work that included night shifts did show an increased risk for long-term sickness absence (>7 days). Single employees or employees without children who worked in a two-shift system were at higher risk of long-term sickness absence compared to single employees or employees without children in day work. These employees, plus divorced and/or widowed employees, were also at higher risk for long-term sickness absence when they changed from one shift schedule to another.

The job classification system used in our study took into account both psychosocial and physical work factors (36). Previous research has shown that employees that work outside regular working hours can be more exposed to low job control and high physical demands compared to day workers (38). In the review of Allebeck & Mastekaasa (20), moderate evidence was found for an effect of physically demanding work, and low psychological control on both short- and long-term sickness absence. More recent studies also found that high physical job demands and psychosocial risk factors can increase sickness absence in various populations of employees (18,22,39,40). Therefore, in order to obtain a precise estimate of the association between exposure to shift work and sickness absence, the multicausality of sickness absence has to be taken into account (17,23,29). This is confirmed by our findings as these indicate that psychosocial and physical work factors, operationalized through job classification variables, are important to include as confounders when analyzing this association.

It has been argued that there is inconclusive evidence for an association between rotating shift work and sickness absence (29). In line with our findings, several studies did not find an association between rotating shift work and sickness absence (41,42). Other studies found higher sickness absence in rotating shift workers in three- (43,44), or two-shift (43,45) schedules. However, Ohayon et al. (45) did not adjust for job characteristics, while Morikawa et al. (44) only took into account physical work demands. Niedhammer et al. (43) did adjust for psychological and physical workload in a large sample of French employees, and found that both employees involved in two- and three-shift schedules had a higher risk of long-term sickness absence (>8 days). However, in all studies above, previous sickness absence of the studied population was not taken into account, although it has been shown that sickness absence in the past is a strong predictor for future sickness absence (21,46), as was also shown in the present study (Table 2). Therefore, taking into account the previous sickness absence of the employees might explain the contrasting results of the present study as compared to others.

Employees who were exposed to the same type of shift schedule during 2005 to 2008 may have learned to cope with their irregular schedules, implementing their working hours into their social and family life (47-49). We found that shift work employees who had children did not have an increased risk for sickness absence,
nor had shift work employees who were married or cohabiting. These findings may seem counterintuitive as non-standard working hours are generally thought to have a negative influence on social activities and work-family life balance, possibly leading to health problems and sickness absence (4,50,51). Haines et al. (4), for instance, showed that work-family conflict partially mediates the relationship between shift work and health deterioration. Demourouti et al. (52), however, did not find an association between rotating shift work and work-family conflict, absenteeism and subjective health. The authors suggest that rotating shift work might increase opportunities for more common time with the family. Moreover, two recent studies showed that work-family conflict decreases if shift workers are able to choose their shift schedule (53,54). Therefore, it might be possible that the married/cohabiting shift workers in our population have actively chosen to continue working in their rotating shift schedules.

Single employees and employees without children showed to have an increased risk for long-term sickness absence, when they switched to working in a three-shift schedule. An even larger relative risk was found for divorced or widowed employees who began working in a schedule that included night shifts (OR 3.96, 95%CI 1.24-12.69). A lack of family support, which can help employees to adapt to a new schedule, might partly explain these findings (50). Adaptation problems can result in sleeping problems and fatigue, possibly leading to medium- and long-term sickness absence (49,55).

We also found that single employees and people without children who were working in a two-shift schedule had a higher risk for long-term sickness absence, compared to singles or people without children in day work. Although it has been shown that rotating between morning and evening shifts can be associated with difficulties falling asleep and high sickness absence compared to that of day workers (45), these findings contradict with those of other studies (42,56). Therefore, more research is needed to confirm our findings and explain the possible involvement of household composition.

Regarding the analyses of the number of sickness absence episodes, it was found that, compared to day workers, all employees involved in shift work had a lower risk for more sickness absence episodes. Frequent night shift exposure led to a lower risk for more sickness absence episodes as well. This lower incidence rate of sickness absence episodes among shift workers has been found before (57). It is suggested that shift workers exhibit greater solidarity towards their shift colleagues and avoid being absent unexpectedly (52). Furthermore, shift workers might regard, as opposed to day workers, non-severe complaints (e.g. not feeling well, fatigue, disturbed sleep) as a part of their work and not as reasons to call in sick (58).

Strengths and limitations

The major strength of this study is the large historic cohort, with extensive, standard available information about more than 7,500 employees over a five-
Chapter 4 | Cumulative exposure to shift work and sickness absence

year period. Because both work schedule and sickness absence data originated from company records, recall bias can be ruled out. The ground staff employees originated from a wide range of jobs throughout the company including both blue and white collar workers (e.g. gate agents, office employees, technical staff, baggage handlers), for which results can be generalizable for other companies as well.

We decided to analyse the association of shift work with sickness absence using an episode of more than seven consecutive days because such an episode is an indication for medically certified sickness absence (34,59,60). Still, a wide variation of sickness absence cut-offs have been used in other studies (from one day up to several weeks), for which results are not always comparable to our findings. The possibility exists that we would have found different results when sickness absence was operationalised differently (28,42-45,56). However, because short-term sickness absence is a good indication for coping strategies and the attitude towards work, we looked at the number of sickness absence episodes as well (20,21,25). Our results showed that the association between shift work exposure and long-term sickness absence differed considerably from the association between shift work exposure and the number of sickness absence episodes. It is therefore important to include both short- and long-term sickness absence outcome measures when analysing the association between shift work and sickness absence.

Although we included numerous potential confounders to determine the association between shift work exposure and sickness absence, previous research showed that health conditions, psychosocial determinants, and coping mechanisms can also play an important role in both the development of sickness absence (17,20,21,23) and the tolerance to irregular working hours (49,61). Because we only used company record data it was not possible to include all of these determinants in our analyses, which can have affected our results. Additionally, it was not possible to include lifestyle factors, such as smoking, alcohol or body weight, which might have confounded the association between shift work exposure and sickness absence. Fekeduleng et al. (62), for instance, showed that the increased sickness absence in night workers only held true for overweight employees, while no significant differences in sickness absence days between day, evening, and night shift workers was found for employees with a normal weight.

Next, it was decided to exclude the employees with missing data on the job classification variables. Since these variables were not available for employees with an expert or high management function, these employees were excluded from the analyses, which affects the external validity of the results.

Finally, our results are probably biased due to selection effects. To make sure that the exposure period for all employees was equal, employees who were employed after 2005, were excluded from the analyses. Moreover, the MORE cohort did
not include employees who terminated their employment before 2010. These employees might have left the company due to health problems as a result of their (shift) work schedules. Consequently, only the employees who managed to keep working during the five-year exposure period were analysed, introducing the healthy worker effect. Therefore, analysing this selection of employees might have led to an underestimation of the association between shift work and sickness absence.

Implications

Our results show that it is important to take into account previous sickness absence and psychosocial and physical work factors to obtain a good estimation of the effects of shift work exposure on sickness absence. In our study population, compared to day work, exposure to different types of shift schedules was not associated with more long-term sickness absence, nor was cumulative night shift exposure. Instead, within the subgroups of single or divorced employees, or employees without children, the risk for more long-term sickness absence increased after a change in shift schedule. Future research is needed to confirm our findings in other populations, and to further explore the influence of household composition and other possible mediating factors. Because it was found that employees that switched into a three-shift schedule showed an increase in long-term sickness absence, it seems useful to support employees who have to adapt to a new shift schedule. For this purpose, counselling and training at work through specific educational programs, involving sleep hygiene, nutrition, physical fitness, and exposure to light, to improve the coping mechanisms of the involved shift work employees, has been recommended (63,64).

CONCLUSION

Taking into account previous sickness absence and psychosocial and physical work factors, it was found that employees who transferred into a shift schedule that included night shifts had an increased risk of future long-term sickness absence compared to day workers. Continuous exposure to a two- or three-shift schedule did not result in an increased risk for sickness absence, neither did cumulative night shift exposure. Instead, shift work employees showed a lower risk for more sickness absence episodes compared to day workers. Employees without children, single employees, and divorced or widowed employees did show a higher risk for long-term sickness absence when exposed to a two-shift schedule, or when they transferred into a new shift schedule.
REFERENCES


Chapter 5

Sickness absence and flight type exposure in flight crew members

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Hynek Hlobil
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ABSTRACT

Background Shift work research has shown that the relationship between exposure to irregular working times and sickness absence may differ between working populations. Not much is known about the prevalence of sickness absence in flight crews or about the relationship between exposure to different flight schedules and sickness absence in this population.

Aims To examine the association between cumulative exposure to different flight types and sickness absence in flight crew members.

Methods The study population consisted of flight crew members from a five-year historic cohort. Flight schedule and sickness absence data were obtained from company records. The association between the cumulative exposure to different flight types and sickness absence episodes of more than seven days was determined using univariate and multivariate logistic regression analyses. Adjusted models were obtained by adding potential confounders. Previous sickness absence was added to compose the fully adjusted models.

Results The records of 8,228 employees were analysed. The fully adjusted univariate analyses showed that the numbers of medium-haul flights and flights with time zone crossings were associated with an increase in the odds for sickness absence. The fully adjusted multivariate analyses showed no significant associations between flight types and sickness absence.

Conclusions Cumulative exposure to flight types was not independently associated with sickness absence in flight crew members when previous sickness absence was taken into account. Because sickness absence in the past can predict future absence, preventive strategies targeted at flight crew members with a history of high sickness absence may be effective.
INTRODUCTION

Flight crew members, both cockpit and cabin crew, have to deal with work-related factors such as long duty days, early starts, night flights, multiple flights per day and crossing time zones (1-3). Several studies have shown that these job aspects can cause reduced sleep quality and quantity as well as jet lag symptoms due to disruption of circadian rhythms (4). In general, flight crew members comprise a relatively healthy population. Cockpit crews and, to a lesser extent, cabin crews need to meet certain health requirements when entering the profession, and undergo regular medical examinations throughout their careers (5). However, possible work-related health problems among these employees have been reported. In a large Norwegian survey on the health of flight crew, respondents reported irritability, digestive disturbances, dry eyes and skin, lower back pain, colds, fatigue and sleep disturbances. Pilots reported the fewest problems while female cabin crew members reported the most (6). It has also been shown that in about 70% of flight crew members fatigue is a common phenomenon that interferes with their normal social activities (7). Sleep problems occur significantly more often in pilots than in civil servants and are associated with fatigue and work stress (8). Fatigue has been linked to exposure to specific flight schedules; both long-haul and short-haul flight crew members report fatigue during and after work (1,6). However, besides fatigue not much is known about the health effects of exposure to different flight schedules. In occupational health research sickness absence is widely used as a health indicator which can be seen as a precursor of work disability and long-term ill health (9,10). Little is known about the prevalence of sickness absence in flight crew although a survey by Steptoe and Bostock (8) reported a mean of 4.8 self-reported sickness absence days per six-month period for short-haul pilots.

In contrast to the effects of flight schedules the effects of different types of shift work schedules on sickness absence have been thoroughly studied, although the results are contradictory. Some studies have found that irregular working hours have no effect on sickness absence days and episodes (11,12), while others identified higher levels of sickness absence as a result of irregular working hours in shift workers (13,14). A recent systematic review therefore concluded that the association between shift work and sickness absence might not only be schedule-specific, but also specific to the working population concerned (15). Consequently the aim of this study was to investigate the association between sickness absence and cumulative exposure to different flight types in the specific population of flight crew members.

METHODS

In this study, data from the MORE (Monitoring Occupational Health Risks in Employees) cohort was used. This five-year historic cohort was set up to analyse the occupational health risks of employees of a large airline company and consisted of all workers employed at January 1, 2010. The cohort data comprised all medical and human resource records for these employees since January 1, 2005.
Additionally work schedules were registered for each day of the cohort period. All datasets were combined, anonymised and coded by an independent occupational physician. This procedure was assessed by the medical ethical committee of the VU University Medical Center, Amsterdam, the Netherlands, which decided that this study was exempt from further medical ethical review according to Dutch law. The study population consisted of the flight crew members in the MORE cohort. Only employees who were already working for the company at January 1, 2005 were included. Women who became pregnant after January 1, 2009 were excluded.

The main outcome variable was sickness absence, defined as an episode of at least seven consecutive registered sickness absence days in 2009. The cut-off of seven days was chosen to match the Dutch social security system (16) and because episodes of more than seven days have been used previously to determine medically certified sickness absence, for instance in the Whitehall II studies (17,18). All absence from scheduled work due to health reasons was registered by the airline occupational health service. The calendar days of the absence episodes were counted as sickness absence days and we recorded whether employees had at least one sickness episode of more than seven days in 2009. Partial absence days were considered as full days of sickness absence (19).

The work schedules of each employee in the period 2005 to 2008 were analysed and classified. For the duration of the flights involved in the schedules, the total
number of short-haul flights (<4 hours), medium-haul flights (≥4 hours and <8 hours), and long-haul flights (≥8 hours) was calculated. A flight was considered a night flight if any part of it took place in between 2am and 6am (based on the local time at the departure), in accordance with European flight time regulations. Finally if a flight crossed four or more time zones it was considered to be a ‘time zone flight’.

Potential confounders such as age, gender, job title (cabin/cockpit), marital status (married/not married), residence (Netherlands/other), multiple employers (yes/no) and having children (yes/no), were retrieved from the MORE database in January 1, 2009. The average contract rate in 2009 was determined for each employee. Each employee’s total number of sickness absence days for the period 2005 to 2008 was also calculated. Means, standard deviations and frequencies were calculated for the demographic variables, sickness absence days and episodes, and the different flight types. The associations between exposure to flight types and sickness absence were assessed using logistic regression analyses.

First, separate models were created for each flight type. After determination of the crude univariate models the potential confounders were added to construct the adjusted univariate models. Next, to determine the association between exposure to the different flight types and change in sickness absence, previous sickness absence was added to compose the fully adjusted univariate models. In the second step, all flight types and potential confounders were analysed together in the adjusted multivariate model. Afterwards, previous sickness absence was added as well to construct the fully adjusted multivariate model.

All analyses were considered statistically significant when p<0.05. Plausible interaction terms were created (potential effect modifier * independent variable) and added to the crude univariate models. If the interaction term proved statistically significant at a level of p<0.05, subgroup analyses were performed. Based on the literature, age, gender, job title (cabin/cockpit), having children (yes/no) and marital status (married/not married) were tested for effect modification (19).

RESULTS

The population characteristics are presented in Table 1. The sample consisted of 8,228 flight crew members (average age 42, 64% female). The majority of the study population were cabin crew members (77%), almost half were not married (48%), and most lived in the Netherlands (94%). Almost 10% of the employees had more than one employer and more than 60% had children. Characteristics of sickness absence and the different flight types are presented in Table 2. On average, employees reported sick for almost 24 calendar days with a mean frequency of one sickness absence episode per year.

The univariate associations between cumulative exposure to different flight types from 2005 to 2008 and sickness absence episodes of more than seven days in 2009
are presented in Table 3. In the crude models, both short-haul and night flights were significantly associated with fewer sickness absence episodes, whereas in the adjusted univariate models short-haul flights, night flights and medium-haul flights were associated with fewer sickness absence episodes. After additionally adjusting for previous sickness absence, only the number of short-haul flights proved to be significantly associated with a lower number of sickness absence episodes. The numbers of long-haul and time zone flights were both significantly associated with a higher number of sickness absence episodes.

The multivariate associations between cumulative exposure to different flight types from 2005 to 2008 and a sickness absence episode of more than seven days in 2009 are presented in Table 4. The influence of the potential confounders is also shown in this table. In the adjusted model the number of short-haul, medium-haul and long-haul flights were all independently associated with fewer sickness absence episodes. The fully adjusted model shows that none of these associations remained significant when previous sickness absence was added to the model. Since none of the added interaction terms proved to have a significant effect on the univariate crude models, no further subgroup analyses were performed.
Table 1. Population characteristics (n=8,228).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>41.5 (7.2)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>3,003 (36)</td>
</tr>
<tr>
<td>Female</td>
<td>5,225 (64)</td>
</tr>
<tr>
<td>Job title</td>
<td></td>
</tr>
<tr>
<td>Cockpit</td>
<td>1,880 (23)</td>
</tr>
<tr>
<td>Cabin</td>
<td>6,311 (77)</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
</tr>
<tr>
<td>Not married</td>
<td>4,245 (52)</td>
</tr>
<tr>
<td>Married</td>
<td>3,983 (48)</td>
</tr>
<tr>
<td>Residence</td>
<td></td>
</tr>
<tr>
<td>Netherlands</td>
<td>7,760 (94)</td>
</tr>
<tr>
<td>Other</td>
<td>468 (6)</td>
</tr>
<tr>
<td>Employer</td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>7,449 (91)</td>
</tr>
<tr>
<td>Multiple</td>
<td>779 (9)</td>
</tr>
<tr>
<td>Children</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>3,067 (37)</td>
</tr>
<tr>
<td>Yes</td>
<td>5,161 (63)</td>
</tr>
<tr>
<td>Type of contract</td>
<td></td>
</tr>
<tr>
<td>Full-time</td>
<td>2,877 (35)</td>
</tr>
<tr>
<td>Part-time</td>
<td>5,351 (65)</td>
</tr>
<tr>
<td>Sickness absence episode (&gt;7 days)^b</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>4,991 (61)</td>
</tr>
<tr>
<td>Yes</td>
<td>3,237 (39)</td>
</tr>
</tbody>
</table>

^aMean (standard deviation)
^bMeasured from January 1, 2009 to January 6, 2010

Table 2. Sickness absence (2009) and flight type characteristics (2005-2008) of the population.

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>sd</th>
<th>25th percentile</th>
<th>75th percentile</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of sickness absence days</td>
<td>23.9</td>
<td>51.6</td>
<td>0.0</td>
<td>21.0</td>
</tr>
<tr>
<td>Number of sickness absence episodes</td>
<td>1.0</td>
<td>1.2</td>
<td>0.0</td>
<td>2.0</td>
</tr>
<tr>
<td>Number of short-haul flights</td>
<td>221</td>
<td>312</td>
<td>25</td>
<td>289</td>
</tr>
<tr>
<td>Number of medium-haul flights</td>
<td>55</td>
<td>33</td>
<td>33</td>
<td>72</td>
</tr>
<tr>
<td>Number of long-haul flights</td>
<td>98</td>
<td>55</td>
<td>62</td>
<td>133</td>
</tr>
<tr>
<td>Number of night flights</td>
<td>82</td>
<td>35</td>
<td>54</td>
<td>109</td>
</tr>
<tr>
<td>Number of time zone flights</td>
<td>106</td>
<td>58</td>
<td>70</td>
<td>143</td>
</tr>
</tbody>
</table>
Table 3. Univariate models for the association between exposure to flight types (2005-2008) and sickness absence episodes in 2009.

