Modelling Exposure-response Relationships for Ionizing and Non-ionizing Radiation

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&
Risk Sciences International

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Outline

- A New Framework for Risk Science
- Key Characteristics of Human Carcinogens
- Ionizing Radiation
  - Sources of exposure
  - Medical uses of radiation
  - Occupational and environmental radiation exposures
  - Radiation hormesis: what do the data Indicate?
- Non-ionizing Radiation
  - Sources of exposure
  - Epidemiological studies of RF fields
- Risk Communication, Risk Perception and Risk Decision Making

The Next Generation Risk Science

Next Generation Risk Assessment

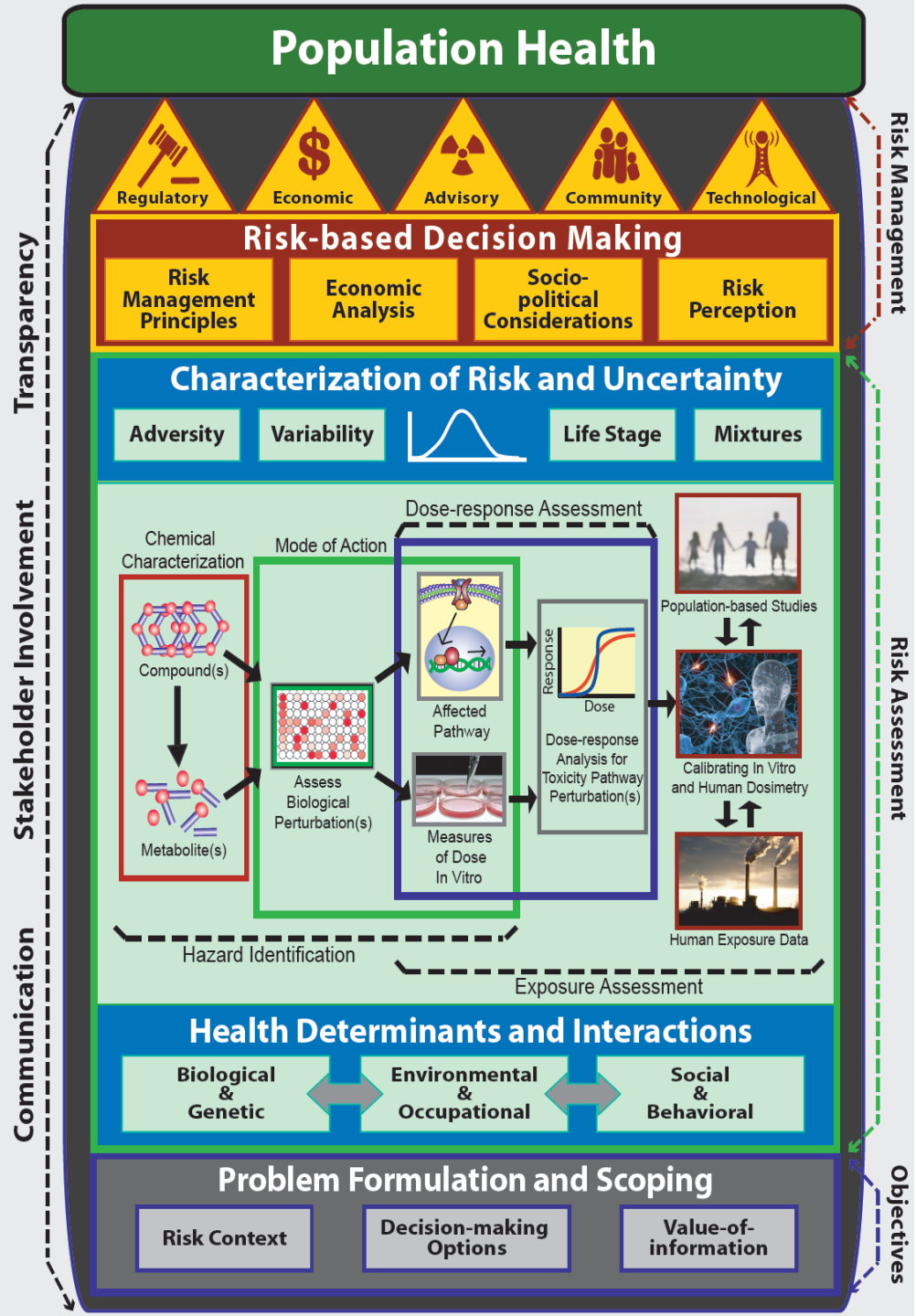
Review

All *EHP* content is accessible to individuals with disabilities. A fully accessible (Section 508–compliant) HTML version of this article is available at http://dx.doi.org/10.1289/ehp.1307260.

