

# Gynaecological cancer and night shift work: A systematic review

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## ABSTRACT

Night shift work can affect hormonal balance, and so might be a risk factor for gynaecological malignancies. This report presents a systematic review on the association between this occupational exposure and the incidence of gynaecological cancers other than breast cancer. We searched for original articles addressing this issue in PubMed/MEDLINE, EMBASE and Web of Science, and used the Newcastle–Ottawa Quality Index to evaluate the methodological quality of those reports selected for review. Globally, we found only six articles, which provided the results of just six research studies: four examined ovarian cancer, two endometrial tumours and two cervical cancer. Our results show that this matter has received scant attention from the research community, and that the little evidence available does not show any clear relationship between night shift work and ovarian, endometrial or cervical cancer. More prospective rigorous studies are needed to evaluate these associations.

## 1. Introduction

Night shift work (NSW) has awakened a growing interest in the research community in the last decade, and its prevalence is increasing. According to the data collected in the sixth EU Survey on Working Conditions in 2015, 14% of the female working population reported working during the night [1]. In 2007, the International Agency for Research on Cancer (IARC), based on strong animal and limited human evidence, concluded that NSW that involves circadian disruption was probably carcinogenic for breast cancer [2]. The most commonly alleged pathway focuses on the effect of the lower melatonin levels caused by exposure to light at night [3,4]. Available information suggests that this hormone may be involved in the regulation of gonadal function by influencing the hypothalamic-pituitary-gonadal axis [5], and it is noteworthy that night shift workers seem to have increased levels of sex hormones [6,7]. Therefore, other hormone-dependent tumours could also be related to NSW [8]. Among female cancers, ovarian, endometrial and cervical cancer represent a significant burden for women, and all together account for more than 220.000 new cases per year according to IARC [9]. Our aim is to summarize the existing evidence on the relationship between NSW and gynaecological tumours

by performing a systematic review conducted according to the PRISMA and MOOSE guidelines [10–13].

## 2. Methods

### 2.1. Data sources, search strategy, eligibility criteria and study selection

We aimed to select all observational studies providing original data that included NSW – defined as night-time work or shift work in hours covering midnight- as risk exposure and gynaecological cancer incidence and/or mortality as outcome. For this purpose, we searched for original articles in PubMed/MEDLINE (<http://www.ncbi.nlm.nih.gov/pubmed/>), EMBASE (<http://www.embase.com/home>), and in the Web of Science (WOS) published until august of 2017, using the terms (nightshift OR “night shift” OR shiftwork OR “shift work” OR night-work) combined with - “cancer” and the corresponding tumour site (i.e. “ovarian”, “endometrial”, “uterine”, “cervical”, “fallopian” or “vulvar”). We only took into consideration results in English, Spanish, German or French. This approach was complemented by a manual search based on the references cited in the papers initially identified.

**Abbreviations:** NSW, night shift work; IARC, International Agency for Research on Cancer; OCA, oral contraception; HRT, hormonal replacement therapy; BMI, body mass index; NHS, nurse health studies; JEM, job-industry exposure matrix; JACC, Japan Collaborative Cohort Study; SIR, standardized incidence ratio; NOS, Newcastle-Ottawa index scale

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## 2.2. Data extraction & quality of studies assessment

Two independent members of our research team performed the abstract/title screening and the full text revision of those reports that addressed our topic of interest. In case of disagreement, a third author's opinion allowed to achieve consensus. Afterwards, they extracted the information of the selected studies using a predefined data collection form. We also evaluated each study using the Newcastle-Ottawa Quality Index [14], a 8-item scale developed to assess the quality of non-randomised studies for meta-analyses with a maximum punctuation of nine stars. It assigns 4 stars to items related to selection and representativeness of the study groups. Another 3 stars correspond to items that evaluate the ascertainment of the exposure or the outcome of interest for case-control or cohort studies respectively. Finally, the remaining 2 points evaluate comparability of the groups in terms of control for potential confounders. In this regard, we defined a minimum (one star) and a preferred (second star) set of confounders to be considered per site location. In ovarian cancer [15], we assigned one star to those studies that adjusted by age, family history, menopausal status, parity, oral contraception (OCA), hormonal replacement therapy (HRT), and body mass index (BMI). The second star was awarded to those including at least four of the following: breastfeeding, age at menarche, age at menopause, hysterectomy, tubal ligation, smoking, diet and physical exercise, exposure to asbestos or perianal use of talcum powder. For endometrial cancer, our minimum set was age, BMI, OCA, menopausal status, parity and unspecified HRT; for the second star studies should additionally control for at least three of the following: unopposed exposure to oestrogens in HRT, polycystic ovarian syndrome, infertility, breastfeeding, age at menarche or menopause [16–19]. Finally, in cervical cancer the criteria for one star was adjusting at least by age, parity and smoking and, for the second star, at least three of the following: sexual behaviour, screening participation, other sexually transmitted diseases, immunodeficiency, vaccination status and family history [20].

