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Scand J Work Environ Health – online first Night-shift work and breast cancer – a systematic review and meta-analysis <sup>1</sup>

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<sup>1</sup> Supplemental appendices A–D
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### Appendix A DATA Extraction Form Shift Work and Breast Cancer Review (sample)

Notes for data extraction:

Please state NR in the response column if an item is not reported in the study

Adjusted values are preferred when provided compared to crude ones. If unable to judge please state next to the values or item, for example, 'not clear if adjusted'

Since data would be available in many formats a general rule is: when in doubt, take out as much data or information as possible. If a column does not seem to fit the data provided in the paper please describe in the authors words or your own with actual values. It is best to extract these variable data formats in the 'other' exposure assessment boxes provided.

In the risk of bias assessment the judgment boxes are supplemented with description of situations where that judgment would apply. Also, text boxes are available next to high and low risk judgments for quotes from the study or your comments that made the decision possible. Any explanations would enable quick agreements possible and are encouraged.

Please cite the references (author 1, title, journal, year, volume and pages) to other potentially relevant studies cited in this included study here:

Any additional report(s) of the same study used /to be used for data extraction (Author 1, title, journal, year, volume, pages) should be indicated here:

Any info not available in the paper that is needed from authors should be cited here:

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### DATA Extraction Form Shift Work and Breast Cancer Review- prospective/ cohort study

| Study Characteristics  |  |           |
|--|--|-----------|
| Aim of the study   |  |           |
| Study design (mark at least one that best describes<br>and any other that may apply) | Cohort (prospective) study with concurrent controls<br>Cohort (retrospective) study with concurrent controls<br>Case-controlled (retrospective) study<br>Cohort (prospective) study with historical controls<br>Mark if the study had defined populations that were prospectively followed in an attempt<br>to determine distinguishing population characteristics with historical controls<br>Nested case-control<br>Mark if the study started with the identification of persons with a disease of interest and a<br>control (comparison, referent) group without the disease that were identified within the<br>cohort of the subjects, participants in prospective cohort study. The relationship of an<br>attribute to the disease was examined by comparing diseased and non-diseased persons<br>with regard to the frequency or levels of the attribute in each group.<br>Other-specify<br>Specify reported study design with terminology different from the definitions of the<br>National Library of Medicine (described above) |           |
| Study Country  |  |           |
| Participants   |  |           |
|  | Exposed  | Unexposed |
| Sources of participants  |  |           |
| Number of Participants (enrolled)  |  |           |
| Number of Participants (analysed)  |  |           |
| Age range or Mean +SD in yrs<br>(describe if reported in another way)                |  |           |
| Gender   |  |           |
| Occupation   |  |           |
| Industry   |  |           |
| Attrition rate   |  |           |
| Excluded from analysis   |  |           |
| Shift Work Exposure Information  |  |           |
| Source of information on<br>shift work exposure (Interviews etc)                     | Exposed  |           |
|  | Unexposed  |           |
| Shift Work Description ( eg night-shift work)  |  |           |
| Shift Work Definition (eg between 0.00 and 6.00 hrs)                                 |  |           |

| Unexposed/Reference Category definition (non-<br>shift work) |                  |              |              |                 |               |
|--|------------------|--------------|--------------|-----------------|---------------|
| Shift Work Exposure Other categories reported                | category name a  | nd / or desc | ription      |                 |               |
| Shift system type<br>(mark all that apply)                   | Rotating For     | ward rotatin | g 🗌 Backward | ls rotating Fix | ed (describe) |
| (mark an unit appry)   | Other (describ   | be)          |              |                 |               |
|  | Not reported     |              |              |                 |               |
| Average Shift exposure duration (yrs $m \pm sd$ )            | Exposed          | Unexposed    |              |                 |               |
| Average Shift exposure intensity (non-day shifts/month)      | Exposed          | Unexposed    |              |                 |               |
| Average Cumulative shift exposure (intensity x duration)     | Exposed Unex     | posed        |              |                 |               |
| Other measure of shift exposure reported                     | exposure measure | re name      | C            | cases controls  |               |
|  |                  |              |              |                 |               |
| Confounders  |                  |              |              |                 |               |
| Confounding factors controlled for                           | Age 🔲 🛛 Bi       | MI 🗌 E       | thnicity 🗌   | Parity Soc      | Ec Stat 🗌     |
|  | Other            |              |              |                 |               |
| Outcome DATA - histologically confirmed Incident             | Breast cancer    |              |              |                 |               |
| risk per year of exposure increase                           | Crude RR 95%C    | CI           | Adjusted RR  | 95%CI           |               |
| categories of exposure duration                              | category<br>name | RR           |              | 95% CI          |               |
|  | cat<br>cat       |              |              |                 |               |
|  | cat              |              |              |                 |               |
|  | cat              |              |              |                 |               |
| risk per unit of intensity increase (eg shift /mo)           | Crude RR 95%C    |              | Adjusted RR  | 95%CI           |               |
| categories of shift work intensity (adjusted for             | category         | RR           | 95% CI       |                 |               |
| confounders yes no)  | name<br>cat      |              |              |                 |               |
|  | cat              |              |              |                 |               |
| risk per year of cumulative dose increase (int * year)       | Crude OR 95%C    |              | Adjusted C   | DR 95%CI        |               |

| categories of cumulative dose (adjusted for<br>confounders yes no)   | category<br>name | RR | 95% CI      |         |
|--|------------------|----|-------------|---------|
|  | cat              |    |             |         |
|  |                  |    |             |         |
| risk per year of other interesting exposure measure<br>unit increase | Crude RR 95%C    | I  | Adjusted RI | R 95%CI |
| categories of other exposure name (adjusted for confounders yes no)  | category<br>name | RR | 95% CI      |         |
|  | cat              |    |             |         |
|  |                  |    |             |         |
| Your name Study ID (author year)                                     | Date:            |    |             |         |

### **Risk of Bias assessment**

Text spaces are available next to the justification of high and low risk categories for your comment or a quote from the study that helped making the decision

| Risk due to Funding source of study  | ☐ high Industry (one or more corporate sponsors), Combined industry +<br>Grant |
|--|--|
|  | low Grant/ not-for-profit sponsors   |
|  | unclear Not reported   |
| Risk due to role of funding organization in data analysis and interpretations of the results | high Sponsoring organization participated in data analyses                     |
|  | low study was clearly not affected by sponsors                                 |
|  | unclear Not reported   |

| Risk due to conflict of interest | high conflict of interest exists (at least one author)   |
|----------------------------------|--|
|                                  | low Reported not having conflict of interest or clear from report/<br>communication that study not affected by author(s) affiliation |
|                                  | unclear Disclosure not reported  |

| Definition of the exposure   | □ high risk   |
|--|---|
| (ideally according to IARC shift work should be measured in 3<br>aspects, duration of shift work (in years), shift work intensity (number<br>of non day shifts per month), shift system (fixed or non fixed, forward | Definition of exposure/ case is categorical with an arbitrary threshold<br>(e.g.1 yr or more, ever done night work) OR  |
| or backward rotating).   | Definition covers only one aspect of exposure (start or end time of shift,<br>duration, intensity, shift system)  |
|  | Dow risk Definition included at least two of the aspects recommended<br>by IARC ((1) shift system: rotating or fixed, forward or backward<br>rotation (2) shift duration: number of years (Houssami et al.) (3)shift<br>Intensity |
|  | unclear risk shift work is not defined in report (shift work or night<br>work is used as a term without elaboration on what it stands for in the<br>study)  |

| Intensity/dose of exposure  | high risk Intensity/dose not assessed in the study |
|-----------------------------|--|
| intensity, dose of exposure |  |

| low risk Intensity/dose of exposure included in the definition/assessment of exposure. |
|--|
| unclear risk Intensity/dose assessment is not reported                                 |

| Source to measure exposure | high risk patient recall, medical or administrative records of job titles etc   |
|----------------------------|---|
|                            | low risk employers' prospectively collected database OR employees prospectively recorded data (logging charts/ diaries) |
|                            | unclear Not reported  |

| Measurement methods used for exposure assessment | high risk subjectively measured: Reported by participants (interviews/questionnaires)  |
|--|--|
|  | subjectively measured: Proxy used to allocate exposure status (job matrix, job title)  |
|  | ☐ low risk objectively measured: direct measurement of exposure (logging data, shift schedule data from the HR or employers records. prospective self measurement of exposure e.g. with diaries) |
|  | unclear risk not reported  |

| Masking of investigators | high risk Not obtained  |
|--------------------------|---|
|                          | low risk assessors were blind to exposure status in cohort studies and to case status in case-control studies |
|                          | unclear risk Not reported   |

| Reliability of exposure estimates- For prospective studies | high risk Intra-observer variability is reported by means of a       |
|--|--|
|  | - j i j  |
|  | subjective judgment of reliability                                   |
|  |  |
|  | low risk Good inter observer reliability achieved with reliability   |
|  | values reported/ not applicable for the measure used                 |
|  | values reported, not appreade for the incusare used                  |
|  | Dunclear rick Not reported   |
|  |  |
|  |  |
| Reliability - For case-control studies                     | high risk The authors used different methods to measure exposure     |
|  |  |
|  | (shift work) in cases and controls                                   |
|  |  |
|  | low risk The authors used same methods for cases and controls to     |
|  | maagura avpogura   |
|  | measure exposure   |
|  |  |
|  | unclear The authors did not state that the same methods were used    |
|  | to manyura avagura risk factors, independent variable) in asses and  |
|  | to measure exposure risk factors, independent variable) in cases and |

|  | controls  |
|--|---|
|  |   |
| Confounding factors  | high risk Major confounding factors/effect modifiers (Age, BMI, |
|  | Ethnicity, Parity (number of children, age at first birth), and |
| Factors that can modify the association between shift work and breast cancer | Socioeconomic status) were not assessed or assessed partially.  |
|  |   |
|  | low risk Major confounding factors/effect modifiers (Age, BMI,  |
|  | Ethnicity, Parity (number of children, age at first birth), and |
|  | Socioeconomic status) were assessed in full.                    |
|  |   |
|  |   |
|  | unclear risk Not reported                                       |
|  |   |

| Measuring of confounding factors | high risk Unknown validity to measure confounding factors OR |
|----------------------------------|--|
|                                  | Non-valid methods to measure confounding factors             |
|                                  | low risk Confounders measured with valid methods             |
|                                  | unclear risk Not reported                                    |

