Occupational Cancer Research Centre

Seeing the Light: How to Minimize the Health Impacts of Shiftwork

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Conference Board of Canada Webinar

September 15, 2015

Towards a cancer-free workplace

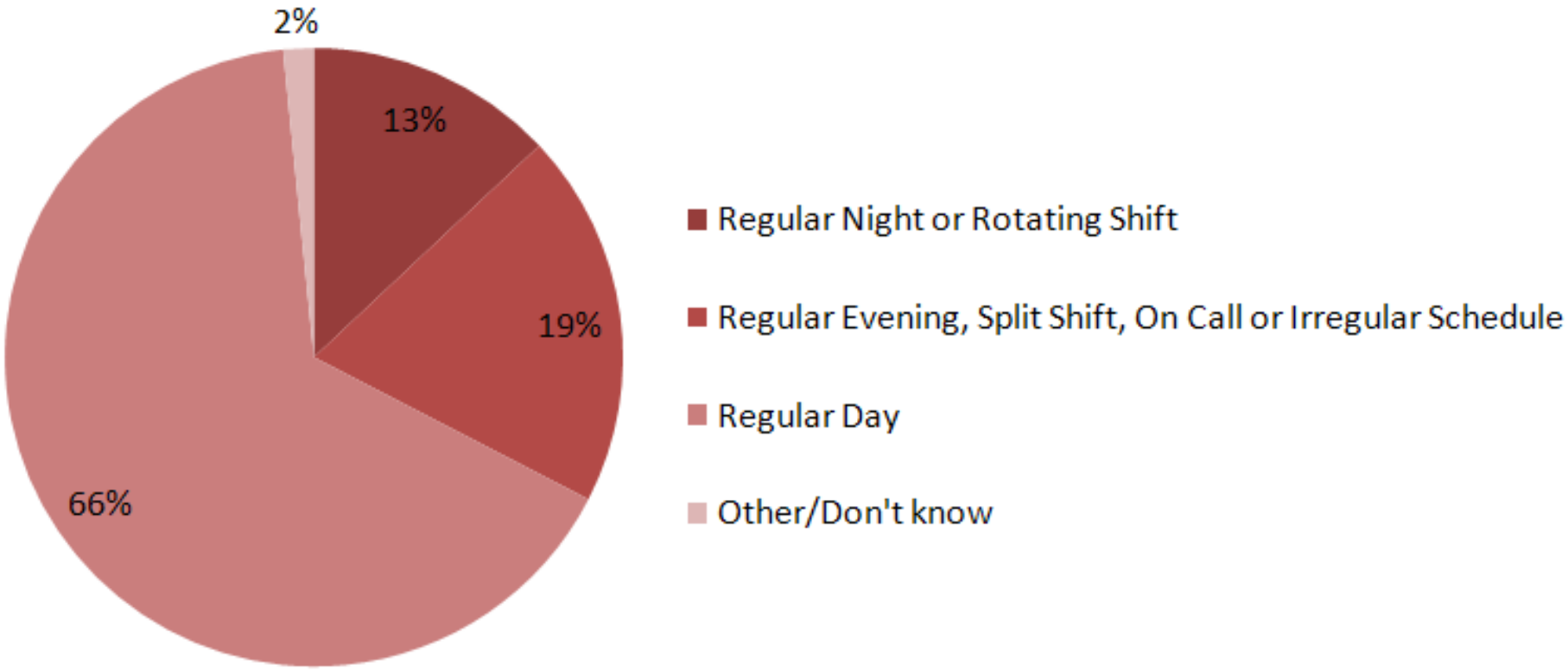
The OCRC & Conflicts of Interest

- Created in 2009 through partnership between:

Canadian Cancer Society
Société canadienne du cancer

- Research program focused on
  - Studies of the causes of workplace cancer
  - Surveillance of cancer and carcinogens
  - Prevention research

Shiftwork in Canada



CAREX Canada 2012. http://www.carexcanada.ca/en/shiftwork/occupational_estimate/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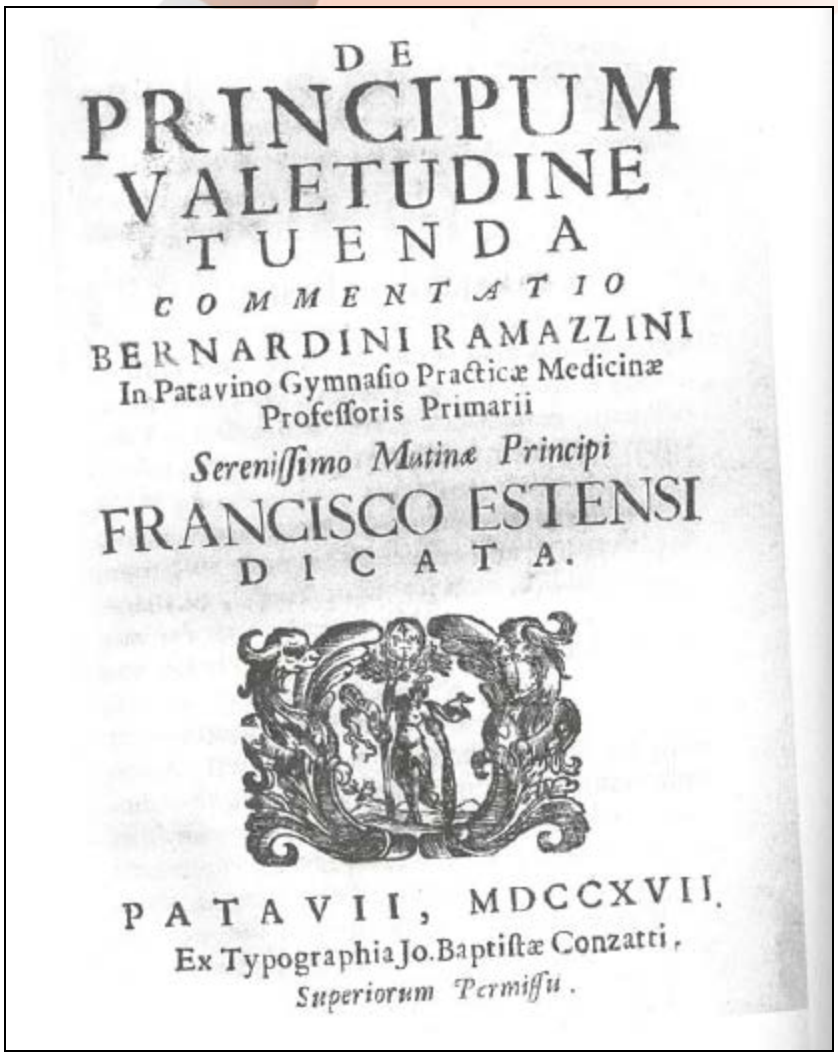
GETTY IMAGES