<table>
<thead>
<tr>
<th></th>
<th>Crude models</th>
<th>Adjusted modelsb</th>
<th>Fully adjusted modelsc</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
<td>95% CI for ORa</td>
<td>OR</td>
</tr>
<tr>
<td></td>
<td>Lower</td>
<td>Upper</td>
<td>Lower</td>
</tr>
<tr>
<td>Number of short-haul flights</td>
<td>0.9996***</td>
<td>0.9995 0.9998</td>
<td>0.9997***</td>
</tr>
<tr>
<td>Number of medium-haul flights</td>
<td>0.9995</td>
<td>0.9981 1.0008</td>
<td>0.9972***</td>
</tr>
<tr>
<td>Number of long-haul flights</td>
<td>1.0005</td>
<td>0.9997 1.0013</td>
<td>0.9994</td>
</tr>
<tr>
<td>Number of night flights</td>
<td>0.9982**</td>
<td>0.9969 0.9995</td>
<td>0.9933***</td>
</tr>
<tr>
<td>Number of time zone flights</td>
<td>1.0005</td>
<td>0.9998 1.0013</td>
<td>0.9995</td>
</tr>
</tbody>
</table>

aOR = Odds Ratio, 95% CI = 95% Confidence Interval.
bAdded confounders in adjusted models: age, gender, job title, marital status, residence, multiple employers, having children and mean contract rate.
p< 0.05, **p< 0.01, ***p< 0.001
Table 4. Multivariate models for the association between exposure to flight types (2005-2008) and sickness absence episodes in 2009.

<table>
<thead>
<tr>
<th></th>
<th>Adjusted model</th>
<th>Fully adjusted model</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
<td>95% CI for OR*</td>
</tr>
<tr>
<td></td>
<td>Lower</td>
<td>Upper</td>
</tr>
<tr>
<td>Number of short-haul flights</td>
<td>0.9991***</td>
<td>0.9987</td>
</tr>
<tr>
<td>Number of medium-haul flights</td>
<td>0.9952***</td>
<td>0.9931</td>
</tr>
<tr>
<td>Number of long-haul flights</td>
<td>0.9934**</td>
<td>0.9888</td>
</tr>
<tr>
<td>Number of night flights</td>
<td>0.9992</td>
<td>0.9956</td>
</tr>
<tr>
<td>Number of time zone flights</td>
<td>1.0034</td>
<td>0.9996</td>
</tr>
<tr>
<td>Age</td>
<td>1.02</td>
<td>1.01</td>
</tr>
<tr>
<td>Gender (male/female)</td>
<td>1.18</td>
<td>1.02</td>
</tr>
<tr>
<td>Job title (cabin/cockpit)</td>
<td>1.28</td>
<td>1.10</td>
</tr>
<tr>
<td>Marital status (yes/no)</td>
<td>0.84</td>
<td>0.76</td>
</tr>
<tr>
<td>Residence (Netherlands/other)</td>
<td>1.17</td>
<td>0.96</td>
</tr>
<tr>
<td>Multiple employers (yes/no)</td>
<td>0.81</td>
<td>0.69</td>
</tr>
<tr>
<td>Children (yes/no)</td>
<td>0.98</td>
<td>0.88</td>
</tr>
<tr>
<td>Mean contract rate</td>
<td>1.02</td>
<td>1.01</td>
</tr>
<tr>
<td>Sickness absence days 2005-2008</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*OR = Odds Ratio, 95% CI= 95% Confidence Interval. *p< 0.05, **p< 0.01, ***p< 0.001

DISCUSSION

Overall our study found that none of the flight types had a significant effect on the likelihood of sickness absence episodes when other flight types were taken into account. The multivariate analyses showed an independent association between cumulative exposure to short-, medium- and long-haul flights and fewer sickness absence episodes of more than seven consecutive days but this relationship was not maintained after including previous sickness absence.

The major strength of this study is its large historic cohort, providing extensive information on more than 8,200 flight crew members over a five-year period. Because both flight schedule and sickness absence data originated from employer registers recall bias can be ruled out. Flight type exposure was analysed separately first, while the independent effect of each flight type was analysed through the multivariate analyses. Because until now little has been known about the prevalence of sickness absence in flight crew members we investigated the association between the exposure to several flight types during several years and sickness absence in the following year. As a result of analysing cumulative exposure we did not take into account alterations between different flight schedules, and the more direct effect on sickness absence over time.
Chapter 5 | Sickness absence and flight type exposure in flight crew members

The results of our study may have been biased by selection effects. To make sure that all participants had the same potential amount of exposure during the study period, flight crew members who were not employed at January 1, 2005 were excluded from the analyses. Furthermore, because the MORE cohort did not include employees who left the company before 2010, for instance because of ill health or failure to meet required fitness standards, we cannot rule out a healthy worker effect.

Although it has been argued that work-related factors, along with medical conditions, psychosocial determinants and coping mechanisms, can lead to health problems and subsequent sickness absence (20-21), the results of our study show that cumulative exposure to different work schedules, in the form of different flight types, was not associated with future sickness absence. It is difficult to compare these findings to those of other studies. Firstly there is little literature on factors affecting sickness absence in flight crew members. Secondly most studies of sickness absence in the shift work literature involve shift workers who are exposed to a single shift work system only (11,13), although flight schedules can resemble the schedules of shift workers (e.g. schedules involving medium- or long-haul flights are comparable to rotating shifts including night work). The employees in a study by Haugli et al. (6) on the health of flight crew were exposed to either short-haul or long-haul schedules, while the flight crew members in our study were exposed to different types of schedules throughout the exposure period. Finally, our findings are difficult to compare because we decided to analyse the association with sickness absence using episodes of more than seven consecutive days as an indication of medically certified sickness absence (16-18). Previous studies have identified sickness absence differently, with cut-offs ranging from one day to more than six weeks (10,15).

In the fully adjusted multivariate model no independent significant associations were found between cumulative exposure to different flight types and sickness absence episodes of more than seven days. Future research with flight crew members exposed to certain flight types only over a longer period of time might give more insight into the effects of different flight types on sickness absence. Additionally, to find out which schedule sequences are best, it is also important to investigate further the effects of specific flight schedule sequences (e.g. specific combinations of short-haul and medium-haul flights) on outcomes such as fatigue and sickness absence.

The outcomes of the fully adjusted multivariate model did show that previous sickness absence can be an important predictor for more sickness absence in the future in flight crew members. Previous studies found that both the number of sickness absence days and the number of episodes were related to future sickness absence in other populations as well (19;22-23). Therefore airlines may wish to identify employees with high sickness absence through company records. Subsequently, they can try to prevent future absence and possible health deterioration in these employees by addressing health and psychosocial determinants (19). Since it has been shown that personality traits, coping
mechanisms, physical fitness and social factors can influence individual tolerance to irregular working hours; these factors should be considered as well (24). As previous studies showed positive results (25-26), this kind of early detection followed by preventive actions targeted at flight crew members with previous sickness absence may be effective.
Chapter 5 | Sickness absence and flight type exposure in flight crew members

REFERENCES


Chapter 6

Flight schedules and occupational accidents among cabin crew: a longitudinal study

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ABSTRACT

**Background** Flight schedules of cabin crew involve early starts, long working hours, night flights, and the crossing of time zones, all of which might contribute to the risk of onboard occupational accidents. Because it is unclear if cumulative flight schedule exposure affects the incidence of occupational accidents, the objective of this study is to examine this association among cabin crew members.

**Methods** Data from the five-year historic MORE cohort was used. The study population consisted of 6,311 cabin crew members. For each employee, all flight schedules from 2005 to 2008, and registered occupational accidents in 2009, were collected. The association between the cumulative exposure to different types of flights and the occurrence of occupational accidents was determined using logistic regression analyses.

**Results** In 2009, 289 cabin crew members reported at least one occupational accident. The adjusted logistic regression models showed that the number of short-haul flights during the period 2005-2008 was positively associated with the occurrence of occupational accidents in 2009. Less exposure to long-haul flights was also associated with reporting an occupational accident.

**Discussion** The results of this study suggest that cumulative exposure to short-haul flights is associated with an increased risk for occupational accidents among cabin crew members. This increased risk may be caused by the specific characteristics of short-haul flights. Future research should focus on possible underlying mechanisms such as fatigue accumulation, and on the influence of adjustments to short-haul schedules. Airline companies can increase their focus on the short-haul operation in order to reduce onboard accidents.
BACKGROUND

Shift work and irregular working hours have become important topics in occupational health since long-term exposure to shift work increases the risk of health problems such as cardiovascular and gastrointestinal diseases (2,6). Additionally, employees with irregular or long working hours have a significantly higher work-related injury rate compared to employees in conventional day shifts (4,11).

In the airline industry, flight schedules of both cabin and cockpit crew involve early starts, long working hours, night flights, and time zone crossings. Irregular working hours can cause fatigue, reduce sleep quality and quantity, and disrupt the circadian rhythm. The crossing of time zones can cause jet lag symptoms, including impairment of alertness and performance (12).

These effects of flight schedules might be associated with the occurrence of occupational accidents among cabin crew. Annual injury rates can be high, and can lead to a considerable amount of sick leave (1,10). In the study of Agampodi et al. (1), one-third of the population called in sick as a result of an accident, with a median of three sickness absence days per six months. Occupational accidents in cabin crew mostly occur onboard, as a result of falls, slips and tripping, and lead to injuries such as sprains and strains, contusions, and burns (1,10). Operational circumstances, such as turbulence or service to customers, or personal factors, such as fatigue, can be involved. Several studies have shown that fatigue is quite common during both short-haul and long-haul flights (3,7,8).

In addition, prolonged exposure to irregular working hours seems to play an important role in accident incidence. While Wagstaff & Lie (11) showed that the risk of the occurrence of accidents increases with extended working hours, Folkard & Åkerstedt (5) argued that the accident risk substantially increases over successive shifts or duty days, indicating a cumulative fatigue effect.

To reduce both accidents and injuries among cabin crew members, it is important to gain more insight into the association between cumulative exposure to flight schedules and occupational accidents. The aim of this study is therefore to examine the longitudinal associations between different flight schedules and the occurrence of occupational accidents among cabin crew members.

METHODS

Study population

This study used data from the MORE (Monitoring Occupational health Risks in Employees) cohort. The 5-year historic cohort was set up to analyze occupational health risks of employees of a large airline company and consists of all workers employed at the company as at January 1, 2010. The cohort data comprised all medical and human resource records of the airline company employees since
January 1, 2005. Additionally, the work schedules were registered for each day of the cohort period. All datasets were combined, anonymized, and coded by an independent occupational physician. According to Dutch law, this study was exempt from Medical Ethical review.

In the present study, all cabin crew members who were already working for the company as at January 1, 2005 were included. Women who had become pregnant after January 1, 2009 were excluded. In total, 6,311 cabin crew members were available for the analyses (Figure 1).

![Flowchart showing the inclusion procedure](image)

**Procedure**

The outcome measure of this study was a registered occupational accident in 2009. All accidents reported to the occupational health services of the airline company were included in the analyses.

Based on the flight schedules between 2005 and 2008, the total number of short-haul flights (<4 hours), medium-haul flights (≥4 hours and <8 hours), and long-haul flights (≥8 hours) was calculated for each employee. Further, the total number of night flights was also calculated. A flight was considered a night flight if any part of it took place in the period between 2am and 6am (based on the location of departure), which is in accordance with the European flight time regulations.
The following potential confounders were retrieved from the database at January 1, 2009: gender, age, residence (Netherlands/other), marital status (married/not married), children (yes/no), job title, multiple employers (yes/no), and mean contract rate. The total number of flights flown was calculated over the years 2005 to 2008.

Statistical analyses

Means and frequencies were calculated for all demographic variables of the study population. Subsequently, differences between the groups with and without accidents were tested using Student t-tests and Chi square tests ($\chi^2$). In order to take the number of working hours into account, accidents were adjusted for the number of hours flown by the reporting crew member during 2009.

Next, the association between the cumulative exposure to flight schedules and the occurrence of occupational accidents in 2009 was determined using a logistic regression analysis, separately for each type of flight schedule. Subsequently, all crude models were adjusted for the potential confounders to construct the adjusted models.

Finally, plausible interaction terms were created (potential effect modifier * independent variable) and added to the adjusted models. If the interaction term proved significant at a level of $p<0.001$, subgroup analyses were performed. Age, job title, gender, children (yes/no), multiple employers (yes/no) and marital status (married/not married) were chosen as potential effect modifiers.

RESULTS

The sample consisted of 6,311 cabin crew members with a mean age of 41.5 years (Table 1). Most cabin crew members were female (81%), a small majority was not married (56%) and most of the employees lived in the Netherlands (95%). A minority of the cabin crew members had multiple employers (12%), and 60% had children.

Cabin crew members without children were more likely to report an accident compared to employees with children. Further, younger employees were more likely to report an accident compared to their older colleagues. After the number of hours flown per cabin crew member was taken into account, only one difference remained (sixth column of Table 1); male cabin crew members experienced significantly fewer accidents per 100 flight hours compared to their female colleagues ($p=0.002$).
Table 1. Characteristics of the cabin crew members as at 1-1-2009.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n (% of characteristic)</th>
<th>Employees with an accident in 2009 (% of n)</th>
<th>p-value</th>
<th>Number of accidents per 100 flight hours</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>1,181 (19%)</td>
<td>44 (4%)</td>
<td>0.120</td>
<td>0.007</td>
<td>0.002</td>
</tr>
<tr>
<td>Women</td>
<td>5,130 (81%)</td>
<td>245 (5%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marital state</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>2,793 (44%)</td>
<td>117 (4%)</td>
<td>0.186</td>
<td>0.013</td>
<td>0.362</td>
</tr>
<tr>
<td>Not Married</td>
<td>3,518 (56%)</td>
<td>172 (5%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Residence</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Netherlands</td>
<td>6,026 (95%)</td>
<td>278 (5%)</td>
<td>0.552</td>
<td>0.012</td>
<td>0.699</td>
</tr>
<tr>
<td>Europe &amp; outside</td>
<td>285 (5%)</td>
<td>11 (4%)</td>
<td></td>
<td></td>
<td>0.010</td>
</tr>
<tr>
<td>Employer</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>5,523 (88%)</td>
<td>255 (5%)</td>
<td>0.759</td>
<td>0.012</td>
<td>0.858</td>
</tr>
<tr>
<td>Multiple</td>
<td>779 (12%)</td>
<td>34 (4%)</td>
<td></td>
<td></td>
<td>0.013</td>
</tr>
<tr>
<td>Children</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>2,522 (40%)</td>
<td>143 (6%)</td>
<td>0.001</td>
<td>0.012</td>
<td>0.939</td>
</tr>
<tr>
<td>Yes</td>
<td>3,789 (60%)</td>
<td>146 (4%)</td>
<td></td>
<td></td>
<td>0.012</td>
</tr>
<tr>
<td>Contract type</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full-time</td>
<td>1,686 (27%)</td>
<td>106 (6%)</td>
<td>0.000</td>
<td>0.011</td>
<td>0.294</td>
</tr>
<tr>
<td>Part-time</td>
<td>4,625 (73%)</td>
<td>183 (4%)</td>
<td></td>
<td></td>
<td>0.013</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 41 years</td>
<td>3,382 (54%)</td>
<td>173 (5%)</td>
<td>0.029</td>
<td>0.013</td>
<td>0.253</td>
</tr>
<tr>
<td>&gt; 41 years</td>
<td>2,929 (46%)</td>
<td>116 (4%)</td>
<td></td>
<td></td>
<td>0.011</td>
</tr>
</tbody>
</table>

During 2009, 289 cabin crew members reported at least one accident, leading to an annual accident incidence per 100 employees of 4.5 ((289/6,311)*100). The mean number of accidents per 100 flight hours was 0.012. Of the involved employees, 71% reported that their accident was related to an onboard customer service. Other, less frequently reported, causes were the landing or taking off of the airplane (6%), and turbulence during the flight (3%).

The crude logistic regression models did not show a significant association between exposure to flight schedules and occupational accidents (Table 2). From the adjusted models it can be seen that exposure to more short-haul flights was positively associated with the occurrence of an occupational accident. Exposure to more long-haul flights was negatively associated with the occurrence of an occupational accident. Since none of the interaction terms proved to be significant (p<0.001), no further subgroup analyses were performed.
Table 2. Crude and adjusted logistic regression analyses results.

<table>
<thead>
<tr>
<th></th>
<th>Crude p-value</th>
<th>OR</th>
<th>95% CI for OR</th>
<th>Adjusted p-value</th>
<th>OR</th>
<th>95% CI for OR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of night flights</strong></td>
<td>0.938</td>
<td>1.000</td>
<td>0.995 - 1.006</td>
<td>0.120</td>
<td>0.994</td>
<td>0.987 - 1.001</td>
</tr>
<tr>
<td><strong>Number of short-haul flights</strong></td>
<td>0.359</td>
<td>1.000</td>
<td>1.000 - 1.001</td>
<td>0.012</td>
<td>1.004</td>
<td>1.001 - 1.007</td>
</tr>
<tr>
<td><strong>Number of medium-haul flights</strong></td>
<td>0.498</td>
<td>0.998</td>
<td>0.993 - 1.003</td>
<td>0.271</td>
<td>0.997</td>
<td>0.992 - 1.002</td>
</tr>
<tr>
<td><strong>Number of long-haul flights</strong></td>
<td>0.123</td>
<td>0.997</td>
<td>0.994 - 1.001</td>
<td>0.011</td>
<td>0.995</td>
<td>0.990 - 0.999</td>
</tr>
</tbody>
</table>

OR = Odds Ratio, 95% CI = 95% Confidence Interval, significant if p < 0.05. All analyses are adjusted for the number of flight hours during 2009. Added confounders in adjusted analyses: age, gender, marital status n/y, children n/y, function, multiple employers n/y, mean contract rate, and number of flights flown 2005-2008.

**DISCUSSION**

Studying the associations between cumulative exposure to flight schedules and the occurrence of occupational accidents among cabin crew members, the number of short-haul flights proved to be predictive for the occurrence of accidents, while the number of long-haul flights was negatively associated with the occurrence of occupational accidents. Hence, the more exposure to short-haul flights, the higher the risk for cabin crew members to experience an occupational accident, and the more exposure to long-haul flights, the lower their risk of experiencing an occupational accident.

This is the first study to investigate the association between exposure to flight schedules and the occurrence of occupational accidents. Although there was no data available about on which type of flight the accidents happened, it can be hypothesized that they predominantly occurred during short-haul flights as well. Because cabin crew members fly fewer short-haul hours compared to long-haul hours on average per year, the presumable increased incidence of accidents during short-haul flights may be explained by the specific characteristics of the short-haul operation. Short-haul is quite different from long- and medium-haul because the operation is characterized by a relatively high workload; a high frequency of onboard services (e.g. serving beverages or meals), and short turnaround times between flights. The data also show that the majority of the accidents are reported to be related to onboard services. Moreover, it is known that workload factors such as time on task, lack of rest breaks, and stressful work contribute to an increased risk of occupational accidents (13).

Since the results of this study indicate that the risk of experiencing an accident increases with increased exposure to short-haul flights, it can also be hypothesized that the cumulative exposure to short-haul flights might lead to more fatigue...
accumulation compared to cumulative exposure to long-haul flights. The long-haul schedules of the studied airline company involve multiple duty days including one or more days of layover, followed by several days off. The short-haul schedules on the other hand, involve three to four successive duty days, followed by one or two days off. It is known that the components of the short-haul duty days (up to four flights a day, long working hours, early starts and late finishes) trigger fatigue among the crew involved (9). It is therefore possible that the days off in between are not sufficient to recover from the days on duty, thereby inducing a cumulative fatiguing effect and increasing the risk of accidents over successive duty days (5).

The major strength of this study is the large historic cohort, with information on 6,311 cabin crew members and detailed and objective information about flight schedules over a period of five years. Because the occupational accidents (with and without sickness absence) were reported through either the employee or the supervisor, and registered by the occupational health services, recall bias was avoided. However, since the report of accidents was on a voluntary basis, underreporting of accidents, in particular accidents where no sickness absence was involved, may have occurred. Further, it is possible that this underreporting differs between subgroups.

