Rotating shift work and colorectal cancer among nurses and midwives: a cross-sectional study

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Conflict of interest
Authors declare no conflict of interest.

KEY WORDS
Rotating shift work, shift work, colorectal cancer, colon cancer, nurses, midwives

ABSTRACT

Objective
The main aim of this study was to explore any association between colorectal cancer (CRC) and rotating shift work in nurses and midwives. The secondary aim of this study was to identify risk factors for CRC in nurses and midwives who are rotating shift workers.

Design
Cross-sectional study.

Setting
Electronic survey of participants from Australia, New Zealand and the United Kingdom.

Subjects
A sample of 8,199 male and female nurses and midwives from Australia, New Zealand and the United Kingdom invited through their registration papers or newsletter advertisement.

Main outcome measure
Prevalence of CRC in participants who have worked rotating shifts for 1-14 years or ≥15 years compared to participants who have never worked rotating shifts. In addition, risk factors for CRC in the rotating shift work population were analysed in a multivariate logistic regression model in order to obtain odds ratio of CRC.

Results
No statistically significant difference was found in the prevalence of CRC between those who have never worked rotating shift work, worked 1-14 years and worked 15 or more years.

Among rotating shift workers, diabetes was associated with a 123-fold (95% CI 39-392; $p<0.001$) increased odds of CRC, while Inflammatory Bowel Disease (IBD) was associated with a 190-fold (95%CI 68-526; $p<0.001$) increased odds of CRC. Screening colonoscopy or sigmoidoscopy for CRC was associated with a 10-fold (95% CI 3-35; $p<0.001$) increased odds of being diagnosed with CRC.

Conclusion
No significant association was found between rotating shift work and colorectal cancer in nurses and midwives. In nurses and midwives who are rotating shift workers, diabetes, IBD and CRC screening significantly increased the odds of CRC.

INTRODUCTION

The twenty-four hour nature of healthcare demands many nurses and midwives work in shifts. Around 40% of nurses and midwives work rotating shifts (Holland et al 2012). Rotating shift work involves shifts that vary regularly between morning, afternoon and night (International Labour Office 2004). Shift work can have deleterious effects on nurses' physical, mental, and social wellbeing (Matheson et al 2014). In recent times, there has been a growing interest in research on the association between shift work and cancer. The International Agency for Research on Cancer in 2007 classified shift work involving circadian disruption as a probable carcinogen (International Agency for Research on Cancer 2007). A number of possible mechanisms have been proposed to explain the suggested carcinogenicity of shift work. Light exposure at night supresses melatonin, a hormone that regulates sleep-wake cycle and appears to have oncostatic effects (Hill et al 2015; Stevens and Zhu 2015). Circadian disruption may affect clock-related gene expression in cells which may lead to tumourgenesis (Masri et al 2015; Kelleher et al 2014).

A recent meta-analysis investigating night shift work and colorectal cancer (CRC) by Wang et al (2015) found odds of CRC is increased by 11% (OR=1.11, 95% CI 1.03–1.20) for every five years of night shift work. Two studies on the association between rotating shift work and CRC among nurses have been conducted in the Nurses' Health Study. Firstly, Schernhammer et al (2003) prospectively followed up a cohort from the Nurses' Health Study between 1988 and 1998. They found a 35% (RR=1.35, 95% CI 1.03-1.77) increased risk of CRC in nurses who worked rotating shifts for 15 or more years in a multivariate hazard ratio analysis. The second study investigated all-cause and cause-specific mortality, including CRC, of nurses from Nurses' Health Study between 1988 and 2010 (Gu et al 2015). They found an increase in CRC mortality and rotating shift work, but when adjusted for a number of variables, the result was not statistically significant.

A meta-analysis by Johnson et al (2013) found a number of risk factors associated with CRC. These were inflammatory bowel disease (IBD), family history, increased BMI, red meat intake, cigarette smoking, low physical activity, and low fruit and vegetable consumption. CRC is the second leading cause of cancer death and it is amongst the top ten leading causes of death in Australia (Australian Bureau of Statistics 2015). Therefore, it is vital to conduct epidemiological studies to investigate the possible link between shift work and CRC. The primary aim of this cross-sectional study is to explore any association between CRC and rotating shift work among nurses and midwives. The secondary aim is to identify prevalence of other risk factors for CRC in this population.

