Exploration of the role of occupational exposures in cancer etiology among participants in the CanPath Study

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Canadian Partnership
for Tomorrow's Health

Partenariat canadien
pour la santé de demain

Conflict of Interest

- None to declare

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The Growing Burden of cancer in Canada

Cancer is the #1 cause of death in Canada

1 in 2 Canadians will develop cancer in their lifetime

82,100 Canadians will die of cancer in 2019

63%

1 in 4 Canadians will die from cancer

"It's untenable to think we can treat our way out of the cancer problem. That alone will not be a sufficient response"

Chris Wild

Canadian Cancer Statistics Advisory Committee. *Canadian Cancer Statistics 2019.* Toronto, ON: Canadian Cancer Society; 2019. Available at: cancer.ca/Canadian-Cancer-Statistics-2019-EN (accessed [Oct. 17, 2019]).

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# Motivations for studying occupational exposures

1. Numerous carcinogens have been discovered through the study of exposures in the workplace

2. Many hazards encountered at work are present in the environment

3. Methodologic advantages

4. Prevention

"Work should be a place where people provide for themselves and their families…not a place where (men) and women increase their risk of disease and injury for themselves or their family"

Zahm and Blair. Am J Ind Med. 2003

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Contextual motivations

Work-related deaths in Canada for which compensation was received, by year
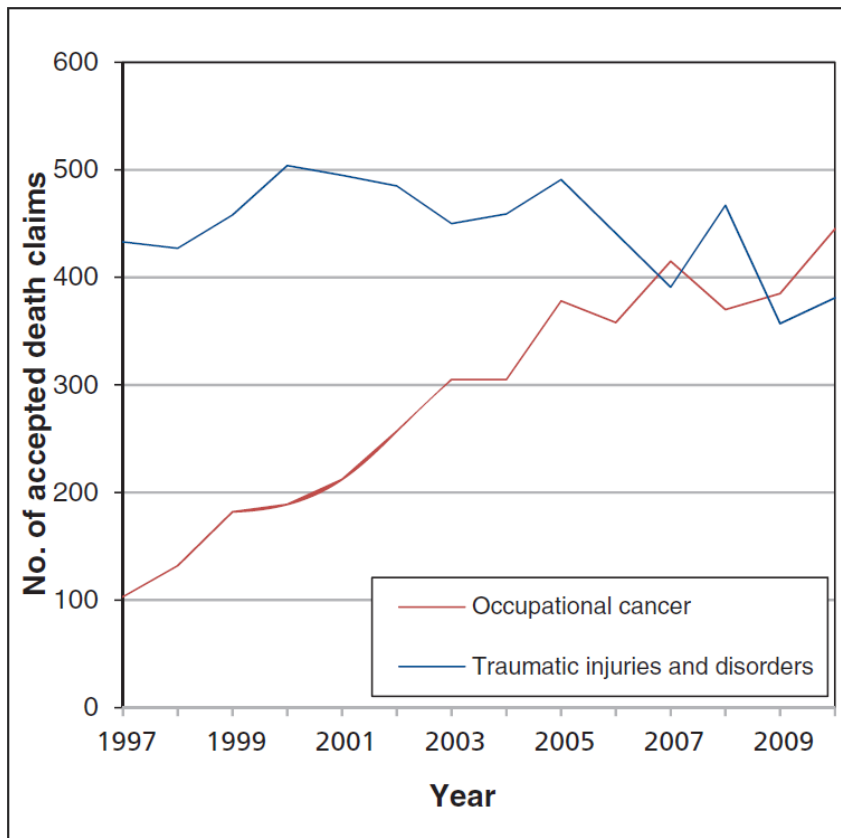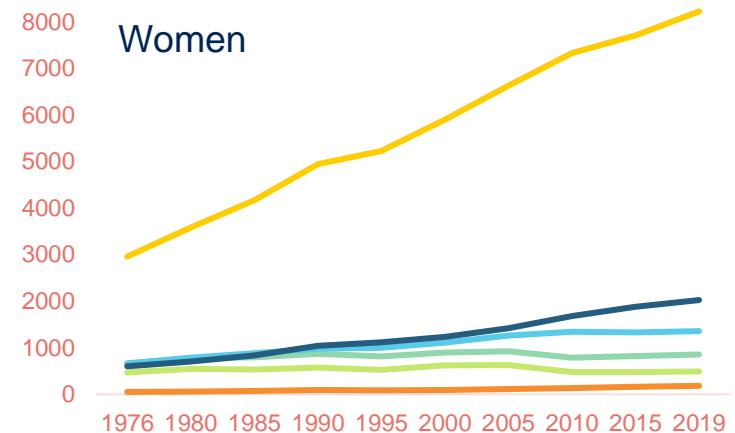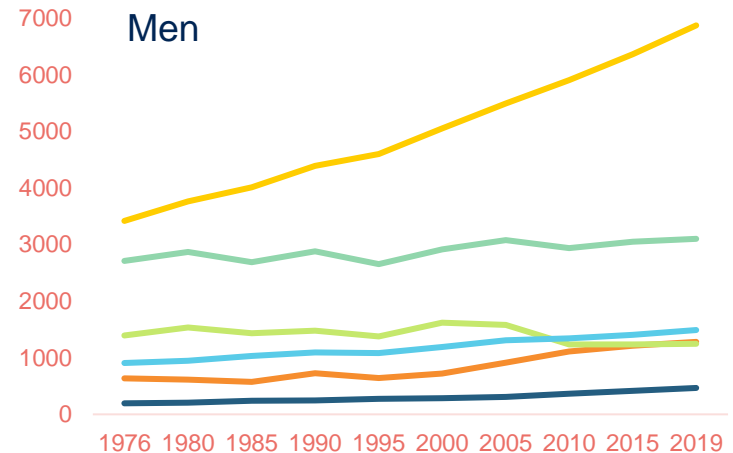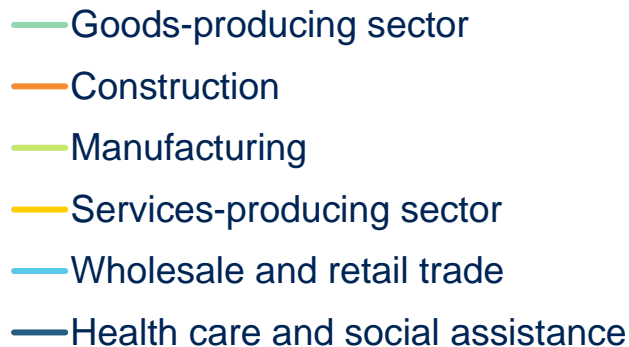