| Attrition bias<br>Loss of follow-up -cohort studies | high risk Total loss to followup is larger than acceptable (20% or<br>more) OR drop out differs between the groups by more than 10% OR<br>the reasons for drop out are different for exposed and non exposed<br>groups |
|---|--|
|   | low risk loss to follow up below 20% in total and not different between the two groups (up to 10% difference)  |
| Non response- For case-control studies              | <ul> <li>unclear risk Not reported</li> <li>high risk% of nonresponse differed among cases and controls OR</li> </ul>  |
|   | % of non response reported for cases only OR reasons for non response<br>not reported/ different between cases and controls  |
|   | I low risk % non response was reported for both cases and controls<br>and did not differ in size and reasons   |
|   | unclear risk Not reported  |

| Analysis of the study<br>Methods to reduce research specific bias | high risk Authors did not obtain methods to reduce bias OR did not justify their choice of statistical models to reduce research specific bias                              |
|---|---|
|   | low risk Authors reported use of one or more methods to reduce<br>bias (standardization, matching, adjustment in multivariate model,<br>stratification, propensity scoring) |
|   | unclear Methods to reduce research specific bias not reported   |
| Dose response analysis  | ☐ high risk Not assessed<br>☐ low risk Dose response assessed in analysis   |
|   | unclear risk Not reported   |

| Reporting of the tested hypothesis | ☐high risk   |
|------------------------------------|--|
|                                    | Incomplete/ selective reporting of the tested hypotheses (compared to aim and objectives) AND/OR |
|                                    | Crude estimates presented only   |
|                                    | low risk Adjusted estimates presented for all hypothesis tested as per aims                      |
|                                    | unclear risk Unclear reporting of tested hypothesis  |

| Sample size justification | high risk Not reported            |
|---------------------------|-----------------------------------|
| Sample Sille Jabaneadon   |                                   |
|                           |                                   |
|                           | low risk Justification by authors |
|                           |                                   |
|                           |                                   |

### **Appendix B**

• Degree of evidence of a causal association between an exposure to a specific risk factor and a specific outcome (Danish Occupational Medicine Association Approach)

The following categories are used.

+++ strong evidence of a causal association

++ moderate evidence of a causal association

+ limited evidence of a causal association

0 insufficient evidence of a causal association

- evidence suggesting lack of a causal association

Description of categories:

Strong evidence of a causal association (+++):

A causal relationship is very likely. A positive relationship between exposure to the risk factor and the outcome has been observed in several epidemiological studies. It can be ruled out with reasonable confidence that this relationship is explained by chance, bias or confounding.

Moderate evidence of a causal association (++):

A causal relationship is likely. A positive relationship between exposure to the risk factor and the outcome has been observed in several epidemiological studies. It cannot be ruled out with reasonable confidence that this relationship can be explained by chance, bias or confounding, although this is not a very likely explanation.

Limited evidence of a causal association(+):

A causal relationship is possible. A positive relationship between exposure to the risk factor and the outcome has been observed in several epidemiological studies. It is not unlikely that this relationship can be explained by chance, bias or confounding.

#### Insufficient evidence of a causal association (0):

The available studies are of insufficient quality, consistency, or statistical power to permit a conclusion regarding the presence or absence of a causal association.

Evidence suggesting lack of a causal association (-):

Several studies of sufficient quality, consistency and statistical power indicate that the specific risk factor is not causally related to the specific outcome.

Comments:

The classification does not include a category for which a causal relation is considered as established beyond any doubt.

The key criterion is the epidemiological evidence.

The likelihood that chance, bias and confounding may explain observed associations are criteria that encompass criteria such as consistency, number of 'high quality' studies, types of design etc.

Biological plausibility and contributory information may add to the evidence of a causal association.

#### Limitations Outcome Advantages **Ouality** of evidence Duration Risk of bias/ design limits Large or very large effect Very low of Very serious limitation No advantage exposure Inconsistency in years Serious limitation Indirectness Dose Response No limitation No advantage Imprecision Confounding does not reduce Serious limitation effect No advantage Publication bias Spurious if no effect observed Size of limitation unknown, likely large Unlikely spurious- no advantage Life time Risk of bias/ design limits Large or very large effect Very low number of Very Serious limitation No advantage night-shifts Inconsistency Serious limitation Indirectness Dose Response No limitation No advantage Imprecision Confounding does not reduce Serious limitation effect No advantage Spurious if no effect observed Publication bias Serious limitation Unlikely spurious- no advantage

#### • GRADE Approach to Assessing the Evidence in shift work breast cancer review

# Appendix C

### 1-Table of excluded studies

| Study ID             | Reason for exclusion   |
|----------------------|--|
| Coogan 1996          | No assessment of shift or night work, no reference working group     |
| Ekpanyaskul 2010     | No assessment of shift work, no reference working group              |
| Elsner 1999          | Translator: no assessment of shift work                              |
| Enderlein 1998       | Translator: no assessment of shift work                              |
| Fritzsch 1979        | Breast cancer not assessed   |
| Geuskens 2011        | Outcome is not brca incidence, but mortality and morbidity due to it |
| Gonthier 1991        | No assessment of shift work. No comparison group                     |
| Gunnarsdottir 1995   | No assessment of shift work  |
| Gunnarsdottir 1997   | No assessment of shift work  |
| Ji 2008              | No assessment of shift work  |
| Kliukiene 1999       | No assessment of shift work  |
| Kocic 1999           | No assessment of shift work  |
| Kojo 2005            | No assessment of shift work  |
| Labreche 2010        | No assessment of shift work  |
| Li 2010              | No assessment of shift work  |
| Lie 2007             | No assessment of shift or night work, no reference working group     |
| Park 2012            | No assessment of shift work  |
| Peplonska 2007       | No assessment of shift work  |
| Petralia 1998        | No assessment of shift work  |
| Petralia 1998a       | No assessment of shift work  |
| Pollan 1999          | No assessment of shift or night work, no reference working group     |
| Pukkala 2009         | No assessment of shift or night work, no reference working group     |
| Rix 1996             | No assessment of shift work  |
| Sankila 1990         | No assessment of shift work  |
| Van Wijngaarden 2001 | No assessment of shift work, no reference working group              |
| Weiderpass 1999      | No assessment of shift work  |
| Zeng 2007            | No assessment of shift work  |

## 2- Studies awaiting classification

| Chu 2010      |  |
|---------------|--|
| Methods       | case-control study   |
| Participants  | Taiwanese women coming for screening of breast cancer                    |
| Interventions | shift work   |
| Outcomes      | incident breast cancer   |
| Notes         | Unable to contact author to confirm methods, comparison and obtain data. |

## Grundy 2011

| Methods       | case-control study                             |
|---------------|--|
| Participants  | female nurses from Vancouver, British Columbia |
| Interventions | Shift work                                     |
| Outcomes      | BrCa incidence                                 |
| Notes         | awaiting full text                             |
|               |  |

## 3- On-going studies

| Hansen 2013 a, b    |  |
|---------------------|--|
| Study name          | Unknown  |
| Methods             | unknown  |
| Participants        | women  |
| Interventions       | Shift work   |
| Outcomes            | Breast cancer incidence  |
| Starting date       | unknown  |
| Contact information | Johnni Hansen <johnni@cancer.dk></johnni@cancer.dk>  |
| Notes               | Author informed in personal communication that <u>two</u> studies will be published within the next year one similar to Hansen 2011 and one prospective study. |

### Papantoniou 2011

| Study name          | Evaluation of breast cancer risk in relation to night-shift work in a case-control study in a Spanish population. |
|---------------------|---|
| Methods             | population case-control study   |
| Participants        | night working females   |
| Interventions       | shift work, compared to day work  |
| Outcomes            | Breast cancer incidence   |
| Starting date       | not known   |
| Contact information | Castano Vinyals, Gemma <gcastano@creal.cat></gcastano@creal.cat>  |
| Notes               | abstract from conference- contacted authors who advised to wait for full publication                              |
| Study name          | Evaluation of breast cancer risk in relation to night-shift work in a case-control study in a Spanish population. |

## Wang 2011

| Study name          | Studying night work and disease in the million women study    |
|---------------------|---|
| Methods             | Cohort prospective- million women study                       |
| Participants        | million women study cohort                                    |
| Interventions       | shift work compared to day work                               |
| Outcomes            | Breast cancer incidence among others                          |
| Starting date       | 1996  |
| Contact information | ruth.travis@ceu.ox.ac.uk                                      |
| Notes               | first publication with baseline characteristics of the cohort |

#### 4- Complete References to Included Studies

#### **Davis 2001**

Davis S, Mirick D K, Stevens R G. Night-shift work, light at night, and risk of breast cancer. Journal of the National Cancer Institute 2001,93(20):1557-62.

#### Hansen 2001

Hansen J. Increased Breast Cancer Risk among Women Who Work Predominantly at Night. Epidemiology 2001,12(1):74-7.

#### Hansen 2011

Hansen J, Stevens R G. Case-control study of shift-work and breast cancer risk in Danish nurses: Impact of shift systems. European journal of cancer 2012,48(11):1722-9.

#### Hansen 2012

Hansen J, Lassen C F. Nested case-control study of night-shift work and breast cancer risk among women in the Danish military. Occupational and environmental medicine 2012,69(8):551-6.

#### Knutsson 2012

Knutsson A, Alfredsson L, Karlsson B, Akerstedt T, Fransson E I, et al.. Breast cancer among shift workers: results of the WOLF longitudinal cohort study. Scandinavian journal of work, environment & health 2012 online first.

#### Li 2011

Camp J E, Seixas N S, Wernli K, Fitzgibbons D, Astrakianakis G, Thomas D B, et al. Development of a cancer research study in the Shanghai textile industry. <u>Int.J.Occup.Environ.Health.</u> 2003,9(4):347-56.

Chang C K, Astrakianakis G, Thomas D B, Seixas N S, Ray R M, Gao D L, et al. Occupational exposures and risks of liver cancer among Shanghai female textile workers--a case-cohort study. Int.J.Epidemiol. 2006,35(2):361-9.

Li W, Ray RM, Lampe JW, Lin M-G, Gao DL, et al.. "Dietary and other risk factors in women having fibrocystic breast conditions with and without concurrent breast cancer: A nested case-control study in Shanghai, China.". International Journal of Cancer 2005,115(6):981-93.

\* Li, Wenjin. Magnetic Fields, Night-shift Work and the Risk of Breast Cancer among Female Textile Workers in Shanghai, China. ProQuest Dissertations and Theses 2011, <u>Thesis</u>.

