





Plant Growth Change



-5

0

5

10

Percent per decade









RESEARCH

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# Breast cancer risk in relation to occupations with exposure to carcinogens and endocrine disruptors: a Canadian case-control study

James T Brophy<sup>1,2\*</sup>, Margaret M Keith<sup>1,2</sup>, Andrew Watterson<sup>1</sup>, Robert Park<sup>3</sup>, Michael Gilbertson<sup>1</sup>, Eleanor Maticka-Tyndale<sup>2</sup>, Matthias Beck<sup>4</sup>, Hakam Abu-Zahra<sup>5</sup>, Kenneth Schneider<sup>5</sup>, Abraham Reinhartz<sup>6</sup>, Robert DeMatteo<sup>6</sup> and Isaac Luginaah<sup>7</sup>

## Abstract

**Background:** Endocrine disrupting chemicals and carcinogens, some of which may not yet have been classified as such, are present in many occupational environments and could increase breast cancer risk. Prior research has identified associations with breast cancer and work in agricultural and industrial settings. The purpose of this study was to further characterize possible links between breast cancer risk and occupation, particularly in farming and manufacturing, as well as to examine the impacts of early agricultural exposures, and exposure effects that are specific to the endocrine receptor status of tumours.

**Methods:** 1005 breast cancer cases referred by a regional cancer center and 1146 randomly-selected community controls provided detailed data including occupational and reproductive histories. All reported jobs were industry- and occupation-coded for the construction of cumulative exposure metrics representing likely exposure to carcinogens and endocrine disruptors. In a frequency-matched case-control design, exposure effects were estimated using conditional logistic regression.

**Results:** Across all sectors, women in jobs with potentially high exposures to carcinogens and endocrine disruptors had elevated breast cancer risk (OR = 1.42; 95% CI, 1.18-1.73, for 10 years exposure duration). Specific sectors with elevated risk included manufacturing (OR = 1.26, 95% CI 1.01-1.58) and agriculture (OR = 2.00, 95% CI 1.01-5.52).



## STATE OF THE EVIDENCE:

THE CONNECTION BETWEEN BREAST CANCER AND THE ENVIRONMENT

by Janet Gray, Ph.D.



AMERICAN CANCER SOCIETY

Sixth Edition 2010

## FROM SCIENCE TO ACTION

by Janet Nudelman, M.A., and Connie Engel, Ph.D.



# 216 mammary carcinogens



1,2-Dibromoethane  
1,2-Propylene oxide  
1,3-Butadiene  
1,4-Dioxane  
2,2-Bis(bromomethyl)-1,3-propanediol  
2,3-Dibromo-1-Propanol  
2,4-Diaminotoluene  
2,4-Dinitrotoluene  
2-Chloroacetophenone  
2-Methylaziridine  
4,4-Methylene-bis(2-chloroaniline)  
5-Nitroacenaphthene  
Acrylamide  
Acrylonitrile  
AF-2 (2-(2-furyl)-3-(5-nitro-2-furyl) acrylamide)  
Benzene  
Chloroprene  
Ethylene oxide  
Glycidol  
Hydrazine  
Hydrazobenzene  
Indium phosphide  
Nitrobenzene  
Nitromethane  
N-Nitroso-di-n-butylamine  
O-N-Nitrotoluene

O-A-Aminoazotoluene  
O-T-Toluidine  
Perfluorooctanoic acid  
Propane sultone  
Styrene  
Toluene diisocyanate mixtures  
Urethane  
Vinyl chloride  
Vinyl fluoride  
Vinylidene chloride  
**Chlorinated solvents (n = 6)**  
1,1-Dichloroethane  
1,2-Dichloroethane  
1,2,3-Trichloropropane  
1,2-Dichloropropane  
Carbon tetrachloride  
Methylene chloride  
**Products of combustion (n = 18)**  
1,3-Dinitropyrene  
1,8-Dinitropyrene  
1-Nitropyrene  
2-Aminoanthracene  
2-Nitrofluorene  
3-Amino-1-methyl-5h-pyrido[4,3-b] indole  
3-Methylcholanthrene  
4-Nitropyrene