METHODS

This cross sectional study utilised self-reported data from Nurses and Midwives e-cohort Study (NMeS). NMeS was an internet-based longitudinal study designed to examine health and workforce factors in nurses and midwives. The present study uses survey 1 from that cohort study. This survey collected data from nurses and midwives from Australia, New Zealand and the United Kingdom (UK). The survey was opened from 1st April 2006 to 31st March 2008. In Australia and New Zealand, nurses and midwives received their invitations along with annual registration papers. In the UK, potential participants were invited through an advertisement in the UK Nursing and Midwifery Council's quarterly newsletter. The participants were directed to a website (http://www.e-cohort.net), where consent, and demographic and work details were obtained. The survey contained various instruments, and answering each question was voluntary. Participants were given a unique ID and were not identifiable in the data analysis. Data collection and management of NMeS are described in papers by Schluter et al (2011) and Huntington et al (2009).

The outcome variable was a self-reported diagnosis of CRC. The participants were asked *"have you ever been professionally diagnosed with colon or rectal cancer?"* for which they could answer either yes or no.

The exposure variable was rotating shift work. The participants were asked "what is the total number of years during which you worked rotating shifts?" Available answers were – never, 1-2 years, 3-5 years, 6-9 years, 10-14 years, 15-19 years, or 20 or more years. For the primary analysis of this study, these were categorised into 3 variables as never, 1-14 years, and 15 or more years. These categories reflect those used in a similar study by Schernhammer et al (2003).

A number of covariates were included. These were age, gender, menopausal status, ever use of oral contraceptives (OC), BMI, smoking, alcohol consumption, red meat intake, vegetable intake, fruit intake, physical activity, sleep duration, family history of CRC, diabetes, IBD and screening colonoscopy or sigmoidoscopy. BMI was calculated from height and weight provided by participants. Smoking status was classified as current smoker, former smoker and never smoker. Pack years were calculated from the number of cigarettes per day multiplied by the number of years smoked, divided by 20. Pack year data was only available for current smokers. Alcohol intake was calculated based on a food frequency questionnaire adapted from Willett et al (1985). Participants provided frequency of consumption for alcoholic beverages - light beer, heavy beer, red wine, white wine, and spirits. This frequency was multiplied by alcohol content of each beverage to derive daily consumption of alcohol. Red meat intake, vegetable intake and fruit intake were extracted from Australian Recommended Food Score (ARFS) (Collins et al 2008) where participants answered yes or no to 74 items relating to diet. Red meat intake variable was derived as having had any of veal, beef, lamb or pork 1-4 times per week which were individually selected by participants as part of ARFS. Data regarding other types of red meat were not available from ARFS. Physical activity was calculated using the long form version of International Physical Activity Questionnaire (IPAQ) (Craig et al 2003). This questionnaire surveys respondents' physical activity from a range of domains such as time spent in leisure, transport, job, and domestic/garden work. Metabolic equivalent of tasks (MET) is the amount of oxygen consumed while sitting at rest. Multiples of MET provide the energy cost of physical activities as multiples of basal metabolic rate at rest (Jetté et al 1990). The number of minutes spent in each activity as surveyed from participants could be weighted according to intensity and converted to MET minutes per week (Craig et al 2003). Sleep duration responses provided by participants were categorised to three groups - 5 hours or less, 6-8 hours, 9 or more hours. These categories are due to two studies indicating a short sleep duration of <6 hours (Thompson et al 2011) and a long sleep duration of ≥9 hours (Zhao et al 2013) may be associated with an increased risk of CRC. Participants were asked whether they have had a colonoscopy or a sigmoidoscopy in the last 2 years, with possible answers – no, yes-for symptoms, and yes-for routine screening. We have excluded those who chose "yes for symptoms".

Statistical analysis was performed using STATA 14.0. Calculations were based on non-missing data. Chi-squared test was used for categorical variables. Fisher's exact test was used instead of chi-squared test when less than 80% of cells had an expected count of less than five. T-test was performed on continuous variables. Frequencies and percentages for categorical variables; and frequencies, percentages, means, and standard deviations are reported for continuous variables. Results with a p-value <0.1 were fed into a backward stepwise logistic regression model. This enabled calculation of odds ratios and 95% confidence intervals. A p-value <0.05 was considered significant.

FINDINGS

The number of participants who answered both the outcome variable and the exposure variable were 7,303 out of 8,199. The prevalence of having ever had diagnosis of CRC was 1.03% (n=7), 0.98% (n=47), 1.32% (n=24) in the never group, 1-14 years group and ≥15 years group respectively. There was no significant association between rotating shift work and colorectal cancer (p=0.481). Due to this large p-value no further analysis from the above data was conducted.