Ray R M, Gao D L, Li W, Wernli K J, Astrakianakis G, Seixas N S, et al. Occupational exposures and breast cancer among women textile workers in Shanghai. <u>Epidemiology</u> 2007,1836:383-92.

Checkoway, H., D. B. Thomas, M. G. Yost, J. E. Camp and W. Li Textile industry exposures and breast cancer in women. (<u>Project protocol</u>). National Institute for Occupational Safety and Health Date of Input: 20120221 Date Record Updated: 20120221:Grant-Number-R01-OH-008149

Wernli K J, Ray R M, Gao D L, De Roos A J, Checkoway H, Thomas D B. Menstrual and reproductive factors in relation to risk of endometrial cancer in Chinese women. <u>Cancer causes and control</u>.2006,17(7):949-55.

Wernli K J, Ray R M, Gao D L, Thomas D B, Checkoway H. Cancer among women textile workers in Shanghai, China: overall incidence patterns. 1989-1998. <u>Am J Ind Med</u> 2003,44(6):595-9.

#### Lie 2006

Lie J A, Roessink J, Kjaerheim K. Breast cancer and night work among Norwegian nurses. <u>Cancer causes & control</u> 2006,17(1):39-44.

#### Lie 2011

Lie J A, Kjuus H, Zienolddiny S, Haugen A, Stevens R G, Kjaerheim K. Night work and breast cancer risk among Norwegian nurses: assessment by different exposure metrics. <u>American journal of epidemiology</u> 2011,173(11):1272-9.

#### Menegaux 2012

Menegaux F, Truong T, Anger A, Cordina-Duverger E, Lamkarkach F, Arveux P, et al. Night work and breast cancer: A population-based case-control study in France (the CECILE study). <u>International journal of cancer</u>. Journal international du cancer 2012,Jun 12(Online First):10.1002/ijc.27669.

Menegaux F, Truong T, Anger A, Kerbrat P, Arveux P, Lamkarkarch F, et al. Night work and breast cancer risk: CECILE study. <u>Cancer Research</u>

2011,71(8): http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L70690109.

Villeneuve S, Fevotte J, Anger A, Truong T, Lamkarkach F, Gaye O, et al. Breast cancer risk by occupation and industry: analysis of the CECILE study, a population-based case-control study in France. <u>Am J Ind Med</u> 2011,54(7):499-509.

#### O'Leary 2006

O'Leary E S, Schoenfeld E R, Stevens R G, Kabat G C, Henderson K, Grimson R, et al. Shift work, light at night, and breast cancer on Long Island, New York. <u>American journal of epidemiology</u> 2006,164(4):358-66.

#### Pesch 2010

Pesch B, Harth V, Rabstein S, Baisch C, Schiffermann M, Pallapies D, et al. Night work and breast cancer - results from the German GENICA study. <u>Scandinavian Journal of Work, Environment & Health</u> 2010,36(2):134-41.

#### Pronk 2010

Pronk A, Ji B T, Shu X O, Xue S, Yang G, Li H L, et al. Night-shift work and breast cancer risk in a cohort of Chinese women. <u>American journal of epidemiology</u> 2010,171(9):953-9.

#### Schernhammer 2001

Schernhammer E S, Laden F, Speizer F E, Willett W C, Hunter D J, Kawachi I, et al. Rotating night-shifts and risk of breast cancer in women participating in the nurses' health study. Journal of the National Cancer Institute 2001,93(20):1563-8.

#### Schernhammer 2006

Schernhammer E S, Kroenke C H, Laden F, Hankinson S E. Night work and risk of breast cancer. <u>Epidemiology</u> 2006,17(1):108-11.

#### Schwartzbaum 2007

Schwartzbaum J, Ahlbom A, Feychting M. Cohort study of cancer risk among male and female shift workers. <u>Scandinavian Journal of Work, Environment & Health</u> 2007,33(5):336-43.

#### **Tynes 1999**

Tynes T, Hannevik M, Andersen A, Vistnes A I, Haldorsen T. Incidence of breast cancer in Norwegian female radio and telegraph operators. <u>Cancer causes and control</u>.1996,7(2):197-204.

#### 5- References to Excluded studies

#### Coogan 1996

Coogan, P. F., R. W. Clapp, P. A. Newcomb, R. Mittendorf, G. Bogdan, et al.. "Variation in female breast cancer risk by occupation." <u>Am J Ind Med</u> 1996,30(4):430-437.

#### Ekpanyaskul 2010

Ekpanyaskul C, Khuhaprema T, Wiangnon S, Sangrajrang S. Case-control study of occupational categories and breast cancer risk in Thailand. <u>Asian Pac J Cancer</u> Prev. 2010,11<sup>37</sup>:793-7.

#### Elsner 1999

Elsner G, Nienhaus A, Hensel N, Roscher G, Kaufmann M, Solbach Chr, et al. Occupational and environmental factors and the risk of breast cancer. <u>Zentralblatt fur Arbeitsmedizin, Arbeitsschutz und Ergonomie</u> 1999,49(10):373-80.

#### Enderlein 1998

Enderlein G, Heuchert G, Stark H. Analysis of work-related cancer risks basing on linkage of registers. <u>Arbeitsmedizin Sozialmedizin Umweltmedizin</u> 1998,33(2):47-55.

#### Fritzsch 1979

Fritzsch, W.. "[Results of sociogynaecological examination for fitness of working women (author's transl)]." Zentralblatt fur Gynakologie 1979,101(15):962-969.

#### Geuskens 2011

Geuskens Goedele, de Vroome Ernest, de Weerd Marjolein, Koppes Lando. Night work and breast cancer – results from a large prospective study in the Dutch general working population. <u>Occupational and Environmental Medicine</u> 2011,68(Suppl 1):A17.

#### Gonthier 1991

Gonthier C, Dell'Accio P, De Gaudemaris R. Detection of breast cancer in occupational medicine. Regional epidemiologic study. <u>Archives des Maladies Professionnelles de Medecine du Travail et de Securite Sociale</u> 1991,5237:208-9.

#### **Gunnarsdottir 1995**

Gunnarsdottir H, Rafnsson V. Cancer incidence among Icelandic nurses. J Occup Environ Med. 1995,37<sup>37</sup>:307-12.

#### **Gunnarsdottir 1997**

Gunnarsdottir H K, Aspelund T, Karlsson T, Rafnsson V V. Occupational Risk Factors for Breast Cancer among Nurses. Int J Occup EnvironHealth 1997,3(4):254-8.

#### Ji 2008

Ji, B. T., A. Blair, X. O. Shu, W. H. Chow, M. Hauptmann, et al.. Occupation and Breast Cancer Risk AmongShanghai Women in a Population-BasedCohort Study. <u>Am J Ind Med</u> 2008,51(100-10).

#### Kliukiene 1999

Kliukiene J, Tynes T, Andersen A. Residential and occupational exposures to 50-Hz magnetic fields and breast cancer in women: a population-based study. <u>Am J Epidemiol.</u> 2004,159(9):852-61.

#### Kocic 1999

Kocic B, Jankovic S, Marinkovic J, Filipovic S, Petrovic B. Case-control study of breast cancer risk factors. Journal of BUON. 1999,4(4):399-403.

#### Kojo 2005

Kojo K, et al. Breast cancer risk among Finnish cabin attendants: a nested case-control study. <u>Occupational and</u> <u>Environmental Medicine</u> 2005;62(7):488-93.

#### Labreche 2010

Labreche F, Goldberg M S, Valois M F, Nadon L. Postmenopausal breast cancer and occupational exposures. <u>Occup</u> <u>Environ Med</u>. 2010,67(4):263-9.

#### Li 2010

Li Q, Zheng T, Holford TR, Boyle P, Zhang Y, et al. Light at night and breast cancer risk: results from a populationbased case-control study in Connecticut, USA. <u>Cancer causes & control</u> 2010,CCC 21(12):2281-85.

#### Lie 2007

Lie J A, Andersen A, Kjaerheim K. Cancer risk among 43000 Norwegian nurses. <u>Scand J Work Environ Health</u> 2007,33(1):66-73.

#### Park 2012

Park Sat Byul, Shin Hai Rim, Lee Soon Young. A population-based cohort study of HRT use and breast cancer in Korea. Asia-Pacific Journal of Public Health 2012,(2):415-22.

#### Peplonska 2007

Peplonska B, Stewart P, Szeszenia-Dabrowska N, Rusiecki J, Garcia-Closas M, Lissowska J, et al. Occupation and breast cancer risk in Polish women: a population-based case-control study. <u>Am J Ind Med</u> 2007,50(2):97-111.

#### Petralia 1998

Petralia S A, Chow W H, McLaughlin J, Jin F, Gao Y T, Dosemeci M. Occupational risk factors for breast cancer among women in Shanghai. <u>Am J Ind Med</u>. 1998,34(5):477-83.

#### Petralia 1998a

Petralia S A, Vena J E, Freudenheim J L, Marshall J R, Michalek A, Brasure J, et al. Breast cancer risk and lifetime occupational history: employment in professional and managerial occupations. <u>Occup Environ Med.</u> 1998,55(1):43-8.

#### Pollan 1999

Pollan M, Gustavsson P. High-risk occupations for breast cancer in the Swedish female working population. <u>Am J</u> <u>Public Health</u> 1999,89(6):875-81.

#### Pukkala 2009

Pukkala E, Martinsen J I, Lynge E, Gunnarsdottir H K, Sparen P, Tryggvadottir L, et al. Occupation and cancer - follow-up of 15 million people in five Nordic countries. <u>Acta Oncol</u>. 2009,48(5):646-790.

#### **Rix 1996**

Rix, B A and Lynge E. Cancer incidence in Danish health care workers. Scand J Soc Med 1996,24(2):114-20.

#### Sankila 1990

Sankila R, Karjalainen S, Laara E, Pukkala E, Teppo L. Cancer risk among health care personnel in Finland, 1971-1980. <u>Scand J Work Environ Health</u> 1990,16(4):252-7.

#### 6- References to studies awaiting classification

Chu 2010

Chu C H, Chen C J, Hsu G C, Liu I L, Christiani D C, Ku C H. Shift work is risk factor for breast cancer among Taiwanese women. <u>European Journal of Cancer, Supplement</u> 2010,837:209.

#### Grundy 2011

Grundy A, Tranmer J, Richardson H, Bajdik C, Graham C, Lai A S, et al. The influence of shift work and light at night exposure on melatonin levels and breast cancer risk. <u>Occupational and Environmental Medicine</u> 2011,68:A87-8.