6-Nitrochrysene  
7,12-Dimethylbenz[a]anthracene  
Benzo[a]pyrene  
Dibenz[a,h]anthracene  
Dibenzo[def,p]chrysene  
IQ  
Isoprene  
MeIQ  
PhIP  
Trp-P-2 acetate  
**Pesticides (n = 10)**  
1,2-Dibromo-3-chloropropane  
Atrazine  
Captafol  
Chlordane  
Clonitralid  
Dichlorvos  
Fenvalerate  
Nifurthiazole  
Simazine  
Sulfallate  
**Dyes (n = 18)**  
2,4-Diaminoanisole sulfate  
3,3-Dichlorobenzidine  
3,3-Dimethoxybenzidine  
3,3-Dimethylbenzidine  
4,4-Methylene-bis(2-methylaniline)

4-Aminobiphenyl  
5-Nitro-*o*-anisidine  
Amsonic acid  
Benzidine  
C.I. Acid Red 114  
C.I. Basic Red 9 monohydrochloride  
C.I. Direct Black 38  
FD&C Violet No. 1  
Guinea green B  
HC Yellow no. 3  
Leucomalachite green  
Malachite green  
N,N-Diacetylbenzidine  
**Radiation and drinking water disinfection (n = 5)**  
Magnetic fields  
MX (3-Chloro-4-(dichloromethyl)-5- hydroxy-2(5h)-furanone)  
Neutrons  
Radionuclide hydrogen-3  
X-rays, gamma rays (ionizing radiation)  
**Pharmaceuticals (n = 47)**  
1-(2-Hydroxyethyl)-3-[(5-nitrofurfurylidene)amino]-2-imidazolidinone  
1,2-Dimethyl-5-nitroimidazole





...cont.

1-[(5-Nitrofurfurylidene)amino]-2-imidazolidinone  
 2-Amino-5-(5-nitro-2-furyl)-1,3,4-oxadiazole  
 2-Amino-5-(5-nitro-2-furyl)-1,3,4-thiadiazole  
 2-Amino-5-nitrothiazole  
 4,4-Sulfonylbisacetanilide  
 4-Methyl-1-[(5-nitrofurfurylidene) amino]-2-imidazolidinone  
 5-(Morpholinomethyl)-3- [(5-nitrofurfurylidene)-amino]-2-oxazolidinone-I form  
 5-Azacytidine  
 Acronycine  
 Doxorubicin (Adriamycin)  
 Amsacrine  
 Anti-(+/-)-trans-7,8,9,10-tetrahydrobenzo[a]pyrene-7,8-Diol-9,10-epoxide  
 Bemitradine  
 Chloroambucil  
 Cyclophosphamide  
 Cytembena  
 Dacarbazine  
 Daunomycin  
 Dibromomannitol

Furosemide  
 Griseofulvin  
 Hexamethylmelamine  
 Indomethacin  
 Isoniazid  
 Isonicotinic acid  
 vanillylidenehydrazide  
 Isophosphamide  
 L-5-Morpholinomethyl-3-[(5-nitrofurfurylidene)amino]-2-oxazolidinone HCl  
 Merphalan  
 Metronidazole  
 Mitomycin-C  
 Nithiazide  
 N,N-Dimethylnitrosourea  
 N-[4-(5-nitro-2-furyl)-2-thiazolyl]acetamide  
 Niridazole  
 Nitrofurantoin  
 Nitrofurazone  
 Norlestrin  
 Phenacetin  
 Phenesterin  
 Procarbazine hydrochloride  
 Reserpine  
 SQ 18506  
 Thiotepe

trans-2-[(Dimethylamino)methylimino]-5-[2-(5-nitro-2-furyl)vinyl]-1,3,4-oxadiazole  
 Uracil mustard

#### **Hormones (n = 17)**

17-Hydroxyprogesterone caproate  
 Chlormadinone acetate  
 Conjugated estrogens  
 Diethylstilbestrol  
 Estradiol-17 Estriol  
 Estrone  
 Ethinylestradiol  
 Ethynodial diacetate  
 Lynestrenol  
 Medroxyprogesterone acetate  
 Megestrol acetate  
 Mestranol  
 Norethisterone  
 Norethynodrel  
 Progesterone  
 Testosterone