- Top 3 industries for deaths claimed from occupational cancer
  - Manufacturing
  - Construction
  - Mining

- Types of occupational cancers
  - Mesothelioma
  - Lung cancer

Del Biano and Demers. CMAJ. 2019

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The changing occupational profiles in Canada

- Changing industrial profile
- Improvements in occupational hygiene
- Sex and gender considerations

Legend:
- Goods-producing sector
- Construction
- Manufacturing
- Services-producing sector
- Wholesale and retail trade
- Health care and social assistance

Statistics Canada

Canada's largest population health research platform

CanPath is a **population-health research platform** for assessing the effect of genetics, behaviour, family health history and environment on chronic diseases.

330,000 Canadians are followed longitudinally

1 in every 100 Canadians participate

Atlantic PATH

36,003

BC Generations Project

29,800

Alberta's Tomorrow Project

41,374

Manitoba Tomorrow Project

Recruiting

Ontario Health Study

213,003

Quebec CARTaGENE

43,609

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Occupational data in CanPath

- **Data collection of CanPath study**
  - In-person assessment
  - Questionnaire
    - Employment information for current job and <u>longest-held job</u>

- Use of longest-held job (in CARTaGENE):
  - 61% of participants self-reported only 1 job (mean duration=16.6 years).
  - 39% of participants held more than one job:
    - Longest-held job still represented 61% (mean duration=15.6 years)

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Overview of occupational exposure assessment approaches

	Method	Strengths	Weaknesses
Expert assessment	Experts assign participants' occupational exposures	Considered as the gold standard	Long and costly; quality depends on the experts and available data
Job exposure matrix (JEM)	Fixed set of rules to associate a list of exposures to any occupational code	Cheap and quick	Dependent on the quality of available data, only provide average estimate of exposure

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The Canadian Job Exposure Matrix (CANJEM)

CANJEM (co-PI: Drs. Siemiatycki and Lavoué) provides Canadian-relevant information on the probability, reliability, intensity and frequency of exposure to a list of 258 agents for given occupational codes in specific time periods

- Developed from the data of four Canadian case-control studies conducted between 1979 and 2004
  - Based on *expert assessment* of **31,673 unique jobs** held by **8,760 participants**

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CANJEM (www.canjem.ca)

CANJEM
OCCUPATIONAL EXPOSURE INFORMATION SYSTEM

OVERVIEW   USER GUIDE   CANJEM DEVELOPMENT   RESEARCH GROUP

SELECT SUBSTANCE FROM LIST → | OVERVIEW | **CANJEM app**

Flexible design

❖ 4 occupational code systems
❖ 3 industry code systems
❖ Any resolution
❖ Customizable time period