Other limitations of this study involve the lack of information about the exact situation of the reported accidents. Information during which type of flight the accident happened, and at what time during the flight it occurred, was not available. Further, although the characteristics of the short-haul operation might have played a role in the reported accidents, there was no objective information available about the involved workload (the number of onboard services or the number of rest breaks during these flights).

Finally, due to differences in registration procedures between companies and because compensation legislation between countries can have a major effect on the number of accidents reported, it is difficult to compare this number of accidents with those reported in other studies (1,10).

Future research should focus on the underlying mechanisms of the association between short-haul exposure and occupational accidents. It would, for instance, be worthwhile to investigate what kind of adjustments to short-haul schedules (duty duration, numbers of flights per day, number of days off) can reduce the number of occupational accidents, improve the wellbeing and fatigue recovery of employees, and can reduce experienced workload during the flights. In these studies, possible accumulation of fatigue as a result of exposure to specific flight schedules should also be measured.

Further, it should be studied how individual factors (such as gender or for instance chronotype) can explain any differences in accident occurrence, job stress and fatigue accumulation. The results of the present study for instance showed that there might be a difference between male and female crew members.
Because the analyses in this study showed that the vast majority, more than 70%, of the reported accidents occurred during onboard services, these tasks should have the main focus of airline companies aiming to reduce onboard accidents and the resulting injuries and sickness absence among cabin crew. Outcomes of future studies could help to create more specific prevention strategies (schedule adjustments, improvement of safety during onboard services) as well as individually tailored ones (training programs, workload reduction).

CONCLUSION

The results of this study show that cumulative exposure to short-haul schedules is associated with an increased risk of occupational accidents among cabin crew. This increase may be caused by the specific characteristics of short-haul flights, such as frequent onboard services per flight. Future research should focus on possible underlying mechanisms such as fatigue accumulation, and the influence of adjustments to short-haul schedules. Airline companies aiming to reduce occupational accidents should focus on the onboard services during short-haul flights.
REFERENCES


Chapter 7

Development and evaluation of an intervention aiming to reduce fatigue in airline pilots: design of a randomised controlled trial

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Tjabe Smid
Cécile R.L. Boot

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ABSTRACT

**Background**  A considerable percentage of flight crew reports to be fatigued regularly. This is partly caused by irregular and long working hours and the crossing of time zones. It has been shown that persistent fatigue can lead to health problems, impaired performance during work, and a decreased work-private life balance. It is hypothesized that an intervention consisting of tailored advice regarding exposure to daylight, optimising sleep, physical activity, and nutrition will lead to a reduction of fatigue in airline pilots compared to a control group, which receives a minimal intervention with standard available information.

**Methods/design**  The study population will consist of pilots of a large airline company. All pilots who posses a smartphone or tablet, and who are not on sick leave for more than four weeks at the moment of recruitment, will be eligible for participation. In a two-armed randomised controlled trial, participants will be allocated to an intervention group that will receive the tailored advice to optimise exposure to daylight, sleep, physical activity and nutrition, and a control group that will receive standard available information. The intervention will be applied using a smartphone application and a website, and will be tailored on flight- and participant-specific characteristics. The primary outcome of the study is perceived fatigue. Secondary outcomes are need for recovery, duration and quality of sleep, dietary and physical activity behaviours, work-private life balance, general health, and sickness absence. A process evaluation will be conducted as well. Outcomes will be measured at baseline and at three and six months after baseline.

**Discussion**  This paper describes the development of an intervention for airline pilots, consisting of tailored advice (on exposure to daylight and sleep-, physical activity, and nutrition) applied into a smartphone application. Further, the paper describes the design of the randomised controlled trial evaluating the effect of the intervention on fatigue, health and sickness absence. If proven effective, the intervention can be applied as a new and practical tool in fatigue management. Results are expected at the end of 2013.

**Trial registration:** NTR2722
BACKGROUND

Long and irregular working hours as well as crossing multiple time zones are common working conditions of flight crew (1). These conditions can cause travel fatigue, reduce sleep quality and quantity, and disrupt the circadian rhythm. The latter can lead to jet lag symptoms as well (1,2). All factors may contribute to increased fatigue. Prolonged fatigue has been shown to cause health problems, impaired performance capability and a disturbed work-private life balance (3). Furthermore, it has become clear that long term exposure to reduced sleep and circadian disruption can lead to cardiovascular diseases, gastrointestinal disorders, and cancer (4-6). More recently, this exposure has also been related to body weight gain, metabolic syndrome, and diabetes (7-9).

Among flight crew, fatigue is experienced regularly (10). In a study conducted in New Zealand for instance, 64% of the participating pilots reported to be fatigued at least once a week due to their working hours (11). In comparison, in a Dutch cohort study of a general working population, the prevalence of fatigue due to work was found to be 22%. Another study among pilots showed that 75% of them acknowledged fatigue as a serious problem during their job. Further, 71% of them admit to have been dozed off at least once during a flight (1).

In recent years, more knowledge has become available about the influencing factors on disturbance of the circadian rhythm, and possible countermeasures of fatigue (12-14). It has been shown that by correct timing of exposure to and avoidance of daylight, the most important biorhythm synchronizer (or zeitgeber) (2,12,13), jet lag symptoms can be reduced. Additionally, an optimal timing and duration of sleep can reduce the disturbance of the biological clock and thereby, reduce fatigue (2,13,14). Further, correct timing of certain types of physical activity can enhance sleep duration and quality (3). Moreover, the intake or avoidance of food may diminish jet lag symptoms during certain phases of the sleep/wake cycle, and caffeine can temporarily alleviate fatigue (3,12-14). Additionally, the specific macronutrient composition of meals has shown to be able to stimulate either alertness or relaxation (15,16). Based on these findings, several measures have been proposed to counter the negative effects of the aforementioned working conditions of flight crew.

These general measures should be translated into practical advice to enhance implementation. For flight crew, the specific advice depends on several variables (e.g. flight direction, flight duration, and number of time zones crossed). This implies that the advice differs per destination and person (e.g. morning vs. evening types), and that the total number of different advices is high. Due to this complexity, translating the theoretical knowledge into training programs for flight crew has proven to be difficult (2,17). Airlines and authorities sometimes provide employees with fatigue-related information at the start of their job, but most often continued education is not assured. And although aircraft companies such as Boeing and Airbus developed training modules aiming to reduce fatigue, the effects of these programs have hardly been examined systematically (17,18).
Chapter 7 | Development of a study aiming to reduce fatigue in airline pilots

The few studies that did study the effects of such training programs, reported some effects (19,20) but they combined their training programs with alterations in work schedules, so that it was impossible to address the measured fatigue reduction and performance improvement to the training program alone. Other studies did find improved knowledge, awareness (21), layover sleep, and in-flight alertness (22) after short term application of fatigue management advice in flight crew, but did not measure the long term effects.

Further, in the aforementioned studies, advice was mostly transferred through the use of paper or in the form of books or instruction materials. This kind of implementation has led to low compliance, which was shown in an article by Flower (23). Their advice cards program among British Airways pilots was received positively, but the compliance of 40% proved to be low. Therefore, it might be possible that the lack of compliance and outcomes in transferring fatigue-related knowledge to flight crew is (partly) due to the chosen medium. There might be a solution for this implementation problem because in more recent health behaviour literature, the large potential of the use of new media sources, such as computers and internet, has become clear (24,25). It has been stated that the use of web-based interventions is more effective in increasing health behaviour knowledge compared to non-web-based interventions (26). Further, to improve adherence, these interventions should be designed to allow individuals to tailor it to their own specific needs. This so called tailoring can significantly affect behaviour regarding safety, smoking, physical activity and dietary intake (24,27,28).

In summary, it can be stated that it is still largely unclear what the effects are of tailored advice regarding exposure to daylight, sleep, physical activity, and nutrition on fatigue of flight crew. Therefore, this paper describes the development of an intervention consisting of tailored advice for airline pilots, and the design of the randomised controlled trial evaluating the effect of the intervention on fatigue, health and sickness absence. The advices are evidence-based and aim to optimise the pilots’ behaviour with regard to:

- Exposure to daylight (timing and duration)
- Sleep (sleep behaviour and timing of sleep)
- Nutrition (dietary behaviour and timing of dietary behaviour)
- Physical activity (form and timing of physical activity)

It is hypothesized that an intervention consisting of easy obtainable tailored advice, will lead to a significant reduction of fatigue in airline pilots compared to a minimal intervention, based on standard fatigue related information available within the airline company.

METHODS/DESIGN

An intervention has been developed and will be evaluated by means of a two-armed randomised controlled trial (RCT). The intervention, named MORE Energy, will
have a follow-up period of six months. The recruitment of the participants will start in autumn 2012. The study design and procedures have been assessed by the Medical Ethics Committee of the VU University Medical Center, Amsterdam, the Netherlands (#2011/065).

Study population

The study population will consist of pilots of all aircraft types of a large internationally operating airline company.

Study procedures

The study design is presented in Figure 1. First, potential participants will be made aware of the project by means of a publicity campaign, using intranet, internet and news bulletins. In addition, meetings with supervisors will be held to make sure they can propagate the study to their employees, and motivate them to participate.

After the publicity campaign, all pilots will receive a postal information brochure. In this brochure, the pilots will be made aware of the participation mail, which they will receive in their company e-mail inbox. In this e-mail, all potential participants will be asked to fill in the baseline questionnaire, by using the included unique internet link.

By filling in the questionnaire the pilots agree to participate in the study, no additional written informed consent will be obtained. After the researchers receive the filled in questionnaire, participants will be allocated to either the control or intervention group.

Inclusion and exclusion criteria

The pilots can participate in the study if they:

• are not on sick leave for more than four weeks at the moment of recruitment;
• own a smartphone or tablet with an Android or iOS (iPhone/iPad) operating system.

Randomisation

Study group allocation will be conducted at individual level, using the minimisation technique. After the baseline measurement the participants will be assigned to one of the two study groups. A minimisation procedure will make sure that the group allocation of the next participant enrolled in the trial takes into account the characteristics of those participants already enrolled. The aim is that each allocation should minimise the imbalance across multiple factors (29). The factors that are considered for minimisation are aircraft type (five different types of aircraft units), and job title (captain, first officer, and second officer).
Chapter 7 | Development of a study aiming to reduce fatigue in airline pilots

Figure 1. Study design.

Development of the intervention

To optimize the content of the advices, a literature study was performed in order to gain insight in the latest scientific knowledge regarding work-related fatigue in flight crew. Based on this literature study, the following intervention objectives were defined (Figure 2).

Figure 2. Intervention objectives.

It is hypothesized that tailoring the relevant fatigue-related information, and making it easy accessible to the flight crew, will lead to improvement of their knowledge about the different aspects. This will be measured using knowledge
tests before and during the intervention. Improved knowledge will enlarge the possibility that the participant will use this knowledge to improve their behaviour regarding exposure to daylight, sleep, physical activity and nutrition, before, during, and after flight schedules. Accordingly, it is hypothesized that if their behaviour is altered, participants’ circadian disruption and fatigue will reduce, leading to an improvement of general health.

To find out what implementation strategy and what medium should be used to optimise compliance to the intervention, focus groups with the target population were held. For each aircraft type, two focus groups were organised. Considering five different types of aircrafts, ten focus groups were held. A total of 30 pilots attended the focus groups, heterogeneous regarding age, gender and job title. The discussions were recorded and field notes were written. The focus groups made clear that the intervention should be easy available, appealing, and to be used by pilots of all ages and ranks. Further, it was made clear that the intervention should be evaluated by means of a test phase first, and that it should be evident that the advice given is evidence based. The advices should be made flight schedule specific; short-haul pilots have a different need for information and advice than long-haul pilots have.

The input from these meetings was used to elaborate the intervention strategy and to take into account the raised facilitators and barriers for implementation. Finally, interviews with key management stakeholders were held, aiming to match the intervention to the present laws and legislation, collective labour agreement, and the policy of the airline company.

After the development of the intervention, it was pretested by pilots and researchers. The group of test pilots was heterogeneous with respect to both aircraft units and job type. In total, 34 pilots were invited to take part in this test phase, which lasted eight weeks in total. At the end of this period, the pilots who had actually participated were asked to fill in a digital evaluation form. Further, they were asked if they were available for a telephone consultation, in case the researchers needed additional information from them. Based on the results of the test phase evaluation, the intervention was reconsidered and optimized where necessary. An important result of the test phase was the report of the short-haul pilots that their advice was not substantive enough. This issue was addressed by adding more extensive advices with regard to short-haul flight schedules.

Description of the intervention

As a result of the focus groups, a tailoring strategy was constructed. It was decided that the best tool to transfer the knowledge would be using a smartphone application. This ensures that the advice can be supplied tailored to flight characteristics (e.g. flight direction, departure and return time, number of time zones crossed) and to personal characteristics (morning vs. evening types).

For each destination with its specific schedule, the participants are provided with
specific advices on optimal light exposure, sleep, nutrition, and physical activity, in order to reduce fatigue. The user can fill in his flight and location, after which he will receive the advices. Subsequently, the user can choose himself to read extensive information about either exposure to daylight, sleep, nutrition, or physical activity in the glossary menu. For each screen of the application, a help menu is available.

A website containing more background information was developed alongside the smartphone app. In the app, the user is guided to the website to read, listen to and see more detailed information. See Appendix 3 for examples of the application and website.

Participants in the intervention group will be stimulated to consider the advice on the application and the website by means of reminders. The first type of reminding occurs through timed alerts; the user receives an alert once he has not opened the app for longer than three weeks. Another reminder strategy that will be used is called geofencing; the user is given an alert each time he is outside the Netherlands, with a maximum of one alert per four days.

**Control intervention**

The participants allocated to the control group will receive a minimal intervention consisting of the available fatigue-related information of the airline company. This information is normally scattered throughout the company and by putting it to the study website it is made sure that the information is available for each participant. Minimal intervention strategies are commonly used for control groups in order to compare them to an intervention group (30).

The researchers will send an e-mail to the participants with instructions how to obtain and use the advices. The members of the intervention group will receive a link to download the smartphone application and a link to access the intervention website. The participants of the control group will be invited to log in to the study website, after which they will be directed to the standard available information. During the intervention period, all participants will be kept involved by sending a regular newsletter with information about the study in general, and upcoming questionnaires. Reminders will be sent to increase compliance among all participants, and communication throughout the airline company will be used to raise awareness.

**Outcomes**

Measurements will take place at three moments; participants will be asked to fill in questionnaires at baseline (T0), and at three (T1), and six months after baseline (T2). Before each follow-up measurement, subjects from both groups will receive an e-mail in which they are asked to fill out the online questionnaires. Reminders will be sent to increase the response rate. All questionnaires are in Dutch.
Primary outcome
The primary outcome variable is fatigue. Fatigue will be measured using the 20-item Checklist Individual Strength (CIS) (31). The questionnaire consists of four dimensions; the subjective experience of fatigue, reduction in motivation, reduction in activity, and reduction in concentration. It has been found that the questionnaire has a good internal consistency: the Cronbach’s $\alpha$ for the total CIS was 0.90 and for the scales the $\alpha$ ranged from 0.83 to 0.92 (31). The questions have seven answer options, ranging from “yes that is correct” to “no that is not correct”.

Secondary outcomes
• **Sleep**
Sleep quantity and quality as well as timing of sleep will be measured using the Jenkins Sleep Scale (32) and the subscales subjective sleep quality, sleep latency, sleep duration, and use of sleeping medication of the Pittsburgh Sleep Quality Index (33).
The Jenkins sleep scale is a short, 4-item, multiple choice questionnaire, which is regularly used in flight personnel (34). The internal consistency has been found to be reasonable, with a Cronbach’s $\alpha$ of 0.79. The used subscales from the Pittsburgh Sleep Quality Index comprise 5 multiple choice items. The total component scores of the PSQI proved to have an overall Cronbach’s $\alpha$ of 0.83, indicating a good internal consistency.
• **Nutrition**
Nutritional behaviour will be measured using a self-developed questionnaire. The questionnaire contains 13 questions concerning the regularity of meals taken, snacking, usage of breakfast, composition of meals, and drinking habits. The questionnaire comprises different types of questions, both open and multiple choice.
• **Physical activity**
The amount of physical activity during leisure time will be measured using questions on the recommended quantity for physical activity and exercise in healthy adults (35,36). These measurements are often used in RCTs and comprise two open-ended questions.
• **Need for recovery**
Need for recovery will be measured using the 11-item ‘need for recovery scale’ from the Dutch Questionnaire on the Experience and Evaluation of Work (Dutch abbreviation VBBA), which has shown to be valid and reliable, and to have a good internal consistency of 0.88 (37). All questions have two answering categories (yes/no).
• **Sickness absence**
Data on sickness absence (number of absence days and number of spells), will be collected from the records of the occupational health service and human resource department of the airline company.
• **Work-private life balance**
Work-private life balance will be measured using the shortened version of the SWING questionnaire (38). This 17-item questionnaire has been developed
to measure and distinguish four types of interaction; negative work-home interference, positive work-home interference, negative home-work interference, and positive home-work interference. It has been shown that the questionnaire measures all constructs reliably, with Cronbach’s α’s ranging from 0.75 to 0.84 (39).

- **General Health**
  General perceived health will be measured using two questions of the Dutch version of the SF-36 Health Survey which have proven to be moderately valid and reliable (0.81) (40).

- **Knowledge**
  During each measurement, the knowledge of the participants regarding the relevant fatigue-related information will be measured by means of 20 true or false statements, containing all sub-domains (exposure to daylight, sleeping, physical activity, and nutrition) of the intervention.

- **Body Mass Index (BMI)**
  Participants will be asked for their body height and body weight. Afterwards BMI will be computed as body weight divided by the square of height (kg/m²).

**Other study parameters**

- **Socio-demographic variables**
  At baseline, socio-demographic data (age, gender, job title, flight unit, and household composition) will be collected.

- **Morningness-eveningness**
  At baseline, personal morningness-eveningness preference will be measured using the VOA, the Dutch version of the Morningness-Eveningness Scale (MEQ) (41).

- **Tobacco and alcohol**
  Smoking tobacco and alcohol consumption are potential effect modifiers. Therefore, tobacco smoking behaviour and alcohol consumption will be assessed at baseline.

- **Chronic disease**
  Having any kind of chronic disease might also be acting as an effect modifier. Therefore having a chronic disease will be measured by one yes or no question: “do you have a chronic disease?”

**Process evaluation**

Besides the effect evaluation, the process of the implementation of the intervention will be evaluated, in accordance with the Steckler&Linnan framework (42). During the intervention period, an extensive userlog will be kept, and the delivery of the intervention will be quantified. Besides, the extent to which participants use the intervention will be objectively measured through the control management system (CMS) of the application. This system will measure the number of times the intervention participants will request an advice, and, each month, all data about usage will be stored in a database. The number and duration of all the participants’ visits to the study website will be stored as well.
Using the questionnaires, the participants will be asked if they have read and used the advices, and if they think their behaviour (regarding exposure to daylight, sleep, physical activity and nutrition) and their timing of this behaviour, has changed due to the advices. Further, they will be asked about their satisfaction with the intervention program, concerning both the smartphone application and the website.

Statistical analysis

To investigate the success of the randomisation procedure, potential confounders or effect modifiers (age, gender, type of aircraft flown, household composition, morningness-eveningness) will be compared between the intervention and control group by Student t-tests for independent samples and Chi square tests ($\chi^2$).