Bernardino Ramazzini (1633-1714)


DE
PRINCIPUM
VALETUDINE
TUENDA
COMMENTATIO
BERNARDINI RAMAZZINI
In Patavino Gymnasio Practicæ Medicinæ
Professoris Primarii
Serenissimo Mutinæ Principi
FRANCISCO ESTENSI
DICATA.

PATAVII, MDCCXVII.
Ex Typographia Jo. Baptistæ Conzatti,
Superiorum Permissu.

Author of the first comprehensive occupational medicine text in 1700.

In 1717 published *The Health of Princes*

> "The inversion of sleep with wakefullness, much in vogue in the courts of princes, is little conducive to maintaining health"

The Melatonin Hypothesis (1987)

"Breast cancer is a disease of modern life. As societies industrialize, risk increases, yet it is unclear which of the myriad changes coming with industrialization drives this increase. One important hallmark of modern life is the pervasive use of electric power. Electric power produces light at night (LAN) and electric and magnetic fields (EMF), either or both of which may alter pineal function and its primary hormone melatonin, thereby, perhaps increasing the risk of breast cancer."

Richard Stephens & Scott Davis, Environmental Health Perspectives 1996;104(suppl 1):125-140.

Shiftwork and Cancer (from Lancet Oncology, 2007)

Policy Watch

Carcinogenicity of shift-work, painting, and fire-fighting

Kurt Straif, Robert Baan, Yann Grosse, Béatrice Secretan, Fatiha El Ghissassi, Véronique Bouvard, Andrea Altieri, Lamia Benbrahim-Tallaa, Vincent Cogliano, on behalf of the WHO International Agency for Research on Cancer Monograph Working Group

In October, 2007, 24 scientists from ten countries met at the International Agency for Research on Cancer (IARC), Lyon, France, to assess the carcinogenicity of shift-work, painting, and fire-fighting. These assessments will be published as volume 98 of the IARC Monographs.[1]

About 15–20% of the working population in Europe and the USA is engaged in shift-work that involves nightwork, which is most prevalent (above 30%) in the health-care, industrial manufacturing, mining, transport, communication, leisure,

on tumour development. More than 20 studies investigated the effect of constant light, dim light at night, simulated chronic jet lag, or circadian timing of carcinogens, and most showed a major increase in tumour incidence. No clear effect was seen for light pulses at night or constant darkness. A similar number of studies investigated the effect of reduced nocturnal melatonin concentrations or removal of the pineal gland (where melatonin is produced) in tumour development and most showed increases in the incidence or growth of

disruption is probably carcinogenic to humans" (Group 2A).[15]