#### van Wijngaarden 2001

van Wijngaarden E, Nylander-French L A, Millikan R C, Savitz D A, Loomis D. Population-based case-control study of occupational exposure to electromagnetic fields and breast cancer. <u>Ann Epidemiol</u>. 2001,11(5):297-303.

#### Weiderpass 1999

Weiderpass E, Pukkala E, Kauppinen T, Mutanen P, Paakkulainen H, Vasama-Neuvonen K, et al. Breast cancer and occupational exposures in women in Finland. <u>Am J Ind Med</u>. 1999,36(1):48-53.

#### Zeng 2007

Zeng C, Mo X Y, Jin L Y. [Study on occupational stress and breast cancer risk among professional women in China]. <u>Zhonghua Liu Xing Bing Xue Za Zhi</u>. 2007,28(10):1046.

#### 7- References to ongoing studies

#### Hansen 2013 a, b

Author communication indicated that two new studies by him will be coming out this year

#### Papantoniou 2011

Papantoniou K, Castano-Vinyals G, Gomez B P, Altzibar J M, Ardanaz E, Moreno V, et al. Evaluation of breast cancer risk in relation to night-shift work in a case-control study in a Spanish population. <u>Occupational and</u> <u>Environmental Medicine</u> 2011,68:A17-8.

#### Wang 2011

Wang X S, Armstrong M E G, Cairns B J, Key T J, Travis R C. Shift work and chronic disease: The epidemiological evidence. <u>Occupational Medicine</u>. 2011,(2):78-89.

Wang X S, Travis R, Beral V. Studying night work and disease in the million women study. <u>Occupational and</u> <u>Environmental Medicine</u> 2011,68:A88.

# Appendix D

Risk of Bias assessment for each included study

| Study ID                          | Davis 2001   |
|-----------------------------------|--|
| Exposure definition               | High risk  |
| Support for the judgment          | Exposure was defined as beginning work after 7:00 PM and leaving work before 9:00 AM: only one of the aspects recommended by IARC  |
| Exposure assessment               | High risk  |
| Support for the judgment          | Subjective assessment. Reported by participants (interviews/questionnaires). Authors say: the exposure is based on an independent simple Job Exposure Matrix. Due to the nature of the study (registry based) such information (number of years of expsoure/ frequency of night work) was not available. |
| Blinding of assessors             | Unclear risk   |
| Support for the judgment          | Not Reported   |
| Reliability of exposure estimates | Low risk   |
| Support for the judgment          | Not clearly stated but both reviewers agreed it was implicit in description that same methods for cases and controls were used to measure exposure   |
| Confounding                       | High risk  |
| Support for the judgment          | Only age and parity assessed.  |
| Attrition                         | High risk  |
| Support for the judgment          | Over 20% non-response however did not differ between cases and controls  |
| Analysis/research specific bias   | High risk  |
| Support for the judgment          | Matching and conditional logistic regression used for analysis. However authors do not provide their considerations for the selection of the sample/ size. Dose response was not assessed adequately   |
| Selective reporting               | Low risk   |
| Support for the judgment          | Baed on methods we assume that estimates were presented for all tested hypotheses  |
| Funding                           | Unclear  |
| Support for the judgment          | Although low risk because of a Non commercial funding source (grant R01CA55844 from the national cancer Institute). The role   |

|                          | of the funding organization in study conduct is not reported. |
|--------------------------|---|
| Conflict of interest     | Unclear   |
| Support for the judgment | Not Reported  |

| Study ID                          | Hansen 2001  |
|-----------------------------------|--|
| Exposure definition               | High risk  |
| Support for the judgment          | Women were considered to work predominantly at night if they had been employed for at least half a year in one or more of the trades in which at least 60% of the female responders had nighttime schedules. None of the aspects recommended for shift work assessment part of definition  |
| Exposure assessment               | High risk  |
| Support for the judgment          | Subjective classification of exposure to shift work: Information on the jobs of each case and control subject was converted into a job classification based on an extended version of the International Standard Industrial Classification of all Economic Activities, used to classify all companies in Denmark by the National Bureau of Statistics. |
| Blinding of assessors             | Low risk   |
| Support for the judgment          | Correspondence: No- investigators assessing exposure were not aware of case or control status of the individual- the exposure was based on an independent simple Job Exposure Matrix.  |
| Reliability of exposure estimates | Low risk   |
| Support for the judgment          | The employment histories of the control subjects were retrieved from the files of the pension fund in the same way as for cases.   |
| Confounding                       | Low risk   |
| Support for the judgment          | 'To adjust for socioeconomic status and reproductive factors (number of children, age at birth of first and last child), we estimated odds ratios (ors) and 95% confidence Intervals (cis) by conditional logistic regression analysis using the statistical package EPICURE."   |
| Attrition                         | Low risk   |
| Support for the judgment          | Register linkage used so non response did not occur  |
| Analysis/research specific bias   | High risk  |
| Support for the judgment          | The division of exposure was binary categorical, even though a dose analysis of sorts was done for a subgroup with 6 yrs or more of employment we do not consider it reflection of exposure.   |
| Selective reporting               | Low risk   |
| Support for the judgment          | Adjusted OR presented for the aim of 'assessing risk of Brca in women who worked predominantly at night'   |
| Funding                           | Low risk   |
| Support for the judgment          | Study was not supported directly abu any organization, but indirectly since my salary was paid by the Danish Cancer Society  |

| Conflict of interest     | Low risk  |
|--------------------------|---|
| Support for the judgment | No conflict of interest based on communication with author: |

| Study ID                          | Hansen 2011  |
|-----------------------------------|--|
| Exposure definition               | Low risk   |
| Support for the judgment          | Definition included at least two of the aspects recommended by IARC (shift duration, shift system)   |
| Exposure assessment               | High risk  |
| Support for the judgment          | Subjective assessment. Reported by participants (interviews/questionnaires)  |
| Blinding of assessors             | Low risk   |
| Support for the judgment          | Correspondence: No, in principle the interviewers were blinded to case-control status. Further, assessing a very objective measure such as shift-work should not be influenced by this. Finally, we didn't directly ask about shift work but rather about normal working time during a 'normal month' in each job.   |
| Reliability of exposure estimates | Low risk   |
| Support for the judgment          | Not stated categorically but clear from report that same method of interview used for both groups  |
| Confounding                       | Low risk   |
| Support for the judgment          | All major confounding factors/effect modifiers addressed. 3 (Age, BMI, Parity), were assessed in full. Of the remaining 2(ethnicity, SES), Ethnicity was considered not applicable and SES deemed similar among the groups based on extrenal data. Authors confirmed: 100% caucasian. Yes we have collected information on e.g education. But SES in itselt is only a crude indicator of potential confounders. Since we had been able to collect information on these there was no need to create a SES-variabel (althought we have data for that). |
| Attrition                         | High risk  |
| Support for the judgment          | Attrition differs between the groups (excluded from analysis13% cases, 16% controls) and has not been explained  |
| Analysis/research specific bias   | Low risk   |
| Support for the judgment          | Authors reported use of one or more methods to reduce bias (standardization, matching, adjustment in multivariate model, stratification, propensity scoring)   |
| Selective reporting               | Low risk   |
| Support for the judgment          | Adjusted estimates presented for all hypothesis tested as per aims   |

| Funding                  | Low risk  |
|--------------------------|---|
| Support for the judgment | 'Unrestricted grants from the Danish Cancer Society and from the National Programme of Environmental Health Research. |
|                          | The funding sources did not involve in the data collection, data analysis, manuscript writing or publication."        |
| Conflict of interest     | Low risk  |
| Support for the judgment | Authors declare no conflict of interest   |
|                          |   |

| Study ID                          | Hansen 2012   |
|-----------------------------------|---|
| Exposure definition               | Low risk  |
|                                   | Definition included 2 of the aspects recommended by IARC (shift duration/ shift time, shift system)   |
| Support for the judgment          |   |
| Exposure assessment               | High risk   |
| Support for the judgment          | Subjective assessment. Reported by participants (interviews/questionnaires)   |
| Blinding of assessors             | Low risk  |
| Support for the judgment          | The trained telephone interviewers were blinded to case or control status   |
| Reliability of exposure estimates | Low risk  |
| Support for the judgment          | Same method of interview used for both groups   |
| Confounding                       | Low risk  |
| Support for the judgment          | All major factors assessed except SES which may well have been different between cases and controls considering its military.<br>Authors communicated: Yes we have collected information on e.g education. But SES in itselt is only a crude indicator of potential confounders. Since we had been able to collect information on these there was no need to create a SES-variabel (althought we have data for that). |
| Attrition                         | High risk   |
| Support for the judgment          | Over 60 % non-response in both groups   |
| Analysis/research specific bias   | Low risk  |
| Support for the judgment          | Authors reported use of one or more methods to reduce bias (standardization, matching, adjustment in multivariate model, stratification, propensity scoring)  |
| Selective reporting               | Low risk  |
| Support for the judgment          |   |
| Funding                           | Low risk  |
|                                   | This study was supported by a grant from the Danish Ministry of Defence. The funding source had no role in the design or analysis   |
| Support for the judgment          | of the study or in the decision to submit the manuscript for publication  |
| Conflict of interest              | Low risk  |