The effectiveness of the intervention (time*group interaction) will be analysed using linear mixed model analyses with the outcome measures at follow-up (T1-T2) as the dependent variables. The dependent variables are fatigue, sleep, physical activity, nutrition, need for recovery, sickness absence, work-private life balance, general health and knowledge, whereas research condition (intervention or control group) is the independent variable. Possible confounding or mediating factors will be considered.

A detailed analysis plan will be developed prior to finalisation of the dataset. For all analyses a two-tailed significance level of <0.05 will be considered statistically significant. The analyses will be performed using SPSS 20.0 (SPSS Inc. Chicago, Illinois, USA).

Sample size

The sample size is based on finding an effect on the primary outcome of the intervention, perceived fatigue. Fatigue will be measured using the 20-item CIS questionnaire (43). The mean total score on this questionnaire for healthy employees is 47.3 (sd = 19.8) according to Beurskens et al. (43) (score range 0–140). Power calculations indicate that to detect a relevant 10% difference in fatigue, 246 subjects are necessary in each study group (with power = 0.80 and alpha = 0.05). Taking the expected loss to follow-up (25%) into account, a sample size of approximately 656 employees is required.
DISCUSSION

This paper describes the development of an intervention consisting of a set of tailored advices (about daylight exposure, sleep, physical activity, and nutrition) delivered through a smartphone application for airline pilots, and the design of a randomised controlled trial evaluating its effect on fatigue, health and sickness absence.

Many authors have called for additional efforts to prevent the detrimental health effects of irregular working hours among the employees involved (9,44). Fortunately, knowledge about the influencing factors of fatigue and disturbance of the circadian rhythm is available. Since educational programs in the past generally did not show a long term fatigue reduction among flight crew, the present study tailors the advices and makes them easy obtainable. By using new forms of media, it aims to improve health behaviour, to reduce experienced fatigue, and to improve general health.

Strengths & limitations

The fact that this intervention uses a smartphone application to transfer knowledge and aims to change behaviour is a strength. A recent estimation in the Netherlands showed that 52% of all phone users own a smartphone and this number is expected to grow to 65% in 2012 (45). Moreover, in the specific target population of this study the percentage of smartphone users is expected to be even higher. Smartphones and tablet computers have several advantages; they are easy to use and to carry on, and do not necessarily need to have access to internet in order to work as an information source. Further, the technology of the smartphone application itself makes it possible that the advices are presented specific per function, chronotype (morningness/eveningness), and flight schedule. Evaluating smartphone apps to improve health behaviour by using a RCT is relatively new. To our knowledge, the study of Quinn et al.(46) was the first to present results of a RCT on mobile health (mHealth). In their study, positive effects were found on the control of blood glucose in diabetes patients. The number of mHealth studies is expected to rise in the upcoming years since several research protocols have been published (47,48). A guideline for both eHealth (web-based interventions to improve health behaviour) and mHealth RCTs was also published recently (49).

The MORE Energy study is the first randomised controlled trial that uses mHealth to improve health behaviour in flight personnel. Advantages of mHealth are partly similar to those of eHealth, and include the unique characteristics of technology (e.g. video transmission, interactiveness), its relative cost-efficiency, the immediate and easy access of information or advice, and the flexibility of user control of the intervention (50). However, the evaluations of these kind of interventions are often complicated by the fact that a substantial proportion of participants may have dropped out because of non-use or loss to follow-up (26,49). Because the effectiveness is dependent on participants actually using the
intervention, in the current study, the usage of the application and website will be measured for each participant. Furthermore, the process evaluation will give insight in compliance, how the intervention was evaluated by participants, and how the advice was used. By tailoring the intervention to the needs of the target population through focus group discussions, it is expected that the risk for low compliance in this intervention is somewhat reduced.

The use of focus groups with the target population is also a strength. Together with the interviews with the key management stakeholders of the company, it resulted in an implementation strategy that took into account a lot of barriers faced by the target population. With this strategy, it is thought that problems faced by similar studies are partly overcome. These studies used other kinds of media to transfer knowledge, and were therefore limited in their capability to tailor their advice. In the MORE Energy study, advice will not only be tailored, but will be offered in such a way that participants can choose the advice that fulfills their specific needs at specific moments.

There are possible limitations to this study as well. Firstly, results from earlier studies and indications from the focus groups point out that there might be a substantial group of pilots that will not participate because they have their own long-lasting routine to cope with flight schedules, and are not open for new insights. This will lead to selection bias (51). Further, because the intervention will use a smartphone application, employees who do not own such a device are excluded from this study. Therefore, even though smartphones and tablets are widely used throughout pilots, a certain subgroup of employees will not be able to participate. Unfortunately, since we do not have information about who does or does not own a smartphone, we can only compare the demographic characteristics of the whole population of airline pilots with those of the participants.

Another limitation of the study is the possible crossover of information. It was decided to randomize the participants at an individual level. This means that, during a flight routine a control group pilot and an intervention group pilot with smartphone application may share the cockpit which makes contamination plausible. Because the application is personalized and both the application and website have a unique login per participant, it is assumed that contamination will have a limited effect on the resulting differences in outcome between groups though. Finally, a possible limitation is that the participants will not be blinded for design. However, because the control group will receive a minimal intervention only, and the intervention group will receive extensive, specific and tailored advice (which is easily accessible through both smartphone application and website) the contrast between groups is considered sufficient. Although we chose to offer the control group a minimal intervention rather than no intervention, more attention was given to the intervention group. Because of this, the Hawthorne effect cannot be fully excluded.

This RCT will investigate whether a tailored mobile health intervention can reduce fatigue and improve general health of airline pilots by improving the knowledge
and behaviour with respect to exposure to daylight, sleep, nutrition and physical activity. If results are positive, it would provide a new tool in fatigue management, possibly reducing the health risks of irregular working times of both flight crew and shift workers. Results of the MORE Energy study will become available at the end of 2013.

Acknowledgement

We would like to thank all pilots and stakeholders who were involved in the development of the MORE Energy intervention.
REFERENCES

33. Buyssse DJ, Reynolds CF, III, Monk TH, Hoch CC, Yeager AL, Kupfer DJ. Quantification of


APPENDIX 3. MORE ENERGY APP SCREENSHOTS

Figure 1. More Energy app

Figure 2. Login & select flight

Figure 3. Selection of specific advice

- **SleepingLight**
  - At arrival:
    - Try to operate as soon as possible and to sleep for a short period of time.
    - Create a dark, quiet and cool environment. Sleep with the curtains closed, and if necessary, use earplugs so you don’t wake up by the noises of the early local morning. Look in the dictionary for more tips on sleep hygiene.
    - Try to wake up at the start of the local afternoon, eat as when close to the target time, and go outside to expose yourself to daylight.
    - Look in the * marathon start time * table when you want to eat daylight, and avoid light as much as possible, in order to adjust to the local rhythm as soon as possible.
Figure 4. Glossary menu

Figure 5. Background information available on project website
Chapter 8

Process Evaluation of a tailored mHealth intervention aiming to reduce fatigue in airline pilots (MORE Energy)

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Tjabe Smid
Allard J. van der Beek

Submitted
ABSTRACT

Background MORE Energy is an mHealth intervention, which aims to reduce fatigue and improve health in airline pilots. The primary objective of this process evaluation was to assess the reach, dose delivered, compliance, fidelity, barriers and facilitators, and satisfaction of the intervention. The second objective was to investigate associations of adherence to the intervention with compliance and with participant satisfaction. Thirdly, we investigated differences between the subgroups within the target population.

Methods The MORE Energy intervention is a smartphone app, supported by a website. It consists of advice on optimal light exposure, sleep, nutrition, and physical activity, tailored to flight and personal characteristics. The reach of the intervention was determined by comparing the intervention group participants and the airline pilots who did not participate. The dose delivered was defined as the total number of participants that was sent an instruction email. Objective compliance was measured through the control management system of the application. To determine the fidelity, an extensive log was kept throughout the intervention period. Subjective compliance, satisfaction, barriers and facilitators, and adherence were assessed using online questionnaires. Next, associations between the extent to which the participants applied the advice in daily life (adherence), compliance, and satisfaction were analysed. Finally, outcomes of participants of different age groups and haul types were compared.

Results Reach was 22% and dose delivered was 99%. Of the intervention group participants, 81% consulted any advice, while 17% did this during more than four weeks. Fidelity was 67%. The participants rated the intervention with a 6.4 (sd 1.6). Adherence was not associated with compliance, but was associated with satisfaction (p≤0.001). Pilots of 35 to 45 year old were significantly more interested in advice regarding physical activity than their colleagues, and short-haul pilots were more interested in advice regarding nutrition compared to long-haul pilots.

Discussion The MORE Energy intervention was well received, resulting in a high reach and dose delivered. The compliance and satisfaction scores indicate that engagement and functionality should be enhanced, and the content and applicability of the advices should be improved to appeal all subgroups.
INTRODUCTION

Due to disruption of the sleep wake pattern and the circadian rhythm, fatigue is inevitable in occupations where individuals are required to work when they normally would be asleep (1). In the aviation industry, fatigue management strategies have been developed to minimize the health effects of these irregular working hours (2,3). Education for flight crew members is an important component of these strategies, for which several educational programs have been developed. Although some of these programs have been studied, the effects, especially on the longer term, remain largely unclear (4-7). Moreover, it can be questioned in what way the available knowledge has to be transferred in order to result in optimal compliance of the employees involved. Flower (8) for instance showed that the compliance of airline pilots was low after being offered a binder of cards with flight schedule specific advices. Other media that have been used involve classroom instructions (4), booklets (5), and CD-ROMs (6).

In general, literature on computerized health education shows that the content of advice should be tailored to the individual needs of the participant and should be applicable for all subgroups within a target population (9,10). Additionally, when translating the relevant knowledge for flight crew members into practical advice, variables such as flight direction, flight duration, and number of time zones crossed have to be taken into account (7). With this in mind, the MORE Energy intervention, aiming to reduce fatigue and improve health in airline pilots through easy obtainable and tailored advice, was developed (11). This intervention provided participants with evidence-based and relevant fatigue-related advice using a mobile application, supported by a website with background information. It was hypothesized that the intervention would improve the pilots’ knowledge and behaviour regarding exposure to light, sleep, nutrition, and physical activity.

The usage of mHealth, mobile phone technologies in health care and public health, has expanded rapidly during the last decade (12). Additionally, because the use of smartphones and tablets keeps increasing, mobile applications (apps) have great potential for promoting health behaviour (13). However, while web-based and text messaging interventions have been shown to be able to positively affect knowledge and behaviour among adults (14,15), evidence for these effects of mobile apps is limited (16,17).

Blackman et al. (18) showed that mHealth studies scarcely report about key implementation factors, while this information is necessary to get more insight in the strength and weaknesses of the implementation of the intervention and to facilitate the interpretation of the results (19,20). Furthermore, such information can not only be used to improve the intervention itself, but also to notify researchers of similar future studies. As Eysenbach (21) emphasized, detailed descriptions of the development, characteristics, revisions and updates of mHealth interventions are necessary for quality improvement of the research domain. Therefore, we performed a process evaluation alongside our randomized controlled trial.
The primary objective of this process evaluation was to assess the reach, dose delivered, compliance (dose received), fidelity, barriers and facilitators (context), and satisfaction of the MORE Energy intervention. The second objective was to investigate whether the MORE Energy intervention was associated with an improvement in relevant behaviour of the participants by exploring the association between compliance to the intervention and the extent to which the pilots adhered, i.e. applied the advice in daily life. We investigated if adherence was associated with the satisfaction of the pilots as well. The third objective was to investigate how the intervention suited the different subgroups within the target population. Therefore, outcome differences between pilots of the different age groups and haul types were analysed for the process evaluation items compliance and satisfaction.

**METHODS**

This process evaluation was carried out alongside the randomized controlled trial on the effectiveness of the MORE Energy intervention that aimed to reduce fatigue in airline pilots. The Medical Ethical Committee of the VU University Medical Center Amsterdam approved the study protocol.

**Participants**

The study population consisted of the pilots of a large internationally operating airline company. The pilots could participate in the study if they were not on sick leave for more than four weeks at the moment of recruitment and if they owned a smartphone or tablet with an iOS (iPhone/iPad) or Android operating system. After inclusion, the participants were equally randomized into the intervention and the control group. For this process evaluation, we focus on the participants of the intervention group only.

**MORE Energy intervention**

The MORE Energy intervention was developed systematically. First, a literature study was performed in order to gain insight in the latest scientific knowledge about optimal behaviour regarding disruption of the circadian rhythm and fatigue in flight crew. Next, focus groups were held to find out what medium and implementation strategy should be used to optimise compliance to the intervention. The focus groups made clear that the intervention should be easy available, appealing, and to be used by pilots of all ages and job types. Further, the advices should be made flight schedule specific and applicable for both short- and long-haul pilots. To match the intervention with the legislation and the policy of the airline company, interviews with key management stakeholders were held as well.

Based on the focus groups and interviews, it was decided to develop a mobile application to transfer the advices to the target population. After the development of the MORE Energy app, it was extensively pre-tested by both pilots and researchers. Based on the results of this first evaluation, the intervention was
optimised where necessary.

The MORE Energy app contained advices on optimal light exposure, sleep, nutrition, and physical activity, tailored to relevant flight (e.g. flight direction, departure and return time, number of time zones crossed) as well as to personal characteristics (e.g. job type, chronotype). The users could choose to consult background information in the glossary menu and the app guided them to a website to read more, or to view and listen to video and audio files concerning the different topics. Participants were encouraged to consider the advices on the app by means of two types of reminders: timed alerts (when the user did not use the app for longer than three weeks) and geofencing alerts (when the user arrived somewhere outside of the Netherlands, with a maximum of one alert per four days). Screenshots of the MORE Energy app can be seen in Appendix 3 (Chapter 7). Further details and exact description, development, and content of the intervention have been published elsewhere (11).

Data Collection

The process evaluation items were taken from the Steckler & Linnan framework (20): reach, dose delivered, compliance (dose received), fidelity, barriers and facilitators (context), and satisfaction. Adherence, the extent to which the participants applied the advices in daily life, was measured as well. Table 1 presents an overview of the different items and the accompanying collection and processing of the data. The airline company provided data about the gender, age, job type, and the haul type of all potential participants.

Reach
Reach is defined as the proportion and representativeness of the intervention group participants in the study, compared to the total group of potential participants (19). Reach was determined by comparing the following characteristics between the intervention group participants and the airline pilots that did not participate: gender, age, job type, and haul type.

Dose delivered
Dose delivered is considered as the total amount of intervention material provided to the participants. In this study, the dose delivered was defined as the total number of participants that was sent an email containing instructions and login details to access the intervention material.

Compliance (dose received)
Compliance is the dose that is received, and refers to the extent to which participants actively engaged with the intervention. In our study, it was objectively measured through the control management system (CMS) of the application. This system stored the number of advices per week requested by each participant through user authentication. Likewise, we used a web-analytic tool (Google Analytics) to register and store the total number of page views per participant to the website of the project. The registered number of app advices of four participants proved to be more than 200. Because this was most certainly
due to malfunctioning of the CMS, the registered data of these participants was excluded from the objective compliance analyses.

The participants were also asked how often they had consulted the advices during the intervention (almost always, sometimes, only a few times, or never) in the online questionnaire at six months after baseline. Further, participants were asked which type of advice they had predominately used (advice regarding preparation for departure, regarding layover, or regarding the return home) and which topics they had consulted the most (exposure to light, sleep, nutrition, or physical activity).

**Fidelity**

Fidelity is defined as the extent to which the intervention program was implemented as planned, representing the quality and the integrity of the implementation (19). Therefore, all changes, updates, and revisions of the app and website that occurred during the intervention period were kept in a log. Fidelity was calculated as the weighted average of the percentage of weeks of the total intervention period that the different components of the intervention were delivered as intended. As the advice delivered through the app was considered the main component of the intervention, this was given the most weight, whereas the remaining four components were weighted equally:

- Access (installation, login, offline functionality): 15%
- Backend (synchronisation of content and flight schedules): 15%
- Advice (tailoring algorithm and glossary): 40%
- Reminders (functioning of push alerts): 15%
- Website with background information (access, functionality): 15%

**Satisfaction**

The satisfaction with the intervention was assessed through the online questionnaire at six months after baseline. First, the participants were asked to give an overall grade for the MORE Energy advice (1 to 10). Next, they were asked to rate four statements about the usability of the intervention on a 5-point Likert scale ranging from ‘disagree’ to ‘agree’. Additionally, participants were asked if they would recommend the MORE Energy application to their colleagues, and to appreciate the effectiveness of the intervention through rating three statements on perceived effectiveness on the 5-point Likert scale.

**Barriers and facilitators (context)**

Context refers to “the larger physical, social, and political environment that either directly or indirectly affects an intervention program” (20). Possible context factors that affected the intervention were registered in a log. Further, in the online questionnaire, we asked the participants which barriers or facilitators they had experienced. First, participants were asked if they would recommend the MORE Energy application to colleagues who do not have access to it yet. If they answered ‘no’, they were asked why they held that opinion. Next, participants
were asked what their reasons were not to consult the advices more often (content already known, no need for further consultation, technical problems, lack of usability, different reason).

Adherence

The extent to which participants applied the MORE Energy advices in daily life was assessed through asking the participants to rate the statement “After reading the advices, I actually applied them as well.” on a 5-point Likert scale ranging from 1 ‘disagree’ to 5 ‘agree’.

Table 1. Overview of the different process evaluation items.

<table>
<thead>
<tr>
<th>Items</th>
<th>Definition</th>
<th>Resources</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reach</td>
<td>Information on the number of participants (%) and their demographics,</td>
<td>Information on all potential participants provided by the airline company</td>
</tr>
<tr>
<td></td>
<td>compared to the non-participants</td>
<td></td>
</tr>
<tr>
<td>Dose delivered</td>
<td>Total amount of intervention material provided to the participants (%)</td>
<td>The number of participants that was sent an email with instructions and login details</td>
</tr>
<tr>
<td>Compliance (dose received)</td>
<td>Measured consultation of the tailored advice</td>
<td>Objective: user authentication through the CMS (app) and Google Analytics (website). Subjective: online questionnaire</td>
</tr>
<tr>
<td>Fidelity</td>
<td>Information on all changes, updates, and revisions that happened with the app during the intervention period. Calculated as the weighted average of the percentage of weeks the different components of the intervention were delivered as intended</td>
<td>Log</td>
</tr>
<tr>
<td>Satisfaction</td>
<td>Participants’ appreciation of the intervention and their opinion on its effectiveness (1-10)</td>
<td>Online questionnaire</td>
</tr>
<tr>
<td>Barriers and facilitators (context)</td>
<td>Barriers and facilitators of the intervention, experienced by both the researchers and the participants</td>
<td>Researchers: log Participants: online questionnaire</td>
</tr>
<tr>
<td>Adherence</td>
<td>The extent to which participants applied the MORE Energy advices in daily life</td>
<td>Online questionnaire</td>
</tr>
</tbody>
</table>

Data Analysis

Regarding the first objective, descriptive analyses were performed. Differences (gender, age, job type, and haul type) between participants and non-participants were analysed with t-tests for independent samples and Chi-square tests.

For the second objective, associations between compliance and the extent to which the participants applied the advice in daily life (adherence) were analysed by calculating Spearman’s (rho) correlation coefficients. Regarding the objective compliance, participants were divided into four groups of equal size related to the amount of compliance. Furthermore, a linear regression analysis was performed.
to explore the association between the level of adherence (independent variable) and satisfaction with the intervention (dependent variable). Participants who indicated not to have applied the advices in daily life, or who had a neutral opinion towards this question, were taken together and used as reference category in the analysis.

