Exploring sex differences in the etiology of cancers: a critical look at endocrine disrupting chemicals in the workplace

Vikki Ho, PhD
Research Scientist/Assistant Professor
CRCHUM/University of Montreal – School of Public Health

Conflict of Interest

- None to declare

Learning objectives

1. Describe the methodological challenges in occupational exposure assessment of endocrine disrupting chemicals (EDCs)

2. Present a framework to classify occupational exposures to EDCs by sex hormone function

3. Apply the framework and assess occupational exposures to EDCs and the risk of developing colorectal cancer

Context of research

Burden of cancer in Canada

"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]).

1. LUNG CANCER *2 CIHR-funded studies* ($175 000)	2. BREAST CANCER *IRSST-funded study* ($501 484)	3. COLORECTAL CANCER *CIHR-funded study* ($252 450)	4. THE CANADIAN EXPOSOME (HEALTH & CHRONIC DISEASE) *L'avenir*
› Environmental factors › Occupational factors › Lifestyle factors › Biomarkers of intermediate effect (epigenetics)	› Occupational factors › Lifestyle factors › Genetic factors	› Occupational factors › Hormonal factors › Biomarkers of intermediate effect (epigenetics)	› Contextual factors › Environmental factors › Occupational factors › Lifestyle factors › Biomarkers of exposure › Biomarkers of intermediate effect (allostatic load)
I. Exploitation of existing databases	> Canadian Partnership for Tomorrow Project > Canadian Health Measures Survey		
II. Exposome: the consideration of multi-exposures	> Big Data > Network analysis, multi-level modelling	> Mise en practique the social theories of health	
III. Sex differences	> Development of tools assessing occupational exposures among women	> Integration of sex in research design	

Colorectal cancer

- In Canada (2019):
  - Men: 71.7 cases per 100,000
  - Women: 50.9 cases per 100,000
- Gap is greatest at 55-74 age range where incidence and mortality rates are ~60% higher in men than women

CRC is not generally considered a hormone-related malignancy

Risk factors?

Screening use?

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]).

Sex hormones and cancer

- Potential mechanisms:
  - Immune system
  - Cell metabolism
  - Renewal of target stem cell populations
  - Tumour microenvironment

- Colorectal cancer

Women:

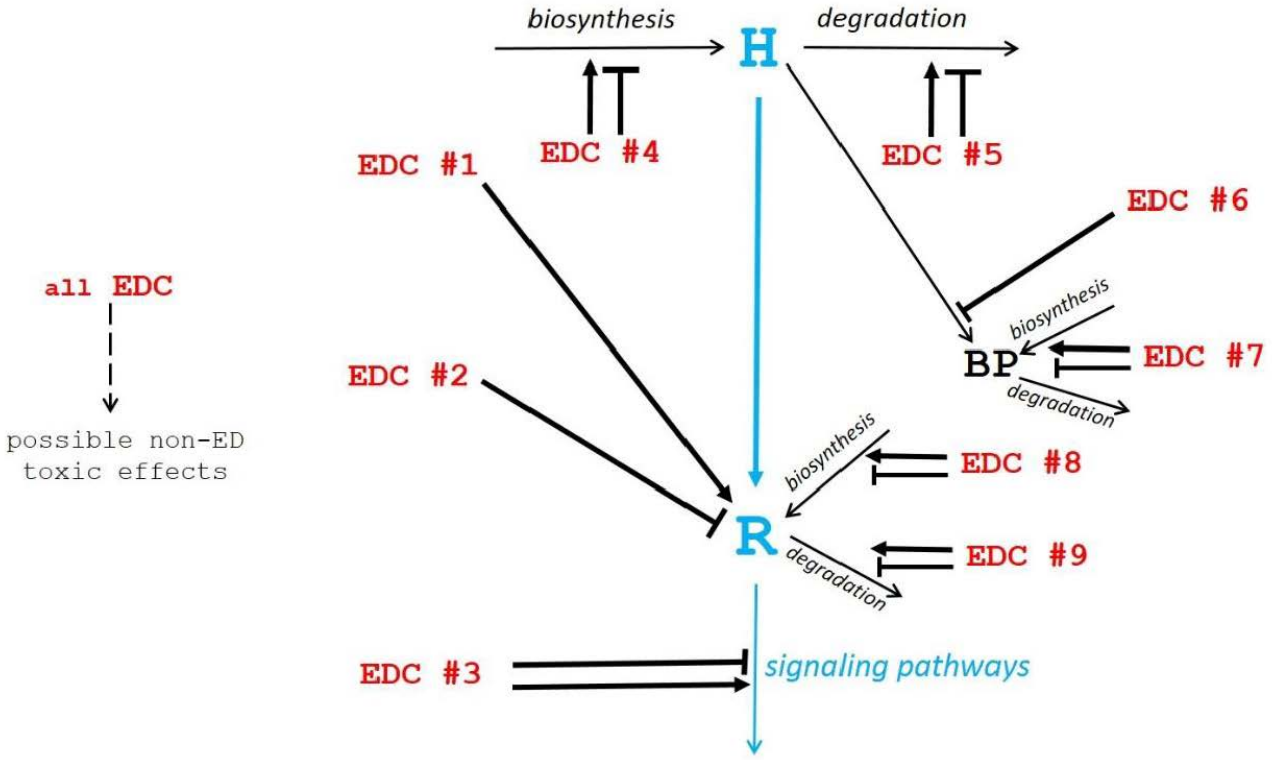
  - Two randomized controlled trials reported a 40% reduction in risk among postmenopausal women taking estrogen plus progestin versus the placebo group
  - Parity, oral contraceptives

Men: Little is known

  - Lower androgenicity appears to increase risk

Endocrine disrupting chemicals (EDCs)