## 3. Results

### 3.1. Search results

Fig. 1 summarizes the search results for NSW and risk of ovarian,

endometrial and cervical tumours. For ovarian cancer, we retrieved 50 records, including two added by manual search; after title and abstract screening and full text revision, four articles were included in this review [21–24]. Regarding endometrial cancer, our search yielded 53 results, with two additional papers found by manual search. In this case, two of the three articles selected for full text revision were considered in this report [24,25]. For cervical cancer, the bibliographic search found 19 results and the manual search recovered two reports. Again, only two papers fulfilled the inclusion criteria and were incorporated in this review [24,26]. One of them did not include material and methods [26], and was partially complemented with information from other papers of the same study [27–29]. Finally, our search did not find any paper focused on NSW and incidence/mortality of vulvar or vaginal cancer.

Overall, we found six reports from six research studies about the relationship between NSW and any gynaecological tumour. Most of them – one case-control [21] and three cohorts [22,23,25] – were carried out in the USA, another cohort study in Sweden [24], and the last one in Japan [26]. Table 1 lists these studies and shows their evaluation according to the quality assessment with Newcastle-Ottawa Scale (NOS). Nurse Health cohort Studies (NHS) I & II had the highest score, obtaining 8 out of 9 stars; they were only penalized for their focus on a single occupation. In contrast, the Japan Collaborative Cohort Study for Evaluation of Cancer, insufficiently described, only got 4 stars, in spite of our effort to look for complementary information. Table 2 summarizes the main characteristics and results of each report.

### 3.2. Ovarian cancer

We identified four reports – five studies – that provided risk estimates on the association between ovarian cancer and NSW: one case-control study [21] as well as NHS I & II and Schwarzbaum cohort studies [23,24] were focused on cancer incidence and the other one, American Cancer Prevention cohort study, studied fatal ovarian cancer [22].

The case-control study was conducted in the USA (Western Washington State) [21]. In this research, Bhatti et al. recruited, interviewed and studied a) 1101 women with invasive ovarian cancer and 394 with borderline tumours, identified through a population-based cancer registry, as well as b) 1832 controls selected from the general

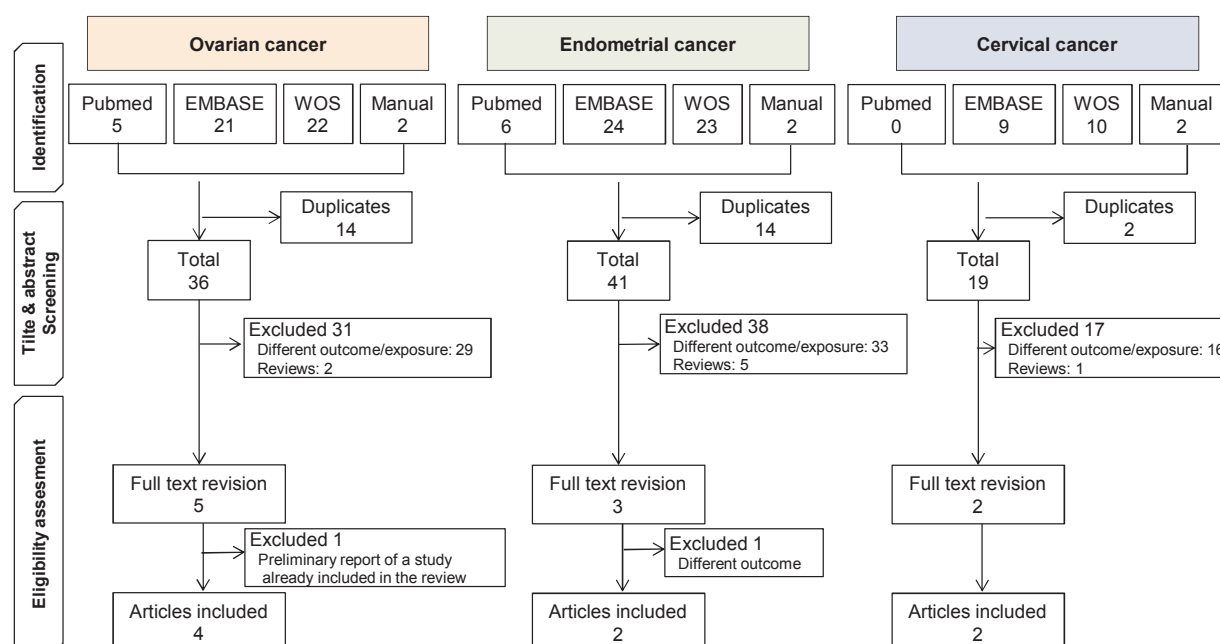


Fig. 1. Night shift work and gynaecological cancer: Search flow diagrams.

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