E

| Study ID                                 | Menegaux 2012  |
|--|--|
| Exposure definition                      | Low risk   |
|  | Definition included 2 of the aspects recommended by IARC (shift duration/shift time, intensity)  |
| Support for the judgment                 |  |
| Exposure assessment                      | High risk  |
| Support for the judgment                 | Subjective assessment. Reported by participants (interviews/questionnaires)  |
| Blinding of assessors                    | High risk  |
| Support for the judgment                 | Correspondence: The interviewers were aware of The case-control status of The participants.  |
| <b>Reliability of exposure estimates</b> | Low risk   |
|  | Authors used same methods for cases and controls to measure exposure: A standardized questionnaire was used and interviewers                                   |
| Support for the judgment                 | were told to conduct the interview in the same way in both groups.   |
| Confounding                              | Low risk   |
|  | Adjusted for all major confounders: Adjusted for age, study area, parity, age at first full-term pregnancy, age at menarche, family                            |
|  | history of breast cancer, current hormonal replacement therapy, body mass index, tobacco and alcohol. These quotas by SES were                                 |
|  | calculated   |
| Support for the judgment                 | from the census data available in each study area, to obtain a distribution by SES among controls identical to the SES distribution                            |
| Attrition                                | I ow risk  |
| Autoni                                   | Low HSK<br>Departed for both asses and controls and did not differ in size and reasons 21% and 24%   |
| Support for the Judgment                 | Leave rick   |
| Analysis/research specific blas          | LOW FISK   |
| Support for the judgment                 | Authors reported use of more than one methods to reduce bias (standardization, matching, adjustment in multivariate model, stratification, propensity scoring) |
| Selective reporting                      | Low risk   |
| Support for the judgment                 | Adjusted estimates presented for all hypothesis tested as per aims   |
| Funding                                  | Low risk   |
| Fullaling                                | Crant sponsor: A gance Nationale de s'acurit, a sonitaire de l'alimentation, de l'anvironnement et du travail (ANSES): Grant                                   |
|  | number: 2010/2/2073: Grant sponsors: Agence Nationale de la Recherche (anot Reported): Fondation de France: Institut National                                  |
|  | du Cancer (INCA): Lique contra le Cancer Grand Quest: Association pour le recherche contra le cancer (ADC). The sponsors had                                   |
|  | no role in the conduct of the study, except funding A final report was provided to them at the end of the contract and validated by                            |
| Support for the judgment                 | a scientific committee   |
| Bupport for the judgment                 |  |

| Conflict of interest     | Low risk  |
|--------------------------|---|
| Support for the judgment | - There is no conflict of interest to disclose. |

| Study ID                                 | Lie 2006   |
|--|--|
| Exposure definition                      | High risk  |
|  | No clear definition provided. Definition of exposure is categorical with an arbitrary threshold (Job at infirmary) which   |
| Support for the judgment                 | covers only one of the recommended aspects of exposure (duration of work at job assumed to have night work exposure).  |
| Exposure assessment                      | High risk  |
|  | Jobs were categorized by authors into exposures: "Work history from the nurse registry was self-reportedIn order to calculate<br>number of years of night work out of total work time as a nurse, some assumptions had to be made. Imputation around the 1970<br>census was mainly based on work history from the last update of the nurse register in 1968." authors elaborated in<br>correspondence: The 2006-study includes cases diagnosed from 1960 to 1982 (and matched controls). The work history we applied<br>in that study came from two registers:<br>1) the Norwegian Board of Health's registry of all nurses, including work sites (years, site, department), however no information on<br>schedules or night work. |
|  | 2) Information from 3 censuses (work and industry codes), no information on night work   |
|  | As we had no information about work schedules or frequency of night-shifts in that study, we used a crude exposure metric for  |
| Support for the judgment                 | night work: cumulative number of years worked in hospitals or other 24-hour institutions.  |
| Blinding of assessors                    | High risk  |
| Support for the judgment                 | Exposure data were coded by researchers into categories after the cases and controls were identified and matched   |
| <b>Reliability of exposure estimates</b> | Low risk   |
| Support for the judgment                 | The authors did not state that the same methods were used to measure exposure risk factors in cases and controls. Report implies linkage was established between cancer cases and the nurses registry before the job categories by Exposure were defined.  |
| Confounding                              | High risk  |
| Support for the judgment                 | All major confounders Age, Parity, SES, were not satisfactorily assessed: ethnicity not an issue: The cohort is ethnically quite homogeneous, most of them ethnical Norwegians. A very small proportion of nurses came from other countries, mainly from Denmark and Sweden. Correspondence: The work history in the 2006-study, which was based on two registers, does not include information on BMI, which was therefore not adjusted for. Since its the same cohort we can assume the BMI to have the same effect as in 2011 study. Self-reported data for confounding factors from health care databases.   |
| Attrition                                | Low risk   |
| Support for the judgment                 | Register linkage used so nonresponse did not occur   |
| Analysis/research sneeific higs          | I ow risk  |
| Anarysis/research specific blas          | Adjustment in multivariate model and sensitivity analyses. Dose response (increasing exposure in 5 and 10 yr categories) assessed  |
| Support for the judgment                 | in analysis. Sample size calculation not provided no justification given   |

| Selective reporting      | Low risk  |
|--------------------------|---|
| Support for the judgment | Adjusted estimates presented for the hypotheses tested as per aims  |
| Funding                  | Low risk  |
| Support for the judgment | Noncommercial funding source (Norwegian Women's Public Health Association). Source had no influence on study conduct. |
| Conflict of interest     | Low risk  |
| Support for the judgment | No conflict of interests to be declared   |

| Study ID                          | Lie 2011   |
|-----------------------------------|--|
| Exposure definition               | Low risk   |
|                                   | Definition included two of the aspects recommended by IARC (shift duration, shift system)  |
| Support for the judgment          |  |
| Exposure assessment               | High risk  |
| Support for the judgment          | Subjective assessment. Reported by participants (interviews/questionnaires)  |
| Blinding of assessors             | Low risk   |
| Support for the judgment          | Interviewers were blind to case status   |
| Reliability of exposure estimates | Low risk   |
|                                   | Implicit even though not stated as investigators were blind to case status so likely that identical interviews for both cases and    |
| Support for the judgment          | controls were carried out  |
| Confounding                       | Low risk   |
|                                   | Although only age and parity adjusted estimates presented, authors did assess all other major confounders and only included the      |
|                                   | ones in analysis which changed the results by more than 10%.   |
|                                   | Ethnicity has not been assessed but likely a low percentage of nonwhite nurses Author confirmed: The cohort is ethnical quite        |
|                                   | Denmark and Sweden • The work history in the 2011 study is based on a telephone interview, and also includes information about       |
|                                   | height and weight at age 18 years and at the time of diagnosis/reference. BMI (at 18 and at time of diagnosis) were not included in  |
| Support for the judgment          | the final model, as it did not seem to be a confounder.  |
| Attrition                         | High risk  |
|                                   | Variation in non-response by group, reasons not provided. Total non-response over 30%. Potential differential bias might have been   |
| Support for the judgment          | introduced by the exclusion of the deceased cases.   |
| Analysis/research specific bias   | Low risk   |
|                                   | Authors reported use of one or more methods to reduce bias (standardization, matching, adjustment in multivariate model,             |
|                                   | stratification, propensity scoring). Dose response assessed in analysis. No justification or calculation for sample size provided in |
| Support for the judgment          | report   |

| Selective reporting      | Low risk  |
|--------------------------|---|
| Support for the judgment | Adjusted estimates presented for all hypotheses tested as per aims  |
| Funding                  | Low risk  |
|                          | Noncommercial funding source (Research Council of Norway (contract 185776/V50) and by grants from the South-Eastern Norway Regional Health Authority (3b-107) and the Norwegian Cancer Society (PK01-2009-0444). Source had no influence on study |
| Support for the judgment | conduct.  |
| Conflict of interest     | Low risk  |
| Support for the judgment | Authors declare no conflict of intrerest  |

| Study ID                          | O'Leary 2006   |
|-----------------------------------|--|
| Exposure definition               | High risk  |
| Support for the judgment          | Definition covers only one aspect of exposure (start or end time of shift)   |
| Exposure assessment               | High risk  |
| Support for the judgment          | Subjectively measured: Reported by participants (interviews/questionnaires)  |
| Blinding of assessors             | Unclear risk   |
| Support for the judgment          | Not Reported   |
| Reliability of exposure estimates | Low risk   |
| Support for the judgment          | Same methods (EBCLIS interview) for cases and controls to measure exposure   |
| Confounding                       | High risk  |
| Support for the judgment          | Age and parity assessed  |
| Attrition                         | Low risk   |
| Support for the judgment          | Non response was reported for both cases(13%) and controls(16%) and did not differ in size and reasons                               |
| Analysis/research specific bias   | Unclear risk   |
|                                   | Authors reported use of one or more methods to reduce bias (standardization, matching, adjustment in multivariate model,             |
|                                   | stratification, propensity scoring). Dose response assessed in analysis. No justification or calculation for sample size provided in |
| Support for the judgment          | report   |
| Selective reporting               | Low risk   |
| Support for the judgment          | Adjusted estimates presented for all hypotheses tested as per aims   |
| Funding                           | Unclear risk   |
|                                   | Although low risk because of Noncommercial funding sources (grant CA/ES 62991 from   |
|                                   | the National Cancer Institute/National Institute of Environmental Health Sciences (NIEHS) (EBCLIS Group); grant                      |
| Support for the judgment          | ES11659 from NIEHS (Dr. Richard Stevens); grant CA/ES 66572 from the National Cancer Institute/NIEHS (LIBCSP);                       |

|                          | and grant P30ES10126 from NIEHS (Dr. Marilie Gammon).) |
|--------------------------|--|
| Conflict of interest     | Low risk   |
| Support for the judgment | Authors declare no conflict of interest                |

| Study ID                            | Pesch 2010  |
|-------------------------------------|---|
| Exposure definition                 | High risk   |
| Support for the judgment            | Definition covers only one aspect of exposure (start or end time of shift)  |
| Exposure assessment                 | High risk   |
| Support for the judgment            | Subjectively measured: Reported by participants (interviews/questionnaires)   |
| Blinding of assessors               | Low risk  |
| Support for the judgment            | Correspondence: Due to the study design it is not possible for interviewers not to realize case-control status (interviews were performed with incident breast cancer patients).  |
| Reliability of exposure estimates   | Low risk  |
| Support for the judgment            | The authors used same methods for cases and controls to measure exposure  |
| Confounding                         | Low risk  |
| Support for the judgment            | Major confounding factors/effect modifiers (Age, BMI, Ethnicity, Parity (number of children, age at first birth, and education(for SES)) were assessed in full.   |
| Attrition                           | High risk   |
| Support for the judgment            | % of nonresponse differed among cases (12%) and controls (33%)  |
| Analysis/research specific bias     | Low risk  |
| Support for the judgment            | Corrected for a potential selection bias using a resampling and bootstrapping procedure with logistic regression models conditional on age in 5-year groups, adjusted for family history of breast cancer, hormone replacement use, and number of mammograms. Dose response assessed in analysis. |
| Selective reporting                 | Low risk  |
|                                     |   |
| Support for the judgment            | Adjusted estimates presented for all hypotheses tested as per aims  |
| Support for the judgment<br>Funding | Adjusted estimates presented for all hypotheses tested as per aims<br>Low risk  |

| Conflict of interest     | Low risk                                |
|--------------------------|---|
| Support for the judgment | Correspondence: No conflict of interest |

