National Toxicology Program
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Draft Report on Carcinogens Monograph on Light at Night

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Running title: Draft RoC Monograph on Night Shift Work and Light at Night

Appendix B: Shiftwork and Cancer

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List of Tables

Appendix B. Shiftwork and Breast Cancer Studies – Quality rankings and results.

This appendix includes the rationales for quality rankings of studies of breast cancer and shift work reported in Section 3.2 by type of quality criteria (e.g., (a) selection bias, (b) exposure assessment, (c) outcome assessment, (d) sensitivity, (e) potential confounding, (f) analysis rating).

Quality rankings are reported in Section 3.2 in Tables 3-2 and 3-3; their rationales are shown in Appendix B: Table B-1a-f for cohort studies of breast cancer and shift work; and in Appendix B: Table B-2a-f for case-control studies of breast cancer and shift work.

Results for the cohort studies of breast cancer and shift work are found in Appendix B, Table B-3; results for case-control studies of breast cancer and shift work are found in Appendix B: Table B-4.

Table B-1a: Breast cancer and shiftwork COHORT studies: Selection bias rationale

Reference	Selection bias rating
Åkerstedt *et al.* 2015	++ ⬇ The cohort is clearly defined. 74% of cohort responded to interview but no information was provided as to how this differed by exposure. This is an older survivor cohort recruited at ages 41–60 years, thus young cases who worked long durations of night work may be missing.
Jørgensen *et al.* 2017	+ ⬇ The cohort was clearly defined by exposed/non-exposed for a specific time period and location. Follow-up did not differ by exposure status. Left truncation is an issue in this older survivor cohort. Authors indicated most nurses have to participate in rotating shift work early in their careers, and this is a > 44 year old cohort, so selection of exposure status may not be appropriate. Mortality analysis is likely to miss cases having longer survival. If fatal cases are more or less likely to be exposed to shift work, selection bias can result.
Knutsson *et al.* 2013	+ ⬌ The cohort is not clearly defined (in that it does not clear elucidate the relevant exposed, non-exposed, or referent group for a specific time period/location); no information is provided to assess whether follow-up differed between exposed and non-exposed subjects. No evidence presented to assess presence of healthy worker survival effect. Overall cohort participation rate for those with information on shift work was 53% from 1992 to 2009. Individuals were added at various points during the study.
Koppes *et al.* 2014	+++ ⬌ Cohort was randomly selected from national survey respondents and linked to national hospital admission data.
Li *et al.* 2015	++ ⬇ The cohort is clearly defined (e.g., includes the relevant exposed, nonexposed, or referent group for a specific time period/location), with no evidence presented to assess if follow-up differed between exposed and non-exposed subjects. This is not necessarily an older cohort (average age is 54.3 at baseline), but the high percentage of ever night workers with half working at least 20 years suggests that it is a survivor cohort.

Reference	Selection bias rating
Pronk *et al.* 2010	++ ⬇ The cohort is clearly defined (e.g., includes the relevant exposed and nonexposed for a specific time period/location), with no evidence offered that follow-up differed between exposed and non-exposed subjects. No evaluation of healthy worker survival effect was conducted in this employed older cohort of women. Initial response rate was 92% from women invited to participate. This was an older group of surviving women (~26% premenopausal at baseline, with questions first asked 6 years later), and if early exposures were related to breast cancer risk, this group may be biased based on left truncation or healthy worker survivor effect.
Schwartzbaum *et al.* 2007	++ ↔ The cohort is clearly defined, with no evidence that follow-up differed between exposed and non-exposed subjects; no evidence of healthy worker effect, as the overall SIR for cancer was 1.02 (95% CI = 1.0–1.05). No discussion of healthy worker survival effect. For the youngest women right truncation may be operating, with insufficient accumulation of night work to assess effect.
Travis *et al.* 2016	++ ⬇ **UK Oxford EPIC**. The cohort of general population and vegetarians is somewhat clearly defined (e.g., includes the relevant exposed, nonexposed, or referent group for a specific time period/location). This is a survivor cohort population aged ~37–90, with a mean of 58 years at the time of data collection and is likely to be unable to detect early breast cancers arising from long-term early exposure.
Travis *et al.* 2016	+ ⬇ **Million Women Study**. The cohort is clearly defined (e.g., includes the relevant exposed, nonexposed, or referent group for a specific time period/location), with no evidence that follow-up differed between exposed and non-exposed subjects. In this general population cohort, no analysis of healthy worker survival effect. This is an older cohort of survivors (mean age 68 at time when questions on night work were asked). If women with night work died, or left night work due to inability to adapt to night work, they wouldn't be present in this cohort to query about night work, and therefore a survivor bias could exist.
Travis *et al.* 2016	+ ⬇ **UK Biobank cohort.** The cohort is clearly defined (e.g., includes the relevant exposed, nonexposed, or referent group for a specific time period/location); No difference in follow-up time between exposed and non-exposed subjects. In this general population cohort, no analysis of healthy worker survival effect. This cohort is on average 56 years of age, and while not the oldest of the cohorts, may still suffer from left truncation due to elimination of early cancers after shift work early in one's career.
Tynes *et al.* 1996	+++ ↔ The cohort is clearly defined and includes the relevant exposed and non-exposed for a specific time period/location. Cases and controls in the nested study were selected from the same population by similar methods and criteria. No evidence that selection was related to both exposure and disease.

Reference	Selection bias rating
Vistisen *et al.* 2017	+ ⬇ The cohort is clearly defined with no evidence that follow-up differed for exposed and non-exposed. Data before January 1, 2007 was unavailable so two analytic cohorts were examined - the total population with records from Jan 1, 2007 and an "inception cohort" including women a) first ever employed Jan 1 2008 or later or no recorded employment in 2007. Both cohorts suffered from left-truncation, and lack of exposure information prior to either 2007 or 2008. Women were 35.5/39.4 years of age in the inception cohort and total population, respectively; the two populations differed in the joint distribution of shift work and education and shiftwork and parity, suggesting unknown selection factors that were operating in this subpopulation beyond simply left-truncation.
Wegrzyn *et al.* 2017	+++ ↔ The cohort is clearly defined (e.g., includes the relevant exposed, nonexposed, or referent group for a specific time period/location), with no evidence that follow-up differed between exposed and non-exposed subjects. Together, the two cohorts cover broad windows of exposure for women of different ages. The authors explored associations separately for the first 10 years of follow-up and the remaining 14 years of follow-up, to understand the long-term findings in the context of the Nurses Health Study their previously published shorter-term associations. In both cohorts, and for both measures of shift work in NHS2, breast cancer risk associated with night shift work was higher in the earlier versus later portion of follow-up. The estimates were higher in NHS2, where the shift work performance was likely closer in proximity to breast cancer risk than in NHS. The inverse finding (< 1.0) in the latter part of follow-up for NHS potentially reflected a healthy worker effect, but the authors did not see any evidence of differential dropping out of the analysis by shift work category, and therefore believe it to be due to chance.

Table B-1b: Breast cancer and shiftwork COHORT studies: Exposure assessment rationale

Reference	Exposure assessment rating
Åkerstedt et al. 2015	+ ⬇ The exposure assessment methods have poor sensitivity and specificity, leading to unreliable classification (or discrimination) with respect to ever-exposure as "night work" was not defined. Thus it was unclear if individuals working late afternoons or early mornings considered themselves "night workers," which would attenuate results. No information on frequency/intensity, timing, or recency. Exposure was assessed prior to diagnosis.
Jørgensen et al. 2017	0 ⬇ Current information on work status at baseline only. No information on past employment status casting doubt on those classified as unexposed. No data on duration of shift schedule and shift work intensity lead to a less sensitive exposure categorization. Furthermore, authors mention the high likelihood of exposure misclassification for nurses whose training involves shift work early in their career.
Knutsson et al. 2013	++ ⬇ The exposure assessment methods have adequate sensitivity and specificity to distinguish ever/never shift work. Most detailed questions concern the current job only and answers to the question on lifetime history of night work is available on only 53% of subjects, and in 36% only baseline information on shift work was available due to the design of their data collection on shift work. However, the comparison group, i.e., day workers, reported working only during the day on current job in 3 follow-ups; while night workers reported in at least one of the follow-ups that they worked some nights. No information on duration or intensity provided. Of those reporting no experince of shiftwork at final follow-up 22% reported shiftwork at baseline; but this figure was only 2% when NIGHT work was considered indicating night work was remembered better.
Koppes et al. 2014	0 ⬇ The study has poor sensitivity and specificity, resulting in poor discrimination between exposed and non-exposed and among exposure categories. Information asked only about current night work and number of hours per week of night work. A poor proxy of lifetime nightwork was estimated based on length of duration in current job. Authors mention that the Dutch have a high proportion of part time workers; also a co-author mentioned that shift workers have a 59% attrition rate over 5 year periods, indicating assumptions in this study are not supported.
Li et al. 2015	++ ⬇ Industry level information on exposure setting (shift work policies) allows for individual level discrimination between exposed and non-exposed to rotating shift work as shift work was mandated by factory. Lifetime # of night shifts measured intensity of night work; 33% day workers. Use of company records avoids recall bias, but no information existed on lifetime exposure to night work.
Pronk et al. 2010	++ ⬇ The exposure assessment methods have moderate to good sensitivity and specificity, leading to reliable classification (or discrimination) with respect to ever-exposure. Duration, intensity, and cumulative # nights were assessed; no assessment of consecutive nights worked or rotations. The job exposure matrix was likely to have over-estimated night work as compared to self-report: 44% worked nights by job exposure matrix; 26% worked nights by self-report.

Reference	Exposure assessment rating
Schwartzbaum et al. 2007	0 ⬇ Exposure assignment is based on aggregate categories, as exposure was defined according to % of those in each job category reporting shift work in an external large national survey. True night workers working in industries with fewer night workers are likely to be missed (sensitivity analyses in men indicated that resulting bias from this misclassification would be small); but women who are less likely to work nights in occupations with significant night work could be misclassifed as exposed. No data on intensity or timing.
Travis et al. 2016	++ ⬇ **UK Oxford EPIC.** The exposure assessment methods have moderate sensitivity and specificity, leading to reliable classification (or discrimination) with respect to ever-exposure and duration of exposure. However, the definition of night work as 1+ shift/month for jobs held at least 1 year likely mixed highly exposed and individuals with minimal exposure.
Travis et al. 2016	++ ⬇ **Million Women Study.** The exposure assessment methods have good sensitivity and specificity leading to reliable classification (or discrimination) with respect to overall ever-exposure and duration of exposure, although the question was asked as a summary question and not as a job-by-job history. Also, no information is presented on level of intensity, timing in relation to first full-term pregnancy, consecutive nights, or rotations. No information on exposure setting across many different types of occupations, none of which were specified, was reported.
Travis et al. 2016	0 ⬇ **UK Biobank Cohort.** The exposure assessment methods have inadequate sensitivity and specificity and are not able to differentiate ever/never exposure, as only current job was assessed. In this population of older survivors, likely that current job with short follow-up would not include the appropriate exposure window.
Tynes et al. 1996	+ ⬇ Exposure assessment methods have low sensitivity and specificity with respect to ever/never exposure and duration as they were based on employment records; intensity was implied but not sufficiently explained; shift work was not defined clearly. Information on rotations, or timing was absent.
Vistisen et al. 2017	+ ⬇ Administrative records avoid recall bias. However, left-truncation of the cohorts may misclassify exposed and unexposed as data from Time 0 is missing. (1) Women classified as "unexposed" may include exposed women working at earlier times in their careers dropping out for various reasons and diluting estimates of effect. (2) Workers on evening shifts could be misclassified as day workers. While sensitivity analyses revealed that bias from such misclassification may be minimal, assumptions about the proportion of women who were previously working may be in error.

Reference	Exposure assessment rating
Wegrzyn et al. 2017	+++ ↔ The exposure assessment methods have moderate to good sensitivity and specificity. The assessment was an improvement over the 2001 and 2006 report as (1) authors specified that women contributed person-time only as long as exposure status was captured; (2) NHS2 included a cumulative SW measure which incorporated follow-up updated information; (3) a secondary assessment was included to conduct analyses by follow-up time period to separate early vs. late associations of rotating night shift work on breast cancer risk; (4) in NHS2, a recency analysis was conducted using time since stopping shift work; and (5) stratified analysis was done by menopausal status, receptor status, shift work before and after first pregnancy, and shift work before and after menopause. A correlation of r = 0.53 was reported between answers to shift work questions about the 1995–1997 period asked in the 2001 follow-up questions and answers provided in 1995–1991. As in previous reports, no information on frequency or intensity was provided.

Table B-1c: Breast cancer and shiftwork COHORT Studies: Outcome assessment rationale

Reference	Outcome Assessment rating
Åkerstedt et al. 2015	+++ ↔ Outcome methods distinguish between diseased and non-diseased subjects, no ICD code indicated, nor detail on validation of case status. Follow-up and diagnoses were conducted independent of exposure status.
Jørgensen et al. 2017	++ ↓ Breast cancer has a very high survival rate, so mortality will miss cases that do not result in death.
Knutsson et al. 2013	+++ ↔ Outcome methods clearly distinguish between diseased and non-diseased subjects. Follow-up and diagnoses were conducted independent of exposure status.
Koppes et al. 2014	+ ↔ Outcome methods do not clearly distinguish between diseased and non-diseased subjects. Using hospital admission data to estimate incidence may lead to bias if differential access to medical treatment exists. Prevalent cases may have been included in the population which may mean there is a different distribution of aggressive and slow growing cancers compared to incident studies.
Li et al. 2015	+++ ↔ Outcome methods clearly distinguish between diseased and non-diseased subjects and cases were verified by pathology/histology. Follow-up and diagnoses were conducted independent of exposure status. No cancer subtypes were examined.
Pronk et al. 2010	+++ ↔ Outcome methods clearly distinguish between diseased and non-diseased subjects. Follow-up and diagnoses were conducted independent of exposure status. No sub-types were examined.
Schwartzbaum et al. 2007	+++ ↔ Outcome methods clearly distinguish between diseased and non-diseased subjects. Follow-up and diagnoses were conducted independent of exposure status. 97% of cases were morphologically verified.
Travis et al. 2016	+++ ↔ **UK Oxford EPIC**. Outcome methods clearly distinguish between diseased and non-diseased subjects. Follow-up and diagnoses were conducted independent of exposure status. No subtypes were ascertained.
Travis et al. 2016	+++ ↔ **Million Women Study**. Outcome methods clearly distinguish between diseased and non-diseased subjects. Follow-up and diagnoses were conducted independent of exposure status. No subtypes were ascertained
Travis et al. 2016	+++ ↔ **UK Biobank Cohort.** Outcome methods clearly distinguish between diseased and non-diseased subjects. Follow-up and diagnoses were conducted independent of exposure status.
Tynes et al. 1996	+++ ↔ Outcome methods clearly distinguish between diseased and non-diseased subjects and follow-up and diagnoses were conducted independent of exposure status.
Vistisen et al. 2017	+++ ↔ Outcome methods clearly distinguish between diseased and non-diseased subjects. Follow-up and diagnosis conducted independent of exposure. Subtypes analyzed.

Reference	Outcome Assessment rating
Wegrzyn et al. 2017	+++ ↔ Outcome methods clearly distinguish between diseased and non-diseased subjects. Follow-up and diagnoses were conducted independent of exposure status. Only confirmed cases were included; estrogen and progesterone receptor status determined but the number of lobular cases was too small to evaluate the risk of breast cancer by histologic type.