A Framework for the Next Generation of Risk Science

Daniel Krewski,[1,2] Margit Westphal,[1] Melvin E. Andersen,[3] Gregory M. Paoli,[2] Weihsueh A. Chiu,[4] Mustafa Al-Zoughool,[1] Maxine C. Croteau,[1] Lyle D. Burgoon,[4] and Ila Cote[4]

[1]McLaughlin Centre for Population Health Risk Assessment, University of Ottawa, Ottawa, Ontario, Canada; [2]Risk Sciences International, Ottawa, Ontario, Canada; [3]Institute for Chemical Safety Sciences, The Hamner Institutes for Health Sciences, Research Triangle Park, North Carolina, USA; [4]National Center for Environmental Assessment, U.S. Environmental Protection Agency, Washington, DC, USA

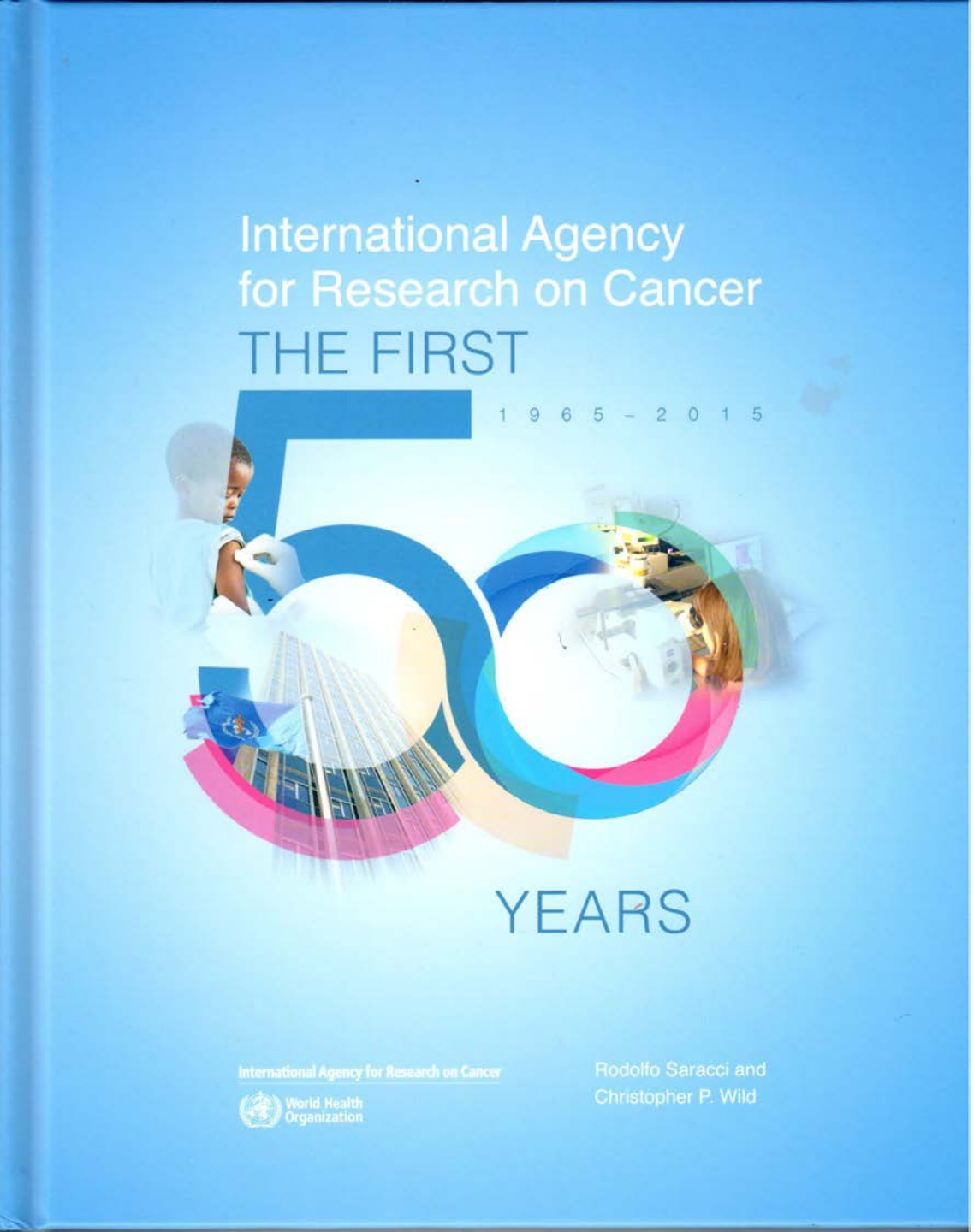


Three Cornerstones

- New paradigm for toxicity testing (TT21C), based on perturbation of toxicity pathways
- Advanced risk assessment methodologies, including those addressed in *Science and Decisions*
- Population health approach: multiple health determinants and multiple interventions