| Study ID                          | Pronk 2010   |
|-----------------------------------|--|
| Exposure definition               | Low risk   |
|                                   | Definition included 2 of the aspects recommended by IARC (shift duration: number of years, shift Intensity)  |
| Support for the judgment          |  |
| Exposure assessment               | High risk  |
| Support for the judgment          | Subjectively measured: Reported by participants (interviews/questionnaires) and proxy used to allocate exposure status (job matrix, job title)   |
| Blinding of assessors             | Low risk   |
| Support for the judgment          | Occupational histories were obtained prior to cancer diagnosis and assignment of night-shift work was conducted without knowledge of case status   |
| Reliability of exposure estimates | Low risk   |
| Support for the judgment          | Correspondence: cases and controls exposure assessed in the same manner  |
| Confounding                       | Low risk   |
| Support for the judgment          | Adjusted for Age, education, family history of breast cancer, number of pregnancies, age at first birth, occupational physical activity. BMI assessed but not controlled for as it had no effect on results and ethnicity was likely not varied. Education as proxy for SES (correspondence)   |
| Attrition                         | Low risk   |
| Support for the judgment          | 7% total loss even though group-wise loss Not Reported   |
| Analysis/research specific bias   | Low risk   |
| Support for the judgment          | <sup>'Cox</sup> proportional hazards regression (PROCPHREG) with age as the time scale and stratification by birth cohort (5-year intervals).<br>Since the self-reported information<br>on night-shift work was obtained during the second follow-up, this analysis was restricted to person-years and cases with incident<br>breast cancer diagnosed after the second follow-up ( $n = 69,982$ , of whom 69,472 provided information on night-shift work)". Dose<br>response analysed. Sample size justification was not clearly stated, not really However, authors elaborate all decisions regarding<br>restricting the sample and why they did it. |
| Selective reporting               | Low risk   |
| Support for the judgment          | Adjusted estimates presented for all hypotheses tested as per aims   |
| Funding                           | Unclear risk   |
|                                   | Although study funded by Noncommercial (US National Institutes of Health (grant R01 CA70867) and the Intramural Research   |
| Support for the judgment          | Program of the National Institutes of Health (contract N02 CP1101066)) organizations the role of these is not reported in study  |

|                          | conduct. Correspondence: I am not sure about this. You could contact my former colleagues in the cc if you want to find out |
|--------------------------|---|
| Conflict of interest     | Low risk  |
| Support for the judgment | Authors declare no conflict of interest   |

| Study ID                          | Schernhammer 2001  |
|-----------------------------------|--|
| Exposure definition               | High risk  |
|                                   | Did not consider the permanent night-shiftworkers who, "being not rotating were included in the control group", as the authors the mealure exclude (here mail guestion mine) only one during the   |
| Support for the judgment          | the whole period of observation  |
| Exposure assessment               | High risk  |
|                                   | Mail Questionnaire once only. Authors explained that unless self-reported data on work cannot be collected from logs in the US   |
| Support for the judgment          | legally. Thus this is a matter out of their control and may be US studies should be considered separately for assessment risks.  |
| Blinding of assessors             | Low risk   |
| Support for the judgment          | Confirmed with authors prospective allocation of exposure  |
| Reliability of exposure estimates | Low risk   |
| Support for the judgment          | Intra-observer variability is reported by means of a subjective judgment of reliability:" it is likely that our results are accurate, because other self-reports have been highly accurate in this cohort (47), and previous validations of similar questions (e.g., electric blanket use) (48) have shown reasonable reproducibility." authos clarified in communication that reliability can't be tested as its not legal to track nurses data unless they self-report in the US. But they measured it for electric blanket use for both studies which was found consistent. |
| Confounding                       | Low risk   |
| Support for the judgment          | Age, BMI, SES, Parity, Age at menarche; age at menopause; age at first birth; alcohol consumption; oral contraceptive use; use of postmenopausal hormones; menopausal status; benign breast disease; family history of breast cancer; Regarding ethnicity and SES author replied: the NHS cohorts are very uniform with over 95% of all women being white/Caucasian.   |
| Attrition                         | Low risk   |
| Support for the judgment          | Groupwise loss not reported however total loss is less than 10% for a very large cohort  |
| Analysis/research specific bias   | Low risk   |
|                                   | Authors reported use of one or more methods (Pooled logistic regression models) to reduce bias. Increasing duration of exposure  |
| Support for the judgment          | assessed in 10 yr categories as supgroup analyses.   |
| Selective reporting               | Low risk   |
| Support for the judgment          | Adjusted estimates presented for all hypotheses tested as per aims   |

| Funding                  | Low risk   |
|--------------------------|--|
|                          | Supported by Public Health Service grants CA/ES62984 (National Cancer Institute [NCI]/National Institute of Environmental      |
|                          | Health Sciences) and CA87969 (NCI), National Institutes of Health, Department of Health and Human Services. E.                 |
|                          | S.Schernhammer was supported in part by a Research Grant in Cancer Prevention from the Austrian Federal Ministry of Education, |
| Support for the judgment | Science and Culture. Confirmed with authors low risk no involvement of the funder  |
| Conflict of interest     | Low risk   |
| Support for the judgment | Confirmed with authors there are no conflicts of interest.   |

| Study ID                          | Schernhammer 2006   |
|-----------------------------------|---|
| Exposure definition               | High risk   |
| Support for the judgment          | Did not consider the pernanent night-shiftworkers separate from rotators. "Years worked rotating night-shifts with at least three nights per month in addition to days or evenings in that month", and "permanent night-shifts for 6 or more months"  |
| Exposure assessment               | High risk   |
| Support for the judgment          | Mail Questionnaire repeated 4 times   |
| Blinding of assessors             | Low risk  |
| Support for the judgment          | Confirmed with authors prospective allocation of exposure   |
| Reliability of exposure estimates | Low risk  |
| Support for the judgment          |   |
| Confounding                       | Low risk  |
| Support for the judgment          | Age, BMI, Parity, SES, Ethnicity. Age at menarche; age at menopause; age at first birth; alcohol consumption; oral contraceptive use; use of postmenopausal hormones; menopausal status; benign breast disease; family history of breast cancer; Regarding ethnicity and SES author replied:the NHS cohorts are very uniform with over 95% of all women being white/Caucasian. SES adjustment was done for husbands' educational attainments as the proxy for SES, since we have no other good indicators of SES. Also because they are all nurses, there is relatively little variation in SES in our cohorts. |
| Attrition                         | Low risk  |
| Support for the judgment          | Differential loss is not reported and unlikely as total loss is under 1%  |
| Analysis/research specific bias   | Low risk  |
| Support for the judgment          | Same as NHS I (Schernhammer 2001)   |
| Selective reporting               | Low risk  |
| Support for the judgment          | Adjusted estimates presented for all hypotheses tested as per aims  |
| Funding                           | Low risk  |
| Support for the judgment          | Supported by Public Health Service grants CA/ ES62984 (National Cancer Institute [NCI]/NationalInstitute of Environmental Health Sciences) and CA87969 (NCI), National Institutes of Health, Department of Health and Human Services. E. S.   |

|                          | Schernhammer was supported in part by a Research Grant in Cancer Prevention from the Austrian Federal Ministry of Education, Science and Culture. Confirmed with authors low risk no involvement of the funder |
|--------------------------|--|
| Conflict of interest     | Low risk   |
| Support for the judgment | Confirmed with authors there are no conflicts of interest.   |

| Study ID                          | Schwartzbaum 2007   |
|-----------------------------------|---|
| Exposure definition               | High risk   |
|                                   | Definition is largely based on proportion of ppl usually involved in night-shift work in an occupation. A job exposure matrix of      |
| Support for the judgment          | sorts prone to bias and missclassification of exposure liekly, as indicated by authors as well  |
| Exposure assessment               | High risk   |
|                                   | Previously recorded data from survey of living conditions (interviews in 1977-1981) was used:   |
|                                   | "Information about work schedules in different occupations within specific industries was obtained from the annual Survey of          |
|                                   | Living Conditions (ULF) conducted by Statistics Sweden during 1977–1981. Over these years, altogether 55 323 persons were             |
|                                   | randomly selected from the Swedish population, and 46 438 (84%) participated in personal interviews conducted by specifically         |
|                                   | trained   |
|                                   | interviewers. The participants answered questions about their usual occupation and workhours [eg, daytime, evening and night          |
|                                   | hours, rotating shift work with twopossible shifts per day, rotating shift work with three ormore possible shifts per day ("three-    |
|                                   | daytime and nighttime workhours. Furthermore, then articipants were asked to give information about when they started and ended       |
|                                   | working each day during theweek preceding the interview" Thus the job-exposure matrix that we constructed                             |
|                                   | contained information about the percentage of shiftworkers in each job title and industry combination and was linked to the census    |
|                                   | data obtained for each personin the cohort. In our analyses, we classified, as shiftworkers, people working in job-title and industry |
| Support for the judgment          | combinations with at least 40% shift workers.   |
| Blinding of assessors             | Low risk  |
| Support for the judgment          | Correspondence: Exposure data was collected completely independent from case status of the participants.                              |
| Reliability of exposure estimates | High risk   |
|                                   | Correspondence: We did not use expert assessments to determine exposure (exposure assessors), so kappa estimates are not              |
|                                   | relevant in the context of the exposure assessment used in our study. The exposure assessment was based on a very large survey        |
|                                   | (almost 50 000 persons) randomly selected from the Swedish population (with high response rate) that were asked about their           |
| Support for the judgment          | working hours and occupational title and industry.  |
| Confounding                       | High risk   |
| Support for the judgment          | Only two of the major confounding factors adjusted for (age and SES). Correspondence: We did not have information about BMI           |

|                                 | or parity. But I believe that adjusted and unadjusted risk estimates in studies that did have information about e.g. Parity did not differ from each other, so these confounders did not seem to have an effect on risk estimates.  |
|---------------------------------|---|
| Attrition                       | High risk   |
|                                 | Participants were not followed as data about them cross linked between registers. Authors report no info on any missing data and  |
| Support for the judgment        | hence excluded ones. However original survey had 16% non response.  |
| Analysis/research specific bias | High risk   |
|                                 | Authors used multivariate model adjustment for major confounders, and assumption also made clear. They performed sensitivity<br>and subgroup analyses to test their assumptions as well.<br>But the starting point (the exposure assessment) was too crude (both in terms of work sectors examined (admitted by the authors<br>themselves) and as cut-off percentages) so that the sophisticated statistical analysis cannot compensate. Plus the sample was based              |
| Support for the judgment        | on a random selection from census. So, in general terms, we believe the risk is high.   |
| Selective reporting             | Low risk  |
| Support for the judgment        | Authors state: "The primary purpose of our present study was to expand research on the association between shift work and cancer<br>by looking at cancer risks at many sites among both male and female night and rotating shift workers in a large occupational<br>cohort." but do not present rotating and night-shift work separately and also do not present some of the analyses done with varying<br>definitions of shift work. Stating the results were almost the same. |
| Funding                         | Low risk  |
| Support for the judgment        | The study was funded by a Swedish research council that was not involved in the conduct of the study.   |
| Conflict of interest            | Low risk  |
| Support for the judgment        | Confirmed with authors there are no conflicts of interest.  |