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



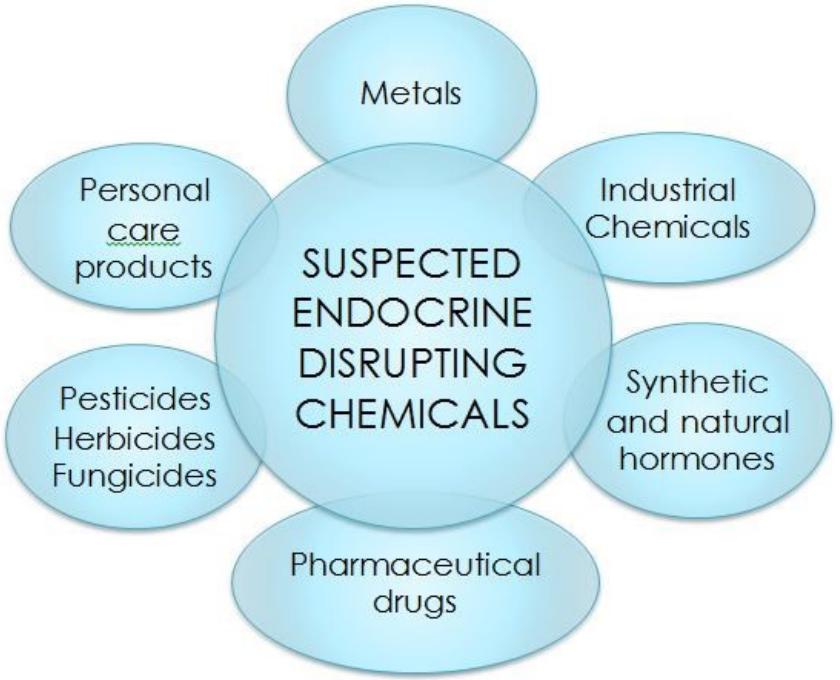
- Inhibiting and/or mimicking the effect of hormones (#1-3)
- Disrupting the production, metabolism and transport of hormones (#4-7)
- Disrupting the production and degradation of hormone receptors (#8-9)

Combarnous, 2019

Exposure to EDCs

- Over 500 chemicals are known/suspected EDCs*
- General population
  - Diet, environment, cosmetics, etc.
- Occupation

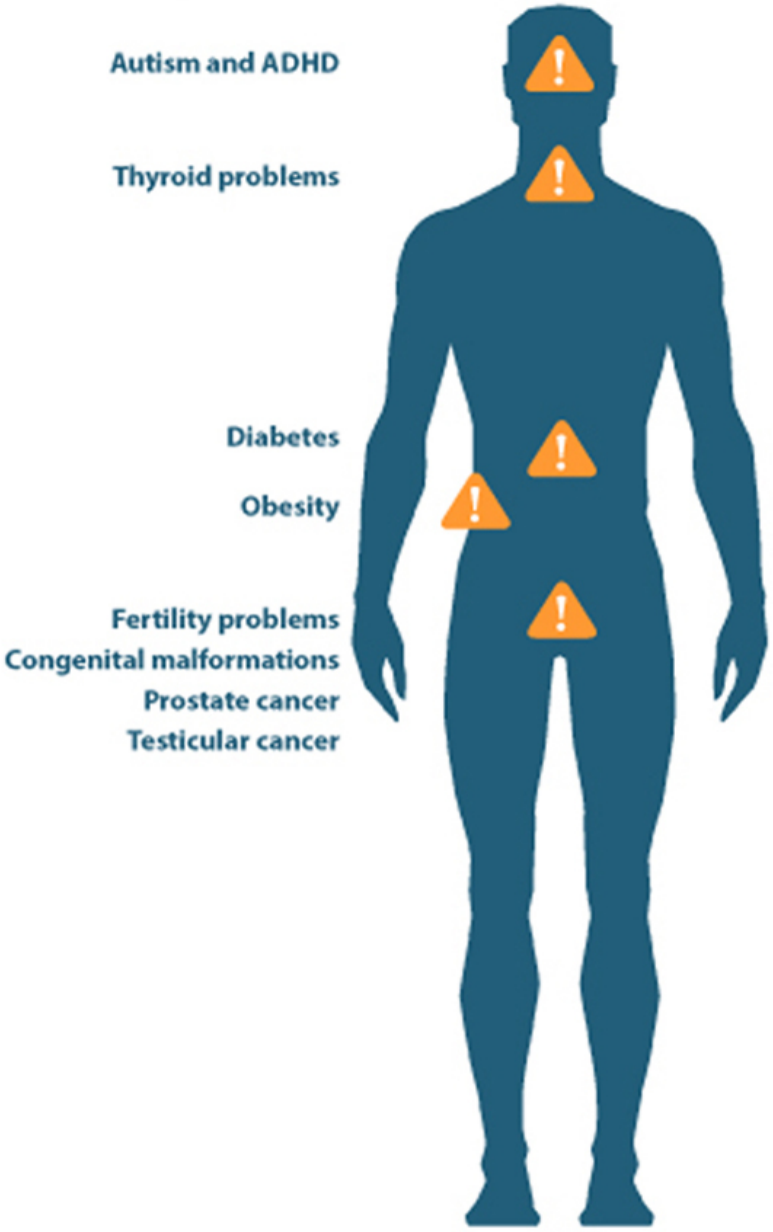
  E.g. Cadmium
  - General population:
    - Non-smokers: 0.4-1.0 µg/L
    - Smokers: 1.4-4 µg/L
  - Occupationally exposed: up to 50 µg/L