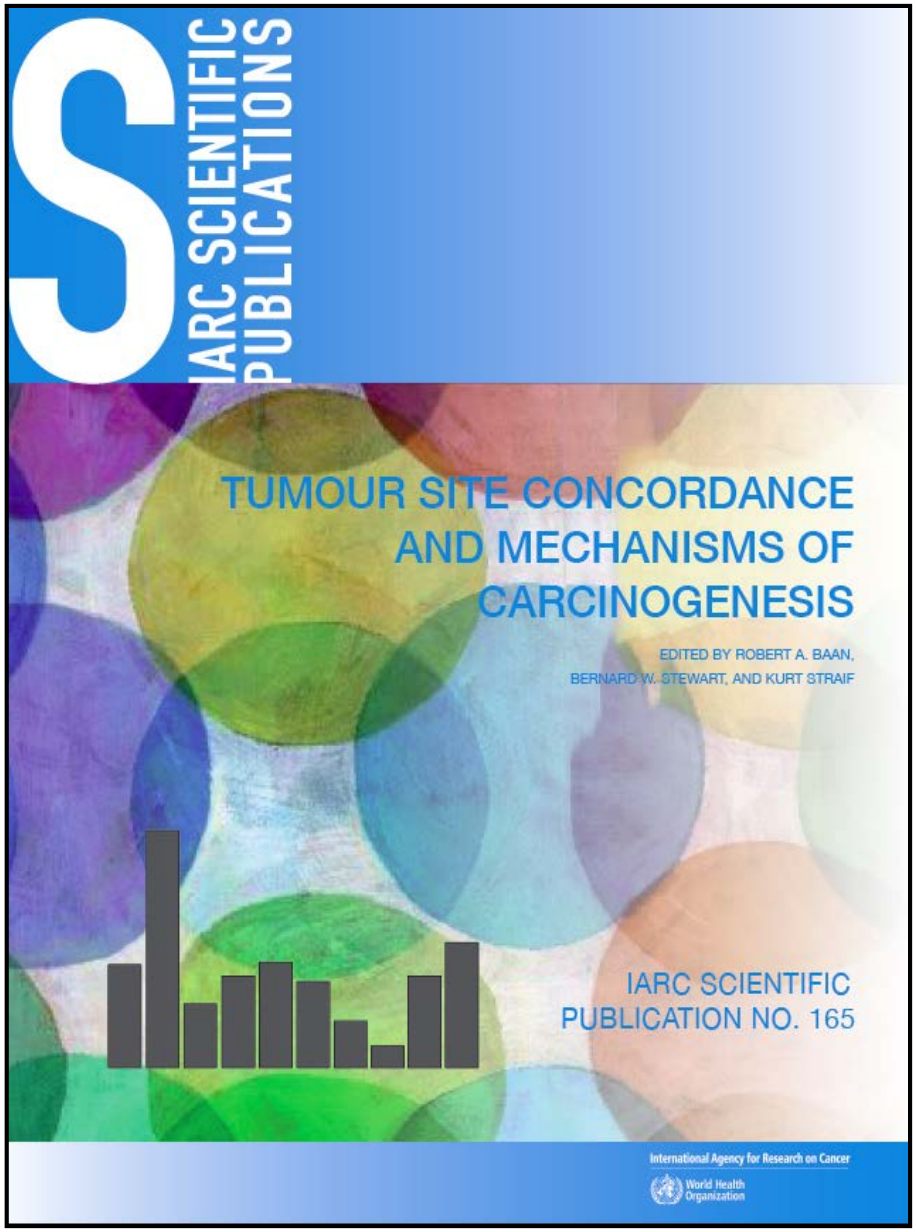
NexGen

Key Characteristics of Human Carcinogens



What can we learn about human cancer based on 50 years of cancer research?

IARC Scientific Publication No. 165