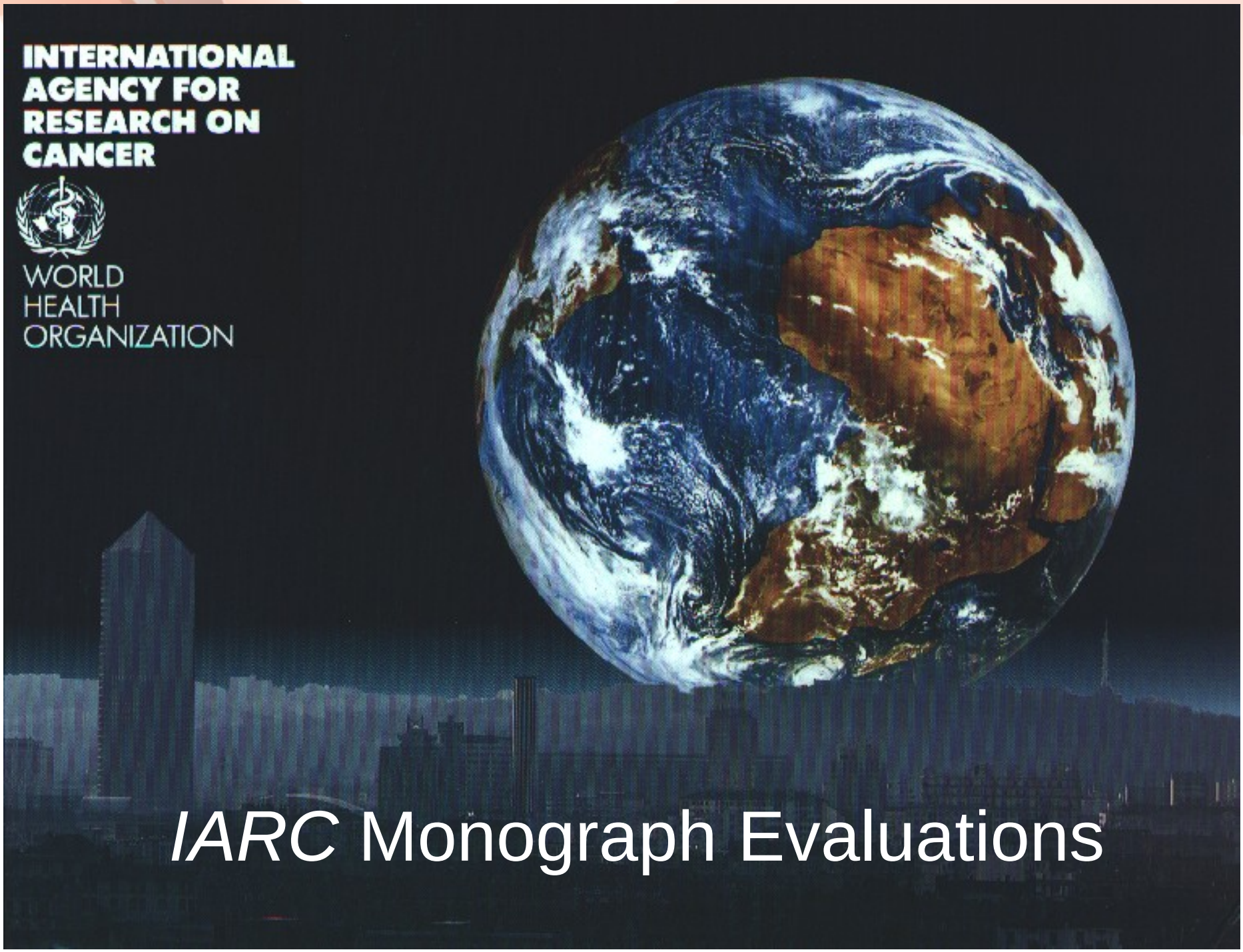
Painters are potentially exposed to many chemicals used as pigments, extenders, binders, solvents, and additives. Painters can also be exposed to other workplace hazards, such as asbestos or crystalline silica.

Cohort and linkage studies of painters have shown consistent and significant increases in lung cancer compared with the general population. No information on tobacco smoking was available in the cohort studies; however, the increases

Upcoming meetings
February 5–12, 2008
Industrial and cosmetic dyes and related exposures
http://monographs.iarc.fr/

Who Decides what Causes Cancer?

- Public opinion?
  - driven by the media, which is often based on the results of a single study…
- Advocacy groups?
  - Often well-intentioned, but highly variable and sometime filtering out conflicting evidence
- Canadian or other regulatory agencies?
  - Generally follow international organizations



IARC Monograph Evaluations

IARC Evaluation of Carcinogens

- Group 1: Carcinogenic in humans (117)
- Group 2A: Probably carcinogenic in humans (74)
- Group 2B: Possibly carcinogenic in humans (287)
- Group 3: Not classifiable, generally inadequate evidence in humans and limited or inadequate in animals (503)
- Group 4: Evidence of a lack of carcinogenicity in both humans & animals (1, caprolactam in 1999)

Disruption of circadian rhythms and melatonin*

- Light at night disrupts circadian rhythms and decreases the production of melatonin, which impacts other hormones
- Melatonin has direct “oncostatic” effects
- 2-10% of genes in mammals are clock controlled
  - Many processes in the body may be disrupted

* IARC Monographs Volume 98, published in 2010 and available on their website

Oncostatic effects of Melatonin

Free radical scavenging and anti-oxidation

- up-regulates anti-oxidant enzymes: glutathione peroxidase, superoxide dismutase…

Anti-proliferative effects

- inhibits the mitotic action of hormones and growth factors: estradiol, EGF, prolactin…
- induces the up-regulation of cell-surface proteins E-Cadherin and b-integrin
- slows down the cell-cycle at G0- S phase transition

Activation of the immune defence

- enhances INFg and IL-1 production

Animal studies of cancer considered by IARC in 2007

	No other exposure	Chemical Initiation / promotion	Tumour cell transplantation	**Total**
Alterations in light exposures*	2 / 3	5 / 6	10 / 10	17 / 19
Experimental jet-lag (chronic)	-	-	2 / 2	2 / 2
SCN lesions	-	-	1 / 1	1 / 1
Pinealectomy	-	2 / 8	11 / 13	13 / 21
Physiological concentrations of melatonin	-	-	5 / 5	5 / 5
Clock gene mutations	1 / 1	1 / 2	-	2 / 3
Total	3 / 4	8 / 16	29 / 31	40 / 51

* Continuous bright light at night, dim light at night, intermittent or pulsed light at night