To answer the third objective, outcomes for the different age groups (<35, ≥35-<45, ≥45) and haul types (short-haul pilots vs. long-haul pilots) on compliance and satisfaction were analysed with t-tests for independent samples, Chi-square tests and one-way ANOVAs.

A two-tailed significance level of p<0.05 was considered to be statistically significant in all analyses. Analyses were conducted with the Statistical Package for Social Sciences (SPSS), version 20.0.

RESULTS

Reach

A total of 2,222 potential participants were made aware of the project by means of a publicity campaign through the airline company, after which they received an email with a link to the baseline questionnaire. From this group, 522 (23%) pilots agreed to participate. A total of 20 pilots (<1%) did not meet the inclusion criteria. Of the remaining pilots, 251 were randomized into the intervention group. At the end of the intervention period, 148 (59%) of these participants completed the process evaluation questionnaire. Baseline characteristics of the intervention group participants and the non-participants are shown in Table 2.

Dose delivered

We sent emails containing the login details and instructions to 251 participants. One email was bounced because the email address proved not to exist. After three months, one other participant reported to have not received the instruction email. The dose delivered therefore was determined to be 99% (249/251).
Table 2. Characteristics of the participants and the non-participants (reach)

<table>
<thead>
<tr>
<th>Reach characteristics</th>
<th>Category</th>
<th>Participants (n=251)</th>
<th>Non-participants (n=1720)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years mean (sd)</td>
<td></td>
<td>41.0 (8.0)*</td>
<td>42.5 (8.3)</td>
</tr>
<tr>
<td>Age group n (%)</td>
<td>&lt;35</td>
<td>60 (23.9)*</td>
<td>313 (18.2)</td>
</tr>
<tr>
<td></td>
<td>≥35-&lt; 45</td>
<td>98 (39.0)*</td>
<td>652 (37.9)</td>
</tr>
<tr>
<td></td>
<td>≥45</td>
<td>93 (37.1)*</td>
<td>755 (43.9)</td>
</tr>
<tr>
<td>Female n (%)</td>
<td></td>
<td>21 (8.4)*</td>
<td>65 (3.8)</td>
</tr>
<tr>
<td>Job type n (%)</td>
<td>Captain</td>
<td>111 (44.2)</td>
<td>750 (43.6)</td>
</tr>
<tr>
<td></td>
<td>First Officer</td>
<td>97 (38.7)</td>
<td>706 (41.0)</td>
</tr>
<tr>
<td></td>
<td>Second Officer</td>
<td>43 (17.1)</td>
<td>264 (15.3)</td>
</tr>
<tr>
<td>Haul type n (%)</td>
<td>Long-haul</td>
<td>179 (71.3)</td>
<td>1287 (74.8)</td>
</tr>
<tr>
<td></td>
<td>Short-haul</td>
<td>72 (28.7)</td>
<td>433 (25.2)</td>
</tr>
</tbody>
</table>

* Significant difference between the participants and non-participants (p<0.05). sd = standard deviation.

Compliance (dose received)

Objective compliance
It was registered that during the intervention period, 54 of the 251 participants never consulted any advice on the app. Two of these participants indicated that they wanted to drop out of the study. Five of them only consulted the website with the background information. The remaining 47 participants either did not download or use the app or website after receiving the instructions, did not receive or read the email with the instructions, or only used the glossary section of the app (consultation of the glossary could not be registered by the CMS).

During the six month intervention period, 68 (27%) participants consulted the advices during one week only, 54 (22%) consulted them during two weeks, and 32 (13%) consulted them during three weeks. A total of 43 (17%) participants consulted the advices on the app during four weeks or more. In total, 1677 advices were requested. The mean number of requested advices per participant was 6.8 (sd 14.0), while the median was 3 advices per participant. If the data of the four participants with outliers was included, the mean number of requested advices would have been 12.6 (sd 55.3).

The CMS registered that the advices regarding the preparation for departure from home were requested the most (49%). The advices concerned with time spent during layover (23%) and the advices about the preparation for the return flight and arrival home (27%) were consulted less often.

In total, 32 (13%) participants went to the website with background information. The mean number of page views of these participants was 9.2 (sd 8.6). As can be seen in Figure 1, 27 (11%) participants used both the app and the website. Most
of the participants did use the app but never logged on to the website (68%).

Subjective compliance
Of the 148 participants that answered the process evaluation questionnaire, 62 (42%) indicated they had never really used the MORE Energy advices, 39 participants (26%) indicated that they had used the advices a few times, and 46 (31%) reported to have used the advices occasionally. One participant reported to have used the advices before and during every flight. Next, of the 86 participants that had used the advices, most of them indicated that they had consulted the advices regarding layovers (70%). Next, 49% indicated to have consulted the advices regarding the return home, and 36% indicated to have consulted the advices concerned with preparation before departure. Further, most of these participants pointed out that they consulted the advices concerned with sleeping behaviour (62%) and nutrition (72%). The advices regarding exposure to light (28%) and physical activity (23%) were consulted less often.

Fidelity
Through the six month intervention period the implementation of the intervention was predominantly affected by the following (detailed explanations of all bugs can be found in Appendix 4):
• After two weeks (second version of app available for iOS): after downloading the update, participants could no longer consult all types of advices. IPhone5 users could not get access to the new version of the app.
• After two months a third version of the app for iOS was released to solve the problems above:
  › This version could not be installed automatically. Participants had to delete the previous version of the app before being able to install the new one.
  › After installation, the reminder alerts malfunctioned. Researchers found out this problem most probably occurred in the Android app as well.
The five components of the intervention were affected to a different extent. Table 3 shows the number of weeks the components could be delivered as intended, and the calculation of the different fidelity scores. The weighted total fidelity score of the intervention was 67%.

Table 3. Fidelity score calculation for the 26-week intervention period.

<table>
<thead>
<tr>
<th>Component</th>
<th>Weight factor</th>
<th>Delivered as intended (in weeks)</th>
<th>Fidelity score</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>App</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Access</td>
<td>15%</td>
<td>16</td>
<td>62%</td>
</tr>
<tr>
<td>Backend</td>
<td>15%</td>
<td>25</td>
<td>96%</td>
</tr>
<tr>
<td>Advice</td>
<td>40%</td>
<td>19</td>
<td>73%</td>
</tr>
<tr>
<td>Reminders</td>
<td>15%</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td><strong>Website</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Access</td>
<td>15%</td>
<td>25</td>
<td>96%</td>
</tr>
<tr>
<td><strong>Weighted total fidelity score</strong></td>
<td></td>
<td></td>
<td><strong>67%</strong></td>
</tr>
</tbody>
</table>

Satisfaction

Figure 2 shows the satisfaction of the 148 participants who completed the process evaluation questions and indicated that they had used the advices of the MORE Energy app. The participants were satisfied with an app as the medium to transfer the advices (>75% agreed) but less than half of the participants found that the advices given were easy to apply in their daily life (46%). 56% of the participants indicated that the MORE Energy advices were useful.

Figure 2. Perceived satisfaction with the MORE Energy smartphone application.
More than 65% of the participants that used the advices thought that the MORE Energy intervention could prevent fatigue and improve fitness. Further, 78% indicated that they would recommend the MORE Energy advices to their colleagues. On average, the participants rated the MORE Energy intervention with a 6.4 (sd 1.6).

Barriers and Facilitators (context)

The 86 pilots that indicated to have used the advices were asked what their reasons were not to consult the advices more often. The most selected reason was that the content of the advice was already known to them (58%). Furthermore, 44% of these participants indicated that they did not need to consult the advices anymore after a few times. Less selected reasons were technical problems with the app (12%) and lack of usability (7%). Out of the additional reasons reported by 24 participants, three main themes could be composed. First, nine participants reported that the advices could not be applied in daily life because that would conflict with their social obligations, both at home and during duty. Predominantly participants with young children and short-haul pilots pointed out that this was a problem. Four participants indicated that they had simply forgotten to consult the app, or that they did not receive an alert to remind them. Similar barriers were addressed by the 19 participants who reported that they would not recommend the MORE Energy app to their colleagues; the advices were too common or not innovative enough (n=5), the advices were not applicable in daily life (n=4), the content was already known (n=3), or the app had too much technical problems (n=2).

Association between compliance, adherence, and satisfaction

Of the 86 participants indicating to have used the advices during the intervention period, 47 (55%) somewhat agreed, and 14 (16%) agreed with the adherence statement that they applied the advices in daily life. Further, 25 (29%) participants somewhat disagreed or had a ‘neutral’ opinion towards the statement.

Spearman’s rho correlation between the objectively and subjectively measured compliance and adherence was 0.04 (p=0.71) and 0.30 (p=0.004), respectively.

Table 4 shows that participants who indicated to have applied the advices after consulting them rated the intervention significantly higher compared to the participants of the reference category. The participants who somewhat agreed with the adherence statement, rated the intervention significantly higher as well (p≤0.001).
Table 4. Linear regression analysis results for adherence and satisfaction with the intervention.

<table>
<thead>
<tr>
<th></th>
<th>β</th>
<th>p-value</th>
<th>95%CI</th>
<th>Lower</th>
<th>Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Agree (n=14)</strong></td>
<td>2.42</td>
<td>0.000</td>
<td>1.41</td>
<td>3.42</td>
<td></td>
</tr>
<tr>
<td><strong>Somewhat agree (n=47)</strong></td>
<td>1.40</td>
<td>0.000</td>
<td>0.68</td>
<td>2.11</td>
<td></td>
</tr>
<tr>
<td><strong>Neutral or disagree (n=25)</strong></td>
<td>Reference</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

95%CI= 95% Confidence Interval.

Subgroup differences

**Compliance**

The objective compliance of the subgroups was comparable with compliance in the total group of participants. As can be seen in Table 5, differences between the groups were small. Because layover advices were not available for short-haul pilots, their registered number of consultations of this type of advice was close to zero.

Results on subjective compliance show that 53% of the pilots younger than 35 indicated to have never consulted the advices. Forty percent of the oldest group of pilots indicated that they used the advices sometimes or always. All age groups indicated they consulted the advices about the time spent during layover the most (63% to 78%), followed by advices concerned with the return flight (46% to 56%), and the advices before departure from home (28% to 43%). With regard to the content of the advices, the youngest group of pilots was more concerned with advice regarding sleep (78% vs. 57/58%, NS), while the oldest group was less concerned with advice regarding nutrition compared to their colleagues (58% vs. 80/83%, p=0.06). Further, significantly more 35 to 45 year old pilots were interested in advice regarding physical activity than their younger and older colleagues (43% vs. 9/11%, p=0.002).

Although layover advice was not available for short-haul pilots, subjective compliance results show that both groups indicated to have consulted this type of advice the most. Next, 50% of the short-haul pilots consulted the advices with regard to departure from home, while 53% of the long-haul pilots consulted the advices regarding the return flight. Advice regarding nutrition was consulted significantly more by short-haul compared to long-haul pilots (91% vs. 66%, p=0.02).

**Satisfaction**

No significant differences in satisfaction were present between the subgroups (Table 6). The youngest group of pilots showed the lowest percentage that agreed that the app was accessible and usable (61%). However, this group showed the highest percentage that reported the advice to be easy to apply (56%) and that indicated to have learned from the intervention (44%). Of the oldest group of pilots, 40% indicated that the advices were easy to apply, and 33% indicated that they learned a lot. Still, 85% of the oldest group of pilots would recommend the
intervention to their colleagues.

Comparing the two haul types, it can be seen that 55% of the short-haul pilots reported that the advices were easy to apply, compared to 43% of the long-haul pilots. However, 40% of the short-haul pilots considered the advices to be useful as well, compared to 61% of the long-haul pilots (p=0.06). Further, 70% of the short-haul pilots would recommend the advices to their colleagues, while 87% of the long-haul pilots would do that (p=0.06).
Table 5. Compliance scores within the subgroups.

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Compliance</th>
<th>Objective (n=247)</th>
<th>Subjective (n=86)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean number of advices (sd)</td>
<td>Median</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Home</td>
<td>During layover</td>
</tr>
<tr>
<td>&lt;35</td>
<td></td>
<td>5.65 (10.76)</td>
<td>2.0</td>
</tr>
<tr>
<td>≥35-&lt;45</td>
<td></td>
<td>6.34 (13.21)</td>
<td>3.0</td>
</tr>
<tr>
<td>≥45</td>
<td></td>
<td>7.98 (16.36)</td>
<td>2.0</td>
</tr>
<tr>
<td>Short-haul</td>
<td></td>
<td>7.42 (14.34)</td>
<td>2.0</td>
</tr>
<tr>
<td>Long-haul</td>
<td></td>
<td>6.53 (13.84)</td>
<td>3.0</td>
</tr>
</tbody>
</table>

* Significant difference (p<0.05). sd = standard deviation.

Table 6. Satisfaction scores within the subgroups.

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Rating</th>
<th>Satisfaction (agree)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean grade (sd)</td>
<td>Pleasant medium</td>
</tr>
<tr>
<td>&lt;35</td>
<td>6.2 (1.5)</td>
<td>83%</td>
</tr>
<tr>
<td>≥35-&lt;45</td>
<td>6.5 (1.5)</td>
<td>67%</td>
</tr>
<tr>
<td>≥45</td>
<td>6.5 (1.9)</td>
<td>83%</td>
</tr>
<tr>
<td>Short-haul</td>
<td>6.1 (1.9)</td>
<td>75%</td>
</tr>
<tr>
<td>Long-haul</td>
<td>6.5 (1.5)</td>
<td>77%</td>
</tr>
</tbody>
</table>

sd = standard deviation.
DISCUSSION

Main findings

The primary objective of this process evaluation was to assess the reach, dose delivered, compliance, fidelity, context, and satisfaction of the MORE Energy intervention. The reach among the target population was 23%. This percentage is quite high compared to the 1.5% to 8% reach published in other mHealth studies (16,22,23), and compared to more conventional studies promoting health behaviour at worksites (24).

The participating pilots were significantly younger compared to the non-participants, possibly because younger pilots are more familiar with mobile apps. Female pilots were also overrepresented, possibly caused by the fact that women tend to exhibit more active information-seeking behaviour and are more likely to participate in scientific studies than men in general (25,26).

It was shown that the dose delivered and initial compliance was high. Of the participants, only 19% never used any advice on either the app or the website. It is even possible that some of these participants never received the email containing the instructions and login details, because of for instance a strict junk-email filter. However, during the intervention period, only one participant reported not to have received the instruction email.

The compliance during the whole intervention period was rather low with 17% of the participants consulting the advices on the app for more than four weeks during six months. Technical problems with some components of the app, as could be seen in the calculation of the fidelity score, might have contributed to this. The fidelity score of 67% is difficult to interpret since we are the first mHealth study to calculate such a score. Moreover, a recent review showed that only 13% of the published mHealth studies, on physical activity promotion, reported fidelity information whatsoever (18).

Our results showed a distinction between the objectively and subjectively measured compliance regarding the type of advices. Despite the registered data displayed that the advice concerned with departure from home was consulted most often, the participants themselves indicated that they used the advice concerned with layovers the most. It might be possible that the participants thought that they were asked when they had used the advice most often. This would also explain the finding that short-haul pilots indicated to have used the layover advice the most although that type of advice was not available for them; they might have predominately considered the advice regarding their next flight at the end of a duty day (i.e. during their layover).

Despite the moderate compliance scores, a majority of the users (65%) was convinced that the intervention was able to fulfill its purpose, preventing fatigue and improving health of pilots. Also, 78% of the participants would
recommend the intervention to their colleagues. In this perspective, the 6.4 (range 1 to 10) appreciation score for the MORE Energy intervention as a whole, is somewhat low. On the other hand, a majority of the pilots (54%) did not agree with the statement that the advices were easy to apply in daily life. This lack of applicability of the flight schedule specific advices was also shown in the barriers and facilitators section. Participants indicated that applying the advices would conflict with their social life at home (e.g. young children) or during duty (e.g. habits during layovers). Furthermore, the correlation between registered compliance and adherence proved to be very low (r=0.041). This indicates that although participants were interested to see what advice the app would provide regarding their upcoming flight schedule, the content could not pursue them to change their behaviour. However, once applied, the advices might have been useful: participants that did indicate to have applied the advices in daily life rated the intervention significantly higher compared to the participants who did not apply them.

Another objective of this process evaluation was to assess whether there was a difference in compliance and satisfaction outcomes between participants of the two haul types and the three age groups present in the population. The results showed that the differences in both objective and subjective compliance between the age groups were small. The oldest participants tended to be the most critical regarding the applicability of the advices. Possibly, these pilots were unwilling to give up the patterns and habits which they developed throughout their career. This was already mentioned during the focus group interviews before the development of the intervention: it would be hard to alter the (social) patterns of the more experienced colleagues. The apparent contradicting high percentage of the oldest group of pilots (85%) that would recommend MORE Energy to their colleagues may be in accordance: the older pilots do not need the advice for themselves but they think it might be useful for their less experienced colleagues.

Regarding the participants of the two haul types, no significant differences in objective compliance existed either. The relatively large number of short-haul pilots that participated in the study did find the advices easy to apply, but found them not very useful. Consequently, short-haul pilots tended to be less satisfied with the intervention compared to the long-haul pilots. Although the operations of the two haul types differ substantially, short-haul schedules can trigger fatigue as much as intercontinental schedules (27). However, most of the scientific knowledge and practical advice available concerns the disruption of the circadian rhythm and is mostly applicable for long-haul pilots. Consequently, the content of our specific advice regarding short-haul schedules was less extensive. The short-haul pilots participating in the test phase of the intervention noticed this already. Although the short-haul advices were reconsidered and extended subsequently, the outcomes of our process evaluation indicate that this elaboration was probably not sufficient enough.
Strength and limitations

This process evaluation is the first evaluating an mHealth intervention promoting health behaviour. One of the major strengths is that we used a combination of objective and self-reported data to evaluate the implementation of the MORE Energy intervention. The compliance with both the app and the website was registered through user authentication, which is more reliable than self-reported information (28). Nevertheless, most probably due to malfunctioning of the CMS, data of four participants had to be excluded from the analyses. We did use self-reported data as well, to gather more detailed information on subject specific compliance, adherence and appreciation.

A limitation of this study is that only 59% of the participants of the intervention group filled out the process evaluation questionnaire. Therefore, selection bias may have occurred, which challenges the reliability and validity of the outcomes. Another limitation of the study is that we could not measure all activities of the users of the mobile app. The number and types of requested advices were registered, but consultation of the background information and time spent on the app was not.

The MORE Energy intervention aimed to improve relevant behaviour among airline pilots. Although we asked participants whether they had applied the advices in daily life, their actual change in behaviour could not be objectively measured. Therefore, to maximize the interpretation of our results, it would have been useful if the app had used more built-in features of smartphones to measure behaviour (e.g. timing of sleep using the motion sensor of the mobile device) (13).

Implications for research and practice

The reach of this study shows that airline pilots are willing to participate in an intervention using an app to promote health behaviour. Although guidelines have been proposed to improve the way the outcomes of mHealth interventions are reported (21), qualitative process evaluations publications are also necessary in order to provide more information about the implementation and working mechanisms of these kind of interventions (18).

High compliance is important for the success of any intervention intending to modify behaviour, but especially so in web-based interventions since there is no direct contact with the participants (14). Because we found that compliance dropped since the start of the intervention, similar studies should put more effort into keeping participants involved throughout the intervention period. Although technical problems were not mentioned as main reasons for non-compliance, time consuming update installations and the resulting loss in functionality, might have been of influence. One of the updates during the intervention period caused the malfunctioning of the reminder alerts. This might have led to a decrease in compliance since well-timed and adequate prompts can be effectively used in mHealth intervention studies. Other possibilities that can keep users engaged involve altering and updating the content of the intervention material, providing
personal feedback, and introducing goal setting (12).