Coverage of population

Over 90% of the recent Canadian working population would be covered by CANJEM
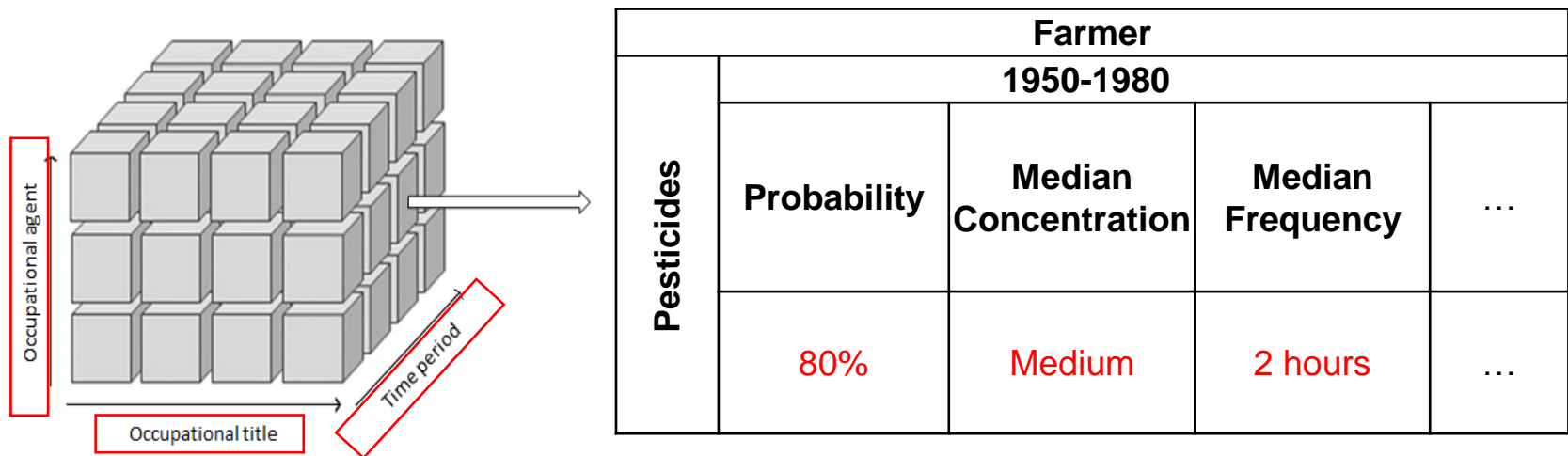

Development of and Selected Performance Characteristics of CANJEM, a General Population Job-Exposure Matrix Based on Past Expert Assessments of Exposure

Annals of Work Exposures and Health, 2018, Vol. 62, No. 7, 783–795
doi: 10.1093/annweh/wxy044

Availability of a New Job-Exposure Matrix (CANJEM) for Epidemiologic and Occupational Medicine Purposes

Journal of Occupational and Environmental Medicine:
July 2018 - Volume 60 - Issue 7 - p e324–e328

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CANJEM (www.canjem.ca)

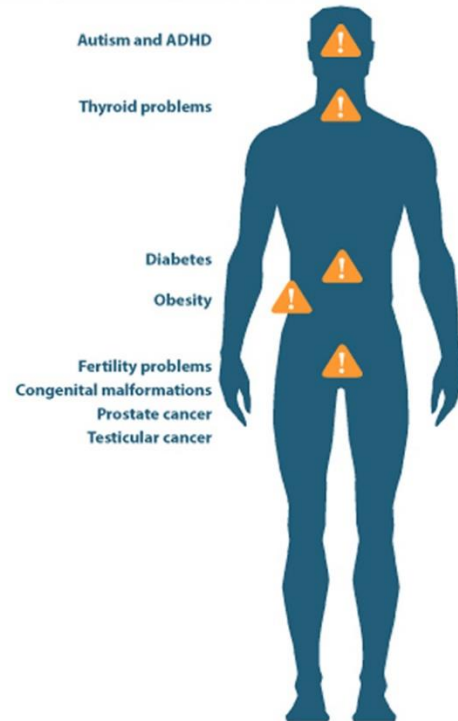| Pesticides	Farmer			
	1950-1980			
	Probability	**Median Concentration**	**Median Frequency**	…
	80%	Medium	2 hours	…

An illustrative example 1:

Occupational exposures and colorectal cancer risk

1. Prevalent occupational exposures
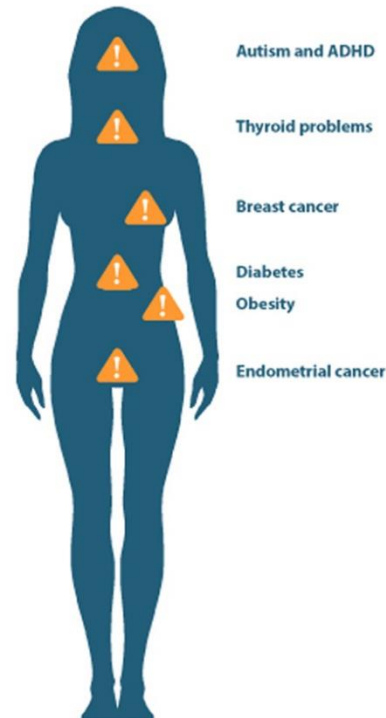2. Endocrine disrupting chemicals

Endocrine disrupting chemicals (EDCs)