Table B-1d: Breast cancer and shiftwork COHORT Studies: Sensitivity rationale

Reference	Sensitivity rating
Åkerstedt et al. 2015	+ ⬇ The study has a moderate number of ever exposed subjects, but a small number of subjects with substantial exposure duration; information about level of intensity or timing unavailable. Follow-up time is only 8.7 years; if cases occur early after night work, this older aged cohort may have missed these cases.
Jørgensen et al. 2017	+ ⬇ Small number of night and rotating breast cancer cases, likely underpowered. Poor sensitivity of exposure status due to lack of level, duration, or range of exposure. Adequate follow-up duration.
Knutsson et al. 2013	++ ↔ The study has an inadequate number of case subjects exposed to night work (N = 14) or shift work without nights (N = 20), without information on level, duration, or range; there is adequate duration of follow-up for latency (average follow-up time is 12.4 years from baseline to censorship).
Koppes et al. 2014	0 ⬇ The study has an adequate number of exposed subjects, but a narrow range of exposure based on the few numbers working full time; and missing information on past or lifetime exposure to night work. Short follow-up time.
Li et al. 2015	+ ⬇ The study has an adequate number of exposed subjects with substantial duration of exposure; however, there was little exposure variation and this is likely a survivor cohort which could miss early cases.
Pronk et al. 2010	+ ⬇ The study has a small number of exposed subjects, with substantial exposure (# nights and duration). However, follow-up for cases once shift work history was known from self-report was only 4.4 years. In this older survivor population, effects would not be seen if any do exist.
Schwartzbaum et al. 2007	0 ⬇ The proportion of ever exposed is 0.06%, much lower than the expected 15%–20% of female nightworkers in the Swedish workforce. Study has small number of exposed cases, without sufficient information about how to characterize the level, duration, or range of exposure. For the youngest women included, duration of work through 1970 may not be sufficient to assess effect. Right truncation may be operating to reduce sensitivity.
Travis et al. 2016	+ ↔ **UK Oxford EPIC Study**. The study has an inadequate number of exposed subjects with substantial exposure duration, and no analyses on direction of shift or intensity. Very short follow-up unlikely to capture effect if there is one. This somewhat older survivor cohort may not be able to capture a relationship with long duration of early night work and breast cancer if one exists. Definition of night work as 1+ shift/month for jobs held at least 1 year mixed likely mixed highly exposed and those with minimal exposure.
Travis et al. 2016	+ ⬇ **Million Women Study**. The study has an adequate number of exposed subjects with substantial exposure duration, but no information on direction of shift, intensity, or contiguous days working. Mean follow-up time is very short (2.6 years); this older survivor cohort may not have captured cases occurring after shift work at an early age

Reference	Sensitivity rating
Travis et al. 2016	0 ↔ **UK Biobank Cohort.** The study did not assess lifetime exposure to nightwork, and the unexposed are likely to have been a mix of previously exposed and currently unexposed. Very short follow-up.
Tynes et al. 1996	+ ↓ The study has a small number of exposed cases with ill-defined moderate duration of exposure.
Vistisen et al. 2017	+ ↓ The study has an adequate number of ever-exposed subjects but follow-up is very short (up to 5 years); intensity (# shifts per period) is included to denote a range of exposure, and duration up to 5 years is incorporated into the analysis.
Wegrzyn et al. 2017	++ ↔ The study has an adequate number of exposed subjects, but small numbers with 20+ years of exposure (N = 13, or 35); the two cohorts together cover broad windows of exposure in relation to the occurrence of breast cancer which increases the sensitivity over the previous two reports

Table B-1e: Breast cancer and shiftwork COHORT studies: Confounding rationale

Reference	Confounding rating
Åkerstedt *et al.* 2015	Breast: ++ ↔ The study measured all relevant potential confounders and addressed alcohol in a separate model which included only cases with these data.
Jørgensen *et al.* 2017	Breast: +++ ↔ None.
Knutsson *et al.* 2013	Breast: +++ ↔ The study measured many relevant potential confounders and used appropriate analyses to address them; no co-exposures were included.
Koppes *et al.* 2014	Breast: + ↔ The study did not measure alcohol, measured occupation as a proxy for SES/education, and used number of children in household as an imperfect proxy for parity.
Li *et al.* 2015	Breast: +++ ↔ The study measured relevant potential confounders. Joint effects of magnetic field exposure and shift work were evaluated by stratifying subjects into 4 groups with 2 levels of exposure for each.
Pronk *et al.* 2010	Breast: +++ ↔ The study measured all relevant potential confounders and addressed alcohol in a separate model which included only cases with these data.
Schwartzbaum *et al.* 2007	Breast: + ↔ The study did not measure all relevant potential confounders as data were not available (e.g., parity, age at first full-term pregnancy, alcohol use)
Travis *et al.* 2016	Breast: ++ ↓ **UK Oxford EPIC**. The study measured and controlled for important potential confounders; however, BMI and age at menarche are in the pathway, and inclusion of these and other variables that are not necessarily confounders may have reduced risk estimate
Travis *et al.* 2016	Breast: ++ ↓ **Million Women Study**. The study measured and controlled for important potential confounders; however, BMI and age at menarche, which are both in the pathway, and inclusion of other variables that are not necessarily related to both exposure and risk may have lowered the estimate of the risk.
Travis *et al.* 2016	Breast: ++ ↓ **UK Biobank Cohort**. The study measured and controlled for important potential confounders; however, BMI and age at menarche, which are both in the pathway, and inclusion of other variables that are not necessarily related to both exposure and risk may have lowered the estimate of the risk.
Tynes *et al.* 1996	Breast: + ↑ The study did not measure all relevant potential confounders. Data on parity, age at first birth were available for a subset of women, but main analyses did not control for these, as these data were only available for the "fertility cohort" within the total cohort. For these women, no control was made for coexposures or alcohol; socioeconomic status was considered to be somewhat homogenous although no data were reported to support this.

Reference	Confounding rating
Vistisen *et al.* 2017	Breast: ++ ⬇ All relevant potential confounders were considered. Given similarity between these for night and day workers, adding them to the models may have reduced estimates. Adjusted and crude estimates were reported, and adjusting tended to move negative values towards 1.0.
Wegrzyn *et al.* 2017	Breast: ++ ⬇ The study measured all relevant potential confounders and used appropriate analyses to address them, but included variables in the pathway (age at menarche, menopause, BMI) in the model, as well as others (benign breast disease, family history of breast cancer, physical activity) which may have resulted in reducing the estimate.

Table B-1f: Breast cancer and shiftwork COHORT studies: Analysis and selective reporting rationales

Reference	Analysis rating	Selective reporting rating
Åkerstedt et al. 2015	+++ ⟷ Study used relevant data and appropriate assumptions and methods of analysis.	+++ ⟷ There is no evidence that reporting of the data or analyses were limited to only a subset of the data that were collected. Timing of nightwork unknown.
Jørgensen et al. 2017	++ ⟷ Inclusion of multiple covariates not related to the exposure and outcome of interest may have attenuated results and widened confidence intervals.	+++ ⟷ There is no evidence that data or analysis were limited to a subset of data.
Knutsson et al. 2013	++ ⟷ The study used appropriate assumptions and methods of analysis but did not use all the information they collected in the analysis.	++ ⟷ Data on various aspects of night work were collected, but only information about ever night work was reported. Only 53% of subjects had information about lifetime exposure to shift work; among these only 36% had baseline information.
Koppes et al. 2014	+++ ⟷ The study used relevant data and appropriate assumptions and methods of analysis. Women with missing data on at least one of the potential confounders were excluded from analyses.	+++ ⟷ There is no evidence that reporting of the data or analyses were limited to only a subset of the data that were collected.
Li et al. 2015	+++ ⟷ The study used relevant data and analyses; Lagged analyses were included.	+++ ⟷ There is no evidence that reporting of the data or analyses were limited to only a subset of the data that were collected.
Pronk et al. 2010	++ ⟷ The study measured all relevant potential confounders and used appropriate analyses to address them. Did not describe stratification analyses sufficiently in detail.	++ ⟷ There is no evidence that reporting of the data or analyses were limited to only a subset of the data that were collected. Did not show results of stratified analyses
Schwartzbaum et al. 2007	++ ⟷ Study used relevant data and appropriate assumptions and methods of analysis. The authors incorporated several sensitivity analyses to test various hypotheses. Sub-analyses used to investigate duration included women who reported working in high shift work occupations in both 1960 and 1970.	+++ ⟷ No evidence that reporting of the data or analyses were limited to only a subset of the data collected.

Reference	Analysis rating	Selective reporting rating
Travis et al. 2016	++ ↔ **UK Oxford EPIC**. The study used appropriate data and analyses or designs to address them.	+ ↔ The authors collected data on many metrics of shift work such as type (permanent), frequency, age at first shift work and provided frequency by duration of night shift work (for total population) but did not calculate or report risk estimates for these metrics. While numbers were small, they may have done some stratification.
Travis et al. 2016	++ ↔ **Million Women Study**. The study measured most relevant potential confounders, and used appropriate analyses or designs to address them. Collected data on chronotype but did not present analysis by chronotype.	++ ↔ There is no evidence that reporting of the data or analyses were limited to only a subset of the data that were collected. However, very little infomation from analyses were shown.
Travis et al. 2016	++ ↔ **UK Biobank Cohort.** The study measured most relevant potential confounders and used appropriate analyses or designs to address them. However, information on analysis was insufficient.	+ ↔ There is no evidence that reporting of the data or analyses were limited to only a subset of the data that were collected. Very little information shown.
Tynes et al. 1996	++ ↔ Analysis methods were satisfactory with given data.	++ ↔ No evidence that reporting of the data or analyses were limited to only a subset of the data that were collected. However, reporting on several key issues was limited which hampered interpretation of study
Vistisen et al. 2017	+++ ↔ The study used relevant data and appropriate assumptions and methods of analysis. Given that the time periods under analysis are short, the Poisson model can be used in lieu of Cox proportional hazards models.	++ ↔ No evidence that reporting of the data or analyses were limited to a subset of the data collected. However, more information about the characteristics of the inception cohort (first time workers and those not working in 2007) would have been helpful.
Wegrzyn et al. 2017	+++ ↔ The study used relevant data and appropriate assumptions and methods of analysis.	+++ ↔ There is no evidence that reporting of the data or analyses were limited to only a subset of the data that were collected.

Table B-2a: Breast cancer and shiftwork CASE-CONTROL studies: Selection bias rationale

Reference	Selection bias rating
Cordina-Duverger *et al.* 2016	+++ ↔ Selection bias was unlikely as all incident cases in both study areas were recruited; cases were frequency-matched to controls by 10-year age strata and by socioeconomic status (SES) calculated from census data in each study area to obtain an SES distribution similar for cases and controls. SES of cases and controls was compared after the selection process and no significant difference was found. Data were collected in detail and factors that differed between cases and controls were included in models. The proportion of night workers among controls was similar to that in the French population and employed in industries where night work is common. However, only 79% of the cases were tested for human epidermal growth factor receptor 2 (HER2), but no information was provided on whether there were any differences in women tested or not tested for HER2.
Davis *et al.* 2001	+++ ↔ Cases and controls were selected from the same population by similar methods and criteria. No evidence that selection of the subjects was related to both exposure and disease.
Fritschi *et al.* 2013	++ ↔ Cases and controls were selected from same population with similar criteria; there was no evidence that selection was related to both exposure and disease. Some attrition bias suspected given the relatively low response fractions; however, the authors used sensitivity analysis to examine what level of selection bias would hide a real effect of 1.5 for ever working the graveyard shift, and found that substantial differences in responses would have to be present to create a bias. However, it may be that they could have missed an elevated risk of 1.2.
Grundy *et al.* 2013	+++ ↔ Cases and controls were not strictly selected from the same population by similar methods and criteria. However, there is no evidence that selection of the subjects was related to both exposure and disease as sensitivity analysis taking selection factors into account produced similar results. Methods differed in the two study areas, but study area was included in all models. Response bias due to differences in response rates of cases and controls is ruled out since participation would have had to be related to night shift work and breast cancer, which is unlikely based on the manner shift work was assessed (e.g., job history).
Hansen 2001	+++ ↔ Countrywide study, thus cases and controls were selected from the same Danish population. There is no evidence that selection of the subjects was related to both exposure and disease.
Hansen and Lassen 2012	++ ↓ Cohort is clearly defined, with cases and controls selected from same population by similar criteria; no evidence that selection of subjects was related to both exposure and disease. Modest participation rates could bias results if night shift workers were more willing to participate than day workers and if this differed by cases and controls. Sensitivity analyses suggested that shift working controls would have to be twice as likely to refuse as shift working cases to negate the observed effect (indicate selection bias). Only 40% of original cohort cases participated, potentially introducing selection bias if cases were more exposed to night shift work than controls. In this older population, such loss is a concern if breast cancer occurs after shift work in early life.

Reference	Selection bias rating
Hansen and Stevens 2012	++ ↓ The prevalence cohort (only living members) from across Denmark is clearly defined (e.g., includes the relevant exposed, non-exposed, or referent group for a specific time period); response rates are similarly high for cases and controls in the nested study. The older survivor population suggests that there may be some selection bias, in that cases occurring at earlier ages after night work early in careers would not be present in the cohort.
Lie *et al.* 2011	++ ↓ Prevalent case inclusion could create a bias as 39% of deceased cases were lost thru death or non-participation in this older cohort leaving long-term survivors; sensitivity analyses using cases from 2004–2007 concluded that this bias is likely to be negligible, although the value of this test late in follow-up is questionable.
Menegaux *et al.* 2013	+++ ↔ Selection bias was unlikely as all incident cases in both study areas were recruited; cases were frequency-matched to controls by 10-year age strata and by SES calculated from census data in each study area to obtain an SES distribution similar for cases and controls. SES of cases and controls was compared after the selection process and no significant difference was found. Data were collected in detail and factors that differed between cases and controls were included in models. The proportion of night workers among controls was similar to that in the French population and employed in industries where night work is common.
O'Leary *et al.* 2006	++ ↔ Highly selected population based on long-term residence. This analytic subset also differed from the full set of cases and controls - they were older, postmenopausal, white, parous, heavier, ever users of alcohol and HRT, and less likely to have more than high school degree or to have breastfed. Likely some selection bias was operating.
Papantoniou *et al.* 2015	++ ↔ Cases and controls were selected from the same underlying population to ensure that they were comparable. There is no evidence that selection of the subjects was related to both exposure and disease; however, attrition bias is a potential as recruitment differed between cases and controls with only 52% of the controls responding. Calls were made repeatedly at different times during the day to avoid missing night shift workers.
Pesch *et al.* 2010	+++ ↔ Cases and controls were selected from the same population by similar methods and criteria. Selection of the subjects was made independent of exposure or disease ascertainment. Bootstrapping analyses was conducted to account for the fact that the 90% of participants taking part in the second round of interviews were more educated than those in the first round; however these analyses indicated no evidence of selection bias. Those reporting shift work were recalled, with another loss of subjects. Data on how these groups compared were not adequately reported.
Wang *et al.* 2015	++ ↔ Whether cases and controls came from the same population is somewhat of a question in any hospital-based case-control study. However, cases and controls were recruited from the same hospital during the same study period, and all subjects must have resided in the Guangzhou area for at least five years. There is no indication if the 3 hospitals are tertiary care hospitals; while controls with chronic disease were not included, if trauma events were over represented among controls, it could be that controls were from a more "local" area than cases and therefore potentially different. In fact, controls were more educated than cases.

Table B-2b: Breast cancer and shiftwork CASE-CONTROL studies: Exposure assessment rationale

Reference	Exposure assessment rating
Cordina-Duverger *et al.* 2016	++ ↔ Type of night work (late evening, early morning, overnight), duration in years, average frequency of nights/week, and duration/frequency combinations were assessed; however, due to large differences between night shift systems across occupations, shift rotation, direction and rate of rotation, and number of consecutive nights on various rotations, could not be assessed.
Davis *et al.* 2001	++ ↓ Exposure assessment methods reliably discriminate ever and never exposure; shift work ascertained only for the 10 years prior to diagnosis/reference date. Intensity and duration were evaluated separately. The unexposed in the reported analysis may have worked early in their careers, thus they may not be completely unexposed. Recall bias is unlikely as lifetime occupational history is queried.
Fritschi *et al.* 2013	+++ ↓ Exposure assessment methods have very good sensitivity and specificity leading to reliable classification with respect to ever/never exposure, intensity, duration, type of rotation, and window of exposure. While exposure assessment was based on expert review, and the study asked about every job, recall bias in this case-control study cannot be completely excluded, particularly as a special interview was conducted for women indicating shiftwork on their questionnaire and data were collected after the 2007 IARC report.
Grundy *et al.* 2013	++ ↓ The exposure assessment methods have only moderate sensitivity as exposure to night work was defined as working either evening or night shifts; permanent and rotating shifts were also not considered separately. Duration was provided for categories of intensity/frequency of evening/night shifts (from 20% to 100%). Duration of lifetime cumulative exposure of night work defined as starting or ending work between 11:00 PM and 7:00 AM. Collection of lifetime job histories reduced likelihood of recall bias.
Hansen 2001	+ ↓ The exposure assessment methods have minimal sensitivity and specificity, with only moderate discrimination with respect to ever-exposure; details of exposure level, timing, or other relevant metrics not available. No individual level information of exposure; to minimize misclassification women working in trades with 40%–59% night work are excluded leaving only those in occupations with little or much shift work.
Hansen and Lassen 2012	+++ ↔ Exposure assessment methods have good sensitivity and specificity for reliably classifying ever/never exposure, intensity/frequency, and duration from lifelong job histories; rotations and permanent shifts could not be differentiated. Recall bias was ruled out after a question on (1) electromagnetic fields or radar exposure (known to be unrelated to breast cancer) was found also to be unrelated to breast cancer in this set of cases and controls, (2) focus of 28-page questionnaire was military exposure, and (3) data were mostly collected before publication of IARC findings.
Hansen and Stevens 2012	+++ ↔ Exposure assessment methods have good sensitivity/specificity leading to reliable discrimination between ever and never exposure, duration and intensity. Various shift systems were ascertained; Recall bias only slightly likely as nurses were told this was an environmental study; data collection took place pre-IARC report; a question about electromagnetic fields (no association with breast cancer) was inserted to assess potential recall.