Table 1: Prevalence of colorectal cancer in nurses and midwives by length of rotating shift work

	Colorectal cancer			
Variable	**Yes**	**No**	**Chi-squared**	**p-value**
	n(%)	**n(%)**		
Rotating shift work (n=7303)			1.47	0.481
Never	7(1.03)	671(98.97)		
1-14 years	47(0.98)	4,759(99.02)		
≥15 years	24(1.32)	1,795(98.68)		

Table 3: Risk factors, as continuous variables, for colorectal cancer among nurses and midwives who are rotating shift workers

	Colorectal cancer				
Variable	**Yes**		**No**		
	n(%)	**M ± SD**	**n(%)**	**M ± SD**	**p-value**
Age (n=6,624)	71(1.07)	47.04 ± 7.97	6,553(98.93)	43.95 ± 9.54	0.007^
BMI (n=6,513)	67(1.03)	28.28 ± 6.11	6,446(98.97)	27.36 ± 5.67	0.187
Physical activity MET/week (n=6323)	69(1.09)	4371 ± 4037	6,254(98.91)	3651 ± 3844	0.122
Pack years* (n=6,601)	70(1.06)	5.51 ± 14.99	6,531(98.94)	3.26 ± 10.69	0.082
Alcohol per day in grams (n=6414)	71(1.11)	9.02 ± 13.71	6,343(98.89)	8.44 ± 13.28	0.717

^p< 0.05; ^^p< 0.001; *for current smokers

Tables 2 and 3 display the prevalence of risk factors in the rotating shift working population. Participants with a history of CRC had a mean age of 47±8 years compared to a mean age of 44±10 in those without a history of CRC ($p<0.05$). A history of CRC was more common in post-menopausal women compared with pre-menopausal women; 1.68% vs 0.81% ($p<0.05$). A history of CRC was significantly far more prevalent in participants with diabetes than those without diabetes; 24.15% vs 0.22% ($p< 0.001$). A history of CRC was significantly far more prevalent in those with IBD than those without IBD; 43.07% vs 0.19% ($p< 0.001$). CRC was also more likely in nurses and midwives who had undergone CRC screening by colonoscopy or a sigmoidoscopy in the last two years. CRC prevalence did not significantly differ at p-value of 0.05 for non-modifiable risk factors of gender and family history. Neither did it differ for modifiable risk factors of OC use, smoking status, red meat intake, vegetable intake, fruit intake, sleep duration, BMI, physical activity, pack years, and alcohol intake.

Table 2: Risk factors, as categorical variables, for colorectal cancer among nurses and midwives who are rotating shift workers

Variable	Colorectal cancer		Chi-squared	p-value
	Yes n(%)	No n(%)		
Gender (n=6,625)			0.24	0.625
Male	7(1.28)	541(98.72)		
Female	64(1.05)	6,013(98.95)		
Menopause (n=6,065)			9.05	0.003^
No	35(0.81)	4,305(99.19)		
Yes	29(1.68)	1,696(98.32)		
Ever use of OC (females) (n=6,023)			0.55	0.458
No	7(1.36)	506(98.64)		
Yes	56(1.02)	5,454(98.98)		
Smoking status (n=6,612)			0.50	0.781
Never smoked	38(1.05)	3,580(98.95)		
Former smoker	22(1.02)	2,129(98.98)		
Current smoker	11(1.30)	832(98.70)		
Red meat intake 1-4 times per week (n=6,596)			0.01	0.921
No	11(1.03)	1,054(98.97)		
Yes	59(1.07)	5,472(98.93)		
4 or more vegetables per day (n=6,608)			0.08	0.779
No	21(1.13)	1,835(98.87)		
Yes	50(1.05)	4,702(98.95)		
2 or more fruit per day (n=6,604)			0.01	0.944
No	22(1.09)	1,999(98.91)		
Yes	49(1.07)	4,534(98.93)		
Sleep duration (n=6,611)			0.51	0.775
≤5 hours	6(1.13)	527(98.87)		
6-8 hours	63(1.09)	5,713(98.91)		
≥9 hours	2(0.66)	300(99.34)		
Family history of CRC (n=6,437)			1.69	0.194
No	60(1.03)	5,752(98.97)		
Yes	10(1.60)	615(98.40)		
Diabetic status (n=6,602)				<0.001^^*
No	14(0.22)	6,352(99.78)		
Yes	57(24.15)	179(75.85)		
IBD status (n=6,571)				<0.001^^*
No	12(0.19)	6,422(99.81)		
Yes	59(43.07)	78(56.93)		
Screening colonoscopy or sigmoidoscopy in the last 2 years (n=6,311)				0.008^*
No	58(0.96)	5,978(99.04)		
Yes	8(2.91)	267(97.09)		