#### **Natural products (n = 5)**

Bracken fern (and its extracted chemicals)  
 Carboxymethylnitrosourea  
 Methyl Eugenol  
 Ochratoxin A

Wood dust methanol extract  
**Research chemicals (n = 15)**

1-Amyl-1-nitrosourea  
 2-Acetylaminofluorene  
 2-Aminofluorene  
 3,2-Dimethyl-4-aminobiphenyl  
 4-(5-Nitro-2-furyl)thiazole  
 4-Bis(2-Hydroxyethyl)amino-2-(5-nitro-2-thienyl)quinazoline  
 4-Hydroxyaminoquinoline 1-oxide hydrochloride  
 Ethyl methane sulfonate  
 N-(4-(5-Nitro-2-furyl)-2-thiazolyl) formamide  
 N-(9-Oxo-2-fluorenyl)acetamide  
 N,N-Diethyl-n-nitrosourea  
 N-N-Butyl-n-Nitrosourea  
 N-Nitroso-n-ethylurea  
 N-Nitroso-n-methylurea  
 Vinyl carbamate epoxide

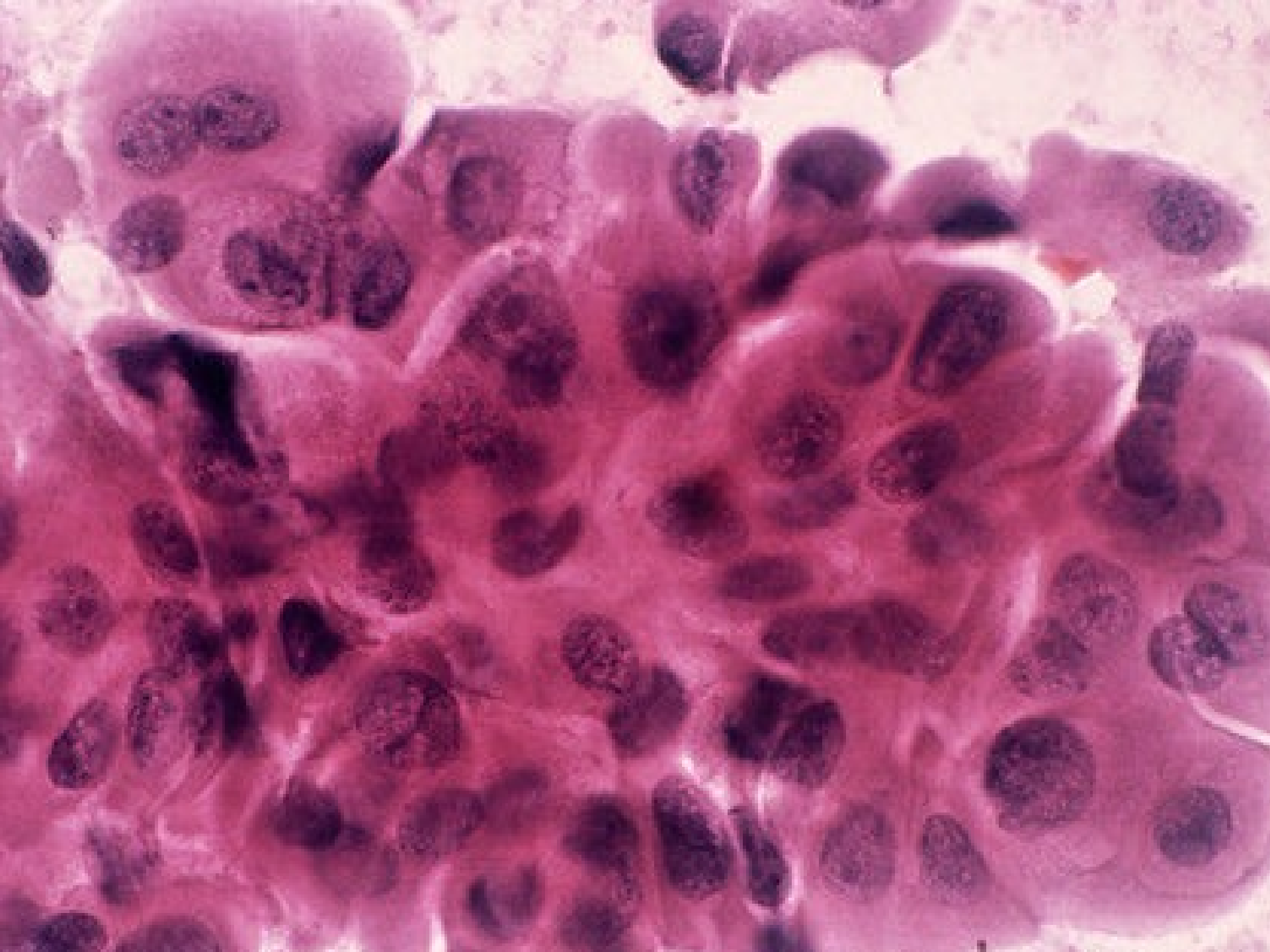
#### **Unclassified (likely research chemicals) (n = 39)**