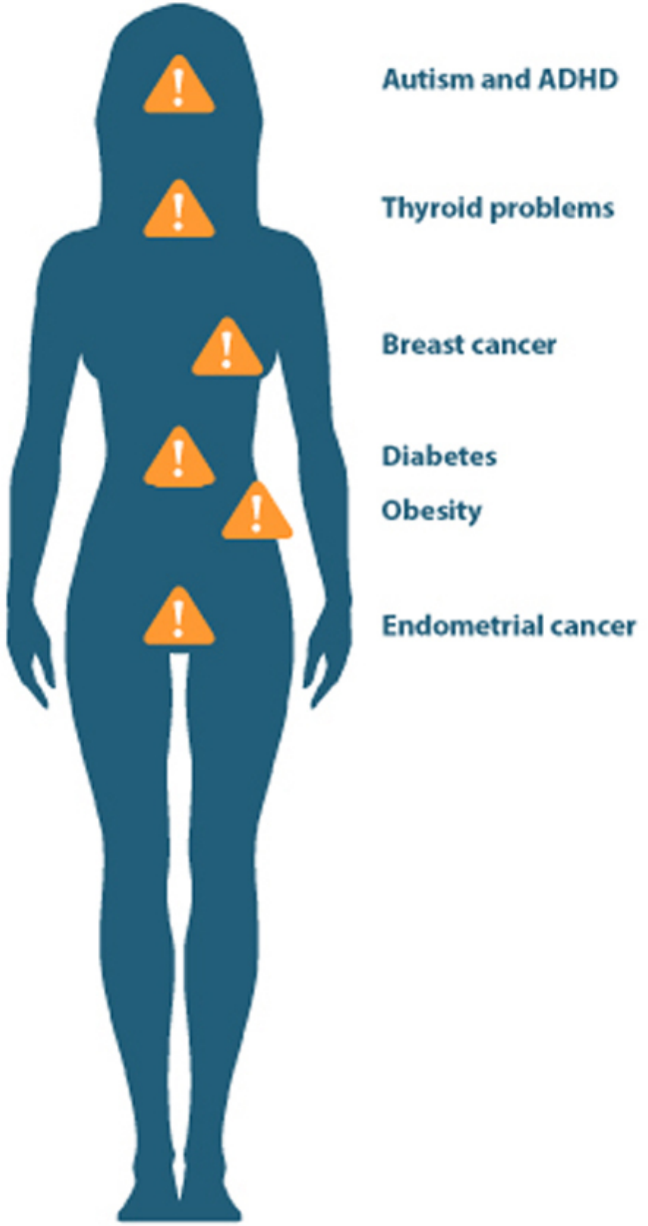
*http://ec.europa.eu/environment/chemicals/endocrine/strategy/substances_en.htm

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

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



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



Study hypothesis &objectives

Exposure to EDCs that alters the proper functioning of sex hormones contributes to colorectal cancer development.

1. To investigate whether occupational exposure to EDCs is associated with the risk of colorectal cancer
2. To investigate whether there are sex differences in Objective 1

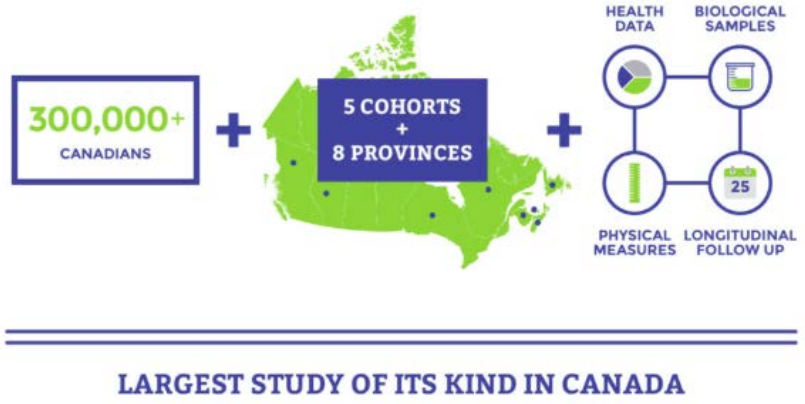
Canadian Partnership for Tomorrow Project (CPTP)

LARGEST STUDY OF ITS KIND IN CANADA

1

Describe the methodological challenges in occupational exposure assessment of EDCs

Exposure assessment



- **Data collection of CPTP study**
  - In-person assessment
  - Questionnaire
    - Employment information for current job and longest-held job

- 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)

Retrospective occupational exposure assessment

	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

EDC-JEM

- Polycyclic aromatic hydrocarbons
- Polychlorinated organic compounds
- Pesticides
- Phthalates
- Organic solvents
- Bisphenol A
- Alkylphenolic compounds
- Brominated flame retardents
- Metals

0=Unlikely
1=Possible
2=Probable

Code	SOC2000 job title	Overall exposure score*	Chemical groups†	Group scores*	Chemical subgroups†	Subgroup scores*	Exposure scenarios
5241	Electricians, electrical fitters	1	Metals (9)	1	Lead (9.4)	1	Lead solder
5491	Glass and ceramics makers, decorators and finishers	2	Organic solvents (5)	1	EGEs (5.1)	1	Glass making chemicals; dyes for glass and ceramics; coatings
					Toluene (5.3)	1	
					Xylene (5.4)	1	
			Metals (9)	2	Arsenic (9.1)	2	
					Cadmium (9.2)	2	
					Lead (9.4)	2	

van Tongeren *et al*., 2002; Brouwers *et al*., 2009

Consideration(s)

- Is the EDC-JEM developed in the UK applicable to Canadian data?
  - Classes of chemicals vs. individual chemicals
  - Probability scores