Animal Studies Considered by IARC

- 51 High Quality Studies of Breast Cancer in Rodents
  - Used a variety of protocols
  - Used altered light patterns or direct disruption of circadian rhythms or melatonin
- 40 Studies were positive (showed increased risk of breast cancer)
  - 19/21 that used altered light patterns

Human studies of cancer considered by IARC in 2007

- Focused almost only on breast cancer
  - 8 studies of breast cancer
  - A very limited number of studies for cancers at other sites
- 9 cohort studies of flight crew initiated because of concern over cosmic radiation

Shiftwork and Breast Cancer

Study	Design/population	Shiftwork	Results
Schernhammer et al, 2001 (USA)	Prospective nurses cohort	Rotating, evening or night shift	RR=1.4 for 30+ yrs
Schernhammer et al, 2006 (USA)	Prospective nurses cohort	Rotating, evening or night shift	RR=1.8 for 20+ yrs
Lei et al, 2005 (Norway)	Registry-based study	Hospital nurses	OR=2.2 for 30+ yrs
Tynes et al, 1996 (Norway)	Radio & telegraph operators	Night shift work on ships	OR=5.9 for 3.2+ yrs night shift, 50+ age
Hansen, 2001 (Denmark)	Registry-based study	4 industries w/ 60+% night shift	OR=1.7 for 6+ yrs
Schwartzbaum et al, 2007 (Sweden)	Registry-based study	Industries w/ 40+% night shift	SMR=1.0 for 10+ yrs
Davis et al, 2001 (USA)	Population-based case-control	Begin after 19:00 & end before 09:00	OR=1.6 for ever
O'Leary et al, 2006 (USA)	Population-based case-control	Begin after 19:00	OR=0.6 for ever

Breast Cancer among Flight Attendants

Study	Design/Population	Results
Pukkala et al, 1995 (Finland)	Finnair flight crew cohort	SIR=1.9, 95% CI=1.2-2.2
Lynge, 1996 (Denmark)	Danish Census follow-up	SIR=1.6, 95% CI=0.9-2.7
Wartenberg et al, 1998 (USA)	Retired flight attendants cohort	SIR=2.0, 95% CI=1.0-4.3
Haldorson et al, 2001 (USA)	Norwegian cabin crew cohort	SIR=1.1, 95% CI=0.8-1.5
Rafnsson et al, 2001 (Iceland)	Icelandic Cabin Crew cohort	SIR=1.5, 95% CI=1.0-2.1
Reynolds et al, 2002 (USA)	California flight attendants cohort	SIR=1.4, 95% CI=1.1-1.8
Linnersjo, 2003 (Sweden)	Swedish SAS cohort	SIR=1.3, 95% CI=0.9-1.7

Evaluating Human Data

Sufficient Evidence	Causal relationship established: chance, bias, & confounding ruled out with reasonable confidence
Limited Evidence	Causal interpretation credible, but chance, bias, or confounding not ruled out
Inadequate Evidence	Studies permit no conclusion about causal association
Evidence suggesting lack of carcinogencity	

Preliminary Default Evaluation

Cancer in Humans	Cancer in Experimental Animals: *Sufficient*	*Limited*	*Inadequate*
Sufficient	*Group* **1**	*Group* **1**	*Group* **1**
Limited	*Group* **2A**	*Group* **2B** **Exceptionally: Group 2A**	*Group* **2B** **Exceptionally: Group 2A**
Inadequate	*Group* **2B**	*Group* **3**	*Group* **3**

Strong mechanistic evidence can move an evaluation up or down a category

Group 1 *Carcinogenic to Humans*
Group 2A *Probably Carcinogenic to Humans*
Group 2B *Possibly Carcinogenic to Humans*
Group 3 *Not classifiable as to its Carcinogenicity to Humans*
Group 4 *Probably Not Carcinogenic to Humans*

IARC Working Group Conclusions

Cancer in humans

- There is *limited evidence* in humans for the carcinogenicity of shiftwork that involves night work.

Cancer in experimental animals

- There is *sufficient evidence* in experimental animals for the carcinogenicity of light during the daily dark period (biological night).

Overall evaluation

- Shiftwork that involves circadian disruption is *probably carcinogenic to humans (Group 2A)*.

IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. *Volume 98: Painting, Firefighting, and Shiftwork*. Lyon: IARC Press, 2010.

Shiftwork and breast cancer case-control studies published since the IARC evaluation

- 4 case-control studies
  - Increased risks associated with long-term (20-30+ years) shiftwork (Grundy et al. 2013, Rabstein et al. 2013, Menegaux et al. 2013, Papantoniou et al. 2015)
- 3 nested case-control studies
  - Elevated risks for long-term day-night rotating shifts, number of years of night shiftwork, and number of lifetime night shifts (Hansen & Lassen 2012; Hansen & Stevens 2011; Lie et al. 2011)

Meta-analyses of studies of shiftwork and breast cancer

- Assessed potential dose-response and evaluated quality of selected studies published to date (Ijaz et al. 2013, Kamdar et al. 2013, Jia et al. 2013, He et al. 2015)
- Modest, non-statistically significant increases in risk for long-term and ever night shiftwork
  - For example He et al, 2015: mRR=1.19 (95% CI=1.08-1.32) for ever shiftwork, 16% (95% CI=1.06-1.27) increase per 10 years
- Heterogeneity observed between studies