(NC6)-  
 (Methylnitroso)adenosine  
 1-(2-Hydroxyethyl)-1-nitrosourea













# Gaps in Breast Cancer Research



- Occupation/Environment
- Endocrine Disrupting Chemicals
- Mixtures
- Cumulative effects
- Periods of vulnerability

# Essex & Kent Counties



- Manufacturing
- Agriculture

# Occupational Histories of Cancer Patients in a Canadian Cancer Treatment Center and the Generated Hypothesis and Farming

JAMES T. BROPHY, MARGARET M. KEITH, ETHAN LAUKKANEN, MD, DEBORAH HELLYER, ABRAHAM REINHARTZ, MD,

Occupational exposures increase cancer risk. The first Canadian cancer treatment center collected occupational histories of its patients, which were reported on a computer-based questionnaire. Breast cancer was the largest respondent group. The occupational histories of 299 women with newly diagnosed cancers were compared with those of 23 women with other cancers. Odds ratios (ORs) were calculated by logistic regression, adjusting for age, social class, and education. The OR for women  $\leq 55$  years of age who had ever farmed, compared with women of the same age with other cancers, was 9.05 (95% CI, 1.6–48.8).

## Occupation and Breast Cancer A Canadian Case-Control Study

JAMES T. BROPHY,<sup>a,b,c</sup> MARGARET M. KEITH,<sup>a,b,c</sup> KEVIN M. GOREY,<sup>c</sup> ISAAC LUGINAAR,<sup>d</sup> ETHAN LAUKKANEN,<sup>e</sup> DEBORAH HELLYER,<sup>a</sup> ABRAHAM REINHARTZ,<sup>a</sup> ANDREW WATTERSON,<sup>b</sup> HAKAM ABU-ZAHRA,<sup>f</sup> ELEANOR MATICKA-TYNDALE,<sup>c</sup> KENNETH SCHNEIDER,<sup>f</sup> MATTHIAS BECK,<sup>g</sup> AND MICHAEL GILBERTSON<sup>b</sup>

<sup>a</sup>Occupational Health Clinics for Ontario Workers (OHCOW), Canada

<sup>b</sup>University of Stirling, UK

<sup>c</sup>University of Windsor, Canada

<sup>d</sup>University of Western Ontario, Canada

<sup>e</sup>Prince Edward Island Cancer Treatment Centre, Canada

<sup>f</sup>Windsor Regional Hospital, Canada

<sup>g</sup>University of York, UK

**ABSTRACT:** A local collaborative process was launched in Windsor, Ontario, Canada to explore the role of occupation as a risk factor for cancer. An initial hypothesis-generating study found an increased risk for breast cancer among women aged 55 years or younger who had ever worked in farming. On the basis of this result, a 2-year case-control study was undertaken to evaluate the lifetime occupational histories of women with breast cancer. The results indicate that women with breast cancer were nearly three times more likely to have worked in agriculture when compared to the controls (OR = 2.80 (95% CI, 1.6–4.8)). The risk for those who