Reference	Exposure assessment rating
Lie *et al.* 2011	++ ↔ Multiple exposure assessment metrics provided sensitivity and specificity with respect to exposure; however, as all nurses had some exposure to night work (3 years during nursing school), there is no unexposed group. Methods of assessing exposure level included consecutive nights worked, duration, intensity, type of pattern (rotation/permanent). Recall bias is a concern, however, as the study was designed to investigate a broad array of work-related factors; no difference was found between cases and controls on duration in jobs reported to include night work; and the structure of questions on lifetime occupational history and schedules is likely to minimize this bias. However, authors note that shift work and cancer was widely discussed in Denmark during this time.
Menegaux *et al.* 2013	++ ↓ Type of night work (late evening, early morning, overnight), duration in years, average frequency of nights/week, and duration/frequency combinations were assessed; due to large differences between night shift systems across occupations, shift rotation, direction and rate of rotation, number of consecutive nights on various rotations was not assessed
O'Leary *et al.* 2006	+ ↔ No lifetime exposure assessment, but only jobs in the last 15 years in this older population of women were queried; frequency and duration were included. Only nights or only evening categories provided information on permanent nights, with the other categories a mix of rotating schedules. Recall bias may be possible given this subset of subjects was selected for a second interview for electromagnetic measurements and light at night which took place on average 200 days later. Categories reported made it difficult to differentiate evening workers who worked through 2:00 AM or earlier, potentially diluting exposure categories which included evening workers (e.g., all but never or permanent night workers)
Papantoniou *et al.* 2015	+++ ↓ The methods were sufficient to differentiate exposed and unexposed with respect to ever-exposure, frequency, and duration. Recall bias is unlikely as the issue of shift work and cancer was not widely discussed in Spain during the study period, and querying lifetime job histories limits opportunity for recall bias.
Pesch *et al.* 2010	++ ↓ Exact methods by which shift information was collected is unclear. Ever shift work, ever night shift work, duration, and frequency were collected, and while the methods were not very detailed, they appeared to allow discrimination between exposed and non-exposed, and those with long/short duration, and timing of work relative to first pregnancy and time since last night shift. No information on rotation vs. permanent shifts, or direction of rotation. The three rounds of interviewing to get to the shift work questions raises the potential for recall bias.
Rabstein *et al.* 2013	++ ↓ The exposure assessment methods rely on self-report, and exact methods by which shift information was collected is unclear based on the two papers (Pesch et al. 2010). Ever shift work, ever night shift work, duration, and frequency were collected, and while not very detailed, appeared to allow discrimination between exposed and non-exposed. No information on rotation vs. permanent shifts, or direction of rotations is provided. The three rounds of interviewing to get to the shift work questions raises the potential for recall bias.

Reference	Exposure assessment rating
Wang *et al.* 2015	+ ↔ Exposure assessment methods have limited sensitivity/specificity and classify with respect only to ever/never lifetime employment at night. No metrics of level, duration, or intensity were collected. Exposure settings vary across the population and are not further described. Interviews in hospitals may introduce observer bias.

Table B-2c: Breast cancer and shiftwork CASE-CONTROL studies: Outcome assessment rationale

Reference	Outcome assessment rating
Cordina-Duverger *et al.* 2016	+++ ↔ Outcome methods clearly distinguish between diseased and non-diseased subjects. Follow-up and diagnoses were conducted independent of exposure status. Appropriate methods used regarding the determination of receptor status.
Davis *et al.* 2001	+++ ↔ Outcome methods clearly distinguish between diseased and non-diseased subjects. Diagnoses were conducted independent of exposure status. No cancer subtypes analyzed.
Fritschi *et al.* 2013	+++ ↔ Outcome methods clearly distinguish between diseased and non-diseased subjects. Diagnoses were conducted independent of exposure status.
Grundy *et al.* 2013	++ ↓ Outcome methods clearly distinguish between cases and non-cases, however, Invasive and in situ cases were combined in analyses, except for estrogen receptor/progesterone receptor (ER/PR) analyses. Authors indicated that there were no differences in results when In situ cases removed. No mention of histologic confirmation.
Hansen 2001	+++ ↔ Outcome methods clearly distinguish between diseased and non-diseased subjects. Follow-up and diagnoses are conducted independent of exposure status.
Hansen and Lassen 2012	+++ ↔ Outcome methods clearly distinguish between diseased and non-diseased subjects; disease follow-up using linkage with the Danish Cancer registry were conducted independent of exposure ascertainment
Hansen and Stevens 2012	+++ ↔ Outcome methods clearly distinguish between diseased and non-diseased subjects (histologically confirmed primary breast cancers). Follow-up and diagnoses were conducted independent of exposure status. Internal comparisons among nurses eliminate concern about lead-time bias that can arise due to nurses' enhanced knowledge of the medical system when compared with general population. No information on subtypes.
Lie *et al.* 2011	+++ ↔ Outcome methods clearly distinguish between cases and controls. Follow-up and diagnoses are conducted independent of exposure status.
Menegaux *et al.* 2013	+++ ↔ Histologic confirmation of cancers is appropriate; companion publication on this cohort provides detail on estrogen, progesterone, and HER2 receptor status (Cordina-Duverger 2013).
O'Leary *et al.* 2006	+++ ↔ Subtypes were evaluated (ER status). Outcome methods clearly distinguish between diseased and non-diseased subjects. Diagnosis was conducted independent of exposure assessment.
Papantoniou *et al.* 2015	+++ ↔ Diagnoses appear to have been conducted independent of exposure assessment; cases were histologically verified.

Reference	Outcome assessment rating
Pesch *et al.* 2010	+++ ↔ Outcome methods clearly distinguish between diseased and non-diseased subjects. Diagnoses were conducted independent of exposure status.
Wang *et al.* 2015	++ ↔ Outcome methods distinguish between diseased and non-diseased subjects; follow-up and diagnosis were conducted independent of exposure status. However, variations in coding across hospitals may have introduced error in the diagnosis of breast cancer.

Table B-2d: Breast cancer and shiftwork CASE-CONTROL studies: Sensitivity rationale

Reference	Sensitivity rating
Cordina-Duverger *et al.* 2016	++ ↔ Adequate number of exposed cases, particularly in ER, PR, and HER2 subgroups. Category of "any night work" may not be a sensitive metric but authors state similar findings were found for other definitions of night shift work.
Davis *et al.* 2001	+ ↓ The study has a low number of exposed subjects with what can be determined at most to be moderate exposure levels; limiting duration to 10 years before diagnosis/reference date in an older population of women is likely to miss any cases due to early exposure in the career.
Fritschi *et al.* 2013	++ ↔ The study has a moderately adequate number of exposed subjects with substantial exposure (medium/high level and high duration) (N = 24 cases). To investigate latency assumptions, authors repeated the analysis indicating whether exposure occurred in the windows of time > 30 years, > 20 and < 30 years, > 10 and < 20 years, and < 10 years before enrollment compared with those who were unexposed during that window of time.
Grundy *et al.* 2013	++ ↓ Combined evening and night work as well as combined permanent and rotating shifts minimized the ability to look at those most highly exposed to night work. The proportion of participants exposed to "night shift work" (combined definition) was relatively high (33%), but only a small percentage worked nights exclusively for 30+ years (N = 16), and no additional information on intensity of night work was available (without including evening work).
Hansen 2001	+ ↓ Large number of exposed cases, and cases classified as having 6+ years in jobs with 60%+ night work. However, as the exposure assessment derives from aggregated data, and not individual level data, uncertainty about actual level of exposure for any specific individual exists.
Hansen and Lassen 2012	+++ ↔ Adequate number of cases with range of exposures and adequate duration of follow-up in the cohort.
Hansen and Stevens 2012	++ ↔ Very small reference group of permanent day workers. There are an adequate number of exposed subjects with substantial duration, or duration that may be meaningful for this exposure. There are also a substantial number of subjects with day-evening-night shifts.
Lie *et al.* 2011	+++ ↔ The study had adequate number of exposed subjects at a substantial exposure level and duration (N = 64 cases with 5+ years working 6+ consecutive nights), and adequate follow-up.
Menegaux *et al.* 2013	++ ↓ Adequate numbers of cases ever working nights; however, less than adequate number of exposed subjects with substantial exposure (duration or intensity).

Reference	Sensitivity rating
O'Leary *et al.* 2006	+ ↓ The study has a very small number of exposed subjects with substantial exposure. The exposure window of 15 years is limited, particularly in this older subset of residentially stable subjects and may or may not be etiologically relevant (60% of overnight shift workers were post-menopausal), which is borderline for being an "older cohort".
Papantoniou *et al.* 2015	++ ↓ For main analyses, the study has an adequate number of exposed subjects, with substantial exposure (level, duration, or range); there was low power to assess possible effect modification by key variables due to small numbers in some subgroups.
Pesch *et al.* 2010	+ ↓ The study had a moderately small number of exposed subjects particularly in the highest exposure category; measures of intensity and duration were included, again with small numbers, and highest exposed intensity not very intense (3+ night shifts per month).
Wang *et al.* 2015	+ ↔ The study has an adequate number of exposed subjects, but no indication of their level, duration, or range of exposure.

Table B-2e: Breast cancer and shiftwork CASE-CONTROL studies: Confounding rationale

Reference	Confounding rating
Cordina-Duverger *et al.* 2016	Breast: +++ ↔ The study measured relevant potential confounders and used appropriate analyses to address them. However, models included additional variables such as BMI and age at menarche (in pathway); both parity and age at first full-term pregnancy were included; and family history of breast cancer was included, as well as tobacco smoking.
Davis *et al.* 2001	Breast: +++ ↔ Study measured all relevant potential confounders with the exception of socioeconomic status/education which was addressed in selection of cases and controls, and did not include variables that had a small effect when added to the models (alcohol, etc.).
Fritschi *et al.* 2013	Breast: +++ ↔ The study measured all relevant confounders and used appropriate methods of analysis to control them.
Grundy *et al.* 2013	Breast: +++ ↔ The study measured all relevant potential confounders and used appropriate analyses to address them, without overloading the model with risk factors that did not change the odds ratio (OR).
Hansen 2001	Breast: ++ ↑ The study did not directly measure SES but used job title; little information on co-exposure, indirect information on alcohol consumption (trade not individual).
Hansen and Lassen 2012	Breast: +++ ↔ The study measured all relevant potential confounders and used appropriate analyses to address them.
Hansen and Stevens 2012	Breast: +++ ↔ The study measured all relevant potential confounders.
Lie *et al.* 2011	Breast: ++ ↑ The study measured all relevant potential confounders with the exception of socioeconomic status, and used appropriate analyses to address them.
Menegaux *et al.* 2013	Breast: +++ ↔ The study measured relevant potential confounders and used appropriate analyses to address them. However, models included additional variables including BMI and age at menarche (in pathway); both parity and age at first full-term pregnancy were included; and family history of breast cancer was included, as well as tobacco smoking.
O'Leary *et al.* 2006	Breast: +++ ↔ All relevant potential confounders measured and appropriate analyses were used to address them.
Papantoniou *et al.* 2015	Breast: +++ The study measured all relevant potential confounders and used appropriate analyses to address them. Included a direct acyclic graph (DAG) in supplemental materials.
Pesch *et al.* 2010	Breast: ++ ↔ The study measured relevant potential confounders with the exception of alcohol use.
Wang *et al.* 2015	Breast: ++ ↔ Given that some variables in the pathway were added to the model even when they were similar between cases and controls likely reduced the estimate towards the null.

Table B-2f: Breast cancer and shiftwork CASE-CONTROL studies: Analysis and selective reporting rationale

Reference	Analysis rating	Selective reporting rating
Cordina-Duverger *et al.* 2016	+++ ↔ The study used relevant data and appropriate assumptions and methods of analysis.	+++ ↔ No evidence that reporting was limited to a subset of the data. Rather, clear statements provided regarding analyses which were run but not included and why.
Davis *et al.* 2001	++ ↔ Study used relevant data and appropriate assumptions and methods of analysis. Given the wide age span in the population (20–74) and the availability of lifetime data on jobs, an age-stratified analysis could have been useful to explore the impact of recent night work among younger and older women in the 10 years preceding diagnosis.	++ ↔ Data on timing of exposure was available given collection of lifetime data, but not reported.
Fritschi *et al.* 2013	+++ ↔ The study used relevant data and appropriate assumptions and methods of analysis. Amount of light was controlled for.	+++ ↔ No evidence that selective reporting of data or analyses compromised the interpretation of the study.
Grundy *et al.* 2013	+++ ↔ The study used relevant data and appropriate assumptions and methods of analysis.	+++ ↔ There is no evidence that reporting of the data or analyses were limited to only a subset of the data that were collected.
Hansen 2001	+++ ↔ The study appeared to use relevant data and appropriate assumptions and methods of analysis, but provided little detail. However, lagging analyses was important in this population.	+++ ↔ No evidence that reporting of the data or analyses were limited to only a subset of the data that were collected.
Hansen and Lassen 2012	+++ ↔ The study used relevant data and appropriate assumptions and methods of analysis and conducted sensitivity analyses which suggested that shift working controls would have to be twice as likely to refuse as shift working cases to negate the observed effect.	+++ ↔ No evidence that reporting of the data or analyses were limited to only a subset of the collected data.
Hansen and Stevens 2012	+++ ↔ Study used relevant data and appropriate assumptions and methods of analysis. Much detail about calculation of various shift types, intensity, and duration.	+++ ↔ There is no evidence that reporting of the data or analyses were limited to only a subset of the data that were collected.
Lie *et al.* 2011	+++ ↔ The study used relevant data and appropriate assumptions and methods of analysis.	+++ ↔ There is no evidence that reporting of the data or analyses were limited to only a subset of the data that were collected.

Reference	Analysis rating	Selective reporting rating
Menegaux *et al.* 2013	+++ ↔ The study used relevant data and appropriate assumptions and methods of analysis.	+++ ↔ No evidence that results were selectively reported.
O'Leary *et al.* 2006	++ ↓ Duration comparisons were made to women with lower frequency of shift work rather than non-workers which may introduce some downward bias.	++ ↔ No evidence that reporting of the data or analyses were limited to only a subset of the data collected. However, information on none of the stratified analyses was shown.
Papantoniou *et al.* 2015	+++ ↔ The study used relevant data and appropriate assumptions and methods of analysis including a DAG.	+++ ↔ No evidence that reporting of the data or analyses were limited to only a subset of the data collected.
Pesch *et al.* 2010	+++ ↔ Study used relevant data and appropriate assumptions and methods of analysis.	++ ↔ There is no evidence that reporting of the data or analyses were limited to only a subset of the data that were collected. Inadequate reporting of loss of shift workers and non-shift workers.
Wang *et al.* 2015	++ ↔ Study used relevant data and appropriate assumptions and methods of analysis. Somewhat thin on detail.	+++ ↔ No indication that reporting of data or analyses were limited to a subset of the data.