- Exogenous substances that cause adverse health effects through interference with the endocrine system

The Endocrine System:
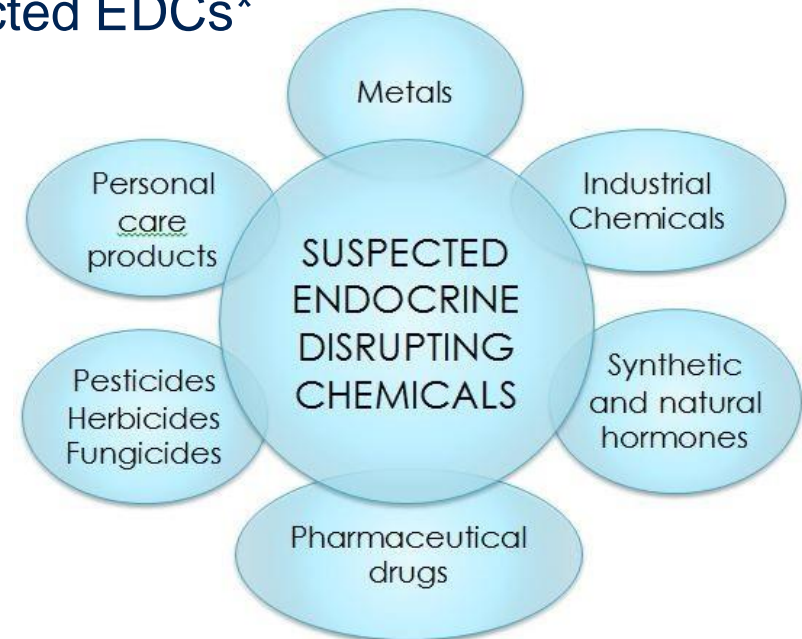Health problems for men related to EDCs?

Autism and ADHD

Thyroid problems

Diabetes

Obesity

Fertility problems
Congenital malformations
Prostate cancer
Testicular cancer

The Endocrine System:
Health problems for women related to EDCs?

Autism and ADHD

Thyroid problems

Breast cancer

Diabetes

Obesity

Endometrial cancer

Combarnous, 2019

Exposure to EDCs

- Over 500 chemicals are known/suspected EDCs*

- General population
  - Diet, environment, cosmetics, etc.

- Occupation
  - E.g. Cadmium
    - General population:
      - Non-smokers: 0.4-1.0 μg/L
      - Smokers: 1.4-4 μg/L
    - Occupationally exposed: up to 50 μg/L

*http://ec.europa.eu/environment/chemicals/endocrine/strategy/substances_en.htm

https://www.meconferences.com/blog/endocrine-disrupting-chemicals-may-be-debilitating-fertility/

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Study hypothesis &objectives

1. To investigate whether occupational exposure to EDCs is associated with the risk of colorectal cancer*, lung cancer**, breast cancer** and prostate cancer**

2. To investigate whether there are sex differences in the EDC-colorectal cancer and EDC-lung cancer relationships
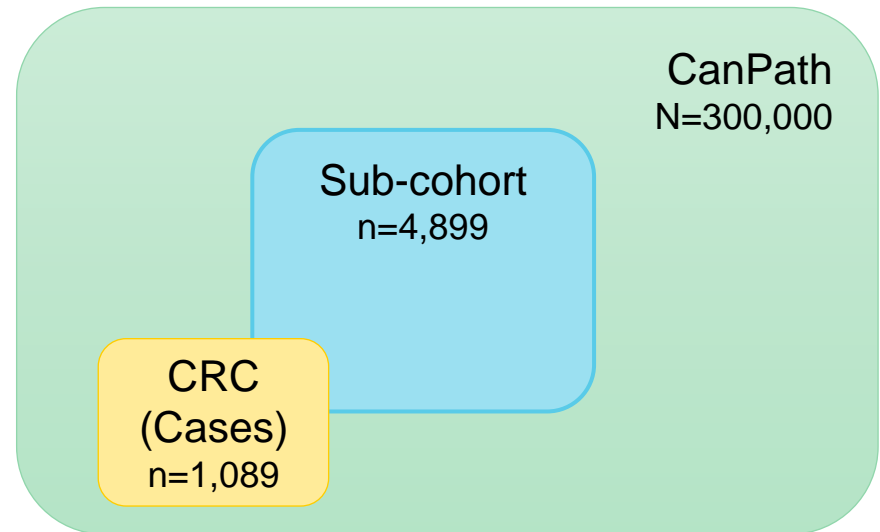
*Funded by CIHR Operating Grant 2018

**Funded by CIHR Chair in Sex and Gender Science in Cancer Research

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Study Design

- **Case-cohort design**
  - 1,089 cases of CRC
  - 4,899 sub-cohort
  - Exclusions:
    - History of cancer
    - Missing information

- **Advantages**
  - Sub-cohort is representative of the full cohort
  - Creation of a sub-cohort can serve as a comparison group for multiple outcomes