**Lifetime Histories  
BREAST CANCER  
Research Study**



*TOWARDS A BETTER  
UNDERSTANDING OF THE  
CAUSES OF*  
**BREAST CANCER**

**IF YOU HAVE RECENTLY BEEN  
DIAGNOSED WITH BREAST CANCER  
YOU CAN HELP  
WITH A ONE-TIME INTERVIEW**

## Current Study

- 1,006 cases
- 1,146 controls

# Questionnaire

## Non-Occupational Factors

- Reproductive factors
- Income
- Smoking
- Family history
- Etc.



# Questionnaire

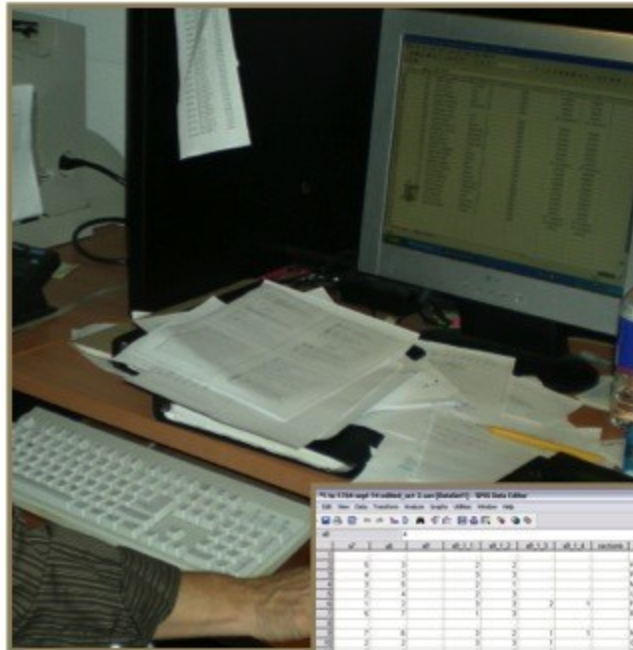