^p< 0.05; ^^p< 0.001; *Fisher's exact

Table 4: Univariate odds ratios for variables with a p<0.1

	Odds of having colorectal cancer		
Variable	**OR**	**95% CI**	**p-value**
Categorical Screening colonoscopy or sigmoidoscopy in the last 2 years			
No	1.00*		
Yes	3.09	1.46 - 6.53	0.003^
IBD status			
No	1.00*		
Yes	404.81	209.31 - 782.91	<0.001^^
Diabetes status			
No	1.00*		
Yes	144.48	79.04 - 264.10	<0.001^^
Menopause			
No	1.00*		
Yes	2.10	1.28 - 3.45	0.003^
Physical activity			
Low	1.00*		
Moderate	0.52	0.21 - 1.29	0.160
High	1.08	0.48 - 2.41	0.857
Continuous			
Age	1.04	1.01 - 1.06	0.007^
Pack years	1.01	1.00 - 1.03	0.086

^p< 0.05; ^^p< 0.001; *reference group

Table 5: Multivariate odds ratios derived from logistic regression modelling

	Odds of colorectal cancer		
Variable	**Adjusted OR**	**95% CI**	**p-value**
Screening colonoscopy or sigmoidoscopy in the last 2 years			
No	1.00*		
Yes	10.13	2.97 - 34.57	<0.001^^
IBD status			
No	1.00*		
Yes	189.62	68.30 - 526.39	<0.001^^
Diabetes status			
No	1.00*		
Yes	123.20	38.75 - 391.77	<0.001^^

^p< 0.05; ^^p< 0.001; *reference group

Table 4 presents univariate odds ratios of variables with a p<0.1. These were input into a backward stepwise logistic regression model to provide adjusted odds ratios in table 5. As per adjusted odd ratios, having IBD increased the odds of having a history of CRC by 190 fold (95%CI 68-526; p<0.001). Nurses and midwives with diabetes also have 123-fold increased odds of having a history of CRC (95% CI 39-392; p<0.001). Having had a screening colonoscopy or sigmoidoscopy in the last 2 years also increased the odds of having a history of CRC by 10-fold (95% CI 3-35; p<0.001).

Age and menopause increased odds of CRC by 1.04 (95% CI 1.01-1.06; p<0.05) and 2.10 (95% CI 1.28-3.45; p<0.05) respectively. However this was not seen in the multivariate analysis.

DISCUSSION

We did not find any association between rotating shift work and CRC. This is in contrast to Schernhammer et al study (2003) which found an increased risk of CRC in nurses who worked 15 or more years (RR=1.35, 95% CI 1.03-1.77). The Schernhammer et al study differs from our study in many respects. It was a prospective longitudinal study that followed participants for 10 years, whereas our study was a cross-sectional study. Schernhammer et al study had a much larger number of participants. Moreover, the participants were American compared to Australian, New Zealander and British participants in our study. Ethnical distribution may be different in these cohorts which could possibly have an impact on the frequency of CRCs. In the present study, statistically significant risk factors in the rotating shift working population were age, menopause, diabetes, IBD, screening colonoscopy or sigmoidoscopy. In Australia, 98% of all CRCs occur in persons over the age of 40 (Australian Institute of Health and Welfare 2014). In our study the mean age in the CRC group was slightly higher. Increased prevalence of cancer in older age is common among many cancers. Accumulation of mutations over time as well as age-related signalling pathways have been hypothesised to explain this association (Bordonaro and Lazarova 2015). The observed association between CRC and menopause may be due to the fact that postmenopausal women tend to be older. Postmenopausal women tend to have lower estrogen levels compared to their younger counterparts (Honma et al 2015). Some studies show a reduction of CRC risk in postmenopausal women having hormone replacement therapy (Honma et al 2015). Our study did not find a statistically significant difference in CRC prevalence between those who have ever used oral contraceptives and those who have not.