Table B-3: Breast cancer and shiftwork COHORT study results

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
Åkerstedt *et al.* 2015 Cohort Sweden **Enrollment or follow-up:** 1998–2003; follow-up 12 yrs	**Population:** Swedish Twin Registry cohort **Exposure assessment method:** questionnaire	**HR Duration (yrs) of night work: Followed to age 60**		Age, education, smoking status, BMI, parity, coffee consumption, previous cancer, hormone and oral contraceptives	**Exposure information:** Number of years with work hours that meant working nights at least "now and then" **Strengths:** Nationwide prospective cohort in unique twin registry population. **Limitations:** Night work poorly defined so that it is not clear if exposed and unexposed were correctly classified. Length of follow-up may not be long enough to detect cases. The study is limited by including only an older age range (41–60) of survivors, such that if starting nightwork early in life is a factor in development of breast cancer some cases may have been missed. **Additional results:** - **Confidence in evidence:** Some evidence
		No night work	1; 354		
		1–45 yr	0.96 (0.74–1.24); 109		
		1–5 yr	0.93 (0.66–1.31); 57		
		6–10 yr	0.79 (0.45–1.38); 16		
		11–20 yr	0.8 (0.45–1.42); 18		
		21–45 yr	1.77 (1.03–3.04); 18		
Gu *et al.* 2015 Cohort 11 U.S. states **Enrollment or follow-up:**	**Population:** Nurses Health Study (NHS) 74,862 **Exposure assessment method:** questionnaire	**HR**		Age, alcohol, physical exercise, multivitamin use, menopausal status, HRT use, physical exam in past	**Exposure information:** Rotating shift work: ≥ 3 shifts/month **Strengths:** Large prospective study of nurses with well documented follow-up procedures and outcome
		Never	1; 269		
		1–5 yr rotating work	1.07 (0.9–1.26); 293		
		6–14 yr rotating work	0.99 (0.76–1.27); 79		

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
Enrolled 1976; follow-up 1988–2008		≥ 15 yr rotating work	0.99 (0.74–1.33); 55	2 years, healthy eating score, smoking status, pack years, BMI, husband's education	definitions and adequate control for potential confounders. **Limitations:** Mortality study likely to miss cases given the high survival rate for breast cancer leading to potential for selection bias if fatal cases are more or less likely to be exposed to shift work. Exposure assessment may have biased results towards the null as permanent night workers may have been classified as unexposed. No analyses on healthy worker survival in this occupational cohort. **Additional results:** - **Confidence in evidence:** Supporting evidence.
Jørgensen *et al.* 2017 Cohort	**Population:** Theh Danish Nurses Cohort (DNC)	**Mortality: HR Type of shift:**		Age, smoking status, pack years, physical activity, BMI, alcohol	**Exposure information:** Current work in evening (3:00 PM to midnight), night (11:00 PM to 7:00 AM) or rotating shifts
		Day shifts	1; 119		
		Night shifts	1.2 (0.7–2.08); 16		

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
Denmark **Enrollment or follow-up:** 1993–2013	18,015 **Exposure assessment method:** questionnaire	Rotating shifts	0.96 (0.66–1.37); 38	consumption, diet (veggies, fruit, meat), pre-existing disease (hypertension, diabetes, MI), self-reported health, stressful work enviornment, marital status, parity, use of HRT, OC use	(day/evening or day/evening/night). **Strengths:** Nationwide prospective cohort of female nurses with detailed information on current work schedules only at baseline, and potential confounders. **Limitations:** Small numbers of breast cancer deaths, no information on duration or intensity, type of rotation schedule, nor past information on shift work. No cancer validation. Due to high breast cancer survival, mortality analyses may select for fatal cases that may or may not be related to shift work. **Additional results:** - **Confidence in evidence:** No confidence, not included in the assessment
Knutsson *et al.* 2013 Cohort Sweden **Enrollment or follow-up:** 1992–95 (Stockholm) and 1996–97 (Norrland); and 2000–2003 (Norrland)	**Population:** Work, Lipids, and Fibrinogen (WOLF) occupational cohort 4,036 **Exposure assessment method:** questionnaire	**HR All ages**		Parity (4 levels), Alcohol consumption (high/low)	**Exposure information:** 3 rounds of questionnaires used to create exposure variable to classify women as day workers, and shift workers with and without night shifts. **Strengths:** Prospectively collected data; unique person ID enabling linkage of data to cancer registry; information on several potential confounders. Relatively young cohort. **Limitations:** Low response rate and high attrition from baseline to follow-up; small numbers of exposed cases; limited information on exposure –only ever/never night work, no information on
		Only day shifts	1; NR		
		Shifts without nights	1.23 (0.7–2.17); 20		
		Shifts with nights	2.02 (1.03–3.95); 14		
		HR Age < 60		Parity (4 levels), Alcohol consumption (high/low)	
		Only day shifts	1; NR		
		Shifts without nights	1.18 (0.67–2.07); 17		
		Shifts with nights	2.15 (1.1–4.21); 12		
		Mean Time in years (cumulative incidence): schedule type			
		Only day shifts	2.4; 60		
		Shifts without nights	2; 20		

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
		Shifts with nights	2.6; 14		intensity, duration or timing. **Additional results:** Shift worker cases had shorter time to diagnosis than day worker cases. incidence info is included in additional results box in the first result for this study. **Confidence in evidence:** Some evidence.
		Trend-test *p*-value: 0.01			
Koppes *et al.* 2014 Cohort Netherlands **Enrollment or follow-up:** 1996–2009; follow-up 1996–2009	**Population:** Netherlands general population prospective cohort 285,723 women **Exposure assessment method:** interview	**HR (RR) Current shift work**		Age, origin, children in the household, education, occupational group, contractual working hours, job tenure	**Exposure information:** Current night work, sometimes or regularly, midnight to 6:00 AM. **Strengths:** Large, general population, prospective study linked with national hospital admission registration. **Limitations:** Only current shift work captured with no data on past exposure. Assumes duration of work at current job is an adequate proxy for lifetime exposure to night work; relevant confounders not adjusted for in analysis; short latency. Admission data as a proxy for incidence data may introduce bias if access to hospital is differential for shift workers and non-shift workers. **Additional results:** - **Confidence in evidence:** No confidence; not included in assessment.
		No current night work	1; 2312		
		Occasional	1.04 (0.85–1.27); 102		
		Regular	0.87 (0.72–1.05); 117		
		HR (RR) Occasional night work in current job: Job tenure (yrs)		Age, origin, children in the household, education, contractual working hours, occupational group	
		No current night work	1; 2312		
		> 0–3 yr	1.05 (0.7–1.57); 25		
		4–9 yr	1.05 (0.71–1.55); 25		
		10–19 yr	1.21 (0.85–1.73); 26		
		≥ 20 yr	0.78 (0.48–1.28); 17		
		Trend-test *p*-value: 0.66			
		HR (RR) Duration (yrs) of regular night work in current job		Same as above	
		No current night work	1; 2312		
		0–3 yr	0.7 (0.47–1.04); 46		
		4-9 yr	0.94 (0.66–1.34); 46		
		10-19 yr	0.91 (0.65–1.28); 47		
		> 20 yr	0.95 (0.62–1.45); 30		

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
		Trend-test *p*-value: 0.26			
		HR (RR) Nurses; Night work in current job		Age, origin, children in the household, education, job tenure, contractual working hours	
		No current night work	1; NR		
		Occasional	1.42 (0.92–2.19); NR		
		Regular	0.93 (0.66–1.31); NR		
Li *et al.* 2015 Nested Case-Control Shanghai, China **Enrollment or follow-up:** 1989–1991: follow-up 2002	**Population:** Female textile workers in Shanghai textile industry Cases: 1,709; Controls: 4,780 **Exposure assessment method:** company records	**HR (RR) Duration (yrs) of rotating night work: All women**		Age	**Exposure information:** Number of years worked on ratiating night shift (continuous work hours between midnight and 5:00 AM); all rotating shift workers with set forwarding schedule; usually 7.5 nights/month. **Strengths:** Well-defined occupational cohort, with sufficient number of cases; work histories complete for all women; detailed shift work information for each job including several metrics. **Limitations:** Older cohort with a high percentage of long-term shift workers may represent a survivor cohort. No information on lifetime exposure history. **Additional results:** For these >50 year-old women, there was a 22%–23% increased nonsignificant risk in both the unlagged (reported here) and 10-year lagged analysis, but not in the 20-year lagged analysis. **Confidence in evidence:** No evidence.
		None	1; 557		
		> 0–12.8 yr	0.99 (0.83–1.17); 286		
		> 12.8–19.92 yr	0.97 (0.82–1.15); 290		
		> 19.92–27.67 yr	0.9 (0.76–1.06); 289		
		> 27.67 yr	0.88 (0.74–1.05); 287		
		Trend-test *p*-value: .095			
		HR (RR) Duration (yrs) worked rotating night shift: < 50 yrs old		Age	
		None	1; 273		
		> 0 –11 yr	0.87 (0.67–1.12); 114		
		> 11–6.8 yr	0.94 (0.73–1.22); 118		
		> 16.8–21.54 yr	1.06 (0.81–1.37); 112		
		> 21.54 yr	0.94 (0.72–1.22); 115		
		Trend-test *p*-value: .453			
		HR (RR) Duration (yrs) worked rotating night shift: ≥ 50 yrs old		Age	
		None	1; 284		
		> 0–14.5 yr	1.23 (0.97–1.56); 173		
		> 14.5 –24.2 yr	0.86 (0.68–1.09); 173		

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
		> 24.2 –31.17 yr	0.85 (0.67–1.07); 174		
		> 31.17 yr	0.96 (0.76–1.23); 173		
		Trend-test *p*-value: .430			
		HR (RR) All women: # rotating night shifts		Age	
		None	1; 557		
		> 0–1,316.79	0.96 (0.81–1.14); 288		
		> 1,316.79–2,018.71	1 (0.84–1.19); 287		
		> 2,018.71–2,880	0.88 (0.74–1.04); 288		
		> 2,880	0.89 (0.75–1.07); 289		
		Trend-test *p*-value: .155			
		HR (RR) # of rotating night shifts: < 50 yrs		Age	
		None	1; 273		
		> 0–1,114.29	0.83 (0.64–1.07); 115		
		> 1,114.29-–1,603.39	0.95 (0.73–1.23); 113		
		> 1,603.39 -– 2,116.61	1.08 (0.83–1.4); 117		
		> 2,116.61	0.96 (0.74–1.26); 114		
		Trend-test *p*-value: .200			
		HR (RR) # of rotating night shifts: ≥ 50 yrs old		Age	
		None	1; 284		
		> 0–1,627.5	1.09 (0.88–1.36); 173		
		> 1,627.5–2,588.21	0.84 (0.68–1.04); 172		
		> 2,588.21 – 3,453.78	0.91 (0.74–1.13); 174		
		> 3,453.78	0.93 (0.74–1.16); 174		
		Trend-test *p*-value: .140			

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
Pronk *et al.* 2010 Cohort Shanghai **Enrollment or follow-up:** 1996–2000; follow-up 2000–2007	**Population:** Shanghai Women's Health Study 73,049 **Exposure assessment method:** interview	**HR (RR) Duration (years) of night work: jobs with JEM scores > 0**		Age, education, Fam hx BRCA, # pregnancies, age at first birth, occupational physical activity	**Exposure information:** Job exposure matrix (JEM) for night shift work 0=no, 1=incidental, 2= likely, 3=probably; self report night shift work: start 10:00 PM ≥ 3 /mo for ≥1yr. **Strengths:** Large, prospective cohort with exposure data collected prior to breast cancer diagnosis; appropriate analysis and control for confounding. Supplementary individual level data collected to verify night shifts assessed by JEM based on job title alone. **Limitations:** This older (ages 40–70) surviving cohort of women may have been subject to the healthy worker survivor effect (HWSE); if breast cancer is likely to occur early on in a person's career, this would not be captured in this survivor cohort; also, very short follow-up time. **Additional results:** A JEM analysis was also performed, but it showed different exposure assessment results from the self-reported data, though the findings were approximately the same. **Confidence in evidence:** No evidence
		Never worked at night	1; 423		
		Ever worked at night	1 (0.9–1.2); 294		
		> 0 and ≤ 14 yr	1.1 (0.9–1.3); 108		
		> 14 and ≤ 25 yr	0.9 (0.7–1.1); 89		
		> 25 yr	1 (0.8–1.3); 97		
		Trend-test *p*-value: 0.72			
		HR (RR) Average shift work JEM score		Same as above	
		0	1; 423		
		> 0 and ≤ 1.29	1 (0.8–1.2); 102		
		> 1.29 and ≤ 2.38	1.1 (0.9–1.3); 109		
		> 2.38	0.9 (0.7–1.2); 83		
		Trend-test *p*-value: 0.73			
		HR (RR) Lifetime cumulative night shift JEM Score		Same as above	
		0	1; 423		
		> 0–< 34	1 (0.8–1.3); 102		
		> 34–< 66	1 (0.8–1.2); 103		
		> 66	1 (0.8–1.2); 89		
		Trend-test *p*-value: 0.84			
		HR (RR) Age started working first job with JEM score > 0		Same as above	
		No shift work	1; 423		
		> 26	1 (0.8–1.2); 87		
		> 20–≤ 26	1 (0.8–1.3); 98		

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
		> 0–≤ 20	1 (0.8–1.2); 109		
		HR (RR) Frequency (night shifts/mo): Self reported		Same as above	
		Never	1; 276		
		Ever	0.9 (0.7–1.1); 73		
		> 0–<8 shfits	0.6 (0.3–1.2); 8		
		8 shifts	0.9 (0.7–1.3); 45		
		> 8 shifts	0.9 (0.5–1.3); 20		
		Trend-test *p*-value: 0.29			
		HR (RR) Duration (years) night shift work: Self-reported		Same as above	
		Never	1; 276		
		> 0–≤ 5 yr	0.9 (0.6–1.3); 25		
		> 5–≤ 17 yr	0.9 (0.6–1.4); 29		
		> 17 yr	0.8 (0.5–1.2); 19		
		Trend-test *p*-value: 0.26			
		HR (RR) Age (years) starting night shift work: self-reported		Same as above	
		Never worked at night	1; 276		
		> 30	0.7 (0.5–1.2); 18		
		> 21–≤ 30 yrs	0.9 (0.6–1.3); 25		
		> 0–≤ 21 years	0.9 (0.6–1.4); 30		
		Trend-test *p*-value: 0.26			
		HR (RR) Ever worked night shift: Both JEM and self report		Same as above	
		Never	1; NR		

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
		Ever	0.9 (0.7–1.3); NR		
		Trend-test *p*-value: 0.26			
Schernhammer *et al.* 2001 Cohort 11 U.S. states **Enrollment or follow-up:** Enrolled 1976; followed June 1988–May 1998	**Population:** Nurses Health Study (NHS) 78,562 **Exposure assessment method:** questionnaire	**RR Duration (years) of rotating night shift work: All**		Age, age at menarche, age 1st ft preg, parity, weight change between 18 yrs and menopause, BMI at age 18 years, Fam hx BRCA, benign breast disease, OC use, current alcohol consumption, age at menopause, use of post menopausal hormones, menopausal status, height, time period of follow-up	**Exposure information:** Rotating night shift work ≥ 3/month **Strengths:** Large prospective study of nurses with well-documented follow-up procedures and outcome definitions, with adequate data on potential confounders. **Limitations:** Exposure assessment may have biased results towards the null as permanent night workers may have been classified as unexposed. No information on intensity. Analysis included many variables unrelated to both exposure and outcome, potentially biasing results towards the null. Shiftwork exposures were assessed once as lifetime exposures near the end of the surviving breast cancer-free nurses' working careers with a follow-up period well into post-retirement years. **Additional results:** - **Confidence in evidence:** Supporting evidence.
		Never worked	1; 925		
		1-14 yr	1.08 (0.99–1.18); 1324		
		15-29 yr	1.08 (0.9–1.3); 134		
		≥ 30 yr	1.36 (1.04–1.78); 58		
		Trend-test *p*-value: .02			
		RR Duration of work (years): Post menopausal		Same as above	
		Never worked	1; 801		
		1–14 yr	1.06 (0.97–1.16); 1146		
		15–29 yr	1.05 (0.87–1.27); 120		
		≥ 30 yr	1.36 (1.04–1.78); 58		
		Trend-test *p*-value: .05			
		RR Duration (years) of work: Pre-menopausal		Same as above	
		Never worked	1; 121		
		1-14 yrs	1.23 (0.97–1.55); 174		
		≥ 15 yrs	1.34 (0.77–2.33); 14		