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N=300,000

Sub-cohort
n=4,899

CRC
(Cases)
n=1,089

Study population

Covariates		% Cases (N=1089)	% Sub-cohort (N=4899)
BMI	Underweight	1	1
	Normal	21	33
	≥Overweight	62	60
Ethnicity	White	76	82
	Asian or Other	10	14
Education	≤ High school	27	20
	Some postsecondary	34	39
	≥ Postsecondary	27	40
Income	10,000$ to < 50,000$	28	24
	50,000$ to < 100,000$	32	33
	≥ 100,000$	27	34
Smoking	Never smoker	32	47
	Past smoker	39	34
	Smoker	13	12
Alcohol consumption	Never drinker	9	10
	≤ Monthly drinker	28	33
	Weekly drinker	32	39
	≥ Nearly daily drinker	13	11
Family history of colorectal cancer	No	90	91
	Yes	10	9

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Top 5 most prevalent jobs in CanPath

All (except OHS)	OHS	CaG	ATP	AP	BCGP
Other Managers	Other Managers	Stenographic Secretary	First-Level Education Teacher	First-Level Education Teacher	Other Managers
Stenographic Secretary	Stenographic Secretary	Finance Clerk	Stenographic Secretary	Auxiliary Nurse	Professional Nurse
First-Level Education Teacher	First-Level Education Teacher	Other Managers	Office Clerk	Office Clerk	First-Level Education Teacher
Office Clerk	Professional Nurse	Retail Trade Salesman	Other Managers	Other Managers.	Office Clerk
Professional Nurse	Office Clerk	Medical Science Technician	General Farmer	Accountant	Accountant

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Assessment of occupational exposure using CANJEM

- Occupation and industry codes assigned to the longest-held job
  - **ISCO 1968**
  - NOC 2011, ISIC 1971 and NAICS 2012

- For this preliminary analysis, we used all time periods in CANJEM to assess exposure to 258 agents in CANJEM
  - 179,212 cells consisting of 696 distinct 5-digit and 3-digit ISCO 1968 codes

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Applying CANJEM to CanPath (excluding OHS)

Study Center	ISCO 68 5-digit	ISCO 68 3-digit	Not Codable/ Linkable
CARTaGENE (CaG)	50%	17%	33%
Alberta's Tomorrow Project (ATP)	80%	4%	16%
Atlantic PATH (AP)	87%	9%	4%
BC Generations Project (BCGP)	86%	9%	6%

Occupational exposure parameterization

- **Probability of exposure:** percentage of jobs considered as exposed within a cell of CANJEM
  - E.g. 8/10 gas welders were exposed to agent X; probability of exposure to agent X = 80% (8/10)

Metrics	Categories	Probability of Exposure
Binary	Never	<25%
	Ever	≥25%
Categorical	Never	<15%
	Potentially	≥15% and <25%
	Ever	≥25%
Substantial exposure	Never	0%
	Potentially	>0 and <25%
	Non-substantially	≥25% and concentration < medium
	Substantially	≥25% and concentration ≥ medium

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Statistical approach

- Weighted Cox regression model

- Minimally adjusted model: age, sex and cohort (random effects)

- Fully adjusted model: + BMI, ethnicity, education, income, smoking, alcohol consumption, family history of colorectal cancer and ever diagnosis of Crohn's disease or colitis

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EDCs in CANJEM

Herbicides	Aluminum compounds*
Polychlorinated biphenyls	Styrene*
Phthalates*	Cadmium
Bisphenol A	Carbon disulphide
Lead*	Ethylene glycol*
Arsenic	Perchloroethylene
Mercury	Phenol
Nonylphenol	Trichloroethylene*
Copper*	Xylene*
Toluene*	

Top 5 most prevalent jobs exposed to EDCs (excluding OHS)

CanPath	Type of EDCs
Farm Worker	Copper
Manager, Retail Trade	Lead
Lorry and Van Driver (Long-Distance Transport)	Lead
Commercial Traveller	Lead
Appraiser	Lead

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Selected results: Any EDCs

Exposure variables	Any EDCs	
	Minimally Adjusted HR (95% CI)	Fully Adjusted HR (95% CI)
Binary exposure		
Never	1.00 (ref)	1.00 (ref)
Ever	**1.49 (1.14 - 1.95)**	**1.40 (1.06 - 1.85)**
Categorical exposure		
Never	1.00 (ref)	1.00 (ref)
Potential	0.66 (0.39 - 1.10)	0.73 (0.43 - 1.24)
Ever	**1.45 (1.11 - 1.90)**	**1.37 (1.03 - 1.82)**
Substantial exposure		
Never	1.00 (ref)	1.00 (ref)
Potential	**0.64 (0.52 - 0.77)**	**0.62 (0.51 - 0.76)**
Non-substantial	1.01 (0.58 - 1.74)	1.11 (0.63 - 1.94)
Substantial	1.21 (0.89 - 1.66)	1.06 (0.77 - 1.47)