Our process evaluation gives insight into the different aspects involved in the implementation of the MORE Energy intervention, and will help to improve the interpretation of the results of the trial. The outcomes of the different items showed which parts of the intervention should be improved before offering the intervention to all flight crew throughout the airline company. First, the app should pursue users more to change relevant behaviour, despite the consequences for their social responsibilities. Further, the content of the advice should be better applicable for both experienced and inexperienced employees, involved in both long- and short-haul schedules. The airline company involved can assist the subsequent implementation of the improved app by integrating it with flight crew scheduling, by giving sustained attention to the topic within the present flight crew members, and by introducing the tool to newly hired employees (7). After the improvement of the MORE Energy intervention, it might be transformed into a ‘white label’ tool in order to make it possible to adapt and implement it as a fatigue management tool for flight crew members or shift workers in other companies as well.

CONCLUSION

The process evaluation of the MORE Energy study showed that this mHealth intervention was well received, resulting in a high reach and dose delivered. Although more than 80% of the participants did use the intervention, most of them were not compliant throughout the intervention period. The intervention could not be delivered as intended and perceived satisfaction was moderate. Further, the combination of compliance and satisfaction scores indicates that the content and applicability of the advices should be improved to appeal all subgroups. The intervention therefore should be improved before making it available for the other flight crew members within the airline company. After the improvement, MORE Energy might be adapted and implemented as a fatigue management tool in other employees and companies as well.
REFERENCES


27. Powell D, Spencer MB, Holland D, Broadbent E, Petrie KJ. Pilot fatigue in short-haul operations: effects of number of sectors, duty length, and time of day. Aviat Space Environ Med
2007;78(7):698-701.
APPENDIX 4. BUGS DURING THE INTERVENTION PERIOD.

• Every month, the researchers uploaded the new flight schedules of the airline company into the control management system (CMS) of the application. The app was designed to synchronise with the CMS automatically so that the users could always consult the advices belonging to the latest flight schedules. During the whole intervention period three users reported that this synchronisation took very long (more than 15 minutes). The only way to resolve this problem proved to be reinstalling the app as a whole. Because the developers of the app could not reproduce this specific problem, it could not be resolved before the end of the intervention period.

• In the second week of the intervention period, an update of the app (version 2) was uploaded in the Apple app store to make the app compatible with the new operation system, iOS6. After the update, several users started to report two problems.
  › Advices concerning the layover after ‘neutral’ flights (flights without time zone crossings) were not shown anymore.
  › Users who used the app on an iPhone5, reported that they could not open the app on their device at all.

• Subsequently, the researchers instructed the app developers to come up with a new version in which these problems were resolved. After two months of the intervention period (February 2013), this third version of the MORE Energy app was made available in the Apple app store.

• In the weeks that followed, however, it became clear that the new version of the app was not compatible with the previous version. Nine participants reported that, whenever opening version 3, an error forced the app to close down. It turned out that the only way to solve this problem was to delete the whole app, and to subsequently download and install the new version again. Three weeks after the upload of version 3, all participants of the intervention group were sent an email instructing them to delete the app before installing version 3.

• At the beginning of April 2013 the researchers themselves noticed that on Apple devices, they did not receive any more push alerts, which were designed to improve app usage. Afterwards, it proved very difficult and time consuming for the app developer to find out what caused this problem. It was not before two weeks before the end of the intervention period that the cause of the problem was detected. Consequently, it is assumed that none of the participants with an Apple device has received any kind of reminder or alert during the last three months of the intervention period. The process evaluation showed that the majority (95%) of the participants that consulted the advices were owners of an Apple device.

• Furthermore, it is possible that the participants with an Android device did not receive all reminders either. Although not reported by participants, the researchers who possessed an Android device, experienced that the geofencing reminders, the alerts which were given outside the Netherlands, with a maximum of one alert per four days, were malfunctioning through the
whole intervention period (e.g. they received a reminder when they were at home, or did not receive anything when abroad).

- Other matters that occurred during the intervention period:
  - Because of a wrong setting in a flight schedule upload, the app provided the users with wrong advices for two days after 3.5 months of the intervention period.
  - After 5.5 months, the project website was offline for two days because of a hosting problem.
  - Three participants reported that the app did not work on their tablet with an older operating system. This was resolved after they updated their operating system.
Chapter 10

General discussion
Since ages, workers in certain occupations have been exposed to working hours outside the dusk to dawn barrier. In earlier days, these people were designated antipodes, indicating their opposite way of living (1). After the introduction of the 24-hour economy more and more workers became involved in irregular working hours. Nowadays, it is estimated that about 19% of the workers in western countries work during the night, and 17% is involved in schedules with permanent or rotating shifts (2,3).

In the airline industry companies operate 24 hours a day, for which a large part of their employees are exposed to a variety of irregular working hours and/or time zone crossings. In this thesis, the health risks of the irregular working hours in airline company employees (flight crew members and ground staff employees) were analyzed. We also investigated the effects of a mobile application that was developed to increase health-related behaviour and sleep, and to reduce fatigue in airline pilots. In this final chapter, the main findings of the thesis are presented. Our results are put in a broader perspective, methodological issues are considered, and the implications of our findings for further research and practice are discussed.

OVERVIEW OF THE FINDINGS

Association between exposure to irregular working hours, body weight change and sickness absence

Previous literature studies found associations between irregular working hours and health outcomes such as gastrointestinal, cardiovascular, and metabolic disorders (4-8). Because body weight gain might have a mediating role in the development of some of these disorders, we summarized the available evidence for an association between shift work including night work and body weight change in Chapter 2. In this systematic review, we found strong evidence for a crude relationship between exposure to several types of shift work and an increase in body weight. The evidence, however, proved to be insufficient when lifestyle related confounders were taken into account. These findings emphasize the effects of an altered lifestyle, such as diminished physical activity and unhealthy food intake, which can be the result of working with irregular working hours (9,10).

Next to the health outcomes mentioned above, the association between exposure to irregular working hours and sickness absence has been studied quite often as well (11-15). We performed a systematic review to further clarify this association (Chapter 3) but had to conclude that due to inconsistent findings, inconclusive evidence for an overall association between shift work and sickness absence exists. Evidence was found for an association between fixed evening shifts and long-term sickness absence in female healthcare workers in this review, implying that the association between exposure to irregular working hours and sickness absence might be dependent on the specific work schedule, and the studied working population.
Cumulative exposure to irregular working hours, sickness absence, and occupational accidents

We investigated the association between cumulative exposure to different types of work schedules and sickness absence using data from the MORE cohort consisting of 26,867 employees of an airline company. Among ground staff employees it was found that the employees who changed into a work schedule that included night shifts had an increased risk for long-term sickness absence (>7 days) (Chapter 4). Exposure to other types of shift schedules did not result in an increased risk for long-term sickness absence when indicators for both psychosocial (e.g. responsibility and social interaction), and physical work-related factors (e.g. physical workload and ergonomic factors) were taken into account. Moreover, we did not find an association between the cumulative number of night shifts that the employees were exposed to, and long-term sickness absence either.

Among flight crew members, we found that cumulative exposure to different flight types (short-, medium- and long-haul flights) was not independently associated with long-term sickness absence (>7 days) (Chapter 5). We did find that female cabin crew members reported significantly more occupational accidents than their male colleagues, and that with more exposure to short-haul flights, cabin crew members had a higher risk for occupational accidents. More exposure to long-haul flights, on the other hand, was found to be associated with a reduced risk for experiencing an occupational accident (Chapter 6).

Development and evaluation of an intervention aimed at reducing fatigue in airline pilots

In close collaboration with airline pilots and key management stakeholders, we developed a mobile application and a supporting website that aimed to reduce fatigue in airline pilots (Chapter 7). The MORE Energy intervention, which contained tailored advice on exposure to daylight, sleep, physical activity, and nutrition, was evaluated during six months, among 502 pilots. The intervention was largely implemented as intended, was well received, and the initial compliance was high (Chapter 8). Yet, the compliance during the whole intervention period was low, as the advice on the app was not consulted very often, and the appreciation of the intervention was moderate. The users indicated that the advice was not always easy to apply in daily life, and that it was difficult to adjust their behaviour according to the advice. Nevertheless, 78% of the participants indicated that they would recommend the intervention to their colleagues. Moreover, a majority of the users (65%), was convinced that the mobile application was able to fulfill its purpose; preventing fatigue and improving health. The results of the RCT indicated that the MORE Energy intervention was indeed effective in reducing the primary outcome fatigue and in some of the secondary outcomes related to health-related behaviour (snacking and physical activity) and sleep (sleep quality) (Chapter 9). We did not find statistically significant differences between the intervention and control group on other outcomes, such as need for recovery and health perception.
REFLECTION AND METHODOLOGICAL CONSIDERATIONS

In the next section, the results of the preceding chapters are put in perspective, considering the methodological issues and the findings of previous research. The theoretical model that was presented in the introduction of this thesis, reflecting the health effects of exposure to irregular working hours, is used as guidance (Figure 1).

Figure 1. Theoretical model reflecting the short- and long-term health effects of irregular working hours (light-grey boxes) and the associated factors. The dark grey boxes were shown to be associated with the health effects of irregular working hours in this thesis.
Working situation

In accordance with our theoretical model, we showed that psychosocial (e.g. job strain, social support) and physical (e.g. physical workload, work environment) work characteristics are able to affect the short-term and long-term health effects of workers involved in irregular working hours (Chapters 3 and 4). This emphasizes the relevance of including both these factors while analyzing the association between exposure to irregular working hours and health-related outcomes such as sickness absence (16-18).

Other researchers have indicated that analyzing exposure characteristics of irregular work schedules as specific as possible could further clarify the health effects of exposure to irregular working hours (19,20). Although it was possible to retrieve specific information about the characteristics of individual work schedules using the MORE database, we chose to analyze them at a higher cumulative level (Chapter 4 to 6). In the ground staff employees, the worked schedules that were used varied that much that it was necessary for the analyses to aggregate them. In addition, for flight crew members, little knowledge existed about the prevalence of sickness absence at all, for which we decided to investigate the association between the cumulative exposure to flight types and sickness absence in this specific population first.

Workers’ capacity

The results of this thesis also demonstrated the importance of including determinants of workers’ capacity (individual characteristics, coping strategies, physical and mental fitness, and lifestyle) while analyzing the health effects of irregular working hours. In the systematic review in Chapter 2 it was found that lifestyle-related factors affected the relation between longitudinal exposure to irregular working hours and body weight gain. In addition, we showed that in the studies where the health status of employees was taken into account, most often, no association between irregular working hours and sickness absence was found, as opposed to studies in which no adjustment for health status was made (Chapter 3). The importance of including previous sickness absence, which can also be considered as an aspect of workers’ capacity, was demonstrated in Chapters 4 and 5, as we found that significant associations between exposure to irregular work schedules and sickness absence disappeared when the analyses were adjusted for previous sickness absence.

Factors outside the working situation

We found that male cabin crew members were at lower risk to be involved in a reported occupational accident compared to their female colleagues (Chapter 6). These findings coincide with those of Wong et al. (21) who analyzed a large Canadian cohort, and might be partly explained by a social rather than biological pathway. Female employees with children might for instance experience less social support and more responsibilities at home (22-24), for which they can have
less time to recover from work, contributing to increased fatigue and chronic sleep loss (25). This pathway might work different for male employees; in a predominantly male population, we found that both marital status and having children was associated with a lower risk for long-term sickness absence among ground staff employees (Chapter 4). These findings underline the important role factors outside the working situation, such as household composition and social responsibilities, can have with regards to the tolerance towards irregular working hours exposure, and that the findings can be gender-dependent.

Health effects

Although it is generally thought that exposure to night work (because of chronic circadian disruption and melatonin suppression) is the main cause for major health effects of irregular working hours (26-29), this assumption was not supported when using sickness absence as outcome measure (Chapter 4 and 5). This could be explained by the fact that sickness absence is not a mere indicator of ill health, but that behaviour, coping strategies, and social, economic and psychological processes are involved as well (30,31). Moreover, because sickness absence has been operationalized in two main concepts, the measure is difficult to interpret. On the one hand, long-term sickness absence is thought to be associated with more sickness absence in the future, an increased risk for work disability, and both social and financial problems (30,32-34). Short-term sickness absence on the other hand is thought to represent a behavioural pattern or coping strategy, which can be used by the individual to prevent future illness or absence (35,36). Previous studies used multiple cut-offs for short and long-term sickness absence (Chapter 3), and the optimal cut-offs for both concepts remain unclear. Despite the cut-offs used, it is worthwhile to include both concepts in the analyses, as we showed that exposure to certain work schedules could increase the risk for long-term sickness absence, but lower the risk for short-term sickness absence (Chapter 4).

In the MORE cohort analyses, we used seven consecutive absence days as the cut-off for long-term sickness absence because earlier research had used this operationalization for medically certified sickness absence, and found it to be a predictor for health deterioration and mortality (31,37,38). It cannot be ruled out, however, that besides medical causes, other factors, such as coping, attitude towards work, and psychosocial determinants, also contributed to this outcome measure (30). Earlier studies did show that maladaptation to a new schedule can lead to disturbed sleep, fatigue, and an affected disturbed work-life balance, possibly developing into sickness absence (39-41). This might explain our finding that changing to a new work schedule that included night work resulted in an increased risk for sickness absence, indicating the difficulties employees can have with adapting to rotating shift work (Chapter 4).

Study population

The theoretical model that we presented can be applicable for all kinds of study
populations involved in irregular working hours. However, we did find that the association between exposure to irregular working hours and sickness absence might not only depend on the specific work schedule, but on the studied population of workers as well. As a result of various factors, similar work schedules might have different effects on, for instance, female nurses compared to the effects of such schedules on predominantly male ground staff employees. Accordingly, the (lack of) associations found between work schedule exposure and sickness absence in the airline company employees should not be generalized to all workers involved in irregular working hours (Chapter 4 and 5). Flight crew members, for instance, are part of a relative healthy population who undergo regular medical examinations (42,43). In addition, their specific work schedules, including layovers and the crossings of time zones, are difficult to compare to the work schedules of non-flying employees. Ground staff employees, on the other hand, do represent a wide range of jobs, including both blue and white collar workers, who are exposed to commonly used, rotating shift schedules. However, compared to the general working population in the Netherlands, the analyzed ground staff employees were relatively old (45.4 years vs. 41.0 years), and contained a large percentage of male employees (82%) (44).

It should be taken into account that the healthy worker effect—the result of selection into work (i.e. unhealthy workers are less likely to start to work irregular hours) and selection out of work (i.e. those with health problems are more likely to drop out), leaving the healthiest workers—might have affected our findings to a certain extent. Because we only included workers who were employed during the whole follow-up period, this phenomenon can have further decreased the possibility to generalize the findings of the analyses of the MORE cohort to other populations (Chapters 4 to 6) (45,46). The healthy worker effect can have influenced the overall conclusions of the systematic reviews as well since a large part of the studies that were included did not assess or report information about the work history of the participants (Chapters 2 and 3).

MORE Energy intervention

Besides analyzing the health effects associated with irregular working hours, the MORE Energy intervention, aiming to increase the workers’ capacity and to decrease the adverse health effects of the work schedule exposure of airline pilots, was developed and evaluated in the current thesis. Some strong methodological points of this intervention concern the use of focus groups and stakeholder interviews to determine the intervention strategy, and the testing of the intervention by means of a one-month test phase. Another strong point involves the use of a randomized controlled trial (RCT), the most suitable design for (occupational) intervention research, to evaluate the effects (Chapter 9). Doing so, interfering factors, such as other health initiatives within the company, or seasonal influences, were negligible (47,48). To analyze the outcomes, we used mixed models analyses that took into account all participants with at least one follow-up measurement, which is in accordance with the intention-to-treat principle. We also performed a process evaluation to obtain more insight in the
strength and weaknesses of the intervention and to facilitate the interpretation of the results (Chapter 8).

One of the weaknesses of the intervention study concerns the fact that the compliance of the intervention group participants was rather low (Chapter 8). In addition, although the goal of the intervention was to increase the relevant knowledge of the participants, we decided to exclude the self-developed knowledge questionnaire as a result of a ceiling effect; at baseline and after three months, participants answered most of the questions regarding the fatigue and circadian disruption correctly. Another critical point involves the fact that, as in other web-based or mobile health intervention studies, it was not possible to blind our participants. Therefore, contamination might have occurred through intervention participants who exchanged information, for instance during their flights, in the cockpit. Due to the lack of blinding, the Hawthorne effect cannot be ruled out either. Finally, although it was our intention to have a 12-month follow-up, we decided to reduce the follow-up period to six months as a result of the long development time of the mobile application.

Notwithstanding, the MORE Energy intervention proved to be effective on the primary outcome measure fatigue, as well on some of the secondary outcome measures linked to the topics of the tailored advice (sleep, nutrition and physical activity). Moreover, although the causes for fatigue in crew members involved in long-haul (night flights, time zone crossings) can be different from those of crew members involved in short-haul (e.g. multiple flights per day, successive early wake-ups) (49-51), both groups did significantly benefit from the intervention. In addition, the good general health and relatively high socio-economic status of flight crew members might make it possible to generalize the positive results of the mHealth intervention to similar working populations. Therefore, although we did not find effects on the outcome measures that represented long-term health effects, our results are promising for flight crew members of other airline companies as well.

**IMPLICATIONS FOR RESEARCH**

The next paragraph discusses how future research could further clarify our findings and could shed more light on the mechanisms that link the exposure to irregular working hours and health problems in- and outside the airline industry.

**Cohort studies**

The airline company data enabled us to investigate which type of work schedules were associated with sickness absence and occupational accidents, taking into account objective data on workload and demographic variables. Because we only obtained retrospective data for those employees who were still employed at the start of 2010, there was no information available about the employees who left the company before this date. Therefore, in order to reduce the impact of the healthy worker effect, future studies using large company databases should try
to follow a cohort prospectively as well. Moreover, by composing a subcohort of newly employed employees, these studies might be better able to determine which individuals tolerate different types of work schedules, and which (individual) factors are involved in this selection process.

A prospective cohort would also be helpful to better determine the characteristics of actual worked schedules, in accordance with the recommendations by Stevens et al. (19) and Bøggild (20). In addition, such a cohort enables monitoring the direct effects of interventions that involve adjustments to work schedules within a specific population. In Chapter 4 we found that cabin crew members were at higher risk for experiencing an occupational accident with increasing exposure to short-haul flights. Prospectively, it could be interesting to determine if adjustments to the short-haul schedules (e.g. in duty duration, numbers of flights per day, or workload) could lead to a reduction in fatigue, or an improvement in wellbeing and recovery, thereby reducing the risk for occupational accidents onboard.