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
		Trend-test *p*-value: .1			
Schernhammer *et al.* 2006 Cohort 14 U.S. states **Enrollment or follow-up:** Enrolled 1989; followed 1989–June 1, 2001	**Population:** Nurses Health Study (NHS2) 115,022 women **Exposure assessment method:** questionnaire	**RR Duration (years) of working shift work: primarily premenopausal**		Age, age at menarche, age 1st ft preg, parity, Fam hx BRCA, benign breast disease, OC use, age at menopause, use of post menopausal hormones, menopausal status, height, BMI, Smoking status, alcohol consumption, physical activity	**Exposure information:** Rotating shift defined as working nights ≥ 3/month **Strengths:** Large cohort of nurses with well-documented follow-up procedures and case definitions. **Limitations:** Small number of women exposed for 20+years; and no information on intensity or timing of exposure. **Additional results:** - **Confidence in evidence:** Supporting evidence.
		Never worked	1; 441		
		1-9 years	0.98 (0.87–1.1); 816		
		10-19 years	0.91 (0.72–1.16); 80		
		≥ 20 years	1.79 (1.06–3.01); 15		
		Trend-test *p*-value: 0.65			
Schwartzbaum *et al.* 2007 Cohort Sweden **Enrollment or follow-up:** 1960 and 1970; follow-up: 1971–1989	**Population:** Swedish working women registered in 1960 and 1970 census data 1,148,661 female workers **Exposure assessment method:** JEM	**SIR Among women working in jobs defined as mostly shift work in the 1969 and 1970 census**		Age, socioeconomic status, occupational position, county of residence	**Exposure information:** Workplace had rotating schedule or work between 1 and 4 AM **Strengths:** Nationwide cohort of working age women in diverse industries followed for 19 years. **Limitations:** Exposure underestimated; small number of exposed cases, aggregate exposure data, lack of data on relevant potential confounders or co-exposures. Misclassification of exposure likely. **Additional results:** - **Confidence in evidence:** No confidence; not included in assessment.
		Shiftwork in 1970	0.94 (0.74–1.18); 70		
		Shiftwork in 1960 and 1970	0.97 (0.67–1.4); 28		
	Population: U.K. EPIC Oxford Study	**RR (Hazard Ratio) Duration (years) of night work**		Age, SES, parity, age at first birth, BMI,	**Exposure information:** Night shift work: Midnight to 6:00 AM for at

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
Travis *et al.* 2016 Oxford, U.K. Cohort **Enrollment or follow-up:** 2010 (4th Survey); follow-up 2012	22,274 women **Exposure assessment method:** questionnaire	Never	1; 153	alcohol consumption, physical activity, Strenuous, age at menarche, OC use, smoking, living with a partner, HRT use, method of recruitment, region of residence	least 3 nights/month **Strengths:** Prospective design and data collection on night work prior to diagnosis; individual level data on potential confounders. Data collected on duration of exposure **Limitations:** Small numbers of exposed, and only 1 exposed case with 20+ years of night work; information on multiple exposure metrics not reported. Follow-up less than 4 years; half of the population over the age of 58, meaning that this may also be somewhat of a survivor cohort with little information about long-term night work at early ages. **Additional results:** An analysis of nurses alone was done to compare these results with the NHS study. No elevated risk, nonsignificant or statistically significant, was found. NTP combined 10–19 and 20+ years into a category of 10+ years estimating it with a fixed effects model. **Confidence in evidence:** Some evidence.
		Ever worked	1.07 (0.71–1.62); 28		
		< 10 yr	1.18 (0.69–2.01); 15		
		10–19 yr	1.92 (1.03–3.57); 11		
		≥ 20 yr	0.22 (0.03–1.61); 1		
		≥ 10 yr	[1.58 (0.88–2.85); 12]		
		Trend-test *p*-value: 0.75			
Travis *et al.* 2016 Cohort England and Scotland **Enrollment or follow-up:** 2009–2012 (4th survey); follow-	**Population:** U.K. Million Women Cohort **Exposure assessment method:** questionnaire	**RR (Hazard Ratio) Duration (years) of night work: women who last worked night shifts in the past 10 years**		Study area, age, SES, parity, age at first birth, BMI, alcohol consumption, physical activity, Strenuous, age at menarche, OC use, smoking, living with a partner, HRT use,	**Exposure information:** Night work: Midnight to 6:00 AM, for at least 3 nights/month. **Strengths:** Prospective design with night shift work data collected prior to diagnosis; large numbers of exposed; individual level data on potential confounders and control for potential confounders. Analysis by time since last worked
		Never worked	1; 4136		
		Ever worked	1.1 (0.94–1.3); 156		
		< 10 yr	0.97 (0.74–1.26); 55		
		10–19 yr	1.41 (1.07–1.86); 52		
		≥ 20 yr	0.98 (0.72–1.33); 42		

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
up 2013		Trend-test *p*-value: 0.42		family history of breast cancer	night shifts. **Limitations:** Lack of exposure assessment regarding intensity, direction of rotation, contiguous shifts. Older cohort of survivors (post menopausal women) may not capture cases occurring after shift work at an early age. **Additional results:** For women last working night shifts more than 10 years in the past, all estimates by duration were similar to 1.0. **Confidence in evidence:** Some evidence.
		RR (Hazard Ratio) Duration (yrs) of night work: All women		Same as above	
		Never	1; 4136		
		Ever	1 (0.92–1.08); 673		
		<10 yr	0.93 (0.83–1.03); 400		
		10–19 yr	1.14 (0.96–1.35); 140		
		≥ 20 yr	1 (0.81–1.23); 89		
		Trend-test *p*-value: 0.68			
Travis *et al.* 2016 Cohort England, Scotland, and Wales **Enrollment or follow-up:** 2006–2010; Follow-up Dec 2012	**Population:** U.K.Biobank Cohort 251,045 **Exposure assessment method:** questionnaire	**RR (Hazard Ratio) Current (main job)**		Study area, age, SES, parity, age at first birth, BMI, alcohol consumption, physical activity, Strenuous, age at menarche, OC use, smoking, living with a partner, HRT use, family history of breast cancer	**Exposure information:** Worked between midnight to 5:00 AM. Low prevalence of exposure (3%) **Strengths:** Prospective design measuring exposure prior to diagnosis; individual level data on potential confounders and control for potential confounders. **Limitations:** Lack of exposure assessment regarding ever/never lifelong exposure to nightwork, Unexposed participants were a mix of previously exposed and currently unexposed. Very short follow-up; cohort of surviving women 40–69 yrs of age. Women working shifts early in their careers and developing cancer may have been excluded from the cohort. **Additional results:** - **Confidence in evidence:** No confidence; no included in assessment.
		Not current night shift work	1; 2653		
		Current night shift work	0.78 (0.61–1); 67		

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
Tynes et al. (1996) Nested Case-Control Norway **Enrollment or follow-up:** 1920–1980; follow-up 1961-1991	**Population:** Norwegian radio and telegraph operators study Cases: 50; Controls: 259 **Exposure assessment method:** company records	**OR < 50 years of age: Cumulative shift work exposure (category x years)**		Duration of employment	**Exposure information:** Shift work defined as frequent presence in radio room both at night and day **Strengths:** Prospective occupational cohort with complete data from occupational and cancer registries. **Limitations:** Exposure assessment was limited; no individual level data for electromagnetic fields and radiofrequency fields, potential co-exposures. Incomplete control for potential confounding by breast cancer risk factors. **Additional results:** - **Confidence in evidence:** Some evidence.
		No shift work	1; 12		
		Low (> 0–3.1 yr)	0.3 (0.1–1.2); 5		
		High (> 3.1– 0.7 yr)	0.9 (0.3–2.9); 12		
		Trend-test *p*-value: 0.97			
		OR < 50 years of age: Cumulative shift work (category x years) before the age of 30.		Duration of employment	
		No shift work	1; 7		
		Low (> 0–2.7 yr)	0.9 (0.2–3); 12		
		High (> 2.7–17.1 yr)	1.9 (0.5–7); 10		
		Trend-test *p*-value: 0.31			
		OR ≥ 50 years of age: Cumulative shift work exposure (category x years)		Duration of employment	
		No shift work	1; 3		
		Low (> 0–3.1 yr)	3.2 (0.6–17.3); 6		
		High (> 3.1– 20.7 yr)	4.3 (0.7–26); 12		
		Trend-test *p*-value: 0.13			
		OR ≥ 50 yrs of age: Cumulative shift work (category x years) before age 30		Duration of employment	
		No shift work	1; 7		
		Low (> 0–2.7 yr)	3.1 (0.7–14.2); 6		
		High (> 2.7–17.1 yr)	4.6 (0.1–7.5); 8		
		Trend-test *p*-value: 0.06			
Vistisen *et al.* 2017 Cohort	**Population:** Danish payroll data cohort. 156,927 (full population);	**RR Ever night (short-term exposure); shiftwork by breast cancer subtype**		Calendar year, age, age at birth of first child, number of	**Exposure information:** Nightwork defined as ≥ 3 hours between midnight and 5:00 AM
		Only day workers	1; 751		

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
Denmark **Enrollment or follow-up:** 2007–2012	55,381 (inception population) **Exposure assessment method:** company records	Ever: All breast cancers	0.9 (0.8–1.01); 425	births, OC use, HRT use, other sex hormone use, medication related to alcoholism, number of mammograms, family education level, family history of breast cancer, family history of ovarian cancer	**Strengths:** Large population with detailed individual level day-to-day information on working hours from a complete countrywide payroll register with linkages to cancer registry, the civil registration system, and family income register. **Limitations:** Left truncation of the dataset with no supplementary information on lifetime history of shiftwork; and there is no information on duration of shiftwork beyond 5 years. The subpopulation of women with a washout period differ from the total population in ways that could bias the results. **Additional results:** - **Confidence in evidence:** No evidence.
		Ever: ER-/HER2-	0.85 (0.59–1.23); 49		
		Ever: ER+/HER2-	0.8 (0.68–0.95); 250		
		Ever: ER-/HER2+	1.49 (0.93–2.39); 37		
		Ever: ER+/HER2+	1.26 (0.84–1.89); 48		
		RR Inception subpopulation: Shift work since entry and during the past 1 to 1–4 years time windows		Same as above	
		Since entry	0.88 (0.66–1.17); 69		
		Past 1–2 yr	0.82 (0.56–1.18); 37		
		Past 1–3 yr	1.14 (0.76–1.71); 36		
		Past 1–4 yr	1.33 (0.82–2.17); 29		
		Past 1–5 yr	1.01 (0.44–2.32); 10		
Wegrzyn *et al.* 2017 Cohort U.S.A. **Enrollment or follow-up:** NHS 1988–2012;	**Population:** Nurses Health Study (NHS and NHS2) NHS 78,516; NHS2 114,559 **Exposure assessment method:** questionnaire	**RR NHS2: Duration (years) of rotating night shift work: exposure at baseline**		Age, age at menarche, Fam hx BRCA, benign breast disease, OC use, age at menopause, use of post menopausal hormones,	**Exposure information:** Working rotating shifts at least 3/month. **Strengths:** The two NHS cohorts together reveal important information about timing of night work in relation to breast cancer. 24 years of follow-up data and large number of breast cancer cases; complete
		Never worked	1; 1318		
		1–9 yr	1.05 (0.98–1.13); 2071		
		10–19 yr	1 (0.85–1.17); 168		
		≥ 20 yr	2.15 (1.23–3.73); 13		

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
NHS2 1989–2013		Trend-test *p*-value: 0.23		menopausal status, height, BMI, alcohol consumption, physical activity, BMI at age 18 years, adolescent body size at age 10 and age 20, ag at first birth and parity combined, breastfeeding duration, duration of estrogen alone HRT, current mammography use	information on potential confounders; ability to analyze by subtype; ability to compare two similar, but age differentiated cohorts. **Limitations:** Potential misclassification of unexposed including permanent night workers and non-shiftworkers as most nurses are exposed to some shift work. Small number of NHS2 women exposed for 20+years; no information on intensity or pattern of nightshift work most disruptive to circadian rhythms. **Additional results:** - **Confidence in evidence:** Moderate to strong evidence.
		RR NHS2: Duration (years) of rotating night shift work in 24 years of follow-up: updated exposure		Same as above	
		Never worked	1; 950		
		1–9 yr	1.04 (0.96–1.12); 2002		
		10–19 yr	0.94 (0.81–1.1); 201		
		≥ 20 yr	1.4 (1–1.97); 35		
		Trend-test *p*-value: 0.74			
		HR NHS2: Women with ≥ 20 years rotating shiftwork by follow-up interval (<10 or ≥ 10 years)		Same as above	
		≥ 20 yr: < 10 yr follow-up, baseline exposure	2.35 (1.04–5.31); 6		
		≥ 20 yr: ≥ 10 yr follow-up, baseline exposure	1.95 (0.92–4.15); 7		

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
		≥ 20 yr: < 10 yr, updated exposure	2.13 (1.19–3.81); 12		
		≥ 20 yr: ≥ 10 yr, updated exposure	1.19 (0.78–1.81); 23		
		HR NHS2: Women with ≥ 20 years rotating shiftwork and ER+PR+ status; baseline or updated exposure information.		Same as above	
		Baseline exposure	1.58 (0.65–3.83); 5		
		Updated exposure	1.62 (1.07–2.45); 24		
		RR NHS: Duration (years) rotating shiftwork in 24 years of follow-up		Age, age at menarche, benign breast disease, OC use, age at menopause, use of post menopausal hormones, menopausal status, height, BMI, alcohol consumption, physical activity, BMI at age 18 years, adolescent body size at age 10 and age 20, ag at first birth and parity combined, breastfeeding duration, duration of estrogen alone HRT, current mammography use, family history of breast cancer	
		Never worked	1; 2382		
		1–14 yr	1.01 (0.96–1.07); 3162		
		15–29 yr	1.06 (0.94–1.19); 331		
		≥ 30 yr	0.95 (0.77–1.17); 96		
		Trend-test *p*-value: 0.63			

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
		RR NHS: Women with ≥30 years rotating shiftwork by follow-up interval		Same as above	
		<10 yr	1.26 (0.97–1.64); 60		
		≥10 yr	0.68 (0.49–0.95); 36		
		RR NHS: ≥30 yrs rotating shiftwork (yrs) in 24 years of follow-up		Same as above	
		ER+/PR+ receptor status	0.96 (0.73–1.27); 54		
		Mortality: RR NHS: Mortality. Rotating shiftwork duration (years) (Gu et al. 2015)		Age, menopausal status, BMI, alcohol consumption, physical activity, multivitamin use, HRT use, physical exam in past 2 years, healthy eating score, smoking status, pack years, Husband's education	
		Never worked	1; 269		
		1–5 yr	1.01 (0.9–1.26); 293		
		6–14 yr	0.99 (0.76–1.27); 79		
		≥ 15 yr	0.99 (0.74–1.33); 55		

Table B-4: Breast cancer and shiftwork CASE-CONTROL study results

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
Cordina-Duverger *et al.* 2018 Case-control Pooled analysis of 5 case-control studies	**Population:** Population-based studies from Australia, Canada, France, Germany, Spain **Exposure assessment method:** Questionnaire	**OR Ever/never worked at night - pooled, All women**		Age, age at menarche, parity, age at first full-term pregnancy, breastfeeding, family history of breast cancer, oral contraceptive (OC) use, body mass index (BMI), alcohol, tobacco, hormone replacement therapy (HRT), menopausal status	**Exposure information:** Jobs that included at least 3 hours of work between midnight and 5:00 AM **Strengths:** Pooled data from 5 studies to create a single definition of nightwork**;** multiple metrics of exposure; large population **Limitations:** Self-reported data, some collected after 2007, the date of the IARC report on shiftwork. **Additional results:** - **Confidence in evidence:** Moderate to strong evidence
		Never worked at night	1; 5,322		
		Ever worked at night	1.12 (1–1.25); 771		
		OR Ever/never worked at night - pooled, Premenopausal women		Age, age at menarche, parity, age at first full-term pregnancy, breastfeeding, Family history of breast cancer, OC use, BMI, alcohol, tobacco	
		Never worked at night	1; 1,669		
		Ever worked at night	1.26 (1.06–1.51); 324		
		OR Ever/never worked at night - pooled, Postmenopausal women		Age, age at menarche, parity, age at first full-term pregnancy, breastfeeding, Family history of breast cancer, OC use, BMI, alcohol, tobacco, HRT	
		Never worked at night	1; 3,652		
		Ever worked at night	1.04 (0.9–1.19); 447		
		OR Duration (years) of night work - pooled, All women		Age, age at menarche, parity, age at first full-term pregnancy, breastfeeding, Family	
		Never worked at night	1; 5,322		
		< 10 yr	1.18 (1.03–1.36); 461		