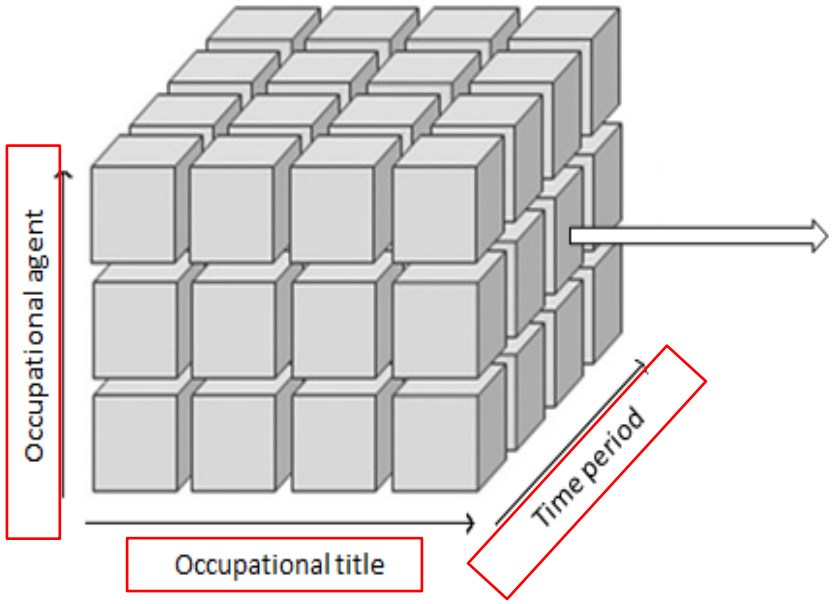
- Cross-walk required for UK-SOC 2000

The Canadian Job Exposure Matrix (CANJEM)

CANJEM 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 (Drs. Siemiatycki and Lavoué)
  - Based on *expert assessment* of **31,673 unique jobs** held by **8,760 participants**

CANJEM



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

CANJEM metrics of exposure

- **Probability of exposure:** percentage of jobs considered as exposed within a cell of CANJEM
  - E.g. if the cell for gas welders during the period 1970 to 1985 for agent X contained 25 exposed jobs over a total of 30 jobs, than the probability of exposure to agent X = 83% (25/30)

- **Median concentration of exposure:** low, medium, high
- **Median frequency of exposure:** hours per week

2

Present a framework to classify occupational exposures to EDCs by sex hormone function

Classifying selected EDCs by hormonal effect

Exposure to EDCs that alters the proper functioning of sex hormones contributes to colorectal cancer development

- Each EDC may affect different sex hormones
- Research Priority: “a new risk assessment approach that would more closely simulate what occurs in nature: that is, a better understanding of the effects of combinations of compounds or mixtures.” *(WHO, Endocrine Society)*

To this end, we propose a new approach to characterize potential EDCs based on effects on sex hormone function

(Anti)-estrogenic

(Anti)-androgenic

Methods

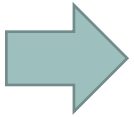
1. Identification of EDCs of interest

2. Literature search focusing on the effect of EDCs on sex hormones

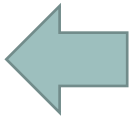
3. Expert panel evaluation

1. EDCs of interest in CANJEM

List of agents with potential ED-effects identified by the European Commission



CANJEM



Agents in EDC-JEM

Potential EDCs in CANJEM

Potential EDCs	CANJEM Agent Code
Bis(2-ethylhexyl) phthalate	531799
Lead	518299
Arsenic	513399
Mercury	518099
Nonylphenol	430201
Copper	512999
Toluene	430102
Aluminum compounds	511399
Diethyl phthalate	531799
Styrene	430104
Bisphenol A (Epoxy)	150023
Butylbenzyl phthalate	531799

Potential EDCs	CANJEM Agent Code
Cadmium	514899
Carbon disulphide	421001
Dibutyl phthalate	531799
Dicyclohexyl phthalate	531799
Diisodecyl phthalate	531799
Diisononyl phthalate	531799
Ethylene glycol	420203
Polychlorinated biphenyl	460029
Perchloroethylene	421303
Phenol	430201
Trichloroethylene	430701
Xylene	430103

2. Literature search

TIER 1 - opinions/risk assessment reports of international bodies

TIER 2 - reviews

TIER 3 - original studies: epidemiological, toxicological (*in vivo, in vitro*)

TIER 4 - *in silico* model (ToxCast)

Summary of Tier 1-4 (Estrogen)

Agents	Tier 1	Tier 2	Tier 3			Tier 4
			Human	*In vivo*	*In vitro*	
Bis(2-ethylhexyl) phthalate	Inconclusive	Not found	5 studies	2 studies	3 studies	No data found
Lead	Not found	Not found	5 studies	2 studies	3 studies	No data found
Dibutyl phthalate	Inconclusive	Not found	Not found	Not found	1 study	Agonist and Antagonist to ER
Dicyclohexyl phthalate	Inconclusive	Not found	Not found	Not found	1 study	Agonist and Antagonist to ER

Summary of the state of evidence

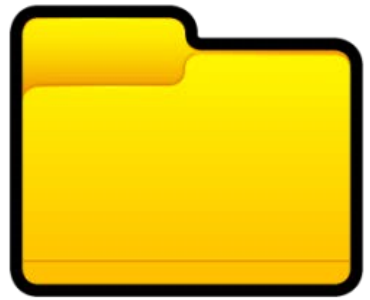
TIER 1

TIER 2

TIER 3

TIER 4

Summary of Scientific Evidence



24 agents

Bis(2-ethylhexyl) phthalate (DEHP)

The literature search of Bis(2-ethylhexyl) phthalate (DEHP) was carried out and key words presented in the following table:

	Tier 1	Tier 2	Tier 3	
Search Terms	Google: "Bis(2-ethylhexyl) phthalate (or DEHP)" and "endocrine effect"	PubMed: Bis(2-ethylhexyl) phthalate (or DEHP)" and "endocrine effect" or "estrogen"	Systematic review: original references (epi, in vivo, in vitro)	

1 DEHP effects on sex hormones / Mode of action

1.1 Tier 1 – Report(s)

The report developed by ECHA is based on literature searches up to 2014 and included risk assessment reports, reviews and original studies. Data collection and the analysis were related to the following topics: adverse health effects, endocrine mode of action (MoA), plausible link between adverse effects and endocrine MoA and human relevance. The most marked adverse effects of DEHP have been described for the male reproductive system and most experimental work focused on elucidating the MoA of DEHP in developing male rats (ECHA, 2014).