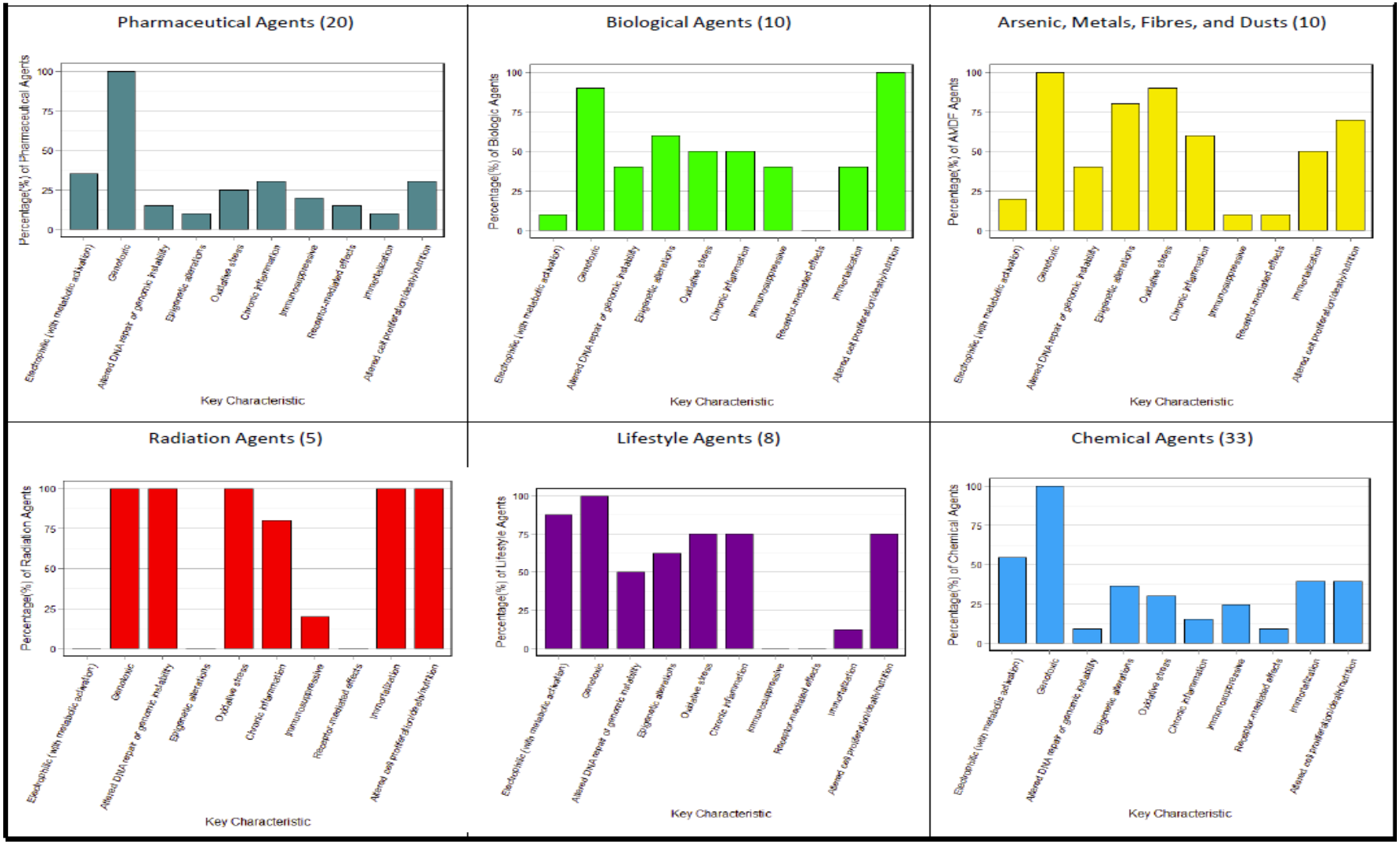
- *Twenty chapters prepared by workshop participants (9 on concordance and 11 on mechanisms)*
- *Five chapters by McLaughlin Centre investigators*
- *Consensus statement from workshop participants*