Shiftwork and prostate cancer

- 4 positive, 1 negative (Schwartzbaum et al. 2007)
- Modest evidence from two Canadian case-control studies (Parent et al. 2012, Conlon et al. 2007), one Spanish case-control study (Papantoniou et al. 2015), and one Japanese cohort study (Kubo et al. 2006) that ever night shiftwork and rotating shiftwork may be associated with increased risk
- Positive link between shiftwork and PSA levels in a cross-sectional study of US men needs to be further assessed (Flynn-Evans et al. 2013)

Some Other Known or Potential Health Effects of Shiftwork

Acute	Chronic	Psycho-social
• Injury • Sleepiness and sleep disorders • Absence due to sickness	• Diabetes & metabolic syndrome? • Gastro-intestinal disorders? • Cardiovascular disease • Reproductive problems?	• Disrupted work-life balance • Depression • Psychological stress • Negative well-being

Shiftwork and Cancer: Some theories (Fritchi, 2011)

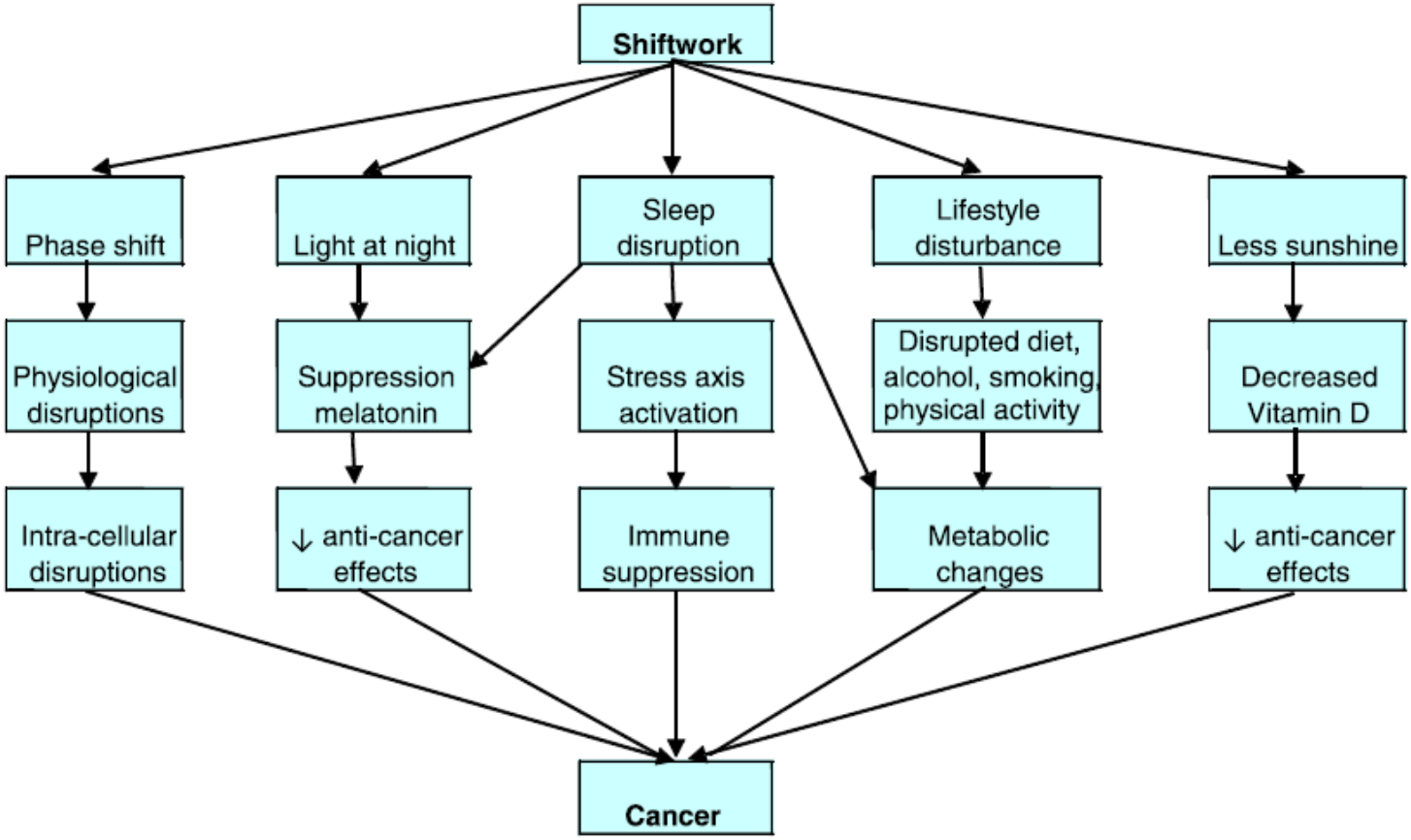
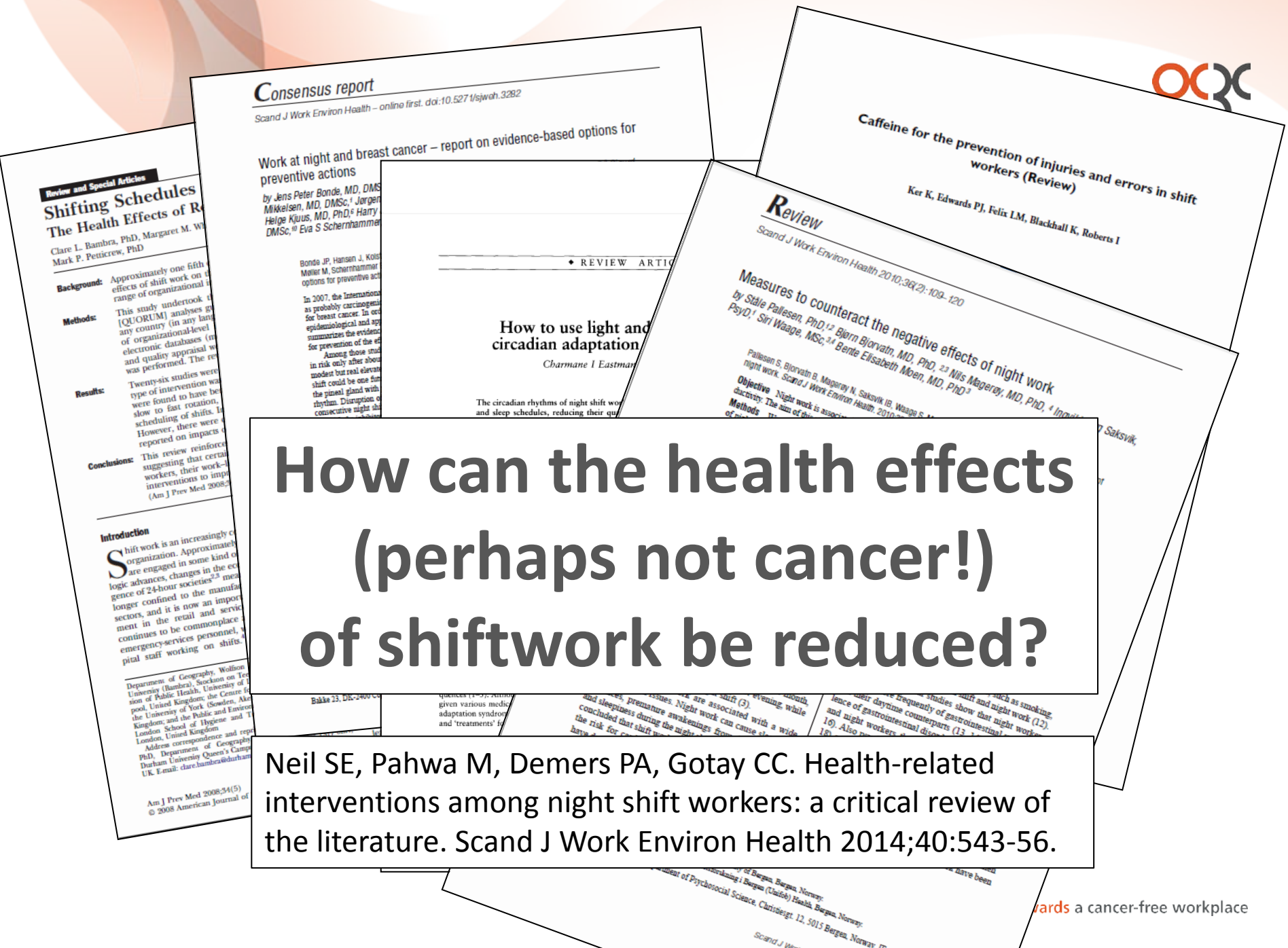