| Study ID                 | Tynes 1996  |
|--------------------------|---|
| Exposure definition      | High risk   |
| Support for the judgment | Definition of exposure/ case is categorical with an arbitrary threshold (e.g.1 yr or more, ever done night work. Also the definition is not exclusive to shift work but includes additional exposures to some extent)   |
| Exposure assessment      | High risk   |
| Support for the judgment | Proxy used to allocate exposure status (job matrix, job title) . In this case ships were classified intoExposurecategories "exposure classification of Norwegian merchant ships"  |
| Blinding of assessors    | High risk   |
| Support for the judgment | Authors state" For cases and controls drawn from the TC, detailed job histories on ships were collected. Shift work (categories 0,1,2,3) and travel through time zones (categories 0,1) were classified for each ship mentioned in the job histories by a shipping journalist and a researcher with detailed knowledge of the recent history (1945-90) of Norwegian merchant ships. " indicating case |

|                                   | and control status were known before exposure metrics were collected.   |
|-----------------------------------|---|
| Reliability of exposure estimates | Unclear risk  |
|                                   | Exposure estimate was mad "a posteriori" by two people not directly involved with this job. No indication that reliability was  |
| Support for the judgment          | assessed in report.   |
| Confounding                       | High risk   |
|                                   | Authors say in text that fertility factors and age were assessed, aparently from tables, none of theses factors have been adjusted for,   |
|                                   | the only adjustment is subgroup results reported by age for under and over 50 yrs and a statement that adjusted OR refer to   |
|                                   | adjustment for employment duration for shift work estimates.  |
| Support for the judgment          | Author explained in correspondence that they don't have access to the data any more.  |
| Attrition                         | Low risk  |
| Support for the judgment          | For cohort the nonresponse is low (TC: 5.4%) Not Reported for nested case-control but unlikely any additional   |
| Analysis/research specific bias   | High risk   |
|                                   | Authors state that they used fertility categories for confounding estimation (For case-control women born 1935 and later, fertility   |
|                                   | data was available and confounding from such factors was evaluated by including a fertility variable with three categories (1 =no   |
|                                   | children; $2 =$ first child born at age 25 years and over; $3 =$ first child born before age 25) but tables indicate only employement   |
| Support for the judgment          | duration was adjusted for and its something they do not explain. No dose assessment, unclear how sample was decided.  |
| Selective reporting               | High risk   |
|                                   | Aims and objectives inconsitent between abtsract and report and results are not a reflection of these completely. Shift work was  |
|                                   | only one of the exposures they aimed to assess. However authors do not report results on the other exposures they aimed to assess,  |
| Support for the judgment          | EWF and KF. Similarly, the the indicates breast cancer only, abstract indicates EWF as a primary cause of breast cancer, nowever<br>SID on all cancers for talacom operators is reported for shift work.  |
| Support for the judgment          | I ow risk   |
| Fullallig                         | Low lisk<br>Lighty no funders, Poport asknowledges, Norwagian Talazam and the Cantral Pursey of Statistics for valuable apparation: Oddwar  |
|                                   | Liekty no funders. Report acknowledges Norwegian Telecom and the Central Bureau of Statistics for variable cooperation, Oduvar<br>Sandvin for help with computing and analysis: Dag S. Bakka for help with exposure classification of Norwegian merchant ships: |
|                                   | Dr Richard Stevens for his thoughtful review of the manuscript: and Kirsten Bolstad for details on the work of radio and telegraph  |
| Support for the judgment          | operators at sea.   |
| Conflict of interest              | Unclear risk  |
| Support for the judgment          | Not reported.   |
| Support for the Judgment          |   |

| Study ID                 | Knutsson 2012  |
|--------------------------|--|
| Exposure definition      | High risk  |
| Support for the judgment | Although the WOLF questionnaire is quite detailed the definition of night-shift worker is simply: If the data indicated shift work |
|                          | with night work on $\geq 1$ occasion, and day work or shift work without night for the rest, the participant was regarded as a     |
|                          | worker with night-shift work.  |

| Exposure assessment               | High risk   |
|-----------------------------------|---|
| Support for the judgment          | 'In order to categorize the participants in three groups (ie, day work and shift work with and without night shifts), we used data from baseline, follow-up in 2000–2003 (WOLFF), and follow-up in 2009 (WOLFU). If data indicated day work on all occasions when the subject participated, she was regarded as a day worker. If data indicated shift work without night work on ≥1 occasion, and day work for the rest, the participant was defined as a worker with shift work without night work. If the data indicated shift work with night work on ≥1 occasion, and day work or shift work without night for the rest, the participant was regarded as a worker with shift work without night for the rest, the participant was regarded as a worker with night-shift work." Comment: subjective allocation of exposure based on available data, even though the questionnaire was detailed the components have not been used in assessing exposure levels.   |
| Blinding of assessors             | Unclear risk  |
| Support for the judgment          | Correspondence: "This is a prospective, longitudinal cohort study. It is not a case-control study. Therefore data on exposure were collected before the participants were diagnosed with cancer. Data on all participants, who entered the study at baseline were checked in the cancer registry at follow-up."<br>Comment: statement does not apply to blind assessment. Although data collected prospectively allocation to exposure is retrospective and likely data driven in our opinion."   |
| Reliability of exposure estimates | Unclear risk  |
| Support for the judgment          | Correspondence: We have reported on that (reliability) in the article (mentioned both in methods and the discussion).<br>In report: The agreement between information given at baseline and follow-up, however, was better when considering shift work<br>with night-shifts. Of those who reported no experience of night-shift work at follow-up, only 2% reported night work at baseline. It<br>appears that retrospective information about night-shift experience is more reliable than information about shifts without night<br>work. In 53% of the subjects, we had retrospective information about lifetime exposure to shift work (with and without night<br>work), in 36% we had only baseline information. The baseline question-naire provided information only on current shift<br>work/night work, and it is probable that some subjects, who were classified as day workers based on this information only, were<br>actually former shift workers. However, it is not possible to draw any conclusions about how this misclassification could have<br>biased our results.<br>Comment: subjective assessments not corroborated by data. 36% had only baseline info and only 2% reported night-shift at<br>baseline. Report acknowledges misclassification potential and reliability of estimates remains in question. |
| Confounding                       | Low risk  |
| Support for the judgment          | BMI, Parity, SES, Ethnicity. Correspondence: "The number of subjects, who were born in another country than Sweden, was 424. We considered that number so small (<10%), that we decided not to control for that variable. We have adjusted for age in the cox regression model. This is described in the method section."   |
| Attrition                         | High risk   |
| Support for the judgment          | Correspondence: Breast cancer and death were the only reasons for drop out. The number or drop-outs with respect to cancer is zero. All participants at baseline have been compared with the data in the Swedish Cancer Registry. The number of drop-outs with respect to answering the questionnaire in 2009 is as suggested by you (60%).   |
| Analysis/research specific bias   | High risk   |

| Support for the judgment | No dose response  |
|--------------------------|---|
| Selective reporting      | Low risk  |
| Support for the judgment | Adjusted estimates presented for all hypotheses tested as per aims  |
| Funding                  | Low risk  |
| Support for the judgment | We got a small funding from a local hospital fund for cancer research (4500 dollars).<br>- They did not take part in planning of conducting the study. The just asked for a final report. |
| Conflict of interest     | Low risk  |
| Support for the judgment | No conflict of interests identified   |

| Study ID                          | Li 2011  |
|-----------------------------------|--|
| Exposure definition               | Low risk   |
|                                   | Definition included 2 of the aspects recommended by IARC (start and end time/duration, shift system)                                 |
| Support for the judgment          |  |
| Exposure assessment               | Low risk   |
| Support for the judgment          | Prospectively collected factory data for shift work were used for exposure   |
| Blinding of assessors             | Unclear risk   |
| Support for the judgment          | Not reported   |
| Reliability of exposure estimates | Low risk   |
| Support for the judgment          | Same methods were used for data collection for all participants by trained field workers   |
| Confounding                       | Unclear risk   |
|                                   | Age and parity assessed according to report, ethnicity entirely Chinese, SES may be similar in factory workers. BMI unknown.         |
| Support for the judgment          | Awaiting communication from authors.   |
| Attrition                         | Low risk   |
| Support for the judgment          | For the nested case-control part of the study the loss is less than 1% for cases and controls each                                   |
| Analysis/research specific bias   | Low risk   |
|                                   | Cox proportional hazards modeling, adapted for the stratified case-cohort design to calculate relative risk estimates (hazard ratios |
|                                   | [hrs] and 95% confidence intervals [cis]) for breast cancer associated with various measures of night-shift work. Subgroup and       |
| Support for the judgment          | dose response analyses conducted.  |
| Selective reporting               | Low risk   |
| Support for the judgment          | Thesis available. All aims assessed  |

| Funding                  | Unclear risk  |
|--------------------------|---|
|                          | Part of a grant funded project, we dont have communication from authors to confirm that the funding body has any role. Though   |
| Support for the judgment | unlikely as it is purely academic research (phd thesis)   |
| Conflict of interest     | Unclear   |
|                          | We dont have communication from authors to confirm that the funding body has any role. Though unlikely as it is purely academic |
| Support for the judgment | research (phd thesis)   |