Our analyses indicated the importance for future occupational cohort studies to try to take into account data on work-related factors, such as the physical and psychosocial workload, as well. Earlier research already showed that both work demands and workload during irregular working hours can be different from those during day work, and that these factors can have an effect on sleep, fatigue, social life, lifestyle, and body weight (17,52,53). Moreover, variables such as individual lifestyle and coping, physical and mental fitness, or previous sickness absence should also be measured and included in the analyses, as they can confound or modify the association between exposure to irregular working hours, circadian disruption, fatigue, and health outcomes. A recent study showed the importance of including these factors, as the association between exposure to irregular working hours and sickness absence was found to be modified by the body mass index (BMI) of the analyzed employees; only shift workers with a high BMI were at risk for more sickness absence (54). A large part of the health-related variables mentioned are regularly collected through medical examinations or checkups. Therefore, future studies could try to combine the data from these periodic measurements with information that is already available within company databases (e.g. human resource and work schedule records), and with other health-related data from occupational health services (55-57). Before combining the data from these different sources, it is important to carefully take into account the privacy of the individual employees. For the present thesis, therefore, we used an independent occupational physician who coded and combined the different datasets of the MORE cohort first, before the data was anonymized and handed over to the researchers.

It is recommended to use the outcomes of the health checkups as dependent variables while analyzing the health effects of irregular working hour exposure, because they (e.g. BMI, cholesterol, metabolic values) can serve as early indicators for more severe, long-term health problems (e.g. cardiovascular diseases, diabetes). If, as in our cohort, sickness absence is the only health-related
outcome variable available, it is important for the researchers to carefully choose the sickness absence concept they want to analyze; dependent on the research question, one should consider including short-term sickness absence, long-term sickness absence, or both.

Interventions to increase workers’ capacity

To be able to conduct the analyses outlined above, close cooperation between the employer, the occupational health service, and the researchers, is necessary. We showed that a structural collaboration agreement between these three parties can result in meaningful epidemiological research, and can enable interventions, such as the MORE Energy intervention, to be tested among employees. The latter is of particular importance since, up to now, there is a lack of good RCTs that translate the knowledge regarding the reduction of circadian disruption and fatigue obtained in laboratory settings towards the workplace (58). Laboratory-based studies mostly involve either rodents or randomly chosen volunteers, which makes it far from clear if the findings of these studies apply to the “real world” as well (58,59).

The intervention studies that have been performed predominantly focussed on the workers’ capacity of night work employees. Therefore, preventive measures regarding the effects of rotating work schedules should be further explored. In addition, because workers with irregular working hours can have problems to retain a stable work-life balance, future research should also try to find better solutions to reduce the social impact and to maintain a stable work-private life balance (59). In that respect, the positive results on objective and subjective outcomes as a result of interventions that implemented self-scheduling (60,61) and chronotype dependent scheduling (62) are promising.

In addition, educational programs to increase the workers’ capacity to cope with their working hours should be further explored as well. Although we showed that it is possible to reduce fatigue, and improve the sleep quality and health-related behaviour of airline pilots through tailored advice, the findings of MORE Energy should be clarified and confirmed by similar interventions that take into account more objective measurements and comprise a longer follow-up period.

Since a further increase in the usage of mobile devices is expected in the coming years, interventions such as MORE Energy have great potential for both primary and secondary prevention (63). Current technologic developments would make it possible to build a mobile app that measures actual behaviour of the user (e.g. movement, location, exposure to light, or sleep) and subsequently produces behaviour dependent advice that aims to reduce circadian disruption as much as possible. Since smartphones and tablets are used among all layers of society (64), such interventions would be able to reach a broad audience. Yet, it has to be taken into account that transferring knowledge using a mobile app is not necessarily the optimal solution for every target population, as a recent poll in the US showed that smartphone possession and app usage is lower in high age groups and people
with lower socio-economic status (65).

It should also be considered to perform a process evaluation alongside the effect study of the intervention. As we showed that this can improve the interpretation of the results, and objective usage data should be included if possible. On top of this, it would be worthwhile to take into account the cost-effectiveness of such an intervention. As employers have to decide whether or not to invest in health promotion for their employees, a return on investment analysis would give more insight, comparing the costs of the intervention to its financial benefits, in terms of productivity, reduced sickness absence, improved health, and increased sustainable employability (66).

IMPLICATIONS FOR PRACTICE

Health effects of irregular working hours can have considerable consequences for the employee and the employer. Since the working population is aging, these work schedule related health-problems can become even bigger in the upcoming years (67,68). Airline companies, employing a lot of workers involved in irregular working hours, might therefore want to consider the following recommendations regarding improvement of the workers’ capacity and reduction of their workload.

Optimizing work schedules

This thesis showed that the effects of exposure to irregular working hours can depend on the population working with them. These findings could suggest that there is no ‘healthiest work schedule’, but that in the most optimal situation, the work is organized in such a way that it can be performed as healthy and productive as possible by the specific working population (69,70). This optimal situation might be reached when it is achieved in cooperation with the employees who have to work irregularly. Several studies showed that in comparison with forced implementation of a new work schedule, a participatory approach might not only lead to better motivation, but to fewer health complaints, and less sickness absence of the employees involved as well (69,71). During such an approach, both the employer and the employees have to weigh the organizational needs, costs, preferences, and the work schedule related health effects and tolerance issues (72). However, while taking into account the preferences of the involved employees, the scheduling guidelines concerned with circadian disruption and sleep regulation should be applied as much as possible (73,74).

Despite the possible benefits of a participatory approach, the subsequently chosen work schedule still does not necessarily fit all individuals within the working population. It might therefore be interesting for the employer to introduce the possibility for employees to choose a schedule that is in accordance with their individual preference (e.g. chronotype, age, familial responsibilities). For flight crew members concerned with short-haul schedules for instance, some will have no problem to get up very early and therefore prefer flight types that involve early starts, while others will prefer later starts and have no problem arriving at night.
Recent intervention studies found improvements in work-life balance, work performance, and need for recovery after implementing such self-scheduling possibilities, that were within the boundaries of the working time legislation (60,61,75).

A much implemented relieve measure for older employees is refraining them from night work. Although this measure might be beneficial for the health of the older employees themselves, from the employers’ perspective, it might become unsustainable for the production process. In addition, it could impose a disproportionate burden on the younger employees who will have to replace their colleagues during the night, and it does not necessarily suit the individual preferences of every older employee. Self-scheduling, therefore, might result in a more spontaneous distribution and hold part of a solution for the growing number of older workers (76,77).

Improving the working situation

Besides seeking opportunities to optimize the work schedules, the employer could also try to accomplish worksite health promotion, taking into account the interplay between the employee, work environment, and social elements (78,79). Possibilities to achieve such prevention include enabling the employee to exhibit a more healthy lifestyle, for instance by creating facilities at the worksite where employees can be physically active during or after working hours (10). In addition, employers could try to promote healthy nutrition by increasing the availability of healthy food at work during both regular and irregular working hours. It has been shown that such adaptations are able to have positive effects on weight loss, quality of life, and sickness absence (80). In addition, prolonged periods of activity should be alternated with rest-breaks to prevent fatigue and accident risks during and after work (81). For this purpose, the workplace could be improved by creating a resting area, other than the company restaurant, that enables employees to take a short nap during these rest-breaks, or before their commuting ride home (82,83). Finally, the worksite should comprise a healthy and safe lighting situation. Given that bright light at night is counter-indicated as it leads to more circadian disruption in the commonly used rotating schedules, new possibilities imply non-blue light or the filtering of a certain area of the light spectrum, using special goggles (28,59).

Increasing workers’ capacity

The workers’ capacity plays an important role in the health effects that arise from exposure to irregular working hours. It has therefore been recommended to improve the coping strategies and health behaviour of employees through providing relevant information about exposure to light, sleep hygiene, nutrition, and physical activity (79,84,85). We showed that providing scientifically-based, tailored advice can reduce the impact of irregular working hours and accompanying circadian disruption in long-haul and short-haul pilots, suggesting benefits for both the individual and the organization. It should therefore be considered to
implement interventions similar to the MORE Energy intervention for all flight crew members, as a component of fatigue risk management. To increase the chance of the individuals to take their responsibility and actually change their behaviour, implementation of such an intervention could be optimized by integrating it with the work schedules, giving sustained attention to the topic within the currently employed flight crew members, and by introducing the intervention to newly hired employees (85).

As discussed in the previous section, other working populations, such as ground staff employees, might also benefit from advice regarding their lifestyle and coping strategies. Our results indicate that this could be of particular importance when employees start working irregularly or have to adapt to a new rotating shift schedule. In addition, employees who are involved in schedules that do not include night work, but alter between late and early morning hours, should receive similar attention since their working hours can have a significant effect on sleep, fatigue, and productivity as well. To attain the highest possible compliance to an intervention, it is important to determine the optimal method to transfer the relevant information first. Therefore, the needs and wishes of a specific working population should be determined, using for instance a needs analysis or focus group interviews. This kind of analysis could also help to determine the most relevant, practical, and socially acceptable information to provide (given the working hours and the characteristics of the employees). Other factors that could be considered are the inclusion of partners or family members as active participants in the program, the continuous attention for the program (e.g. through internal communication channels), and the permanent accessibility of the information (on- and offline availability) (79).

Prevention through early detection

Despite all possible prevention measures provided, irregular working hours will still lead to problems for some employees. The employer, together with the occupational health service, could try to recognize these employees at an early stage. Once identified, they could be provided with targeted interventions to prevent further problems and future health effects (86,87). Such individual interventions could involve increasing the workers’ capacity (e.g. lifestyle, behaviour) and work-private life balance with the help of a health consultant, or decreasing the workload through altering the individual work schedule. Afterwards, the employees at risk should be monitored for a longer period of time, to find out if their capacity to cope with their working hours has improved.

Because employees with high sickness absence in the past are known to be at higher risk for more sickness absence in the future as well, sickness absence records can be used to identify employees at an early stage (88,89). Managers should try to address the workers’ capacity towards irregular working hours during (regular) bilateral consultations, especially with those employees who just started with a new job or work schedule, and with employees whose situation at home has recently changed. Companies could try to help managers who find
it difficult to conduct such personal interviews, for instance by training them in motivational conversational techniques. Occupational physicians could also help the employer to identify employees at risk by frequently conducting open consultation hours.

Employees at risk could also be identified using the outcomes of health checkups. Flight crew members already undergo regular medical examinations, although these are directed somewhat more towards safety rather than health. The European Working Time Directive, however, states that all European employees involved with night work are entitled to have free regular health checkups aimed at protecting their health (74). Companies could therefore consider to implement these regular checkups for all their employees involved in irregular working hours. The outcomes can lead to better support for the employee, better monitoring of the results of interventions at the workplace, and a better overall understanding of the health effects of exposure to irregular working hours (74). Although it remains the own responsibility of the employee to attend such a health checkup, an extensive publicity and incentive campaign could help to raise the participation rate.

CONCLUSIONS

The ongoing globalization and technological developments ensure that an increasing number of workers are active outside the traditional dawn to dusk barrier, and the once called antipodes are here to stay. This thesis showed that the overall association between exposure to irregular working hours and sickness absence remains unclear. The results of our analyses did indicate that health-related outcomes (sickness absence or occupational accidents) and preferences of irregular working hours can differ between (subgroups of) the studied working populations. In addition, we showed that a mobile application providing tailored advice could reduce fatigue, and improve sleep quality and aspects of health-related behaviour. Besides population-specific optimization of the work schedules and the working situation, we therefore recommend to provide employees involved in irregular working hours with target population-specific, tailored advice, in order to improve their workers’ capacity (e.g. coping strategies and health behaviour) and to reduce the potential adverse health effects of their irregular working hours.
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Summary
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SUMMARY

In Europe and the US, about 19% of the workforce has to work during the night, while 17% is involved in schedules with permanent or rotating shift schedules. These irregular working hours disturb the circadian rhythm and sleep/wake pattern of the workers, and can interfere with their social life and work-family balance. On the short-term, irregular working hours have been shown to lead to fatigue, sleep loss, and digestive disturbances. More chronic health effects include gastrointestinal, reproductive, metabolic and cardiovascular disorders. Both short- and long-term health effects are thought to be determined by a combination of factors: work schedule characteristics and working conditions (working situation); familial and social responsibilities (factors outside work); and personal characteristics, physical and mental fitness, coping strategies and lifestyle (workers’ capacity) (Chapter 1).

Research with company databases, containing objective data on work-related and individual factors, might further clarify the association between specific work schedules and health outcomes. In addition, it should be determined if especially developed interventions are able to support employees involved in irregular working hours. This would be of special interest for airline companies who have to operate 24 hours a day. A large part of their employees are exposed to a variety of irregular working hours and/or time zone crossings, possibly contributing to an increased sickness absence, and a loss in productivity. The first objective of this thesis was therefore to better determine the health effects of exposure to irregular working hours in the airline industry, by investigating the associations between cumulative exposure to irregular working hours and adverse work-related health outcomes, such as sickness absence and occupational accidents, within an airline company. The second objective was to increase the workers’ capacity and reduce the impact of exposure to irregular working hours, by developing and evaluating an intervention aimed at reducing fatigue, and improving the health-related behaviour of airline pilots.

In the first section of this thesis, the current status of the scientific literature regarding the association between exposure to irregular working hours and two health outcomes were summarized. Chapter 2 presented a systematic review in which the available evidence for an association between shift work including night shifts and body weight change was analyzed. A systematic search strategy was performed on longitudinal studies, after which the methodological quality was assessed by a standardized quality checklist, and the results were summarized using a levels of evidence synthesis. The results showed that there was strong evidence for a crude relationship between exposure to several types of shift work and an increase in body weight. This evidence proved to be insufficient when health-related confounders such as age, gender, body weight and physical activity were taken into account. These findings implicate that altered health-related factors, which could be the result of working irregularly, influence the association between exposure to irregular working hours and body weight gain.
In Chapter 3, we systematically reviewed the literature to clarify the association between exposure to irregular working hours and sickness absence. A systematic search strategy on observational studies was performed after which the selected relevant articles were scored on methodological quality. The studies were categorized according to shift work characteristics and summarized using the levels of evidence synthesis. Due to inconsistent findings, there was no evidence for an association between different types of shift work and sickness absence. Evidence was found for an association between fixed evening shifts and long-term sickness absence in female healthcare workers. These findings imply that the association between exposure to irregular working hours and sickness absence depends on both the work schedule and the studied working population.

In the second section of this thesis, we analyzed the MORE (Monitoring Occupational Health Risks in Employees) cohort, a five-year historic cohort consisting of all workers employed at an internationally operating airline company at January 1, 2010. The cohort data comprised all work and human resource records of the employees since January 1, 2005, combined with sickness absence and occupational accident data, provided by the occupational health service of the airline company. Chapter 4 described a study that involved the ground staff employees of the MORE cohort, analyzing the association between cumulative exposure to different types of shift schedules, the number of night shifts, and sickness absence. For each of the 7,652 included employees, work schedules and sickness absence days during 2005 to 2009 were obtained. Sickness absence outcome measures were long-term sickness absence (>7 consecutive sickness absence days), and the number of sickness absence episodes during 2009. The associations of exposure to different shift schedule types, and to cumulative night shifts during 2005 to 2008, with the sickness absence outcome measures were determined using logistic and Poisson regression analyses. It was found that employees who changed into a work schedule that included night shifts had an increased risk for long-term sickness absence (>7 days). Exposure to other types of shift schedules did not result in an increased risk for long-term sickness absence, when indicators for both psychosocial and physical work-related factors were taken into account. In addition, no significant association between exposure to night shifts and long-term sickness absence was found. Compared to day workers, shift work employees showed a lower risk for more sickness absence episodes. Subgroup analyses did show that employees who were single and employees without children had an increased risk for long-term sickness absence when their shift schedule was changed and when they worked in a two-shift schedule. Among other, the results of this study imply that work schedule changes can be associated with more sickness absence, possibly induced by adjustment problems of the employee.

In Chapter 5, the association between cumulative exposure to flight types and sickness absence among both cockpit and cabin crew members was described. The study population consisted of 8,228 flight crew members from the MORE cohort. For each employee, all flight schedules and sickness absence days from 2005 to 2009 were obtained. The flights involved in the schedules were classified into night flights, and short-, medium-, and long-haul flights. The associa-
tions between the cumulative exposure to the flight types during 2005 to 2008 and sickness absence episodes of more than seven days in 2009 were determined using univariate and multivariate logistic regression analyses. We found that cumulative exposure to the different flight types was not independently associated with sickness absence when previous sickness absence was taken into account. The results imply that flight type exposure can not explain sickness absence in flight members. To prevent future sickness absence, strategies targeted at flight crew members with a history of high sickness absence may be effective.

Chapter 6 described a study in which the association between cumulative flight schedule exposure and occupational accidents among cabin crew members was analyzed. The study population consisted of 6,311 cabin crew members. For each employee, all flight schedules from 2005 to 2008, and registered occupational accidents in 2009, were collected. The association between the cumulative exposure to different flight types and the occurrence of occupational accidents was determined using logistic regression analyses. It was found that female cabin crew members reported significantly more occupational accidents than their male colleagues, and that with more exposure to short-haul flights, cabin crew members had a higher risk for occupational accidents. On the other hand, more exposure to long-haul flights was associated with a reduced risk for experiencing an occupational accident. The increased risk as a result of short-haul schedules may be caused by the specific characteristics of short-haul flights, and future research should focus on possible underlying mechanisms.

The third section of this thesis focused on the development and evaluation of a mobile health intervention (MORE Energy), aiming to reduce fatigue and improve health of airline pilots. Chapter 7 described the development of the intervention that consisted of tailored advice on exposure to (day)light, sleep, physical activity, and nutrition. It was decided to provide the MORE Energy intervention through a mobile application, supported by a website, as a result of focus group interviews with a representative sample of pilots, and interviews with key management stakeholders. The advice that aimed to reduce fatigue and circadian disruption as much as possible was evidence-based, and discussed with experts in the field of chronobiology, physical activity, and nutrition. In addition, the advice was tailored to flight schedules and personal characteristics. Personal characteristics that were used to tailor the advice were job title (captain, first officer, second officer) and chronotype (morning vs. evening type). Flight schedule characteristics that were used included haul type (short-haul vs. long-haul), flight direction (neutral, eastward, westward), departure time (morning, afternoon, evening/night), arrival time (morning, day, night), return time (morning, afternoon, evening/night), and the number of time zones crossed (<4 vs. ≥4). The intervention group participants were advised to either hold on to the home based time, or to adjust to the local time, depending on the length of the layover (<48 hours vs. >48 hours). The MORE Energy app enabled users to switch manually between the advised time (local or home-based), depending on their personal preference and situation.
Chapter 8 presented the process evaluation of the intervention. This evaluation was performed to get more insight in barriers and facilitators, strengths and weaknesses of the implementation of the MORE Energy intervention, and to facilitate the interpretation of the results of the effect study. The outcomes that were determined were reach, dose delivered, compliance, fidelity, satisfaction, barriers and facilitators, and adherence. The evaluation showed that the intervention was largely implemented as intended, and that it was well received. Of the participants, only 19% never used any advice on either the app or the website. Yet, the compliance during the whole intervention period was low; only 17% of the intervention group participants consulted the advices for more than four weeks. The appreciation of the intervention was moderate, users indicated that the advices were not always easy to follow up in daily life, and that it was difficult to actually change their behaviour. Nevertheless, 78% of the participants indicated that they would recommend the intervention to their colleagues. Moreover, 65% of the users were convinced that the intervention was able to fulfill its purpose; preventing fatigue and improving their health.

In Chapter 9, the effects of the randomized controlled trial on health-related behaviour, fatigue, sleep, and health perception among 502 airline pilots were presented. After randomization, the intervention group was given access to the MORE Energy app with tailored advice, and to the website with background information. The control group was directed to a website with standard fatigue-related information. The outcomes were measured through online questionnaires at baseline and at three and six months after baseline. The effectiveness of the intervention was determined using linear and Poisson mixed model analyses. The results showed that the MORE Energy intervention was effective in reducing the primary outcome fatigue and in improving some of the secondary outcomes related to sleep (sleep quality) and health-related behaviour (snacking behaviour and the amount of physical activity). Other outcomes related to health-related behaviour, sleep, and health perception did not show statistically significant improvements. The results of the trial imply that it is possible to effectively support flight crew members who have to cope with irregular working hours and the crossing of time zones by providing tailored advice through an mHealth intervention.