Fig. 1. Theoretical framework of possible mechanisms by which shiftwork might cause breast cancer.

Fritschi et al. Medical Hypotheses 2011;77(3):430-436.


Review and Special Articles
Shifting Schedules
The Health Effects of R
Clare L. Bambra, PhD, Margaret M. Wh
Mark P. Petticrew, PhD
Background:
Methods:
Results:
Conclusions:
Introduction
Am J Prev Med 2008;34(5)
© 2008 American Journal of
Consensus report
Scand J Work Environ Health – online first. doi:10.5271/sjweh.3282
Work at night and breast cancer – report on evidence-based options for preventive actions
by Jens Peter Bonde, MD, DMS
Mikkelsen, MD, DMSc,[1] Jørgen
Helge Kjuus, MD, PhD,[6] Harry
DMSc,[10] Eva S Schernhammer
Bonde JP, Hansen J, Kols
Møller M, Schernhammer
options for preventive act
In 2007, the Internationa
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REVIEW ARTI
How to use light and
circadian adaptation
Charmane I Eastman
The circadian rhythms of night shift wo
and sleep schedules, reducing their qu
Caffeine for the prevention of injuries and errors in shift workers (Review)
Ker K, Edwards PJ, Felix LM, Blackhall K, Roberts I
Review
Scand J Work Environ Health 2010;36(2):109–120
Measures to counteract the negative effects of night work
by Ståle Pallesen, PhD,[1,2] Bjørn Bjorvatn, MD, PhD,[2,3] Nils Magerøy, MD, PhD,[4] Ingu
PsyD,[1] Siri Waage, MSc,[3,4] Bente Elisabeth Moen, MD, PhD[3]
Pallesen S, Bjorvatn B, Magerøy N, Saksvik IB, Waage S,
night work. Scand J Work Environ Health. 2010;
Objective
Methods
Saksvik,
How can the health effects (perhaps not cancer!) of shiftwork be reduced?
Neil SE, Pahwa M, Demers PA, Gotay CC. Health-related interventions among night shift workers: a critical review of the literature. Scand J Work Environ Health 2014;40:543-56.
ards a cancer-free workplace