Summary of the ECHA report about the anti-androgenic effect and plausible estrogenic effect

Animal studies demonstrated the adverse effects of DEHP in male reproductive organs such as: testicular changes, decreased number of spermatocytes, decreased ano-genital distance and nipple retention. It was considered highly plausible that these effects are induced by an endocrine MoA of DEHP. These findings are further supported by other *in vivo* mechanistic findings as DEHP exposure has been associated with a down-regulation of genes (e.g. StAR, Cyp11, insl3) in the steroidogenic biosynthesis pathway. The range of adverse effects observed in rats includes a reduced number of spermatocytes and testicular changes including multinucleated gonocytes, tubular atrophy and Leydig cell hyperplasia. Further, studies on exposure to DEHP and its metabolite mono(2-ethylhexyl)phthalate (MEHP) also showed decreased levels of testosterone and other effects on steroidogenesis confirming an endocrine disrupting MoA of DEHP. The anti-androgenic related effects of DEHP that are evaluated to be relevant in humans include congenital malformations of the male reproductive organs, reduced semen quality and reduced male reproductive hormone levels. DEHP has been shown to affect the endocrine system of mammals primarily through *in vivo* studies on reduced fetal testosterone (ECHA, 2014).

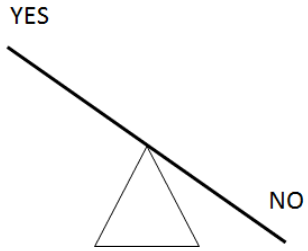
Reference	Type of study	Chemical under Investigation	Hormone(s) under Investigation	Description of Assay used	Results
(Morgan, Deoraj, Felty, & Roy, 2017)	Cross-sectional study: Females who participated in NHANES 2003-2010	PCBs, BPA and seven phthalates (MEP, MCPP, MZP, **DEHP**, MEHP,MEHHP, MEOHP)	Indirectly estrogen, via the diagnosis of breast cancer	Phthalates were measured in urine. Geometric means were calculated to compare levels of phthalates in women who self-reported a breast cancer diagnosis and those who reported never being diagnoses.	Risk of breast cancer was not significantly associated with phthalate concentrations or phthalate metabolites.
(Wang et al., 2016)	Cross-sectional study in 509 males from China	MMP, MEP, MBP, MBzP, **MEHP**, MEHHP, MEOHP, MOP	LH, FSH, testosterone, estradiol	Men provided 1 semen sample and 1 blood sample and 2 urine samples. Phthalates were measured in urine samples. Hormones were measured in serum. Semen parameters were measured.	MEHP was associated with a decrease in estradiol and testosterone. MEHP, MEHHP and MEOHP were associated with higher spermatozoa apoptosis and DNA damage
(Specht et al., 2014)	Cross-sectional study: Between 2002-2004, 938 pregnant women and 401 male spouses from Greenland, Poland and Ukraine	**DEHP metabolites** (MEHP, 5cx-MEPP, 5OH-MEHP, 5oxo-MEHP) and DiNP metabolites (MiNP, 7cx-MMeHP, 7OH-MMeOP, 7oxo-MMeOP)	Androgen and estrogen levels measured indirectly by calculating the time to pregnancy (TTP) and fecundability ratio (FR), which is the probability of conceiving during a time period within one group compared to the probability	Interviews were conducted to establish the TTP of each woman. Phthalates were measured in serum of both parents	In women with high levels of DEHP, the FR was slightly higher (suggesting a shorter TTP). In pregnant women from Greenland, high serum DiNP was associated with longer TTP. No significant adverse effects on couple fecundity.

Reference	Type of study	Chemical under Investigation	Hormone(s) under Investigation	Description of Assay used	Results
(Fong et al., 2015)	Cross-sectional study: 82 male plastic workers	**DEHP and metabolites**: MEHP, MEOHP, MEHHP	Testosterone, estradiol, FSH, LH	Hormones measured in plasma. DEHP metabolites were measured in urine. Aromatase activity was estimated by calculating the molar ratio of estrogen to testosterone.	Positive association between DEHP metabolites and estradiol and ratio of estradiol to testosterone. Positive association between the sum of DEHP metabolites and aromatase activity.

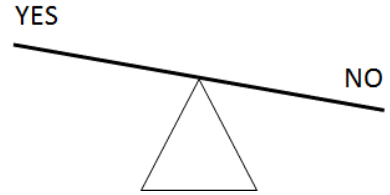
3. Expert panel

- The aim of this expert panel evaluation was **to categorize the most likely effect(s) or mechanism(s) of 24 EDCs as estrogenic, anti-estrogenic, androgenic and/or anti-androgenic** based on the current scientific evidence and personal expertise
- 7 Experts
  - International
  - Toxicology, environmental sciences and epidemiology

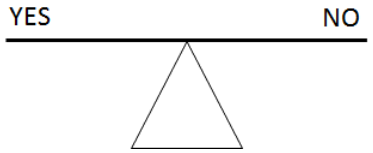
No
= there is no or very little evidence suggesting that there is such effect