In the General Discussion (Chapter 10), the main findings of this thesis were presented and put in a broader perspective, considering the methodological issues and the findings of previous research. Recommendations for future research and implications for practice were provided as well. Regarding our first objective, we did not find clear overall associations between work schedule characteristics and sickness absence. Our findings emphasized the influence of the health status and a possible altered lifestyle of the employees. In addition, they indicated that adverse health effects and preferences of irregular working hours can differ between (subgroups) of the studied working population. We therefore recommended to include psychosocial and physical work factors, determinants of workers’ capacity (individual characteristics, coping strategies, physical and mental fitness, and lifestyle), and factors outside the working situation (work-life balance and social responsibilities) while analyzing the health effects of irregular working hours in
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future studies. We think that more structural collaboration between companies, occupational health services, and research institutes could enable such meaningful epidemiological research.

These collaborations make it possible to study more interventions in real life work settings as well. The second aim of this thesis was to develop and evaluate such an intervention, aimed at reducing fatigue, and improving health of airline pilots. The results of the randomized controlled trial showed that a mobile application providing tailored advice could reduce fatigue, and improve health-related behaviour and sleep quality. We therefore recommended airline companies to try to optimize the work schedules, improve the working situation, and to increase the workers’ capacity of both flight crew members and ground staff employees. The latter could be possible through implementing interventions similar to MORE Energy, providing scientifically-based, tailored advice about exposure to light, sleep, nutrition, and physical activity. Since the detrimental health-effects of prolonged exposure to irregular working hours concern employees outside the airline industry just as well, these kinds of target population-specific interventions might also be beneficial for working populations in other industries.
SAMENVATTING

Een groot aantal mensen heeft te maken met onregelmatige werktijden. De 24-uurs economie en de toenemende internationale betrekkingen hebben er mede voor gezorgd dat nog maar 25% van de werkende populatie Europa en de Verenigde Staten reguliere “negen tot vijf” werktijden heeft. Het is bovendien gebleken dat 19% van de werkenden regelmatig tijdens de nacht werkt, en 17% te maken heeft met een bepaalde vorm van ploegendiensten. Verscheidene onderzoeken hebben aangetoond dat onregelmatige werktijden de biologische klok (het circadiane ritme) en het slaap/waak patroon verstoren en daardoor tot gezondheidsproblemen kunnen leiden. Onregelmatige werktijden kunnen daarnaast ook van invloed zijn op het sociale leven en de werk-privé balans. De gerapporteerde korte termijn effecten van het werken met onregelmatige werktijden zijn vermoeidheid, slaapgebrek en spijsverteringstoornissen. Op de langere termijn zijn onder andere associaties gevonden met aandoeningen aan het maag-darmstelsel, en het reproductieve, metabole en cardiovasculaire systeem. Omdat niet iedereen die onregelmatig werkt ook daadwerkelijk gezondheidsklachten krijgt zijn wetenschappers van mening dat klachten mede beïnvloed worden door een combinatie van de volgende factoren: de kenmerken van het werkschema en andere belastende factoren op het werk (de werksituatie); de sociale verplichtingen en werk-privé balans (factoren buiten het werk); en persoonskenmerken, lichamelijke en mentale fitheid, coping-strategieën en leefstijl (belastbaarheid van het individu) (Hoofdstuk 1).

Om de gezondheidseffecten van het werken met onregelmatige werktijden beter te bepalen is er meer onderzoek nodig. Zulke onderzoeken kunnen worden uitgevoerd met behulp van werk- en persoonsgerelateerde gegevens die algemeen beschikbaar zijn bij (grote) bedrijven. Het is eveneens belangrijk om te onderzoeken of er interventies kunnen worden ontwikkeld die voorkomen dat het werken met onregelmatige werktijden tot gezondheidsklachten leidt. De uitkomsten van beide vormen van onderzoek zouden in het bijzonder van belang kunnen zijn voor de luchtvaartindustrie, waarvan de 24-uurs operatie een groot gedeelte van de werknemers blootgesteld wordt aan onregelmatige werktijden en/of tijdzoneoverschrijdingen. De eerste doelstelling van dit proefschrift was dan ook om de gezondheidseffecten van de specifieke werktijden binnen een luchtvaartmaatschappij beter te bepalen. Daartoe werden de associaties tussen cumulatieve blootstelling aan onregelmatige werktijden, ziekteverzuim en arbeidsongevallen onderzocht. De tweede doelstelling was om te achterhalen of het mogelijk was om het effect van onregelmatige werktijden op gezondheid terug te dringen. Daartoe werd een interventieprogramma met als doel de fitheid en gezondheid van piloten te bevorderen, ontwikkeld en vervolgens geëvalueerd.

In het eerste deel van dit proefschrift wordt de huidige wetenschappelijke kennis met betrekking tot het verband tussen blootstelling aan onregelmatige werktijden en twee gezondheidsgerelateerde uitkomsten samengevat. Hoofdstuk 2 beschrijft een systematische review naar het verband tussen werken in ploegendiensten
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(inclusief nachtdiensten) en een verandering in lichaamsgewicht. Met behulp van een systematische zoekstrategie werden studies met een longitudinale opzet (prospectief of retrospectief) verzameld, waarna de methodologische kwaliteit van deze studies werd bepaald door middel van een gestandaardiseerde checklist. De resultaten van deze studies zijn samengevat met een ‘levels of evidence’ synthese. We vonden sterk bewijs voor een relatie tussen blootstelling aan onregelmatige werktijden en een toename van lichaamsgewicht. Echter, wanneer er rekening werd gehouden met de invloed van verstorende variabelen zoals leeftijd, geslacht, lichaamsgewicht en fysieke activiteit, bleek er onvoldoende bewijs te zijn voor deze relatie. Deze uitkomst impliceert dat het ouder, zwaarder, en fysiek minder actief worden van werknemers met onregelmatige werktijden een belangrijke rol kan spelen in de relatie tussen blootstelling aan het werk en een toename van het lichaamsgewicht.

In Hoofdstuk 3 hebben we eveneens door middel van een systematische review het bewijs voor een verband tussen blootstelling aan onregelmatige werktijden en ziekteverzuim samengevat. De observationele studies die werden gevonden als gevolg van de systematische zoekstrategie werden gescoord op methodologische kwaliteit. Vervolgens werden de studies gecategoriseerd op basis van het type roosters waar onderzoek naar werd gedaan (bijvoorbeeld roterende wisseldiensten of vaste nachtdiensten) en werden de resultaten aan de hand van deze categorieën samengevat door middel van de ‘levels of evidence’ synthese. Er bleek geen bewijs te zijn voor een generiek verband tussen het werken met onregelmatige werktijden en ziekteverzuim. Er werd wel een verband gevonden tussen het vast werken in avonddiensten door vrouwelijke medewerksters in de gezondheidszorg en langdurig verzuim. De uitkomsten impliceert dat de associatie tussen blootstelling aan onregelmatige werktijden en ziekteverzuim niet alleen afhangt van het roostertype maar ook van de populatie die hieraan wordt blootgesteld.

hadden op langdurig verzuim in 2009. Een toename van het aantal gewerkte nachtdiensten bleek niet geassocieerd te zijn met langdurig ziekteverzuim. Werknemers met onregelmatige werktyd bleken wel een lager risico op meer ziekmeldingen te hebben in vergelijking met werknemers die alleen overdag werkten. De uitkomsten van deze studie impliceren dat het wisselen tussen een type rooster kan bijdragen aan verzuim, mogelijk veroorzaakt door aanpassingsproblemen van de betreffende medewerker. Begeleiding van werknemers die in een ander type rooster gaan werken zou daarom op zijn plaats kunnen zijn.

**Hoofdstuk 5** beschrijft een onderzoek naar het verband tussen de cumulatieve blootstelling aan verschillende vluchttypen en ziekteverzuim bij het vliegend personeel (cabine- en cockpitpersoneel) van het MORE cohort. Van 8.228 personeelsleden werden de vluchtschema’s en dagen ziekteverzuim tussen 2005 en 2009 verzameld. Er werd onderscheid gemaakt tussen nachtvluchten, short-haul vluchten (korter dan 4uur), medium-haul vluchten (tussen 4 en 8 uur) en long-haul vluchten (langer dan 8 uur). De statistische analyses toonden aan dat cumulatieve blootstelling aan de verschillende vluchttypen tussen 2005 en 2008 niet onafhankelijk geassocieerd was met ziekteverzuim van meer dan 7 dagen in 2009, nadat er gecorrigeerd was voor verzuim in het verleden. De uitkomsten impliceren dat blootstelling aan bepaalde vluchttypen niet van invloed is op het ziekteverzuim van vliegend personeel. Om ziekteverzuim van deze doelgroep te voorkomen zouden preventieve strategieën zich meer kunnen richten op vliegend personeel met veel verzuim in het verleden.

In **Hoofdstuk 6** wordt een studie naar het verband tussen cumulatieve blootstelling aan de verschillende vluchttypen en arbeidsongevallen bij cabinepersoneel gepresenteerd. De onderzoekspopulatie bestond uit 6.311 cabinepersoneelsleden uit het MORE cohort. Voor elk van deze werknemers werden de vluchtschema’s en geregistreerde arbeidsongevallen tussen 2005 en 2009 verzameld. De uitgevoerde logistische regressie analyses toonden aan dat vrouwelijke cabinepersoneelsleden significant meer arbeidsongevallen rapporteerden dan hun mannelijke collega’s. Daarnaast werd gevonden dat cabinepersoneelsleden een groter risico op een arbeidsongeval in 2009 hadden naarmate men meer blootgesteld was aan short-haul vluchten tussen 2005 en 2008. Meer blootstelling aan long-haul vluchten daarentegen was geassocieerd met een lager risico op een arbeidsongeval. De uitkomsten kunnen mogelijk verklaard worden door de specifieke werkzaamheden tijdens short-haul vluchten en de kenmerken van short-haul schema’s, al is er meer onderzoek naar de onderliggende mechanismen nodig voordat hier conclusies uit getrokken kunnen worden.

Het derde en laatste deel van dit proefschrift richt zich op de ontwikkeling en evaluatie van MORE Energy. Het interventieprogramma had als doel de fitheid en gezondheid van piloten te bevorderen. In **Hoofdstuk 7** wordt de ontwikkeling van MORE Energy beschreven. De interventie bestond uit advies op maat met betrekking tot de onderwerpen blootstelling aan (dag)licht, slaap,
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fysieke activiteit en voeding. Naar aanleiding van focusgroep interviews met de doelgroep en gesprekken met verschillende stakeholders, werd besloten om de adviezen te verstrekken met behulp van een mobiele applicatie (app), ondersteund door een website met achtergrondinformatie. De advisering op maat was er op gericht de verstoring van de biologische klok en de vermoeidheid van de piloten zoveel mogelijk te beperken. De inhoud van de adviezen was gebaseerd op wetenschappelijke kennis en afgestemd met deskundigen op het gebied van chronobiologie, fysieke activiteit en voeding. De advisering werd op maat aangeboden aan de hand van de vluchtschema’s en de persoonlijke kenmerken van de piloten. De persoonlijke kenmerken die werden gebruikt waren: functie (captain, first officer en second officer) en chronotype (ochtendmens vs. avondmens). De kenmerken van de vluchtschema’s waar de adviezen op werden gebaseerd waren: type (short-haul vs. long-haul), richting (neutraal, westwaarts, oostwaarts), vertrektijd van de heenvlucht (ochtend, middag, avond/nacht), tijdstip van aankomst (ochtend, dag, nacht), vertrektijd van de terugvlucht (ochtend, middag, avond/nacht) en het aantal overschreden tijdzones. In het geval dat het verblijf op locatie korter dan 48 uur was werd de gebruiker geadviseerd om zoveel mogelijk het Nederlandse ritme aan te houden. In het geval het verblijf op locatie langer dan 48 uur duurde werd de gebruiker geadviseerd zich aan te passen aan de lokale tijd.

In Hoofdstuk 8 wordt de procesevaluatie van de MORE Energy interventie beschreven. Een procesevaluatie wordt doorgaans uitgevoerd om de resultaten van een studie beter te kunnen interpreteren en om inzicht te krijgen in de belemmerende en bevorderende factoren, de sterke en zwakke punten van de implementatie van de interventie, en de mate waarin de deelnemers de interventie hebben gevolgd en gewaardeerd. De resultaten van de procesevaluatie toonden aan dat MORE Energy grotendeels volgens plan was uitgevoerd en dat deelnemers op de voorgenomen wijze toegang tot de app en de website hadden gekregen. Bovendien bleek dat een groot deel van de deelnemers van de interventiegroep (81%) op enig moment gebruik had gemaakt van de app of de website. De mate waarin men tijdens de gehele onderzoeksperiode van zes maanden gebruik van de advisering had gemaakt (compliance) bleek echter laag te zijn; 17% van de deelnemers raadpleegde de app of website gedurende vier weken of meer. De waardering voor de interventie was middelmatig, de deelnemers gaven een gemiddeld cijfer van 6.4. De deelnemers gaven aan dat de advisering soms lastig op te volgen was in hun dagelijks leven en dat het moeilijk was om hun gedrag daadwerkelijk aan te passen aan de hand van de adviezen. Toch gaf 78% van de deelnemende piloten aan dat ze de interventie aan hun collega’s zouden aanraden. Daarnaast gaf 65% van de deelnemers aan overtuigd te zijn dat de interventie daadwerkelijk de fitheid en gezondheid van vliegers kon bevorderen.

In Hoofdstuk 9 worden de effecten van het onderzoek naar MORE Energy op de uitkomstmaten fitheid, slaap, leefstijl en gezondheid beschreven. In totaal deden 502 piloten mee aan het onderzoek (22% van de totale populatie). De geïncludeerde piloten werden via loting verdeeld over de interventiegroep die beschikking kreeg over de MORE Energy app en website, en de controlegroep
die werd verwezen naar een website met algemene, aan het onderwerp gerelateerde achtergrondinformatie. Bij het begin van het onderzoek en na drie en zes maanden kregen alle deelnemers een online vragenlijst toegestuurd. De vragenlijst werd door 405 deelnemers (80,7%) ingevuld en door 390 deelnemers (77,7%). Uit de resultaten bleek dat de interventiegroep na zes maanden significant beter scoorde dan de controlegroep op de voornaamste uitkomstmaat van het onderzoek, fitheid. Daarnaast bleek ook de slaapkwaliteit en de mate van fysieke activiteit van de deelnemers uit de interventiegroep te zijn toegenomen en bleken deze deelnemers minder snacks te eten in vergelijking met hun collega’s uit de controlegroep. De andere uitkomstmaten met betrekking tot leefstijl, slaap en algemene gezondheid bleken niet significant te zijn veranderd. De uitkomsten van het onderzoek impliceren dat het mogelijk is om met behulp van advies op maat, toegepast via een app, vliegend personeel effectief te ondersteunen tijdens de omgang met hun onregelmatige werkmaten en tijdzone overschrijdingen.

Tot slot worden in Hoofdstuk 10 de voornaamste bevindingen van dit proefschrift gepresenteerd en in een breder, maatschappelijk perspectief geplaatst. Dit hoofdstuk bevat bovendien aanbevelingen voor toekomstig onderzoek en implicaties voor gezondheidsbevordering van werknemers met onregelmatige werktijden. We hebben in dit proefschrift geen duidelijk verband gevonden tussen blootstelling aan bepaalde typen roosters of vluchten en ziekteverzuim. Onze bevindingen onderstreepten wel de invloed van gezondheid en van leefstijlfactoren die kunnen veranderen als gevolg van het werken met onregelmatige werkmaten. Daarnaast bleek dat de gezondheidsgerelateerde effecten van blootstelling aan onregelmatige werktijden af kan hangen van de werkende populatie die wordt onderzocht. Mede daarom wordt aangeraden om in toekomstig onderzoek naar de gezondheidseffecten van werk met onregelmatige werkmaten de invloed van psychosociale en fysieke blootstelling op het werk, determinanten van de belastbaarheid van de werknemer (zoals coping en fysieke en mentale fitheid) en factoren buiten het werk om (zoals de werk-privé balans) op een juiste manier te includeren. Zulke onderzoek kan, net als het onderzoek in dit proefschrift, mogelijk gemaakt worden door een structurele samenwerking tussen een bedrijf, een arbodienst en een onderzoeksinstituut. Een dergelijke samenwerking maakt het tevens mogelijk om interventies ter bevordering van de gezondheid van medewerkers met onregelmatige werkmaten in de praktijk te toetsen. Bij deze wijze werd in dit proefschrift een interventie getest bij een grote groep piloten. De uitkomsten lieten zien dat het mogelijk is om met behulp van advies op maat, toegepast via een app, fitheid, slaapkwaliteit en leefstijl te bevorderen.

Advisering met betrekking tot blootstelling aan licht, slaap, voeding en fysieke activiteit lijkt dan ook een goede manier om de belastbaarheid van werknemers met onregelmatige werkmaten te bevorderen en negatieve gezondheidseffecten te voorkomen. We bevelen luchtvaartmaatschappijen (maar ook bedrijven in andere bedrijfstakken waarin met onregelmatige werkmaten gewerkt wordt) aan om, naast het optimaliseren van de roosters en de werkomgeving, deze informatie structureel aan het personeel aan te bieden, rekening houdend met de
wensen en behoeften van de specifieke doelgroep.
ABOUT THE AUTHOR

Alwin van Drongelen was born in Axel (Zeeuws-Vlaanderen), the Netherlands, in 1980. After successfully finishing VWO at the ZSC College in Terneuzen in 1998, he started studying Human Movement Sciences at the VU University in Amsterdam. While he obtained his master’s degree in 2004, Alwin also studied Physical Therapy at the Hogeschool Utrecht, and graduated in 2006.

During 2005 and 2006, he worked as a research assistant at the EMGO+ Institute for Health and Care Research, VU University Medical Center, Amsterdam. At the end of 2006, Alwin started working at the occupational health service ArboNed. Halfway 2007 he was employed as health consultant by KLM Health Services at Schiphol Airport. In February 2009, Alwin started his PhD at the department of Public and Occupational Health at the VU University Medical Center, on the effects of irregular working hours in the airline industry. During his PhD, Alwin remained working at KLM Health Services for one day a week and was involved in many projects concerned with the irregular working hours, lifestyle and physical workload of KLM employees. Meanwhile, he obtained a master’s degree in Epidemiology after following the Postgraduate Epidemiology Program at the VU University Medical Center, and held several oral presentations at international congresses. As of February 2014, Alwin is working fulltime for KLM Health Services again, as a occupational health consultant and project manager.

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LIST OF PUBLICATIONS

International publications


National publications


International presentations


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DANKWOORD

“Dit is een goed stel hoor!” (Evert ten Napel, 1988)

Vijf jaar durend empirisch onderzoek met mezelf als proefpersoon heeft aangetoond dat het dankwoord het meest gelezen onderdeel van een proefschrift is. En dat is niet voor niets. Het uiteindelijke promoveren mag dan wel een sologeburtenis zijn, de weg ernaartoe wordt bepaald door de steun, inzet en hulp van anderen.

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“En dan houden we er mee op, hier in Amsterdam.” (Hugo Walker, 1998)