Group 1 Radiation Agents in Volumes 100A-F, 105, 106, 107 and 109

100 D	Radiation	18	Fission products including Sr-90; Haematite mining with exposure to radon (underground); Ionizing radiation (all types); Neutron radiation; Phosphorus-32, as phosphate; Pu-239; Radioiodines, including I-131; Internalized radionuclides that emit alpha particles; Internalized radionuclides that emit beta particles; Ra-224 and its decay products; Ra-226 and its decay products; Ra-228 and its decay products; Rn-222 and its decay products; Solar radiation; Th-232 (as Thorotrast); UV radiation (bandwidth 100-400 nm, encompassing UVC, UVB and UVA); UV-emitting tanning devices; X- and Gamma radiation

Radiation well-studied in humans and animals

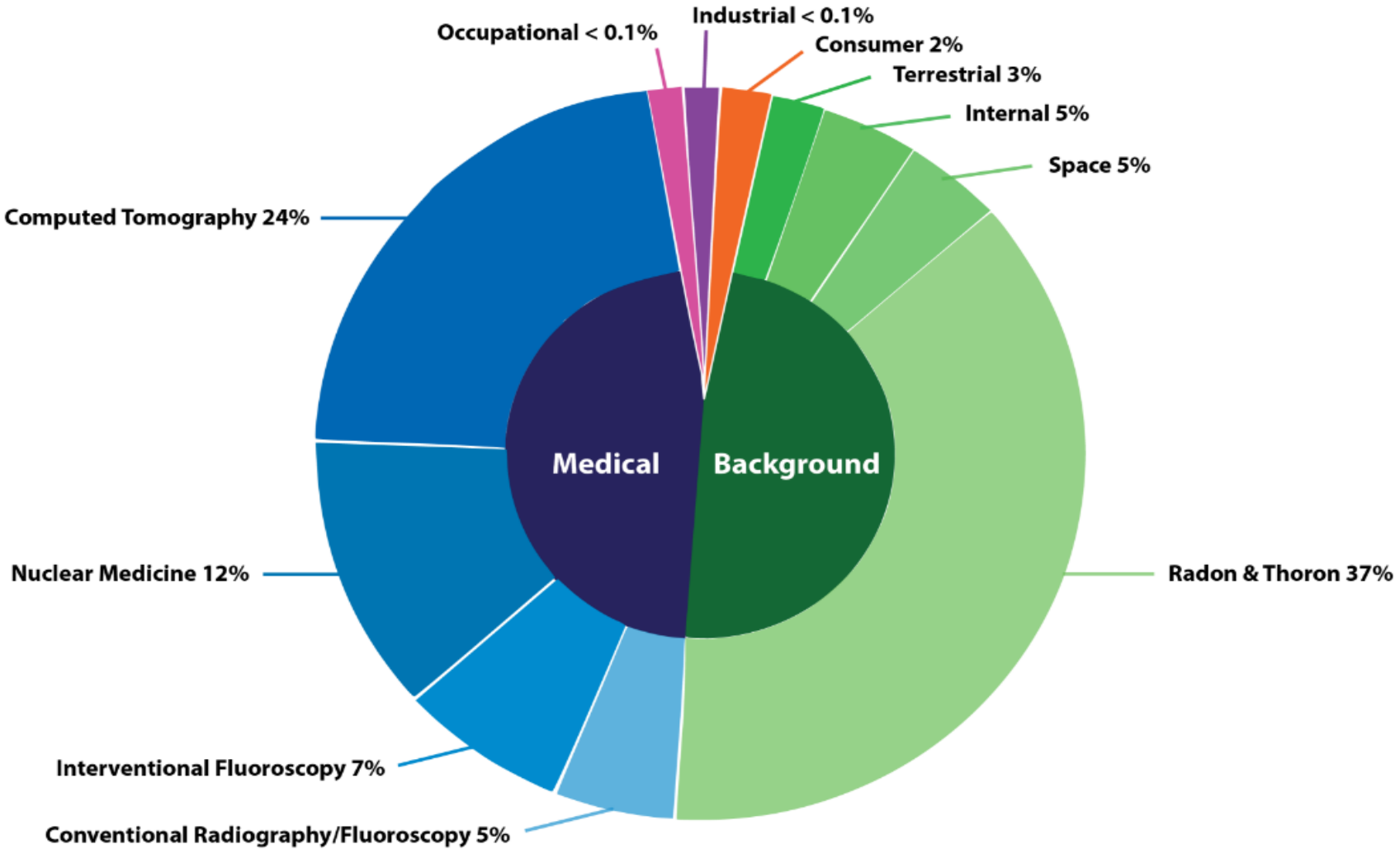
Key Characteristics of 86 Group-1 Agents by Type of Agent