### Unpublished information on included studies

| Study ID             | Authors' input<br>Provided kindly by: Schernhammer E., Rabstein S., Pronk A., Tynes T., Knutsson A., Hansen J., Guenel P, Lie J-A S., Feychting M.  |
|----------------------|---|
| Hansen 2001          | <ul> <li>Sponsor: No not directly, but indirectly since my salary was paid by the Danish Cancer Society.</li> <li>No (assessor aware of case status) – the exposure is based on an independent simple Job Exposure Matrix.</li> <li>All information in the study is taken from available registry data about one year before submission.</li> <li>No. Due to the nature of the study (registry based) such information (number of years and/ or frequency in shift work) was not available.</li> </ul>  |
| Hansen 2011          | <ul> <li>The interviewers were blinded to case-control status. Further, assessing a very objective measure such as shift-work should not be influenced by this. Finally, we didn't directly ask about shift work but rather about normal working time during a 'normal month' in each job.</li> <li>100% caucasian. We have collected information on e.g education. Since we had been able to collect information on these there was no need to create a SES-variable (although we have data for that).</li> <li>We had a response rate of about 90% in both cases and controls</li> </ul>  |
| Hansen 2012          | <ul> <li>Assessments for socioeconomic status: we have collected information on e.g education. But SES in itself is only a crude indicator of potential confounders. Since we had been able to collect information on these there was no need to create a SES-variable (although we have data for that).</li> <li>100% were Caucasians.</li> <li>Reasons for nonresponse: We don't know the answer beyond the normal reasons for this potential problem. We have actually discussed the consequences of differential non-response in the text.</li> </ul>   |
| Menegaux 2011        | <ul> <li>-In our population-based case-control study, the selection of population controls was made carefully in order to avoid selection bias, and to obtain a representative sample of the study base. There were 109 women (4.4%) who had never been employed (36 cases and 73 controls). Study results were unchanged when never working women were excluded from the analyses.</li> <li>The interviewers were aware of the case-control status of the participants. A standardized questionnaire was used and interviewers were told to conduct the interview in the same way in both groups.</li> <li>The sponsors had no role in the conduct of the study, except funding! A final report was provided to them at the end of the contract and validated by a scientific committee.</li> <li>There is no conflict of interest to disclose.</li> <li>Based on data ethnicity was only white</li> </ul> |
| Lie 2006<br>Lie 2011 | -Both the 2006- and the 2011 studies of Norwegian nurses are case-control studies nested within the same cohort of nurses. However, the 2011 study is not an update of the 2006 study.<br>-The 2006-study includes cases diagnosed from 1960 to 1982 (and matched controls). The work history we applied in that study came from two registers:<br>1) the Norwegian Board of Health's registry of all nurses, including work sites (years, site, department), however no information on schedules or night work.<br>2) Information from 3 censuses (work and industry codes), no information on night work<br>As we had no information about work schedules or frequency of night-shifts in that study, we used a crude exposure metric for night work: cumulative number of years worked in<br>hospitals or other 24-hour institutions.  |

|                   | -A main objective of the 2011 study was to obtain data of better quality, concerning work history and night work, but also concerning potential confounders. To obtain this, we conducted telephone interviews, of all cases diagnosed with breast cancer between 1990 and 2007, alive at the time of the interview in 2009, and frequency matched controls. The nurses  |
|-------------------|--|
|                   | were interviewed about each job held as a nurse, whether it included night-shifts, and if yes, the average number of night-shifts per month and the number of consecutive night-shifts.  |
|                   | -In the 2011 study we also included analyses applying the same exposure metric as in the 2006-study (cumulative number of years worked in institutions). In contrast to the elevated risk seen in 2006, no increased risk was found in 2011, when using this metric. A contributing factor for this discrepancy of results, may be that exposure to night work has decreased over the relevant period (2006 study cases were diagnosed 1960-1982, 2011 study-cases were diagnosed 1990-2007).<br>-We did not adjust for socioeconomic status or ethnicity in any of the two studies.   |
|                   | -The cohort is ethnical quite homogeneous, most of them ethnical Norwegians. A very small proportion of nurses came from other countries, mainly from Denmark and Sweden.  |
|                   | <ul> <li>The work history in the 2006-study, which was based on two registers, does not include information on BMI, which was therefore not adjusted for.</li> <li>The work history in the 2011-study is based on a telephone interview, and also includes information about height and weight, at age 18 years and at the time of diagnosis/reference.</li> <li>BMI (at 18 and at time of diagnosis) were not included in the final model, as it did not seem to be a confounder.</li> <li>In our 2011-study, 19.9 years (~ 20 years) was the mean duration of work in schedules including night-shifts in the open category of 12+ years. In our study from 2006 there were only 24 subjects in the 30+ year category, and maximum number of years with night work was 42 0 years. I guess the median was approximately 36 years.</li> </ul>   |
| Schernhammer 2001 | -The NHS cohorts are very uniform with over 95% of all women being white/Caucasian.  |
| Schernhammer 2006 | -As far as SES adjustment is concerned - are you referring to the nurses' or their husbands' educational attainments (the proxy we sometimes use for SES, since we have no other good indicators of SES)? Also, keep in mind that, because they are all nurses, there is relatively little variation in SES in our cohorts.  |
|                   | -We used a full cohort approach, not a case-control study design.<br>Author also provided unpublished frequency distribution data in their sample: 'Firstly, you may find this small pilot study which we conducted in NHS2 a while ago, rather reassuring as far as your estimation for average number of nights/mo is concerned, and perhaps you want to use this pilot data to support your choice: From a small pilot study of approximately 60 women from within the NHS2 cohort (unpublished data), we know that there is a relatively large spread of number of nights worked: among rotating night workers, the average number of nights worked per month was 6.4 (SD, 4.1) with a range from 1 to 21 nights per month, whereas among permanent night workers, the average number of nights worked per month was 6.4 (SD, 4.1) with a range from 1 to 21 nights per month, whereas among permanent night workers, the average number of nights worked per month was 12.3 (SD, 4.8) with a range from 3 to 30 nights per month. Secondly, when looking at the tables and proposed numbers you sent upfront, - I generally agree with your estimates; I would advice, however, to be equally conservative with your estimate for the average duration of shift work in years in the highest groups in both cohorts; for 30+ years of shift work, I would propose to use 30 years, and not 43 years; likewise, in NHS2, I would use 20 years, and not 28 years. This is most consistent with your otherwise always (in my view very wisely chosen) conservative approach and if you pick the average duration as 43 and 28 years in these upper categories as 30 and 20 years, respectively, when we calculated p for trends), so it would also be consistent with us.' |
| Schwartzbaum 2007 | <ul> <li>The study was funded by a Swedish research council that was not involved in the conduct of the study.</li> <li>Reliability estimates for the exposure assessors/assessments</li> <li>We did not use expert assessments to determine exposure (exposure assessors), so kappa estimates are not relevant in the context of the exposure assessment used in our study. The exposure assessment was based on a very large survey (almost 50 000 persons) randomly selected from the Swedish population (with high response rate) that were asked about their working hours and occupational title and industry.</li> <li>The authors have no conflicts of interest.</li> </ul>  |
|                   | - As described in the paper, we have information about the occupation held at the 1960 and 1970 censuses, but we have no information in between the censuses (the 1965 year census did not include occupational information). Therefore we cannot provide duration in 5 year categories. Exposure assessment was made in a similar way as in the first Danish paper about shift work. Exposure was not assessed for each individual person, but for an occupational title. In the paper we write: "Information about work schedules in different occupations within specific industries was obtained from the annual Survey of Living Conditions (ULF) conducted by Statistics Sweden during 1977-1981." These are interview based surveys made with 46 438 participants, who answered questions about their usual occupation and workhours. Our goal was to identify occupations in which a large proportion of workers had workhours that could affect melatonin levels, i.e. Workhours during the night. From the ULF survey we   |

|            | <ul> <li>identified combinations of occupation and industry where a large proportion of the workers had workhours including night work. We analyzed cancer risk in occupation-industry combinations where at least 40% were shift workers according to our definition (i.e. Included night work), and also combinations where at least 70% were shift workers. Duration of exposure to shift work was taken into consideration by analyzing cancer risk in persons who had an occupation-industry combination defined as shift work in both the 1960 and the 1970 censuses.</li> <li>Blind to the case status</li> <li>Exposure data was collected completely independent from case status of the participants.</li> <li>Confounders</li> <li>We did not have information about BMI or parity. But I believe that adjusted and unadjusted risk estimates in studies that did have information about e.g. Parity did not differ from each other, so these confounders did not seem to have an effect on risk estimates.</li> </ul> |
|------------|---|
| T 100/     |   |
| Tynes 1996 | Explained in correspondence that they didn't have access to the data any more so were unable to help.   |
| Knutsson   | - We got a small funding from a local hospital fund for cancer research (4500 dollars).   |
|            | - They did not take part in planning or conducting the study. The just asked for a final report.  |
|            | - No connect of interests identified, expert study, it is not a see control study. Therefore data on experimental subort depends the participants were discreted with support. Data on all  |
|            | - This is a prosective, longitudinar conor study, it is not a case-control study. In therefore data on exposite were conected before the participants were diagnosed with cancer. Data on an  |
|            | - We have reported on that (reliability of exposure estimates) in the article (mantional both in methods and the discussion)  |
|            | - Breast capter and death were the only reasons for dron out. The number or dron-outs with respect to cancer is zero. All participants at baseline have been compared with the data in the  |
|            | Swedish Cancer Registry. The number of drop-outs with respect to answering the questionnaire in 2009 is as suggested by you (60%).  |
| Pesch 2010 | -Due to the study design it is not possible for interviewers not to realize case-control status (interviews were performed with incident breast cancer patients).   |
|            | -No, the sponsors of the study did not have any role in the conduct of the study.   |
|            | -There is no conflict of interests.   |
|            | statistics for the highest night exposure groups of our GENICA shift work population:   |
|            | Cumulative lifetime night-shift exposure (highest exposure group), cases:   |
|            | Max= 6695, mean = 2118, median = 1607   |
|            | Cumulative lifetime night-shift exposure (highest exposure group), controls:  |
|            | Max = 5915, mean= 2094, median =1655  |
|            | Number of Years with night-shift above 20 years, cases:   |
|            | Max = 35 years, mean = 27.3, median = 27.8  |
|            | Years of night-shift above 20 years, cases:   |
|            | Max = 29 years, mean 25.5, median = 26.5  |
| Pronk 2010 | -Assignments of exposure status carried out in the same way for cases and controls? Yes they were   |
|            | -Assessment of socioeconomic status: We have used education level to adjust for socioeconomic status. There may have been other potential proxies as well, but -I don't remember  |
|            | exactly all the variables.  |
|            | -Role of sponsors in the conduct of the study? I am not sure about this. You could contact my former colleagues in the cc if you want to find out. (no response yet)  |
|            | -There were no conflicts of interest.   |
|            | -Open ended Exposure category: 1 assigned median values for each category for the trend analyses, I think very similar to what you intend to do. For duration I used 25 as the median for the highest category (3 and 10 years for the other cats). For cumulative I used 2496 as the median for the highest category (3 and 960 for the other cats).   |