In our study, IBD, diabetes, and screening colonoscopy or sigmoidoscopy considerably increased the odds of CRC. This may be due to the increased capacity of colonoscopy to diagnose CRC. The screening is done amongst specific population groups and therefore colonoscopy itself should not be seen as a risk factor, instead a mean for early detection. In terms of diabetes, a meta-analysis (Luo et al 2015) found that diabetes was associated with an increased risk of CRC (RR=1.37, 95% CI 1.30–1.45). Activation of insulin and insulin-like growth factor 1 receptors expressed in cancer cells due to hyperglycemia and hyperinsulinemia along with increased inflammatory cytokines have been proposed as possible mechanisms explaining this association (Sharma et al 2014). An Australian cohort study (Selinger et al 2014) reported a 7% (95% CI 4-10%) cumulative incidence of CRC among persons with ulcerative colitis (UC) and 2% (95% CI, 0%–4%) with Crohn's disease (CD) at 30 years of follow-up. Selinger compared this incidence to corresponding age and gender matched general population, which were 1.9% for UC and 1.1% for CD. Over recent decades, there has been a substantial decrease in risk. A Danish study reported a RR of UC over background population of 1.34 (95% CI, 1.13–1.58) in 1979–1988 compared to 0.57 (95% CI 0.41–0.80) in 1999–2008 (Jess et al 2012). In the study, CD RR was 0.85 (95% CI, 0.67–1.07), which did not change over time. A 2013 meta-analysis states that IBD increases the risk of CRC but not as much as previously thought (Lutgens et al 2013). In patients with IBD, CRC is increased with the duration of the disease, the extent of colonic inflammation, family

history of CRC, and coexisting primary sclerosing cholangitis. It has been proposed that chronic inflammation causes DNA damage through oxidative stress. This can cause a loss of tumour suppression gene function leading to increased proliferation of tumour cells (Beaugerie and Itzkowitz 2015). About 30% of CRC cases have a positive family history (Brosens et al 2015); however we were unable to find a statistically significant difference in our population. Notably, we did not find any statistically significant relationship with many other risk factors such as increased BMI, red meat intake, cigarette smoking, low physical activity, and low fruit and vegetable consumption, as found in the meta-analysis by Johnson et al (2013).

This study has a number of noteworthy limitations. This study analysed data from a pre-existing database which limited the inclusion of a number of important covariates such as vitamin d level, fibre intake, and familial syndromes. For example, between 2-5% of all CRC can be attributed to hereditary syndromes such as lynch syndrome and familial adenomatous polyposis, which considerably increase the risk of CRC in those individuals (Jasperson et al 2010). We were not able to gather data from participants regarding these syndromes; even though we asked them about their family history of CRC. Some data were missing as respondents did not answer all the questions. For example, out of 8199 participants only 7303 answered both questions on shift work and CRC, which amounts to around 11 percent missing observations. It is also notable that there are generally a small number of observations in the positive CRC group for each variable compared with the negative CRC group. This results in large differences in odds. This perhaps gives a greater effect size than it otherwise would have been if we had a much larger sample size (Nemes et al 2009). This study being cross-sectional, the results should be interpreted cautiously as it is possible for CRC to have preceded the risk factor which means causation cannot be assumed. The study contained data from three countries – Australia, New Zealand and the UK which means these findings may not translate to nurses and midwives of other countries. There could be a social desirability bias where respondents may have provided data which they thought were more socially appropriate. The objectivity of some data (for example, height and weight) should also be questioned as data were received through self-report. There could be a response bias inherent in this study design as those people who decided to take part in the survey may have been different from those who did not decide to participate. Some nurses may have been more comfortable using non-electronic means such as paper-based surveys.

Observational studies such as this attempt to identify risk factors that affect the health and wellbeing of nurses and midwives. Identification and mitigation of these risk factors may help ensure a sustainable workforce into the future. Future studies may consider if different work schedules such as permanent night shifts have different outcomes, and whether these differ from other shift worker populations such as police officers. Future studies may also evaluate costs associated with the loss of nurses and midwives from the workforce due to CRC. This may help with workforce planning. Other research opportunities may involve exploring how nurses and midwives manage their diabetes or IBD in the context of CRC.

CONCLUSION

In this cross-sectional study we did not find any significant association between rotating shift work and CRC in nurses and midwives. However, IBD and diabetes were correlated with an increased probability of CRC in nurses and midwives who were rotating shift workers. Further research should be conducted using a large prospective cohort design to investigate the effect of rotating shift work on CRC.

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