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
		10–19 yr	0.98 (0.78–1.22); 154	history of breast cancer, OC use, BMI, alcohol, tobacco, HRT, menopausal status	
		≥ 20 yr	1.1 (0.87–1.39); 151		
		OR Duration of night work - pooled, Premenopausal women		Age, age at menarche, parity, age at first full-term pregnancy, breastfeeding, family history of breast cancer, OC use, BMI, alcohol, tobacco	
		Never worked at night	1; 1,669		
		< 10 yr	1.33 (1.07–1.65); 210		
		10–19 yr	1.05 (0.74–1.47); 69		
		≥ 20 yr	1.34 (0.85–2.13); 42		
		OR Duration of night work - pooled, Postmenopausal women		Age, age at menarche, parity, age at first full-term pregnancy, breastfeeding, family history of breast cancer, OC use, BMI, alcohol, tobacco	
		Never worked at night	1; 3,652		
		< 10 yr	1.09 (0.91–1.31); 251		
		10–19 yr	0.92 (0.68–1.23); 85		
		≥ 20 yr	1.04 (0.8–1.36); 109		
		OR Length of nightshifts - pooled, All women		Age, age at menarche, parity, age at first full-term pregnancy, breastfeeding, family history of breast cancer, OC use, BMI, alcohol, tobacco, HRT, menopausal status	
		Never worked at night	1; 5,322		
		< 8 hr	1.06 (0.78–1.43); 84		
		8–9 hr	1.15 (0.98–1.34); 324		
		≥ 10 hr	1.12 (0.96–1.31); 344		
		OR Length of night shifts - pooled, Premenopausal women		Age, age at menarche, parity, age at first full-term pregnancy, breastfeeding, family history of breast	
		Never worked at night	1; 1,669		
		< 8 hr	1.03 (0.65–1.64); 37		

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
		8–9 hr	1.2 (0.91–1.6); 111	cancer, OC use, BMI, alcohol, tobacco	
		≥ 10 hr	1.36 (1.07–1.74); 167		
		OR Length of night shifts - pooled, Postmenopausal women		Age, age at menarche, parity, age at first full-term pregnancy, breastfeeding, family history of breast cancer, OC use, BMI, alcohol, tobacco, HRT	
		Never worked at night	1; 3,652		
		< 8 hr	1.09 (0.73–1.65); 47		
		8–9 hr	1.12 (0.92–1.36); 213		
		≥ 10 hr	0.96 (0.78–1.19); 177		
Cordina-Duverger *et al.* 2016 Case-control France, Cote d'Or and Ille-et-Vilaine departments **Enrollment or follow-up:** 2005-2007	**Population:** CECILE Study Cases: 975; Controls: 1,317 **Exposure assessment method:** questionnaire	**OR Any night shift: post menopausal women**		Age, study area, age at menarche, parity, age at first full-term pregnancy, breastfeeding duration, OC use, menopausal hormone therapy, alcohol consumption, tobacco consumption, BMI, Fam hx BRCA	**Exposure information:** Night work is defined as working the entire time period between 11:00 PM and 5:00 AM. **Strengths:** Large, well-designed general population based case-control study with detailed, quality data on HER2, and ER and PR status. **Limitations:** Some subtypes with small numbers (e.g., ER-, PR-, and combinations of various subtypes) **Additional results:** - **Confidence in evidence:** Moderate to strong evidence
		Never worked at night	1; 540		
		Ever worked at night	0.97 (0.61–1.54); 39		
		ER+	0.96 (0.59–1.58); 33		
		ER-	1.08 (0.43–2.72); 6		
		PR+	0.92 (0.54–1.57); 25		
		PR-	1.06 (0.54–2.07); 14		
		ER+/PR+	0.91 (0.53–1.56); 24		
		ER+/PR-	1.2 (0.52–2.75); 9		
		HER2+	1.03 (0.38–2.81); 5		
		HER2-	0.96 (0.59–1.57); 34		
		HER2+ and (ER+ or PR+)	1.59 (0.55–4.59); 5		
		HER2+ and (ER- and PR-)	-		
		OR Any night shift: all women		Age, study area, age at menarche, parity, age at first full-term	
		Never worked at night	1; 876		
		Ever worked at night	1.38 (1.01–1.88); 99		

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
		ER +	1.49 (1.08–2.05); 87	pregnancy, breastfeeding duration, OC use, family history of breast cancer, menopausal hormone therapy, alcohol consumption, tobacco consumption, menopausal status, BMI	
		ER-	0.86 (0.44–1.7); 12		
		PR+	1.48 (1.06–2.06); 74		
		PR-	1.12 (0.68–1.84); 25		
		ER+/PR+	1.48 (1.06–2.07); 73		
		ER+/PR-	1.56 (0.82–2.98); 14		
		ER-/PR-	0.83 (0.41–1.67); 11		
		HER2+	1.91 (1.09–3.33); 20		
		HER2-	1.29 (0.93–1.78); 79		
		HER2+ and (ER+ or PR+)	2.52 (1.36–4.68); 17		
		HER2+ and (ER- and PR-)	0.75 (0.16–3.38); 3		
		OR Any night shift: pre-menopausal women		Age, age at menarche, study area, parity, age at first full-term pregnancy, breastfeeding duration, OC use, family history of breast cancer, alcohol consumption, tobacco consumption, BMI	
		Never worked at night	1; 336		
		Ever worked at night	1.77 (1.14–2.73); 60		
		ER +	2.04 (1.3–3.19); 54		
		ER -	0.7 (0.25–1.9); 6		
		PR +	1.98 (1.25–3.12); 49		
		PR -	1.12 (0.52–2.43); 11		
		ER+ PR+	2.02 (1.28–3.19); 49		
		ER+ PR-	2.24 (0.73–6.84); 5		
		HER2+	2.8 (1.36–5.76); 15		
		HER2-	1.58 (1–2.52); 45		

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
		HER2+ and (ER+ or PR+)	3.3 (1.42–7.67); 12		
		HER2+ and (ER- and PR-)	2.3 (0.36–14.7); 3		
Davis *et al.* 2001 Case-control Seattle, WA **Enrollment or follow-up:** 1992–1995	**Population:** Population-based study Cases: 813; Controls: 793 **Exposure assessment method:** questionnaire	**OR Duration of work (years) graveyard shift (≥ 1/week) within the past 10 years before diagnosis**		Parity, family history of breast cancer, OC use, use of HRT discontinued <5 years, age	**Exposure information:** At least 1 graveyard shift (7:00 PM–9:00 AM) per week within the 10 years before diagnosis **Strengths:** Detail on graveyard shifts; strong population based methods; limited potential for recall bias. **Limitations:** Small numbers of exposed; exposure window limited and excludes early exposures among the older women. **Additional results:** - **Confidence in evidence:** Moderate to strong evidence
		Never graveyard shift	1; 713		
		Ever graveyard shift	1.6 (1–2.5); 54		
		< 3 yr	1.4 (0.6–3.2); 15		
		≥ 3 yr	1.6 (0.8–3.2); 19		
		Continuous (per yr)	1.13 (1.02–1.27); 767		
		Trend-test *P*-value = 0.04			
		OR Hours of graveyard shift per week		Parity, Fam hx BRCA, OC use, use of HRT discontinued < 5 years, age	
		Never graveyard shift	1; 713		
		< 1.2 hr/wk	1.3 (0.5–3.1); 11		
		1.2–2.7 hr/wk	1.4 (0.6–3.2); 13		
		2.7–5.7 hr/wk	1.5 (0.6–3.6); 13		
		≥ 5.7 hr/wk	2.3 (1–5.3); 17		
		Continuous (per hr/wk)	1.06 (1.01–1.13); 767		
		Trend-test *P*-value = 0.04			
Fritschi *et al.* 2013, 2018 Case-control Western Australia **Enrollment or follow-up:**	**Population:** Population-based study Cases: 1,202; Controls: 1,785 **Exposure assessment method:** expert assessment	**OR Graveyard shift: Ever/Never, 2013 and 2018 reclassified exposure, All women**		For 2017 analysis, only age. For 2018 analysis, age, age at menarche, age at first full-term pregnancy, parity, breastfeeding,	**Exposure information:** **2013 Report:** Night shift: midnight to 5:00 AM. Phase shift: High exposure (> 4 nights forward or > 6 nights backward rotation); medium (3–4
		Never, 2013	1; 914		
		Ever, 2013	1.16 (0.97–1.38); 288		
		Never, 2018	1; 949		

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
May 2009 - January 2011		Ever, 2018	1.27 (1.05–1.54); 250	family history of breast cancer, OC use, BMI, alcohol, tobacco, HRT, menopausal status.	forward, or 4–6 backward rotation); low (3 nights backward rotation). **2018 Report:** Reclassified exposure data by incorporating concepts of chronotype and circadian disruption into the definition of exposure. Circadian disruption (CD) was defined as occurring if working ≥ 1 hour during preferred hours of sleep ("biological night"). Late CD occurred if ≥ 1 hour of evening work day was after the start of the biological night; early CD occurred if start of the morning work day was before the end of biological night. **Strengths:** Large population-based study with exposure assessment closely linked to biological mechanisms; good examination of and control for potential confounders occurring at relevant time periods. Strong analytic methods. Adequate number (N = 24) of exposed cases at medium/high levels of exposure for long duration. **Limitations:** Low response rate, particularly among controls. **Additional results:** - **Confidence in evidence:** Some evidence
		OR Graveyard shift: Ever/Never, 2018 reclassified, premenopausal women		Age, age at menarche, age at first full-term pregnancy, parity, breastfeeding, family history of breast cancer, OC use, BMI, alcohol, tobacco	
		Never, 2018 reclassified	1; 276		
		Ever, 2018 reclassified	1.48 (1.02–2.15); 79		
		OR Graveyard shift: Ever/Never, 2018 reclassified, postmenopausal women		Age, age at menarche, age at first full -erm pregnancy, parity, breastfeeding, family history of breast cancer, OC use, BMI, alcohol, tobacco, HRT	
		Never, 2018 reclassified	1; 673		
		Ever, 2018 reclassified	1.24 (0.99–1.55); 171		
		OR Graveyard shift: Duration (years)		Age	
		Never	1; 914		
		< 10 yr	1.25 (1–1.56); 164		
		10–19 yr	1.09 (0.79–1.5); 71		
		≥ 20 yr	1.02 (0.71–1.45); 53		
		OR Phase shift: Intensity and duration (years)		Age	
		Never phase shift	1; 959		
		Ever phase shift	1.22 (1.01–1.47); 242		
		Low phase shift	1.09 (0.7–1.68); 36		
		Medium phase shift	1.24 (0.97–1.57); 140		

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
		High phase shift	1.25 (0.9–1.75); 66		
		< 10 yr medium/high phase shift	1.35 (1.06–1.72); 140		
		10–19 yr medium/high phase shift	1.12 (0.74–1.68); 42		
		≥ 20 yr medium/high phase shift	0.96 (0.58–1.61); 24		
		OR Circadian preference: Morning type		Age	
		Graveyard shift	1.12 (0.81–1.55); 344		
		Phase shift	1.23 (0.87–1.72); 77		
		OR Circadian preference: Neutral type		Age	
		Graveyard shift	1.34 (1.04–1.73); 594		
		Phase shfit	1.34 (1.02–1.77); 119		
		OR Circadian preference: Evening type		Age	
		Graveyard shift	0.95 (0.66–1.38); 248		
		Phase shift	1.02 (0.68–1.52); 57		
		OR Menopausal status: premenopausal and postmenopausal		Age	
		Premenopausal: Graveyard shift	1.13 (0.81–1.57); 92		
		Postmenopausal: Graveyard shift	1.18 (0.96–1.45); 196		
		Premenopausal: Phase shift	1.22 (0.85–1.74); 74		
		Postmenopausal: Phase shift	1.21 (0.97–1.51); 168		
		OR Early and Late CD, 2018			

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
		Early CD: ever	1 (0.82–1.21); 204	Age, age at menarche, age at first full -erm pregnancy, parity, breastfeeding, family history of breast cancer, OC use, BMI, alcohol, tobacco, HRT	
		Early CD: > 11.5 yr	0.94 (0.65–1.35); 48		
		Late CD: ever	1.17 (0.97–1.41); 254		
		Late CD: > 11.5 yr	0.88 (0.65–1.19); 74		
Grundy *et al.* 2013 Case-control Vancouver, BC and Kingston, ON **Enrollment or follow-up:** 2005–2010	**Population:** Population-based study Cases: 1,134; Controls: 1,179 **Exposure assessment method:** questionnaire	**OR Duration (years) of night work starting or ending 11:00 PM-7:00 AM**		Age, study center, household income, education, age at first mammogram	**Exposure information:** Night work: jobs starting or ending between 11:00 PM and 7:00 AM. **Strengths:** Use of lifetime occupatonal history; start and end times collected, categories created for intensity/frequency of night or evening shifts worked for each job. Compared risk in health workers and non-health workers. **Limitations:** Analyses combined evening and night workers and those working permanent and rotational shifts. *In situ* and invasive cancers combined. **Additional results:** The interaction with yrs of 50% eve/nights and menopausal status was p=0.01 (>0-14 yrs); p=0.7 (15-29 yrs); and p=0.2 (≥30 yrs). **Confidence in evidence:** Moderate to strong evidence
		None	1; 826		
		> 0–14 yr	1.29 (1.01–1.65); 172		
		15–29 yr	1.27 (0.83–1.95); 49		
		≥ 30 yr	1.68 (0.74–3.79); 16		
		OR 50% evenings and/or nights: Duration (years of work)		Age, study center	
		None	1; 751		
		> 0–14 yr	0.95 (0.79–1.16); 283		
		15–29 yr	0.93 (0.67–1.3); 72		
		≥ 30 yr	2.21 (1.14–4.31); 28		
		Trend-test *P*-value = 0.5			
		OR 80% evenings and/or nights: Duration (years) of work		Same as above	
		None	1; 941		
		> 0–14 yr	0.95 (0.75–1.2); 162		
		15–29 yr	0.98 (0.53–1.82); 20		
		≥ 30 yr	3.73 (1.04–13.42); 11		
		Trend-test *P*-value = 0.5			
		OR 100% evenings and/or nights: Duration (years) of shift work		Same as above	

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
		None	1; 976		
		> 0–14 yr	1.05 (0.82–1.35); 136		
		15–29 yr	1.93 (0.86–4.36); 17		
		≥ 30 yr	2.63 (0.51–13.64); 5		
		Trend-test *P*-value = 0.5			
		OR Type of occupation: ≥ 30 years working shifts (50% evening and/or nights)		Same as above	
		Health occupations	3.11 (1.1–8.77); 12		
		Non-health occupations	2.25 (0.92–5.52); 16		
		OR Premenopausal: Duration (years) of working shifts (50% evenings and/or nights)		Age, study center, BMI	
		None	1; 220		
		> 0–14 yr	1.32 (0.97–1.8); 126		
		15–29 yr	0.99 (0.57–1.7); 27		
		≥ 30 yr	1.3 (0.66–2.58); 18		
		Trend-test *P*-value = 0.3			
		OR Postmenopausal: Duration (years) of working shifts (50% evenings and/or nights)		Age, study center, BMI	
		None	1; 531		
		> 0–14 yr	0.75 (0.58–0.97); 142		
		15–29 yr	0.97 (0.63–1.49); 48		
		≥ 30 yr	1.63 (0.8–3.35); 22		
		Trend-test *p*-value: 0.8			
		OR Hormone receptor status: ≥ 30 yrs working 50% night and/or eventings		Age, study center	
		ER+/PR+	2.37 (1.18–4.76); 22		

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
		ER-/PR-	1.06 (0.24–4.75); 2		
Hansen 2001 Case-control Denmark **Enrollment or follow-up:** NR	**Population:** Danish female breast cancer cases and matched controls from the central population registry 30-54 years of age linked to national pension fund data on employment. Cases: 7,035; Controls: 7,035 **Exposure assessment method:** job title	**OR Work trades with ≥ 60% night time jobs, 5 year lag**		Age, age at first birth, age at last birth, social status	**Exposure information:** Ever working in trades with ≥60% night work **Strengths:** Nationwide study of breast cancer. Employment histories assessed independently of cancer diagnoses. **Limitations:** The exposure assessment methods have only weak sensitivity and specificity; confounders were not all measured on an individual level. Aggregated data from a separate survey were used to estimate exposure to night work. **Additional results:** The upper confidence interval (CI) for the estimate on all night trades for duration of > 6 years is incorrect in the publication. **Confidence in evidence:** Some evidence
		Ever work in trades with < 40% night time work	1; 5,847		
		Ever work in trades with ≥ 60% night time work	1.5 (1.3–1.7); 434		
		Work in trades with ≥60% night time work for > 6 years	1.7 (1.3–1.7); 117		
Hansen and Lassen 2012 Nested case-control Denmark **Enrollment or follow-up:** 2005–2006	**Population:** Danish female military workers Cases: 141; Controls: 551 **Exposure assessment method:** questionnaire	**OR Duration (years) of night work**		Age, HRT use, age at menarche, education, parity/nulliparity, smoking status	**Exposure information:** Night shift work beginning by 5:00 PM and ending before 9:00 AM for 1 year (includes both rotating and permanent) **Strengths:** Well-defined cohort based on complete routinely collected employment data and identification of all breast cancer cases from the national registry. Exposure assessment methods have good sensitivity and specificity for reliably classifying ever/never exposure, intensity/frequency, and duration from lifelong job histories; low chance of recall bias.
		Never	1; 89		
		Ever	1.4 (0.9–2.1); 43		
		1–5.9 yr	0.9 (0.4–1.7); 13		
		6–14.9 yr	1.7 (0.9–3.2); 18		
		≥ 15 yr	2.1 (1–4.5); 12		
		Trend-test *P*-value: 0.03			
		OR Cumulative # of night shifts		Same as above	
		Never	1; 82		
		< 416	0.8 (0.4–1.9); 9		