## Occupational Factors

- All jobs
- Industry
- Occupation
- Exposure
- Vulnerability factors





# Exposure Assessment

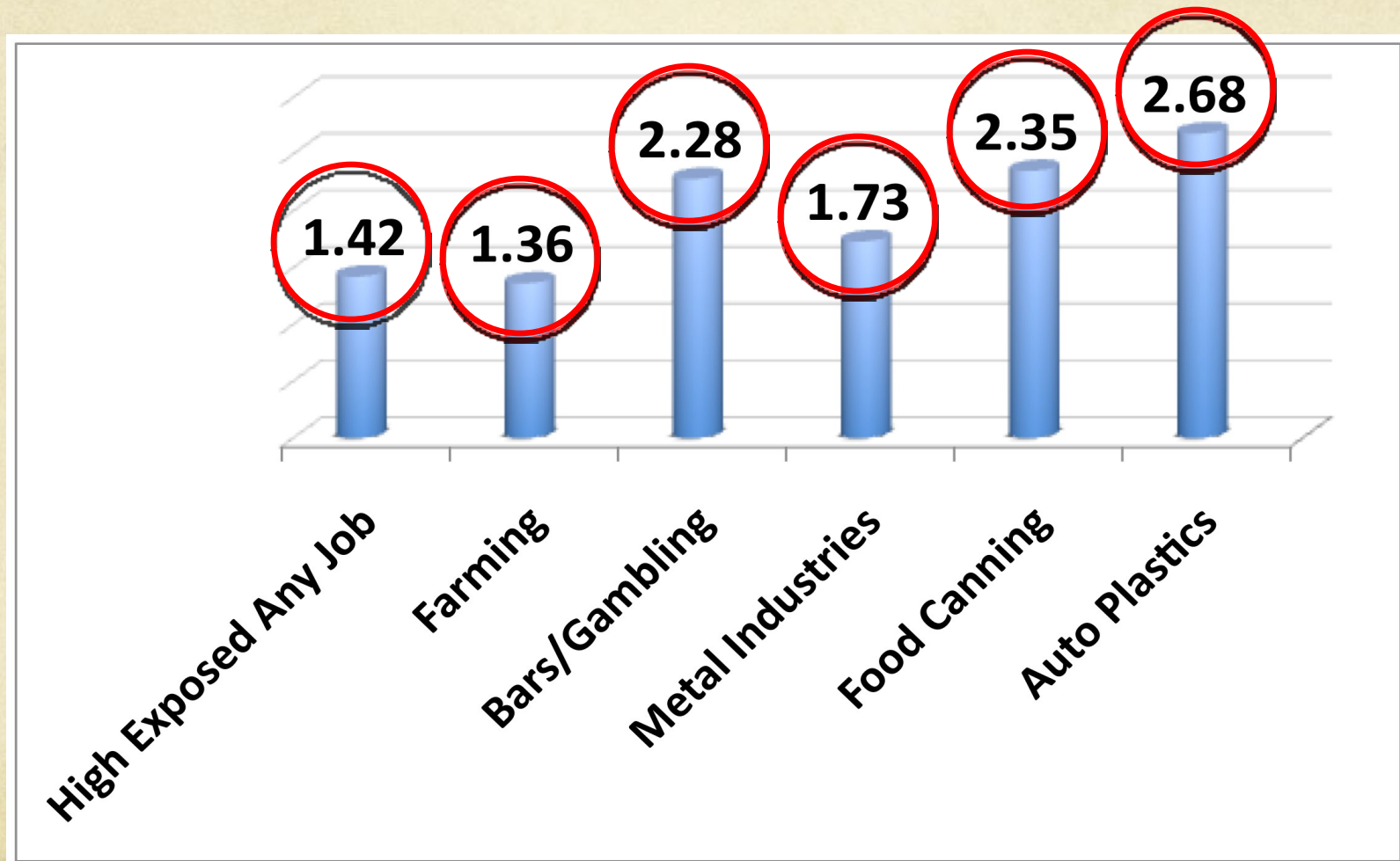
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- Low
- Moderate
- High

## Non-Occupational Findings

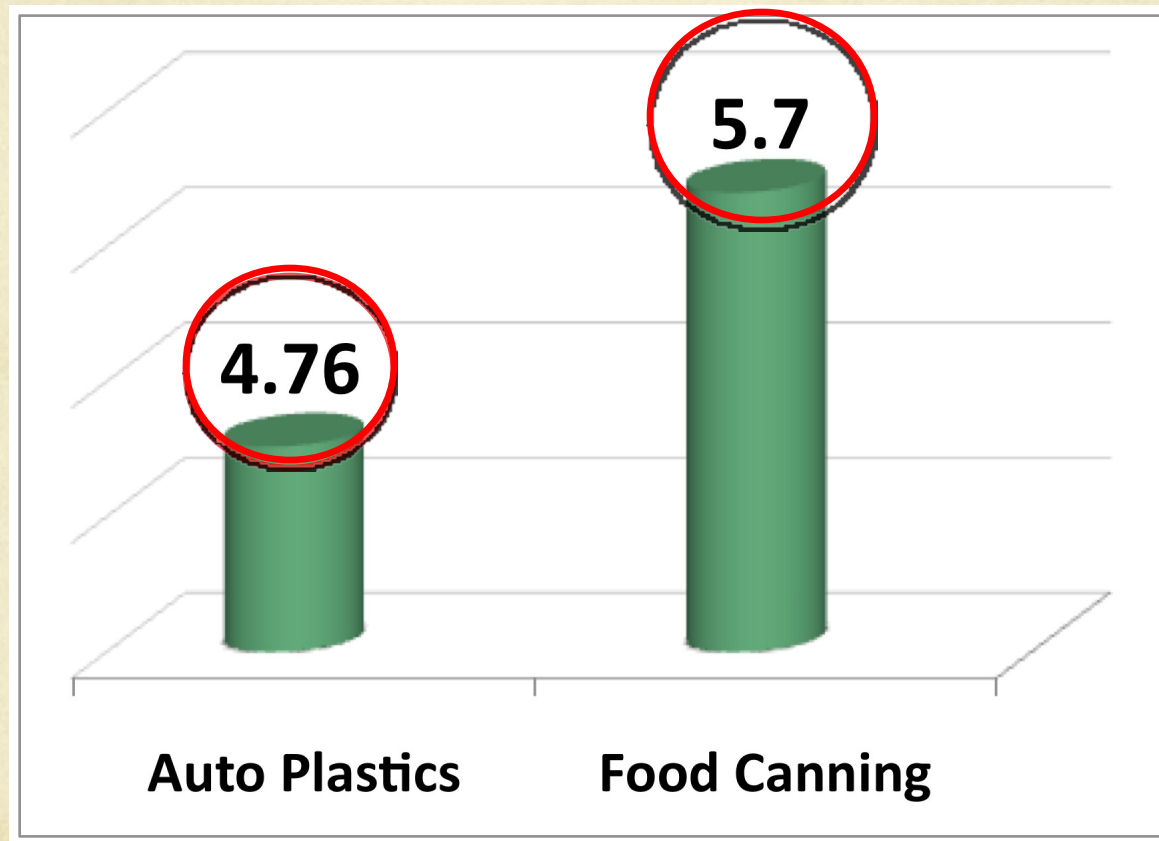
- High postmenopausal BMI
- Less education and income
- Number of pregnancies
- Duration of child-bearing years
- Smoking