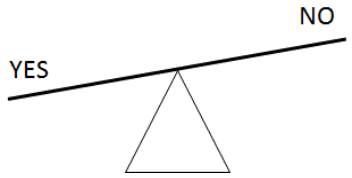
Unlikely
= given the weight of the evidence it is more likely than not that there is no the effect



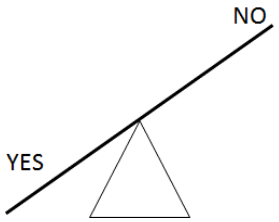
Possibly
= there is equal evidence for and against effect

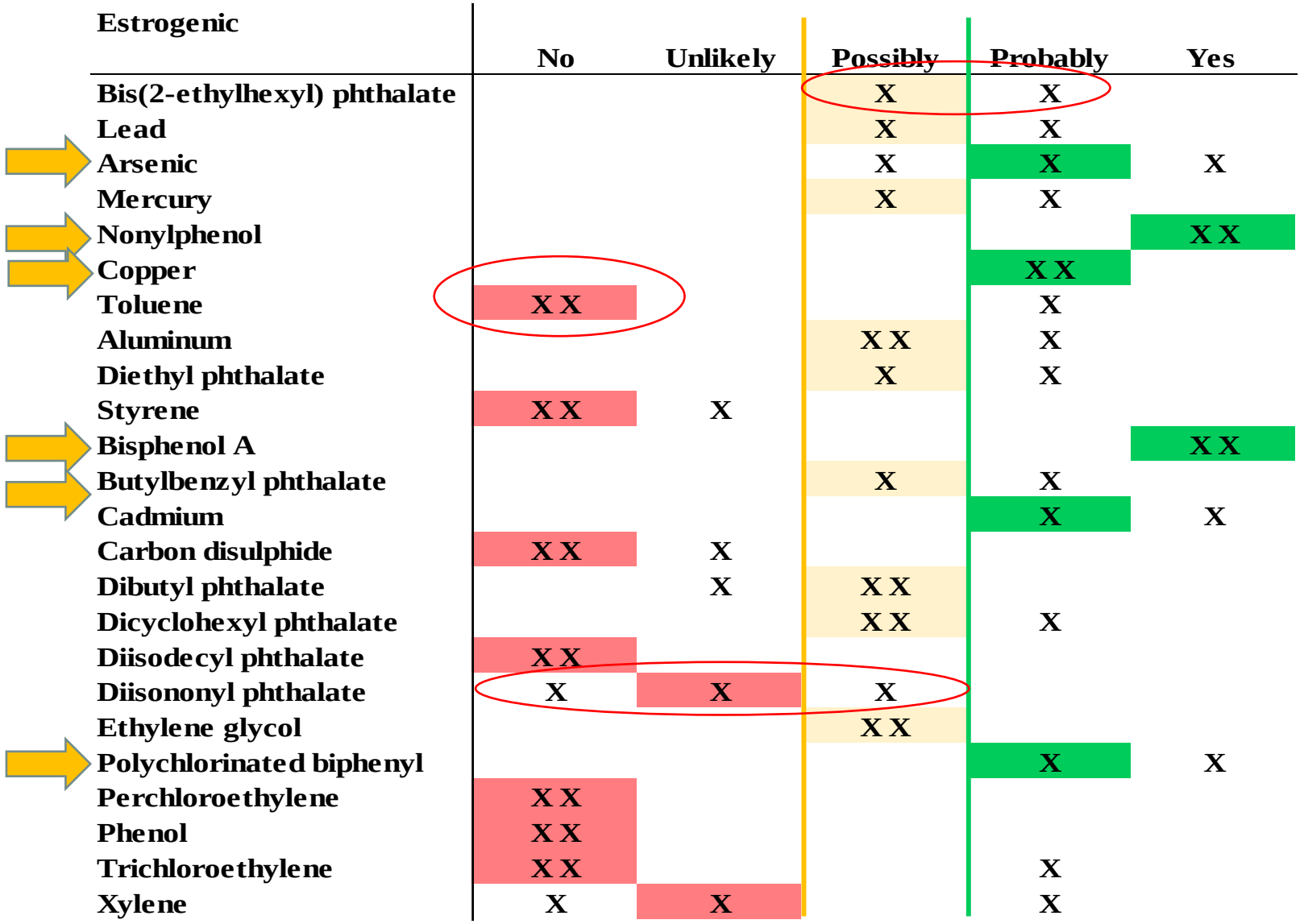


Probably
= given the weight of the evidence it is more likely than not that there is this effect



Yes
= there is strong evidence suggesting the effect




Estrogenic
No
Unlikely
Possibly
Probably
Yes
Bis(2-ethylhexyl) phthalate
Lead
Arsenic
Mercury
Nonylphenol
Copper
Toluene
Aluminum
Diethyl phthalate
Styrene
Bisphenol A
Butylbenzyl phthalate
Cadmium
Carbon disulphide
Dibutyl phthalate
Dicyclohexyl phthalate
Diisodecyl phthalate
Diisononyl phthalate
Ethylene glycol
Polychlorinated biphenyl
Perchloroethylene
Phenol
Trichloroethylene
Xylene