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
		416–1,560	1.4 (0.7–2.9); 14		**Limitations:** Potential exposure misclassification due to broad exposure definition.
		≥ 1,560	2.3 (1.2–4.6); 17		
		Trend-test *P*-value = 0.02			**Additional results:** -
		OR Duration (years) and frequency (shifts/wk)		Same as above	**Confidence in evidence:** Moderate to strong evidence
		Never	1; 82		
		1–2 night shifts/wk, all durations	1 (0.5–1.9); 15		
		1–5.9 yr, ≥ 3/wk	1.1 (0.5–2.3); 9		
		6–14.9 yr, ≥ 3/wk	2.1 (1–4.8); 11		
		≥ 15yr, ≥ 3/wk	2.5 (1–6.6); 9		
		Trend-test *P*-value = 0.02			
		OR > 844 total night shifts and chronotype		Same as above	
		Morning	3.9 (1.6–9.5); 12		
		Evening	2 (0.7–5.8); 10		
		Neither	0.7 (0.1–3); 3		
Hansen and Stevens 2012 Nested case-control Denmark **Enrollment or follow-up:** 2002–2005	**Population:** Danish Female Nurse Cohort Cases: 267; Controls: 1,035 **Exposure assessment method:** questionnaire	**OR Shift work schedule type**		Age, weight regularity, HRT use, family history of breast cancer, age at menarche, menstrual regularity, menopausal status, age at first birth, parity, breastfeeding duration	**Exposure information:** Night shift 11:00 PM to 9:00 AM; permanent and type of rotating: day-evening, day-night, day-evening-night **Strengths:** Large nationwide cohort of female nurses in Denmark with similar shift systems; detailed exposure assessment of various shift systems with opportunity to look at duration and intensity; sufficient numbers of exposed subjects; control of potential confounders
		Permanent day shifts	1; 28		
		Ever evening, never night	0.9 (0.4–1.9); 9		
		Ever night,rotating (no permanent nights)	1.8 (1.2–2.8); 212		
		Ever permanent + rotating nights	2.9 (1.1–8); 18		
		OR Duration (yrs) working night			
		Day/evening workers	1; 37		

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
		1–5 yr	1.5 (0.99–2.5); 55		**Limitations:** Limited number of referents; overlapping shift system categories. **Additional results:** - **Confidence in evidence:** Moderate to strong evidence
		5–10 yr	2.3 (1.4–3.5); 70		
		10–20 yr	1.9 (1.1–2.8); 66		
		≥ 20 yr	2.1 (1.3–3.2); 39		
		Continuous (per year)	1.018 (1.01–1.027); 267		
		OR Cumulative number of night shfts		Same as above	
		Day/evening workers	1; 37		
		< 468	1.6 (1–2.6); 63		
		468–1,095	2 (1.3–3); 80		
		≥ 1,095	2.2 (1.5–3.2); 87		
		OR # Rotating day-night shifts		Same as above	
		Permanent day	1; 28		
		< 732	1.5 (0.9–2.4); 30		
		≥ 733	2.6 (1.8–3.8); 11		
		Other non-day shifts	2 (1.3–3.1); 198		
		OR # Rotating day/evening/night shifts		Same as above	
		Permanent day	1; 28		
		< 732	1.8 (1.2–3.1); 127		
		≥ 733	1.9 (1.1–3.3); 86		
		Other non-day shifts	1.2 (0.7–2.3); 26		
Lie *et al.* 2013 Nested case-control Norway **Enrollment or**	**Population:** Norwegian nurses cohort. Cases: 513; Controls: 757 **Exposure assessment method:** questionnaire	**OR ER positive; duration of work with ≥ 6 consecutive nights**		Period of diagnosis, parity, history of breast cancer in mother and/or sister, alcohol consumption	**Exposure information:** Working for ≥ 5 yr working for on average ≥ 6 consecutive nights, midnight to 6:00 AM **Strengths:** Large cohort of nurses with large number of
		Never worked nights	1; 63		
		Never worked ≥ 6 consecutive nights	1.2 (0.9–1.8); 274		

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
follow-up: Jan 1996–Dec 2007, restricted		< 5 yr	1.3 (0.8–2); 73	at time of diagnosis, age at diagnosis, hormonal treatment within 2 years of diagnosis	breast cancer cases; complete cancer registration for the study period. Exposure metrics based on prior detailed analysis in same cohort. **Limitations:** Small numbers of ER/PR subgroups; limited sensitivity in some subgroups. **Additional results:** - **Confidence in evidence:** Moderate to strong evidence
		≥ 5 yr	1.8 (1–3.1); 36		
		Trend-test *P*-value = 0.06			
		OR ER negative; duration of work (years) with ≥ 6 consecutive nights		Same as above	
		Never worked nights	1; 6		
		Never worked ≥ 6 consecutive nights	2 (0.8–4.8); 45		
		< 5 yr	1.7 (0.6–4.8); 10		
		≥ 5 yr	2.8 (0.8–9.2); 6		
		Trend-test *P*-value = 0.19			
		OR PR positive; Duration of work (years) with ≥ 6 consecutive nights		Same as above	
		Never worked nights	1; 45		
		Never worked ≥ 6 consecutive nights	1.3 (0.9–2); 203		
		< 5 yr	1.4 (0.9–2.4); 57		
		≥ 5 yr	2.4 (1.3–4.3); 33		
		Trend-test *P*-value = 0.01			
		OR PR negative; Duration of work (years) with ≥ 6 consecutive nights		Same as above	
		Never worked nights	1; 22		
		Never worked 6+ consecutive nights	1.4 (0.8–2.4); 114		
		< 5 yrs	1.2 (0.7–2.3); 26		
		≥ 5 yrs	1.2 (0.5–2.8); 9		

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
		Trend-test *p*-value: 0.76			
		OR ER+/PR+: Duration of work (years) with ≥ 6 consecutive night shifts		Same as above	
		Never worked nights	1; 45		
		Never worked ≥ 6 consecutive nights	1.3 (0.9–1.9); 197		
		< 5 yr	1.4 (0.9–2.3); 56		
		≥ 5 yr	2.2 (1.2–4.1); 31		
		Trend-test *P*-value = 0.01			
		OR ER+/PR-: Duration of work (years) with ≥ 6 consecutive night shifts		Same as above	
		Never worked nights	1; 16		
		Never worked ≥ 6 consecutive nights	1.3 (0.7–2.3); 75		
		< 5 yr	1.1 (0.5–2.4); 17		
		≥ 5 yr	0.9 (0.3–2.6); 5		
		Trend-test *p*-value: 0.89			
		OR ER-/PR-: Duration of work (years) with ≥ 6 consecutive night shifts		Same as above	
		Never worked nights	1; 6		
		Never worked ≥ 6 consecutive nights	1.7 (0.7–4.2); 39		
		< 5 yr	1.5 (0.5–4.4); 9		
		≥ 5 yr	1.9 (0.5–7); 4		
		Trend-test *P*-value = 0.45			
Lie *et al.* 2011 Nested case-	**Population:** Norwegian nurses cohort	**OR Duration of work (years) with ≥ 3 consecutive night shift**		Period of diagnosis, parity, history of	**Exposure information:** Night shiftw were those shifts lasting at least

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
control Norway **Enrollment or follow-up:** Jan 1990–Dec 2007, update	Cases: 699; Controls: 895 **Exposure assessment method:** Questionnaire	Never worked nights	1; 102	breast cancer in mother and/or sister, alcohol consumption at time of diagnosis, age at diagnosis	from midnight to 6:00 AM. **Strengths:** Large cohort of nurses with large number of breast cancer cases; complete cancer registration for the study period; thorough analysis of multiple exposure metrics. **Limitations:** Potential recall bias; loss of cases in this prevalent cohort may have introduced a selection bias towards the null. **Additional results:** - **Confidence in evidence:** Moderate to strong evidence
		Never worked 3 consecutive nights	1.4 (1–2.1); 125		
		< 5 yr	1.1 (0.8–1.6); 194		
		≥ 5 yr	1.1 (0.8–1.5); 278		
		Trend-test *p*-value: 0.92			
		OR Duration of work (years) with ≥ 4 consecutive nights		Same as above	
		Never worked 4 consecutive nights	1.1 (0.8–1.5); 306		
		< 5 yr	1.2 (0.8–1.6); 160		
		≥ 5 yr	1.4 (0.9–1.9); 131		
		Trend-test *p*-value: 0.10			
		OR Duration of work (years) with ≥ 5 consecutive nights		Same as above	
		Never worked 5 consecutive nights	1.1 (0.8–1.5); 386		
		< 5 yr	1.2 (0.8–1.7); 137		
		≥ 5 yr	1.6 (1–2.4); 74		
		Trend-test *P*-value = 0.05			
		OR Duration of work (years) with ≥ 6 consecutive nights		Same as above	
		Never worked 6 consecutive nights	1.1 (0.8–1.5); 414		
		< 5 yr	1.2 (0.8–1.7); 119		
		≥ 5 yr	1.8 (1.1–2.8); 64		
		Trend-test *P*-value = 0.02			

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
		OR Duration of work (years) with ≥ 7 consecutive nights		Same as above	
		Never worked 7 consecutive nights	1.1 (0.9–1.5); 430		
		< 5 yr	1.1 (0.8–1.6); 109		
		≥ 5 yr	1.7 (1.1–2.8); 58		
		Trend-test *P*-value = 0.05			
Menegaux *et al.* 2013 Case-control France, Cote d'Or and Ille-et-Vilaine departments **Enrollment or follow-up:** 2005–2007	**Population:** CECILE Study Women 25–75 years of age living in two administrative departments. Cases: 1,232; Controls: 1,317 **Exposure assessment method:** questionnaire	**OR Type of shift**		Age, study area, age at menarche, parity, age at first full-term pregnancy, alcohol consumption, tobacco consumption, BMI, Current menopausal hormone therapy, family history of breast cancer	**Exposure information:** Working ≥ 6 months for at least 6 hours between 11:00 PM and 5:00 AM was defined as overnight work. Any night work could also include late evening (work shift ending between 11:00 PM and 3:00 AM) or early morning (work shift starting between 3:00 AM and 5:00 AM. **Strengths:** Large, well-designed general population-based case-control study able to categorize type of night work, and intensity and duration and timing of night work relative to first full-term pregnancy. **Limitations:** Rotating types of night work, direction and rate of rotation, and number of consecutive nights at work were not quantified due to large number of work systems represented in the population. **Additional results:** - **Confidence in evidence:** Moderate to strong evidence
		Never worked at night	1; 1,068		
		Ever worked overnight)	1.35 (1.01–1.8); 120		
		OR Duration of work (years)		Age, study area, age at menarche, parity, age at first full-term pregnancy, family history of breast cancer, alcohol consumption, tobacco consumption, BMI, current menopausal hormone therapy	
		< 4.5 yr overnight	1.27 (0.83–1.94); 51		
		≥ 4.5 yr overnight	1.4 (0.96–2.04); 69		
		OR Frequency(shift/wk)		Age, study area, age at menarche, parity,	
		< 3 overnight	1.61 (1.07–2.42); 64		

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
		≥ 3 overnight	1.13 (0.76–1.68); 56	age at first full-term pregnancy, alcohol consumption, tobacco consumption, BMI, Current menopausal hormone therapy, family history of breast cancer	
		OR Any night shift: Pre-menopausal status		Age, study area, age at menarche, parity, age at first full-term pregnancy, family history of breast cancer, alcohol consumption, tobacco consumption, BMI, Current menopausal hormone therapy	
		Never worked	1; 492		
		Ever worked	1.36 (0.98–1.87); 110		
		Ever worked overnight	1.48 (1.03–2.13); 85		
		< 4.5 yr	1.4 (0.89–2.21); 49		
		≥ 4.5 yr	1.32 (0.87–2); 61		
		< 3 any night shift/wk	1.32 (0.87–2.01); 61		
		≥ 3 any night shift/wk	1.4 (0.89–2.21); 49		
		1st worked before first full-term pregnancy	1.59 (1.05–2.4); 55		
		OR Any night shift: post menopausal		Age, study area, age at menarche, parity, age 1st ft preg, family history of breast cancer, alcohol consumption, tobacco consumption, BMI, Current menopausal hormone therapy	
		Never	1; 576		
		Ever	1.08 (0.72–1.63); 54		
		Ever overnight	1.03 (0.62–1.71); 35		
		< 4.5 yr any night shift	0.63 (0.33–1.2); 17		
		≥ 4.5 yr any night shift	1.54 (0.91–2.61); 37		
		< 3 shifts/wk	1.82 (0.92–3.61); 23		
		≥ 3 shifts/wk	0.82 (0.5–1.36); 31		

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
		First worked before first full-term pregnancy	1.13 (0.62–2.06); 21		
		OR All women, duration (years) and frequency (overnight shift/wk)		Age, study area, age at menarche, parity, age at first full-term pregnancy, family history of breast cancer, alcohol consumption, tobacco consumption, BMI, Current menopausal hormone therapy	
		≥ 4.5 yr and < 3 nights/wk	1.83 (1.15–2.93); 54		
		≥ 4.5 yr and ≥ 3 nights/wk	1.1 (0.71–1.69); 44		
		≥ 4.5 yr and < 3 nights/wk	2.09 (1.26–3.45); 49		
		≥ 4.5 yr and ≥ 3 nights/wk	0.91 (0.55–1.5); 31		
		OR Parous women: 1st worked before first full-term pregnancy (FFTP) and type of night shift		Age, study area, age at menarche, parity, age at first full-term pregnancy, family history of breast cancer, alcohol consumption, tobacco consumption, BMI, Current menopausal hormone therapy	
		Never night work	1; 954		
		1st work after first full-term pregnancy	1.09 (0.77–1.55); 66		
		1st work before first full-term pregnancy	1.47 (1.02–2.12); 76		
		Late evening work before first full-term pregnancy	1.89 (0.87–4.08); 18		
		Early morning work before first full-term pregnancy	1.09 (0.38–3.12); 6		
		Overnight work before first full-term pregnancy	1.49 (0.96–2.32); 52		

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
		OR Parous women: Duration (years) of any night work before the first full-term pregnancy		Age, study area, age at menarche, parity, age at first full-term pregnancy, family history of breast cancer, alcohol consumption, tobacco consumption, BMI, Current menopausal hormone therapy	
		≤ 4 yr	1.15 (0.7–1.89); 33		
		> 4 yr	1.95 (1.13–3.35); 43		
		< 3 shifts	2.24 (1.35–3.71); 47		
		≥ 3 shifts	0.96 (0.56–1.62); 29		
		> 4 yr and < 3 shifts	3.03 (1.41–6.5); 26		
		> 4 yr and ≥ 3 shifts	1.3 (0.61–2.77); 17		
O'Leary *et al.* 2006 Case-control Long Island, NY **Enrollment or follow-up:** August 1996–June 1997	**Population:** Electromagnetic fields and breast cancer on Long Island Cases: 487; Controls: 509 **Exposure assessment method:** questionnaire	**OR Type of shift work**		Age, parity, family history of breast cancer, education, benign breast disease	**Exposure information:** Any shift work in the past 15 years including evenings (afternoon to 2:00 AM) and overnight (7:00 PM to morning) shifts **Strengths:** Population-based study nested in well-conducted larger study; analytic control for potential confounders. **Limitations:** Highly selected population based on long term residence; exposure assessment was limited to the past 15 years in this somewhat older subset of participants. Small number of women with overnight exposure history. **Additional results:** - **Confidence in evidence:** No evidence
		No evening or overnight	1; 313		
		Any overnight	0.55 (0.32–0.94); 26		
		Only overnight	0.64 (0.28–1.45); 10		
		Any evening	1.08 (0.81–1.44); 164		
		Only evening	1.21 (0.9–1.64); 148		
		OR Duration (years) of any overnight work with > 1 shift/wk		Same as above	
		< 1 shift/wk	1; 469		
		< 8 yr	0.74 (0.32–1.68); 11		
		≥ 8 yr	0.32 (0.12–0.83); 6		
		OR Duration (years) of any evening work with > 1 shift/wk		Same as above	
		< 1 shift/wk	1; 356		
		< 5 yr	0.91 (0.6–1.38); 51		
		≥ 5 yr	1.24 (0.86–1.8); 79		
		OR Type of shift			