# Occupational Findings



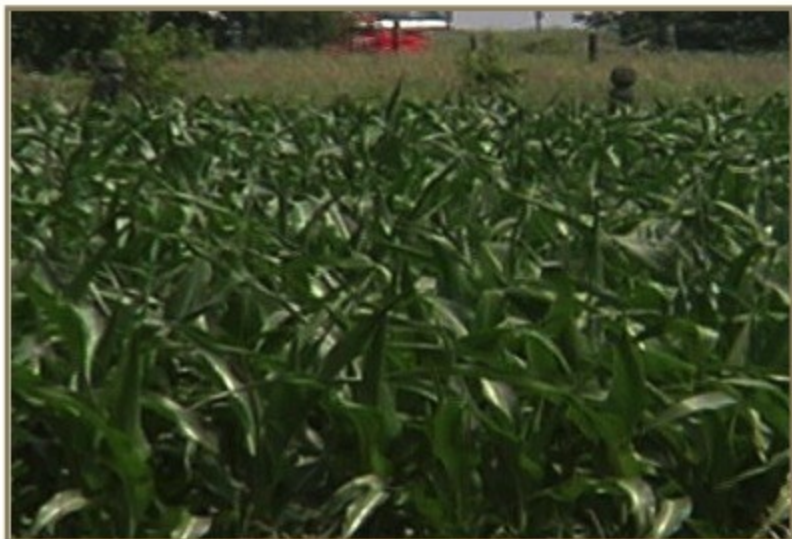


# *... Premenopausal*



## Farming Exposures (1.36)

- Pesticides
- Fungicides
- Fertilizers
- Diesel exhaust
- Other agricultural chemicals?



# Bars/Gambling Exposures (2.28)

- Second-hand tobacco smoke
- Night work
- Other?



# Metal Work Exposures (1.73)

- Metals
- Solvents
- Metalworking fluids
- Smoke/exhaust/PAHs
- Other chemicals





# Food Canning Exposures (2.35)

- Plastic can linings
- Pesticides
- Other?



# Automotive Plastics Exposures (2.68)

- Plastic resins
- Additives
- Flame retardants
- Solvents/glues/paints
- Other chemicals



# What Are The Implications?

- Occupational histories
- Regulations
- Workplace compensation
- More research
- **PREVENTIVE ACTION**