Radiation agents have a distinct profile of key characteristics

Exposure to Ionizing Radiation

Exposure to Ionizing Radiation in the United States



https://www.epa.gov/radiation/radiation-sources-and-doses

Computed Tomography

Examination	Effective dose (mSv)
Head CT	2
Chest CT	7
Abdomen CT	8
Pelvis CT	6
Coronary artery calcification CT	3
Coronary CT angiogram	16

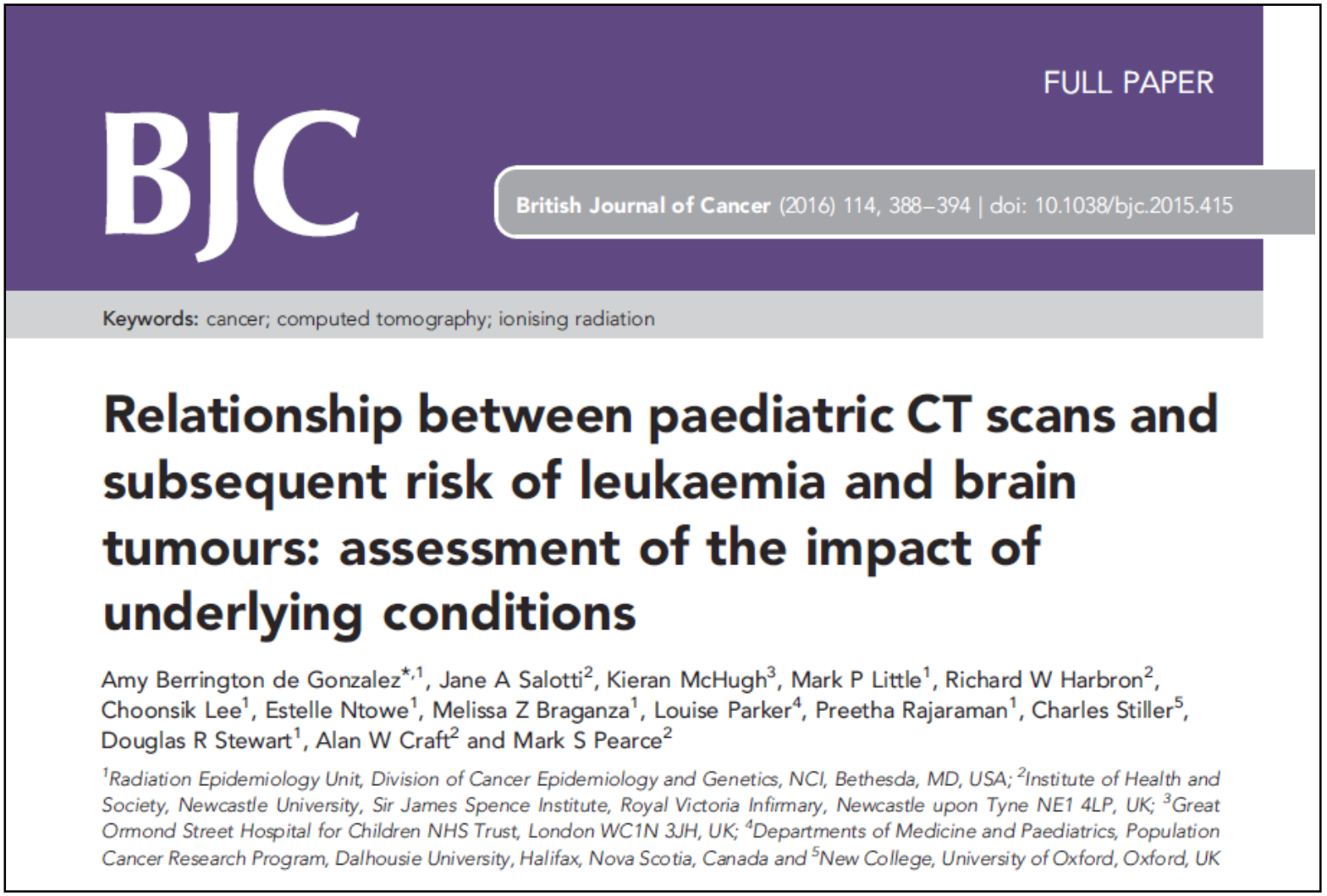
C. H. McCollough, J. T. Bushberg, J. G. Fletcher, and L. J. Eckel. Answers to Common Questions About the Use and Safety of CT Scans. Mayo.Clin.Proc. 90 (10):1380-1392, 2015.