Schedule Changes

- Backward (counter-clockwise) → forward (clockwise) and changing the speed of rotation
  - ↑ sleep length and sleep quality
  - ↑ triglycerides, glucose, blood pressure
- 8 hours → 12 hours
  - ↑ sleep length and sleep quality
  - ↑ physical fitness
- Work schedule flexibility
  - ↑ health, work-life balance, performance, motivation
  - ↓ stress, absenteeism, turnover

Controlled Exposure to Light/Dark

- Timed bright light
  - Positive effects on body temperature, cortisol, melatonin
  - Various effects on sleep
- Glasses or goggles that block or filter light
  - Little effects on health

- Timed bright light AND glasses or goggles
  - Evidence of circadian adaptation
  - More effective than bright light or glasses/goggles alone

Behavioural Changes

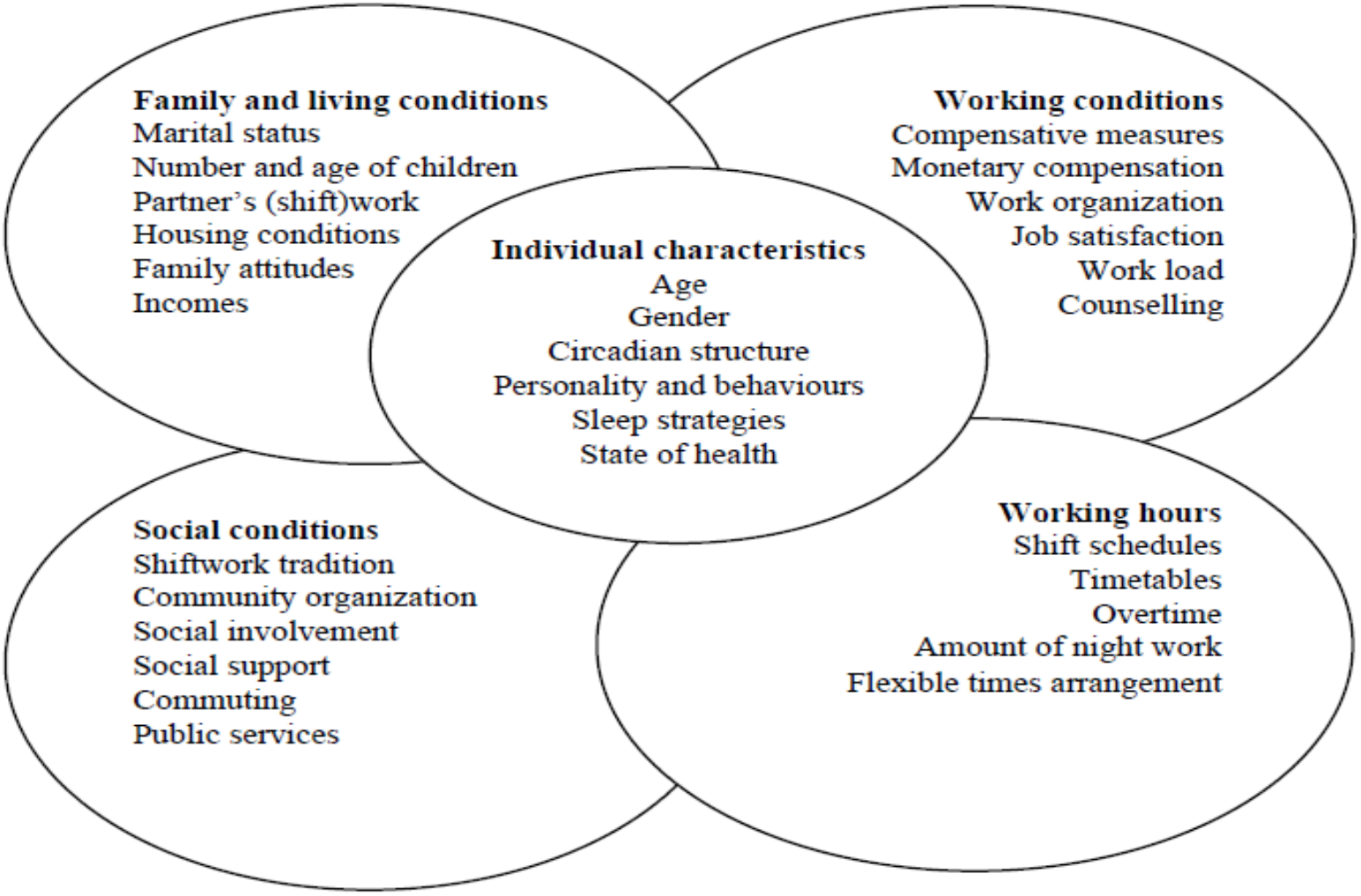
- Physical training and lifestyle changes
  - ↑ strength, lung capacity, sleep length, weight/BMI, blood pressure
- Scheduled rest period
  - ↑ quality of life
  - Adopting strategies in the workplace is important

Harma MI et al. Ergonomics 1988a;31:39-50; Harma MI et al. Ergonomics 1988b;31:51-63; Morgan PJ et al. Prev Med 2011;52:317-325; Bonnefond A et al. Ergonomics 2001;44:937-945; Smith-Coggins R et al. Acad Emerg Med 1997;4:951-961.