# THE PRECAUTIONARY PRINCIPLE



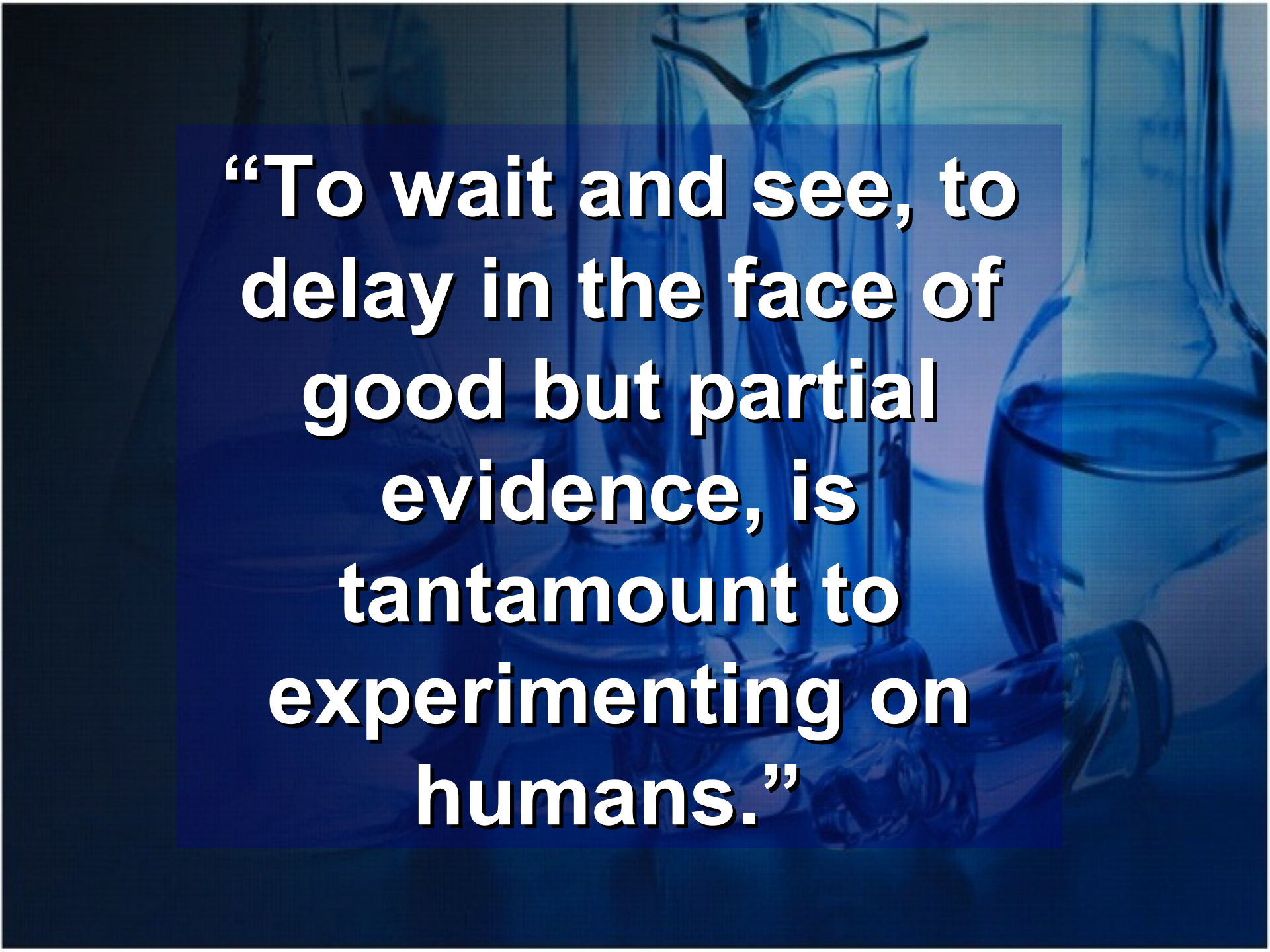
to protect  
what we have

not mourn  
what we've lost

A STANDARD WE CAN LIVE WITH!





The background of the slide features a blue-tinted image of laboratory glassware, including several Erlenmeyer flasks and beakers, some containing liquids, arranged on a surface. The text is overlaid on a dark blue rectangular area in the center.

**“To wait and see, to  
delay in the face of  
good but partial  
evidence, is  
tantamount to  
experimenting on  
humans.”**





*Contains photos taken by the presenters as well as images publicly available on the internet.*