Agent	Estrogenic	Anti-estrogenic	Androgenic	Anti-Androgenic
Bis(2-ethylhexyl) phthalate	Possibly	No	No	Probably
Lead	Possibly	Probably	No	Yes
Arsenic	Probably	Probably	Unlikely	Yes
Mercury	Possibly	Unlikely	No	Possibly
Nonylphenol	Yes	No	Unlikely	Probably
Copper	Probably	No	No	Possibly
Toluene	No	Possibly	No	Probably
Aluminum	Possibly	Possibly	No	Possibly
Diethyl phthalate	Possibly	No	No	Possibly
Styrene	No	No	No	No
Bisphenol A	Yes	No	No	Probably
Butylbenzyl phthalate	Possibly	No	No	Yes
Cadmium	Probably	No	Probably	No
Carbon disulphide	No	Unlikely	No	Possibly
Dibutyl phthalate	Possibly	Unlikely	No	Yes
Dicyclohexyl phthalate	Possibly	Possibly	No	Yes
Diisodecyl phthalate	No	No	Unlikely	No
Diisononyl phthalate	Unlikely	Unlikely	Unlikely	Probably
Ethylene glycol	Possibly	No	No	No
Polychlorinated biphenyl	Probably	Probably	No	Possibly
Perchloroethylene	No	No	No	No
Phenol	No	No	No	No
Trichloroethylene	No	Unlikely	Unlikely	Possibly
Xylene	Unlikely	No	No	No

This manuscript was written in accordance with the instructions for authors provided by Environmental Health, a peer-reviewed journal.

Title:
A new tool to classify occupational exposures to endocrine disrupting chemicals by sex hormone function

Authors:
R. Prichystalova[1], E. Caron-Beaudoin[2], L. Richardson[3], Dirkx E.[3], A. Amadou[4], T. Zavodna[5], R. Cihak[6], V. Cogliano[7], J. Hynes[8], L. Pelland-St-Pierre[3], M.A. Verner[2,9], M. van Tongeren[10], V. Ho[3, 11]

3

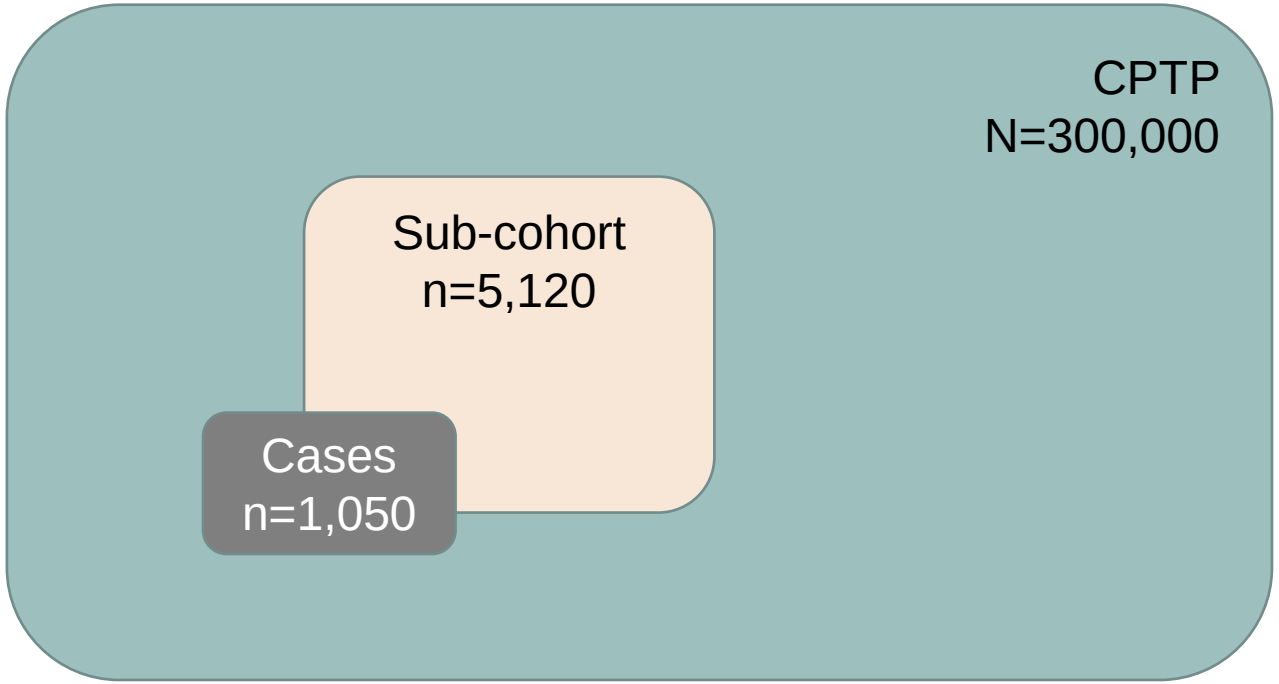
Apply the framework and assess occupational exposures to EDCs and the risk of developing colorectal cancer

Preliminary results from a CIHR-funded study on "Occupational exposures to endocrine disrupting chemicals and colorectal cancer risk" (PI: V. Ho)

Study Design

Canadian Partnership for Tomorrow Project (CPTP)

- **Case-cohort study**
  - 1,050 cases
  - 5,120 sub-cohort



Assessment of occupational exposure to EDCs using CANJEM

- All data from all participating cohorts of CPTP (except Ontario) have been received and job 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 17 potential EDCs
  - 11,849 cells consisting of 697 distinct 5-digit and 3-digit ISCO 1968 codes

EDC exposure parameterization

- **Probability of exposure:** percentage of jobs considered as exposed within a cell of CANJEM

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

EDC exposure parameterization by hormonal effect

- For example: Estrogenic
  - Select only agents that were evaluated as “yes” or “probably” estrogenic: arsenic, nonylphenol, copper, bisphenol A, butylbenzyl phthalate, polychlorinated biphenyl
  - For each agent, dichotomize into Never (<25% probability) vs. Ever Exposed (≥25% probability)

Estrogenic = (0/1) Arsenic + (0/1) Nonylphenol + (0/1) Copper….