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
Papantoniou *et al.* 2015 Case-control Spain **Enrollment or follow-up:** 2008–2013	**Population:** MCC-Spain population-based Cases: 1708; Controls: 1778 **Exposure assessment method:** questionnaire	Never night work	1; 1,438	Age, study center, education, menopausal status, family history of breast cancer, BMI, Smoking status, OC use, leisure time physical activity, alcohol consumption	**Exposure information:** Partly or entirely working midnight–6:00 AM at least 3 nights/month; duration and cumulative frequency. **Strengths:** Large population-based case-control study; detailed exposure assessment including differentiation of rotating and permanent night work; duration and frequency of night shifts. Detailed analysis used to control multiple potential confounders. **Limitations:** Some attrition in control recruitment **Additional results:** - **Confidence in evidence:** Some evidence
		Ever night work	1.18 (0.97–1.43); 270		
		Permanent night work	1.19 (0.89–1.6); 114		
		Rotating night work	1.17 (0.91–1.51); 156		
		OR Excluding housewives and rotating shift workers without night shift		Same as above	
		Never shift work	1; 1,190		
		Permanent night work	1.13 (0.84–1.51); 114		
		Rotating night work	1.11 (0.86–1.43); 156		
		OR Cumulative years of total night work		Same as above	
		Never shift work	1; 1,438		
		1–4 yr	1.21 (0.83–1.76); 67		
		5–14 yr	1.13 (0.83–1.53); 103		
		≥ 15 yr	1.21 (0.89–1.65); 97		
		OR Cumulative years of permanent night work		Same as above	
		Never night work	1; 1,438		
		1–4 yr	1 (0.59–1.66); 32		
		5–14 yr	1.17 (0.74–1.87); 46		
		≥ 15 yr	1.49 (0.88–2.53); 34		
		Trend-test *P*-value = 0.109			
		OR Cumulative years of rotating night work		Same as above	
		Never night work	1; 1,438		

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
		1–4 yr	1.58 (0.94–2.66); 40		
		5–14 yr	0.96 (0.65–1.41); 56		
		≥ 15 yr	1.22 (0.82–1.81); 59		
		Trend-test *P*-value = 0.369			
		OR Cumulative number of total night shifts		Same as above	
		Never night work	1; 1,438		
		36–599	1.15 (0.8–1.64); 62		
		600–1,799	1.2 (0.85–1.7); 53		
		≥ 1,800	1.18 (0.83–1.69); 56		
		Trend-test *P*-value = 0.248			
		OR Cumulative number of permanent night shifts		Same as above	
		Never night work	1; 1,438		
		36–599	0.96 (0.5–1.85); 14		
		600–1,799	1.15 (0.65–2.04); 16		
		≥1,800	1.48 (0.81–2.68); 20		
		Trend-test *P*-value = 0.149			
		OR Cumulative number of rotating night shifts		Same as above	
		Never night work	1; 1,438		
		36–599	1.34 (0.77–1.67); 14		
		600–1,799	1.32 (0.83–2.08); 16		
		≥ 1,800	1.08 (0.66–1.79); 20		
		Trend-test *P*-value = 0.519			
		OR Morning chronotype: Type of work		Same as above	

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
		Never night work	1; 425		
		Ever night work	1.17 (0.83–1.65); 89		
		Permanent night work	1.26 (0.76–2.09); 37		
		Rotating night work	1.11 (0.71–1.74); 52		
		OR Morning chronotype: Night work cumulative duration and # of shifts		Same as above	
		Never night work	1; 425		
		1–4 yr	2.09 (1.03–4.22); 24		
		5–14 yr	1.14 (0.66–1.98); 32		
		≥ 15 yr	0.91 (0.54–1.51); 31		
		36–599 shifts	2.1 (1–4.42); 23		
		600–1,799 shifts	1 (0.57–1.8); 19		
		≥ 1,800 shifts	0.9 (0.5–1.59); 17		
		OR Evening chronotype: Type of shift		Same as above	
		Never night work	1; 275		
		Ever night work	1.27 (0.81–2); 56		
		Permanent night work	1.11 (0.59–2.12); 25		
		Rotating night work	1.43 (0.79–2.59); 31		
		OR Evening chronotype: Night work cumulative duration and # of shifts		Same as above	
		Never night work	1; 275		
		1–4 yr	0.95 (0.44–2.03); 13		
		5–14 yr	1.17 (0.55–2.48); 20		
		≥ 15 yr	1.76 (0.85–3.67); 23		
		36–599 shifts	0.8 (0.37–1.72); 9		

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
		600–1,799 shifts	1.9 (0.86–4.22); 14		
		≥ 1,800 shifts	1.38 (0.59–3.24); 10		
		OR Night shift and menopausal status		Same as above	
		Premenopausal: Never	1; 552		
		Premenopausal: Ever	1.33 (0.98–1.79); 140		
		Postmenopausal: Never	1; 1037		
		Postmenopausal: Ever	1.08 (0.82–1.42); 130		
		OR Night shift and first full-time pregnancy		Same as above	
		1st exposure before first full-term pregnancy	1.25 (0.93–1.67); 130		
		1st exposure after first full-term pregnancy	1.14 (0.81–1.6); 81		
		OR Subtypes: Premenopausal		Same as above	
		ER+	1.38 (1–1.89); 552		
		ER-	1.01 (0.56–1.82); 103		
		PR+	1.44 (1.05–1.99); 498		
		PR-	0.9 (0.54–1.51); 154		
		ER+/PR+	1.44 (1.04–1.98); 485		
		ER+/PR-	0.87 (0.4–1.89); 61		
		ER-/PR+	2.56 (0.49–13.29); 9		
		ER-/PR-	0.91 (0.48–1.72); 93		
		Her2 nue+	1.56 (0.94–2.59); 116		
		Her2 nue-	1.25 (0.9–1.73); 501		
		Invasive	1.35 (0.99–1.83); 607		

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
		In situ	1.37 (0.67–2.79); 58		
		I–II grade	1.27 (0.88–1.81); 359		
		III–IV grade	0.86 (0.51–1.45); 159		
		Ductal	1.37 (1–1.89); 524		
		Lobular	1.74 (0.82–3.7); 46		
		OR Postmenopausal: Subtypes		Same as above	
		ER+	1.05 (0.78–1.41); 791		
		ER-	1.2 (0.75–1.94); 181		
		PR+	0.95 (0.7–1.31); 652		
		PR-	1.43 (0.99–2.1); 309		
		ER+/PR+	0.94 (0.68–1.29); 640		
		ER+/PR-	1.81 (1.11–2.95); 138		
		ER-/PR+	1.15 (0.18–7.32); 10		
		ER-/PR-	1.2 (0.73–1.97); 169		
		Her2 nue+	1.07 (0.65–1.79); 174		
		Her2 nue-	1.1 (0.82–1.48); 733		
		Invasive	1.15 (0.87–1.53); 1,470		
		In situ	0.68 (0.35–1.34); 170		
		I–II grade	0.9 (0.64–1.27); 540		
		III–IV grade	1.65 (1.07–2.54); 200		
		Ductal	1.1 (0.82–1.47); 741		
		Lobular	1.62 (0.8–3.28); 65		
Pesch *et al.* 2010 Case-control		**OR Cumulative number of night shifts (adjusted PR not bootstrap)**		Family history of breast cancer, use of	**Exposure information:** Night work: Ever working midnight to 5:00 AM

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
Bonn, Germany Enrollment or follow-up: 2000–2004	Population: GENICA Study Cases: 857; Controls: 892 Exposure assessment method: interview	Never worked at night	1; 698	post menopausal hormones, number of mammograms, age	full time ≥1 year; duration and cumulative number of shifts. **Strengths:** Large population based case-control study with precise definition of night work; assessed both intensity and duration and timing of shift work. **Limitations:** Low prevalence of shift work and long term night shift work limited the power of the study to detect an effect. **Additional results:** - **Confidence in evidence:** Some evidence
		Ever worked at night	1.01 (0.68–1.5); 55		
		< 807 (total)	0.66 (0.4–1.11); 25		
		≥ 807 (total)	1.78 (0.89–3.58); 23		
		< 1056 (≥ 3/mo)	0.8 (0.47–1.36); 25		
		≥ 1056 (≥ 3/mo)	1.66 (0.8–3.46); 20		
		OR Duration (years) of night work (adj. OR not boot strap)		Same as above	
		0–4 yr	0.64 (0.34–1.24); 15		
		5–9 yr	0.93 (0.41–2.15); 11		
		10–19 yr	0.91 (0.38–2.18); 10		
		≥ 20 yr	2.49 (0.87–7.18); 12		
		OR Age (years) at 1st night shift (adj OR not bootstrap)		Same as above	
		< 20 yr	0.53 (0.28–1.03); 14		
		20–29 yr	1.51 (0.8–2.83); 25		
		30–39 yr	1.25 (0.38–4.15); 6		
		≥ 40 yr	0.98 (0.19–5.09); 3		
		OR Years since last night shift (adjusted OR not bootstrap)		Same as above	
		Currently working night shifts	1.1 (0.51–2.38); 14		
		1–9 yr	1.04 (0.31–3.53); 6		
		10–19 yr	1.69 (0.69–4.14); 13		
		≥ 20 yr	0.62 (0.33–1.19); 15		
		OR Postmenopausal women: Cumulative number of night shifts		Same as above	

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
		Employed, but never in shiftwork	1; 510		
		< 807 nights	0.65 (0.34–1.23); 16		
		≥ 807 nights	2.29 (0.91–5.78); 14		
		< 1,056 and > 3/month	0.71 (0.39–1.36); 16		
		≥ 1,056 and > 3/month	2.09 (0.76–5.78); 11		
		OR Postmenopausal women: Duration (years) of night shift work		Same as above	
		Employed, but never in shiftwork	1; 510		
		> 0–< 5 yr	0.46 (0.21–1.03); 9		
		5–9 yr	1.54 (0.48–4.97); 7		
		10–19 yr	1.45 (0.38–5.57); 5		
		≥ 20 yr	2.6 (0.89–8.57); 9		
		OR Postmenopausal women: Years since last night shift		Same as above	
		Employed, but never in shiftwork	1; 510		
		Current night work	1.76 (0.48–6.31); 6		
		1–9 yr	0.84 (0.16–4.39); 3		
		10–19 yr	1.91 (0.55–6.67); 7		
		≥ 20 yr	0.71 (0.36–1.4); 14		
Rabstein *et al.* 2013 Case-control Bonn, Germany **Enrollment or**	**Population:** GENICA Study	**OR ER positive: Cumulative # of night shifts**		Age, family history of breast cancer, use of post menopausal hormones, number of mammograms	**Exposure information:** Night work: Ever working midnight to 5:00 AM full time ≥1 year; duration and cumulative number of shifts.
		Never worked at night	1; 539		
		Ever worked at night	0.98 (0.63–1.5); 39		
		< 807 total shifts	0.66 (0.37–1.16); 18		

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
follow-up: 2000–2004	Cases: 857; Controls: 892 **Exposure assessment method:** questionnaire	≥ 807 total shifts	1.56 (0.73–3.33); 15		**Strengths:** Large population-based case-control study with detailed analysis by breast cancer subtypes. **Limitations:** Low prevalence of long term night shift work for subtypes. The study had limited power to assess the association between night shift work and estrogen receptor status. **Additional results:** - **Confidence in evidence:** Some evidence
		< 1,056 (≥ 3/mo)	0.74 (0.41–1.36); 17		
		≥ 1,056 (≥ 3/mo)	1.46 (0.65–3.28); 13		
		OR ER positive: Duration (years) of night shifts		Same as above	
		> 1–< 5 yr	0.58 (0.27–1.22); 10		
		5–< 10 yr	0.96 (0.39–2.4); 8		
		10–19 yr	1.04 (0.41–2.64); 8		
		≥ 20 yr	1.81 (0.56–5.83); 7		
		OR ER negative: Cumulative # of night shifts		Age, family history of breast cancer, use of post menopausal hormones, number of mammograms	
		Never worked at night	1; 134		
		Ever worked at night	1.16 (0.62–2.18); 14		
		< 807 (total)	0.71 (0.29–1.75); 6		
		≥ 807 (total)	2.34 (0.89–6.14); 7		
		< 1,056 (≥ 3/mo)	1.02 (0.44–2.4); 7		
		≥ 1,056 (≥ 3/mo)	2.11 (0.76–5.9); 6		
		OR ER negative: Duration (years) of night shift		Same as above	
		> 1–< 5 yr	0.89 (0.3–2.64); 4		
		5 – < 10 yr	0.98 (0.26–3.64); 3		
		10–19 yr	0.58 (0.1–2.72); 2		
		≥ 20 yr	4.73 (1.22–18.36); 4		
Wang *et al.* 2015 Case-control Guangzhou, China	**Population:** Hospital based case-control study in women 22–85 years of age.	**OR Ever worked night shift: All women and menopausal status**		Age, education, age at menarche, menopausal status, parity, physical	**Exposure information:** Ever/never worked night shifts **Strengths:** Large, young cohort of premenopausal women
		Never worked nights	1; 443		
		All	1.37 (1.07–1.74); 218		

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
Enrollment or follow-up: 2010–2012	Cases: 661; Controls: 714 **Exposure assessment method:** questionnaire	Premenopausal	1.47 (1.07–2.01); 144	activity, breastfeeding, family history of breast cancer, BMI, sleep duration	with a range of occupations; controls for a range of breast cancer risk factors. **Limitations:**. Hospital-based case-control study may be subject to selection bias, limited exposure assessment, and low sensitivity; traditional risk factors for breast cancer did not vary by case status. **Additional results:** Combined effect of nightwork and no daytime napping or longer sleep duration is greater than their independent effects. Interaction p < 0.054. Combined effect of nightwork and no daytime napping or longer sleep duration is greater than their independent effects. Interaction p < 0.009 for long duration (0.473 for short duration). **Confidence in evidence:** Some evidence
		Postmenopausal	1.17 (0.77–1.8); 74		
		OR Ever night work: ER/PR/HER2 status		Same as above	
		Never worked nights	1; NR		
		HER2-	1.39 (1.05–1.83); 146		
		HER2+/equivocal	1.35 (0.94–1.94); 66		
		ER-	1.1 (0.74–1.62); 53		
		ER+	1.48 (1.13–1.93); 160		
		PR-	1.34 (0.93–1.93); 66		
		PR+	1.39 (1.05–1.82); 147		
		Localized: OR Ever night work: Clinical stage		Same as above	
		Never	1; NR		
		Localized	1.47 (1.09–1.99); 120		
		Regional/distant	1.22 (0.89–1.67); 89		
		OR Night shift work and daytime napping		Same as above	
		No nightwork and never daytime napping	1; 179		
		No nightwork and ever daytime napping	1.01 (0.75–1.33); 260		
		Ever nightwork and never daytime napping	1; 113		
		Ever nightwork and ever daytime napping	0.62 (0.4–0.95); 1.04		

Reference, study-design, location, and year	Population description & exposure assessment method	Exposure category or level	Risk estimate (95% CI); exposed cases	Co-variates controlled	Comments, strengths, and weaknesses
		Trend-test *P*-value <.054			
		OR Night shiftwork and sleep duration (hours/night)		Same as above	
		No nightwork and 6.1–8.9 hr/night	1; 289		
		No nightwork and short duration (≤ 6.0 hr/night)	1.41 (0.94–2.11); 69		
		No nightwork and long duration (≥ 9.0 hr/night)	1.16 (0.81–1.67); 79		
		Ever nightwork and 6.1–8.9 hr/night	1; 47		
		Ever nightwork and short duration (≤ 6.0 hr/night)	2.08 (1.18–3.64); 119		
		Ever nightwork and long duration (≥ 9.0 hr/night)	3.22 (1.72–6.04); 49		
		Trend-test *P*-value < 0.009			

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