“Answers to Common Questions About the Use of CT Scans”

1. How is radiation dose in CT quantified?
2. How much radiation does CT use?
3. How much radiation is dangerous?
4. Is there any direct evidence that CT scans cause cancer?
5. Are estimates of how many people exposed to CT will die of radiation-induced cancer accurate?
6. Children are much more sensitive to radiation than are adults: is it appropriate to use examinations like CT in children?
7. What is being done to lower radiation exposures and why?
8. Why do the doses provided in radiation reports vary so much?
9. At what point does the cumulative dose from repeated examinations become dangerous? Should previous examinations be considered when ordering new examinations?
10. Should I order examinations that use lower doses of radiation (such as chest radiographs) or nonionizing radiation (such as ultrasound and magnetic resonance imaging) rather than CT scans?
11. What important points should I consider discussing with patients concerned about radiation exposure?

C. H. McCollough et al. Mayo.Clin.Proc. 90 (10):1380-1392, 2015.

“Is there any direct evidence that CT scans cause cancer?”



FULL PAPER

BJC

British Journal of Cancer (2016) 114, 388–394 | doi: 10.1038/bjc.2015.415

Keywords: cancer; computed tomography; ionising radiation

Relationship between paediatric CT scans and subsequent risk of leukaemia and brain tumours: assessment of the impact of underlying conditions

Amy Berrington de Gonzalez*[,1], Jane A Salotti[2], Kieran McHugh[3], Mark P Little[1], Richard W Harbron[2], Choonsik Lee[1], Estelle Ntowe[1], Melissa Z Braganza[1], Louise Parker[4], Preetha Rajaraman[1], Charles Stiller[5], Douglas R Stewart[1], Alan W Craft[2] and Mark S Pearce[2]

[1]Radiation Epidemiology Unit, Division of Cancer Epidemiology and Genetics, NCI, Bethesda, MD, USA; [2]Institute of Health and Society, Newcastle University, Sir James Spence Institute, Royal Victoria Infirmary, Newcastle upon Tyne NE1 4LP, UK; [3]Great Ormond Street Hospital for Children NHS Trust, London WC1N 3JH, UK; [4]Departments of Medicine and Paediatrics, Population Cancer Research Program, Dalhousie University, Halifax, Nova Scotia, Canada and [5]New College, University of Oxford, Oxford, UK

“ . . . increased cancer risk after low-dose radiation exposure from CT scans in young patients.”