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Top 5 most prevalent agents in CanPath (excluding OHS)

All (except OHS)	CaG	ATP	AP	BCGP
PAHs from any source	PAHs from any source	PAHs from any source	Organic solvents	PAHs from any source
Organic solvents	Organic solvents	Carbon monoxide	Cleaning agents	Organic solvents
PAHs from petroleum	PAHs from petroleum	PAHs from petroleum	Aliphatic aldehydes	PAHs from petroleum
Engine emission	Lead	Engine emission	PAHs from any source	Engine emission
Carbon monoxide	Abrasive dust	Organic solvents	Alkanes (C18+)	Carbon monoxide

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PAHs from any source

Exposure variables	PAHs from any source	
	Minimally Adjusted HR (95% CI)	Fully Adjusted HR (95% CI)
Binary exposure		
Never	1.00 (ref)	1.00 (ref)
Ever	**1.79 (1.13 - 2.82)**	1.40 (0.88 - 2.21)
Categorical exposure		
Never	1.00 (ref)	1.00 (ref)
Potential	0.51 (0.16 - 1.59)	0.51 (0.13 - 1.95)
Ever	**1.77 (1.12 - 2.78)**	1.39 (0.87 - 2.20)
Substantial exposure		
Never	1.00 (ref)	1.00 (ref)
Potential	**1.82 (1.30 - 2.53)**	0.95 (0.66 - 1.36)
Non-substantial	1.28 (0.48 - 3.46)	1.04 (0.38 - 2.83)
Substantial	**2.19 (1.32 - 3.62)**	1.50 (0.89 - 2.53)

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Selected results: Organic solvents

Exposure variables	Organic solvents	
	Minimally Adjusted HR (95% CI)	Fully Adjusted HR (95% CI)
Binary exposure		
Never	1.00 (ref)	1.00 (ref)
Ever	0.82 (0.45 - 1.50)	1.05 (0.57 - 1.93)
Categorical exposure		
Never	1.00 (ref)	1.00 (ref)
Potential	1.67 (0.69 - 4.04)	1.62 (0.60 - 4.41)
Ever	0.82 (0.45 - 1.51)	1.06 (0.57 - 1.94)
Substantial exposure		
Never	1.00 (ref)	1.00 (ref)
Potential	**2.22 (1.62 - 3.05)**	0.90 (0.63 - 1.28)
Non-substantial	0.76 (0.24 - 2.38)	0.80 (0.25 - 2.51)
Substantial	0.98 (0.48 - 2.00)	1.16 (0.57 - 2.38)

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An illustrative example 2:

Occupational physical activity and lung cancer risk

Physical activity

- Physical activity (PA) is any bodily movement produced by skeletal muscles that results in energy expenditure
  - Complex behavior
    - Type
    - Intensity
    - Frequency
    - Duration

- Metabolic equivalent of task (MET):
  - Ratio of metabolic rate during a specific PA to a reference metabolic rate
    - 1 MET: resting metabolic rate during quiet sitting
    - 2 MET: metabolic rate for walking at a slow pace