Pharmaceuticals

- Pharmaceutical melatonin
  - Improved sleep length in some studies
  - May facilitate adaptation to long-term night work
- Stimulants (e.g. caffeine, amphetamines) and hypnotics (e.g. zopiclone, nitrazepam) likely pose health risks to workers and public safety

Factors that can Affect Tolerance to Shiftwork



Costa G. Factors influencing health and tolerance to shift work. *Theor Issues Ergon Sci* 2003;4:263-288.

Conclusions

- Evidence for shiftwork & cancer slowly growing
- Many other potential health effects of concern
- Some interventions show promise
  - Direction and speed of rotation, flexible scheduling, possible others
- Much more research needed on interventions
- New research focusing on combinations (e.g. melatonin + bright light + scheduling)

Folkard S et al. Chronobiol Int 1993;10:315-320; Cavallo A et al. Ambul Pediatr 2005;5:172-177; Burgess et al. Sleep Medicine Reviews 2002;6:407-420; Pallesen S et al. Scand J Work Environ Health 2010;36:109-120.

Some Resources

IARC Monograph on Shiftwork

From the Occupational Cancer Research Centre:
http://www.occupationalcancer.ca/2012/shiftwork-interventions-symposium/
From the Occupational Health Clinics for Ontario Workers:
Shiftwork: Health effects & solutions:
http://nupge.ca/sites/nupge.ca/files/Shiftwork.pdf
From the Canadian Centre for Occupational Health and Safety:
Shiftwork – OHS Answers:
http://www.ccohs.ca/topics/hazards/ergonomic/shiftwork/#ctgt_wb-auto-3

Some References: Recent Meta-analyses of Shiftwork and Breast Cancer

He C, Anand ST, Ebell MH, Vena JE, Robb SW. Circadian disrupting exposures and breast cancer risk: a meta-analysis. International Archives of Occupational and Environmental Health 2015;88:533-547.

Ijaz SI, Verbeek J, Seidler A, Lindbohm ML, Ojajärvi A, Orsini N, Costa G, Neuvonen K. Night-shift work and breast cancer - a systematic review and meta-analysis. Scand J Work Environ Health. 2013 39(5):431–447.

Kamdar BB, Tergas AI, Mateen FJ, Bhayani NH, Oh J. Night-shift work and risk of breast cancer: a systematic review and meta-analysis. Epidemiology 2013;138:291-301.

Wang F, Yeung KL, Chan WC, Kwok CCH, Leung SL, Wu C, Chan EYY, Yu ITS, Yang XR, Tse LA. A meta-analysis on dose-response relationship between night shift work and the risk of breast cancer. Annals of Oncology 2013;24:2724-2732.

Jia Y, Lu Y, Wu K, Lin Q, Shen W, Zhu M, Huang S, Chen J. Does night work increase the risk of breast cancer? A systematic review and meta-analysis of epidemiological studies. Cancer Epidemiology 2013;37:197-206.

Some References: Selected intervention studies

Neil SE, Pahwa M, Demers PA, Gotay CC. Health-related interventions among night shift workers: a critical review of the literature. Scand J Work Environ Health 2014;40:543-56.

Controlled light exposure:

Tanaka K, Takahashi M, Tanaka M, Takanoa T, Nishinoue N, Kaku A, et al. Brief morning exposure to bright light improves subjective symptoms and performance in nurses with rapidly rotating shifts. J Occup Health. 2011;53(4):258-66.

Boivin DB, Boudreau P, James FO, Kin NM. Photic resetting in night-shift work: impact on nurses' sleep. Chronobiol Int. 2012;29(5):619-28.

Boivin DB, Boudreau P, Tremblay GM. Phototherapy and orange-tinted goggles for night-shift adaptation of police officers on patrol. Chronobiol Int. 2012;29(5):629-40.

Changes in shift scheduling:

Viitasalo K, Kuosma E, Laitinen J, Härmä M. Effects of shift rotation and the flexibility of a shift system on daytime alertness and cardiovascular risk factors. Scand J Work Environ Health. 2008;34(3):198-205.

Hakola T, Paukkonen M, Pohjonen T. Less quick returns- -greater well-being. Ind Health. 2010;48(4):390-4.

Some References: Selected intervention studies

Behavioural:
Morgan PJ, Collins CE, Plotnikoff RC, Cook AT, Berthon B, Mitchell S, et al. Efficacy of a workplace-based weight loss program for overweight male shift workers: the Workplace POWER (Preventing Obesity Without Eating like a Rabbit) randomized controlled trial. Prev Med. 2011;52(5):317-25.

Morgan PJ, Collins CE, Plotnikoff RC, Cook AT, Berthon B, Mitchell S, et al. The impact of a workplace-based weight loss program on work-related outcomes in overweight male shift workers. J Occup Environ Med. 2012;54(2):122-7.

Pharmacological: Czeisler CA, Walsh JK, Roth T, Hughes RJ, Wright KP, Kingsbury L, et al. Modafinil for excessive sleepiness associated with shift-work sleep disorder. N Engl J Med. 2005;353(5):476-86.

Multiple types of interventions: . Bjorvatn B, Stangenes K, Øyane N, Forberg K, Lowden A, Holsten F, et al. Randomized placebo-controlled field study of the effects of bright light and melatonin in adaptation to night work. Scand J Work Environ Health. 2007;33(3):204-14.

Towards a cancer free workplace

http://occupationalcancer.ca

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Action Cancer Ontario

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Ministère du Travail