Metrics	Categories	Probability of Exposure
Binary	Never	<25%
	Ever exposure to at least 1 “estrogenic agent”	≥25%
Categorical	Never	<25%
	Exposure to 1 “estrogenic agent”	≥25% to 1 agent
	Exposure to >1 “estrogenic agent”	≥25% to >1 agent

*No androgenic variable was created since cadmium was the only agent

Statistical approach

- Weighted Cox proportional hazards

- Minimally adjusted model: age, sex and cohort (random effects)
- Fully adjusted model: + BMI, ethnicity, education, income, smoking, alcohol consumption, family history of colorectal cancer, ever diagnosis of Crohn’s disease or colitis

Preliminary results

Covariates		% Cases (N=534)	% Sub-cohort (N=2450)
BMI	Underweight	1	1
	Normal	21	35
	≥Overweight	67	60
Ethnicity	White	74	84
	Asian or Other	5	11
Education	≤ High school	25	21
	Some postsecondary	32	41
	≥ Postsecondary	20	38
Income	10,000$ to < 50,000$	28	21
	50,000$ to < 100,000$	34	33
	≥ 100,000$	25	40
Smoking	Never smoker	68	67
	Past smoker	13	20
	Smoker	12	12
Alcohol consumption	Never drinker	9	1
	≤ Monthly drinker	22	30
	Weekly drinker	28	40
	≥ Nearly daily drinker	11	10
Family history of colorectal cancer	No	89	91
	Yes	11	9

Applying CANJEM to CPTP

Study Center	ISCO 68 5-digit	ISCO 68 3-digit	Not 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%

Top 5 most prevalent jobs in CPTP

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

Top 5 most prevalent jobs exposed to EDCs

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

Selected results: Any EDCs

Exposure variables		Any EDCs	
		Minimally Adjusted	Fully Adjusted
Binary exposure			
	Never	1.00 (ref)	1.00 (ref)
	Ever	1.04 (0.96 - 1.14)	0.94 (0.84 - 1.06)
Categorical exposure			
	Never	1.00 (ref)	1.00 (ref)
	Potential	0.63 (0.54 - 0.73)	1.30 (1.10 - 1.55)
	Ever	1.02 (0.93 - 1.11)	0.95 (0.84 - 1.06)
Substantial exposure			
	Never	1.00 (ref)	1.00 (ref)
	Potential	1.12 (1.06 - 1.18)	0.95 (0.90 - 1.01)
	Non-substantial	1.02 (0.85 - 1.22)	0.73 (0.57 - 0.93)
	Substantial	**1.15 (1.04 - 1.28)**	0.97 (0.85 - 1.10)

Selected results: Lead

Exposure variables		Fully Adjusted
Ever exposure		
	Never	1.00 (ref)
	Ever	0.94 (0.84 - 1.05)
Categorical exposure		
	Never	1.00 (ref)
	Potential	**1.34 (1.05 - 1.72)**
	Ever	0.94 (0.84 - 1.06)
Substantial exposure		
	Never	1.00 (ref)
	Potential	0.98 (0.93 - 1.04)
	Non-substantial	0.81 (0.64 - 1.04)
	Substantial	0.96 (0.85 - 1.09)

Selected results: Copper

Exposure variables		Fully Adjusted
Ever exposure		
	Never	1.00 (ref)
	Ever	**4.40 (2.69 - 7.21)**
Categorical exposure		
	Never	1.00 (ref)
	Potential	**1.67 (1.29 - 2.17)**
	Ever	**4.38 (2.68 - 7.17)**
Substantial exposure		
	Never	1.00 (ref)
	Potential	**0.58 (0.54 - 0.62)**
	Non-substantial	3.91 (0.54 - 28.26)
	Substantial	**3.76 (2.26 - 6.25)**

Selected results: Hormonal effect

Exposure variables		Estrogenic	Anti-estrogenic	Anti-androgenic
Ever exposure				
	Never	1.00 (ref)	1.00 (ref)	1.00 (ref)
	Ever	**2.62 (1.62 - 4.24)**	0.94 (0.84 - 1.05)	0.93 (0.83 - 1.04)
Categorical				
	Never	1.00 (ref)	1.00 (ref)	1.00 (ref)
	Exposure to 1 agent	**2.82 (1.69 - 4.70)**	0.94 (0.84 - 1.05)	0.93 (0.83 - 1.04)
	Exposure to >1 agent	1.66 (0.40 - 6.85)	-	0.42 (0.06 - 3.04)

Discussion

Summary

- Suggestive increased risk of colorectal cancer associated with:
  - Copper (but likely correlated with other agents)
  - Estrogenic agents

- Methodological considerations
  - Bias
  - Sample size

Future Directions

Within CPTP Study

- Addition of data from Ontario Health Study
- Exploration of metrics of exposure in CANJEM
- Use of EDC-JEM to assess occupational exposures
- Interactions by sex and menopausal status

- CANJEM-female

- Complementary study using UK-Biobank data
  - *To determine the association between occupational exposure to EDCs and sex hormone levels in the total population and, separately in men and women*

Acknowledgements

This research was supported by the Canadian Institutes of Health Research

- Co-PI: Jack Siemiatycki
- Co-Is:
  - Trevor Dummer
  - Will King
  - Anita Koushik
  - Jerome Lavoue
  - Marie-Helene Mayrand
  - Harriet Richardson
  - Marie-Pierre Sylvestre
  - Martie van Tongeren
- Staff
  - Lesley Richardson
- Trainees:
  - Laura Pelland-St Pierre
  - Romain Pasquet

Salary Support:

- Cancer Research Society, Fonds de recherche du Québec – Santé (FRQS) and Ministère de l'Économie, de la Science et de l'Innovation du Québec (MESI)

CRCHUM
CENTRE DE RECHERCHE

Exploring sex differences in the etiology of cancers: a critical look at endocrine disrupting chemicals in the workplace

Vikki Ho, PhD

Research Scientist/Assistant Professor

Université de Montréal