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Men

Women
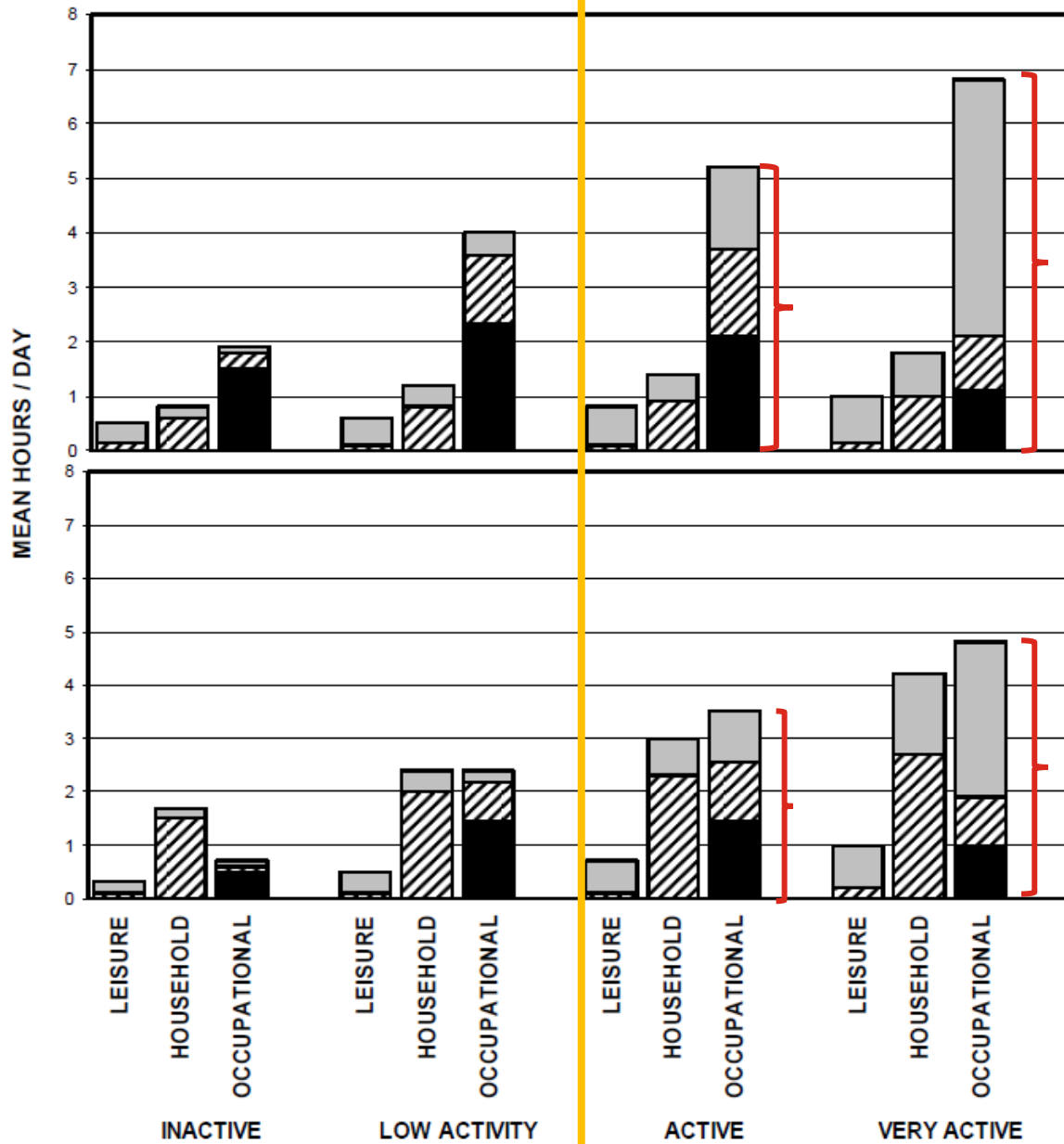
Hours/day spent in occupational PA by physical activity levels

Moderate-to-Vigorous Activity

Light Activity

Sedentary Behaviour

MEAN HOURS / DAY

LEISURE HOUSEHOLD OCCUPATIONAL

INACTIVE **LOW ACTIVITY** **ACTIVE** **VERY ACTIVE**

Csizmadi, et al., Int. J. of Behav. Nut. And Phys Act. 2011

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Summary of the Literature

Effect size of 1.15 (1.04-1.28)
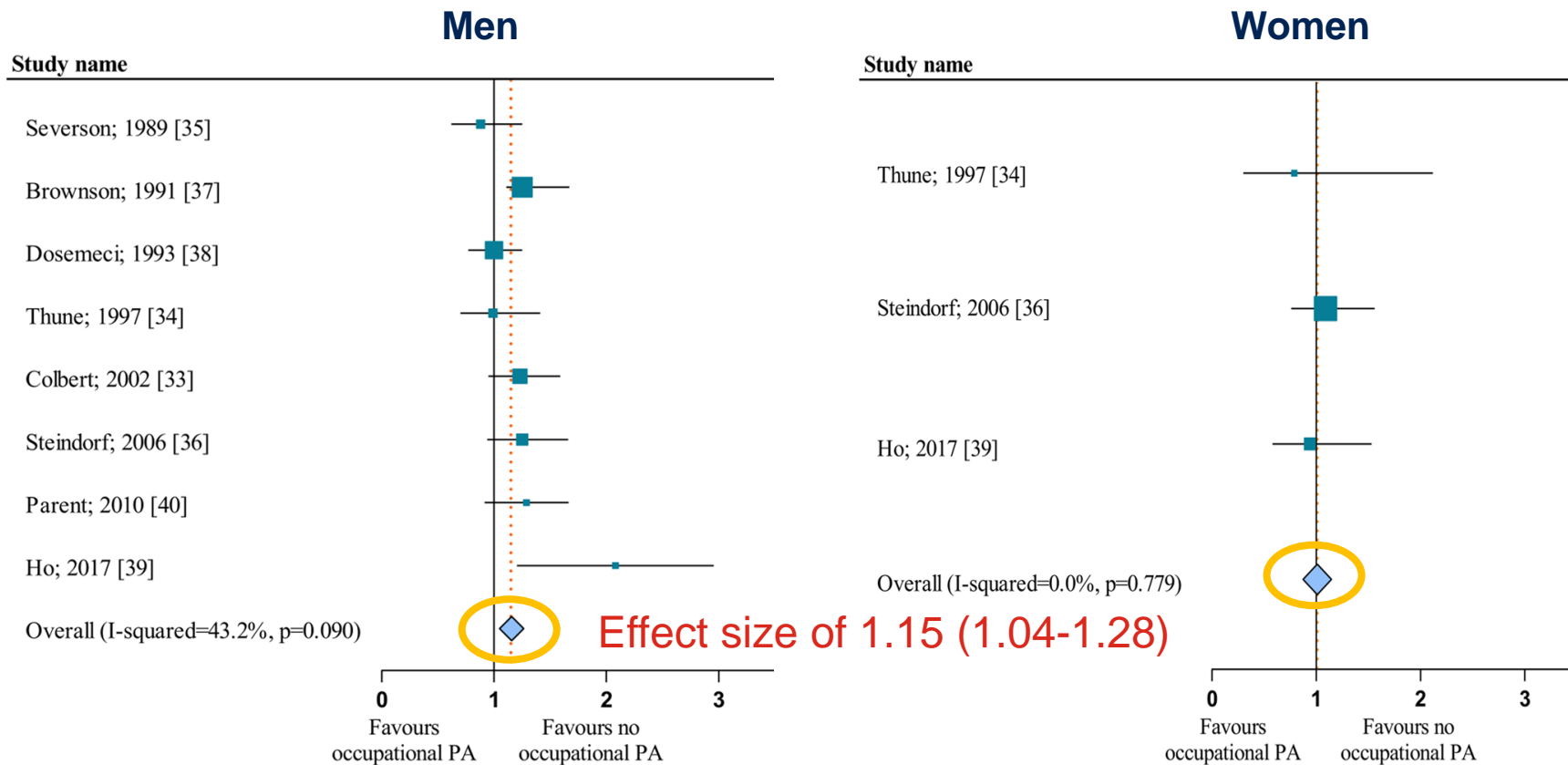
Rana *et al,* Sports Med. 2020

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Occupational Physical Activity Assessment

- For each major task within a job a MET value was assigned by an industrial hygienist and an exercise physiologist using the Compendium of Physical Activity as a reference

	Job	%	Activity Code	Activity Description	MET
1	Logger	70	11290	Forestry, felling trees	12
		30	11250	Forestry, ax chopping. very fast	9
2	Carpenter	100	11120	Constructionoutside	5.5

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Occupational physical activity database

- The median level of occupational physical activity in METs are available in ISCO 1968 codes

- The list of ISCO 1968 codes include 2- to 5-digits codes, as well as combinations of code (e.g. 0-61/0-62)

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Study population (excluding OHS)

Covariates		% Cases (N=335)	% Sub-cohort (N=2309)
BMI	Underweight	38	36
	Normal	34	37
	≥Overweight	24	23
Ethnicity	White	92	87
	Asian or Other	6	8
Education	≤ High school	38	21
	Some postsecondary	44	41
	≥ Postsecondary	18	39
Income	10,000$ to < 50,000$	45	21
	50,000$ to < 100,000$	37	33
	≥ 100,000$	14	41
Occupational exposure to lung carcinogens	Ever	11	8
	Never	89	92
Chronic obstructive pulmonary disease	Yes	17	3
	No	82	96

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Occupational physical activity (excluding OHS)

Men	MET range	Top 3 Jobs
High	2.16 - 6.50	Retail trade salemen, other service workers, Construction workers
Medium	1.58 - <2.16	Teachers, Government executive official, Medical doctors or assistant
Low	1.30 - <1.58	Other managers, Finance clerks, Accountant

Women	MET range	Top 3 Jobs
High	2.00 - 4.80	Medical doctors or assistant, Teachers, Retail trade salemen
Medium	1.50 - <2.00	Stenographic Secretary, Finance clerk, Other managers
Low	1.30 - <1.50	Accountant

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Occupational physical activity and lung cancer risk by sex (excluding OHS)

METs Tertiles	Occupational physical activity	
	Men* Adjusted HR (95%CI)	Women** Adjusted HR (95%CI)
Low	1.00 (ref)	1.00 (ref)
Medium	**3.66 (1.50 - 8.91)**	**0.32 (0.16 - 0.65)**
High	**4.24 (1.29 - 13.86)**	0.81 (0.36 - 1.84)

*Adjusted for age, ethnicity, number of years of schooling, income, smoking history and occupational lung carcinogen exposure

**Adjusted for age, ethnicity, number of years of schooling, income, smoking history, and vegetable intake

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Future Directions

- Parallel analyses in OHS

- Exploration of additional occupational exposures in CANJEM

- CANJEM-female

Thank you to CanPath participants across the seven regional cohorts who generously donate their time, information and biological samples. **CanPath is a success because of the participants' ongoing commitment.**

Acknowledgements

My research program within CanPath is supported by the Canadian Institutes of Health Research

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Opportunities!!!

- Postdoctoral Fellow
  - PhD in epidemiology, occupational health or a related field

- Research Assistant
  - MSc in epidemiology, occupational health or a related field

- Biostatistician
  - MSc in biostatistics

Accessing CanPath Data

CanPath.ca

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Partenariat canadien
pour la santé de demain