Occupational Radiation Exposure

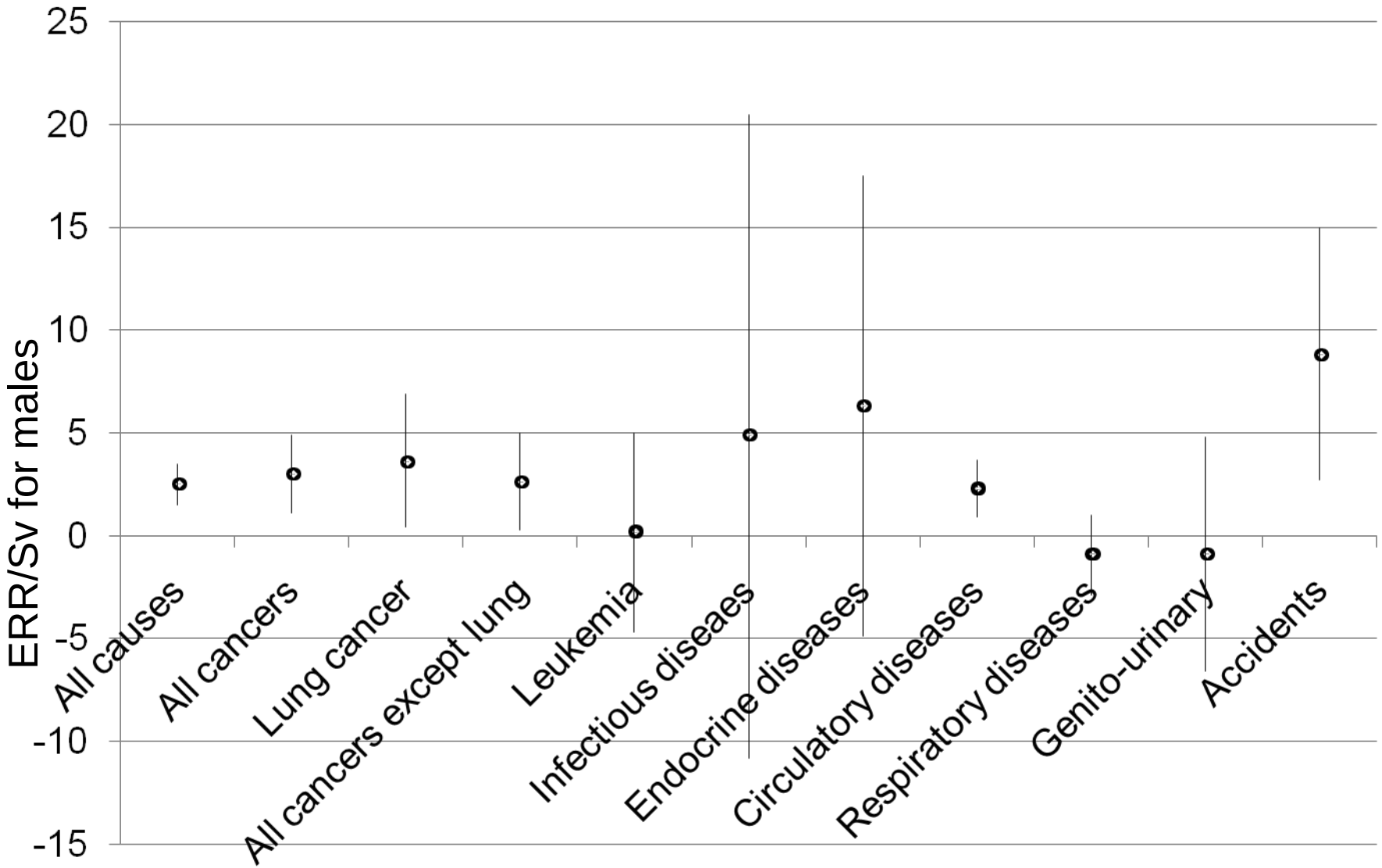
National Dose Registry of Canada

American Journal of Epidemiology
Vol. 148, No. 6
Printed in U.S.A.

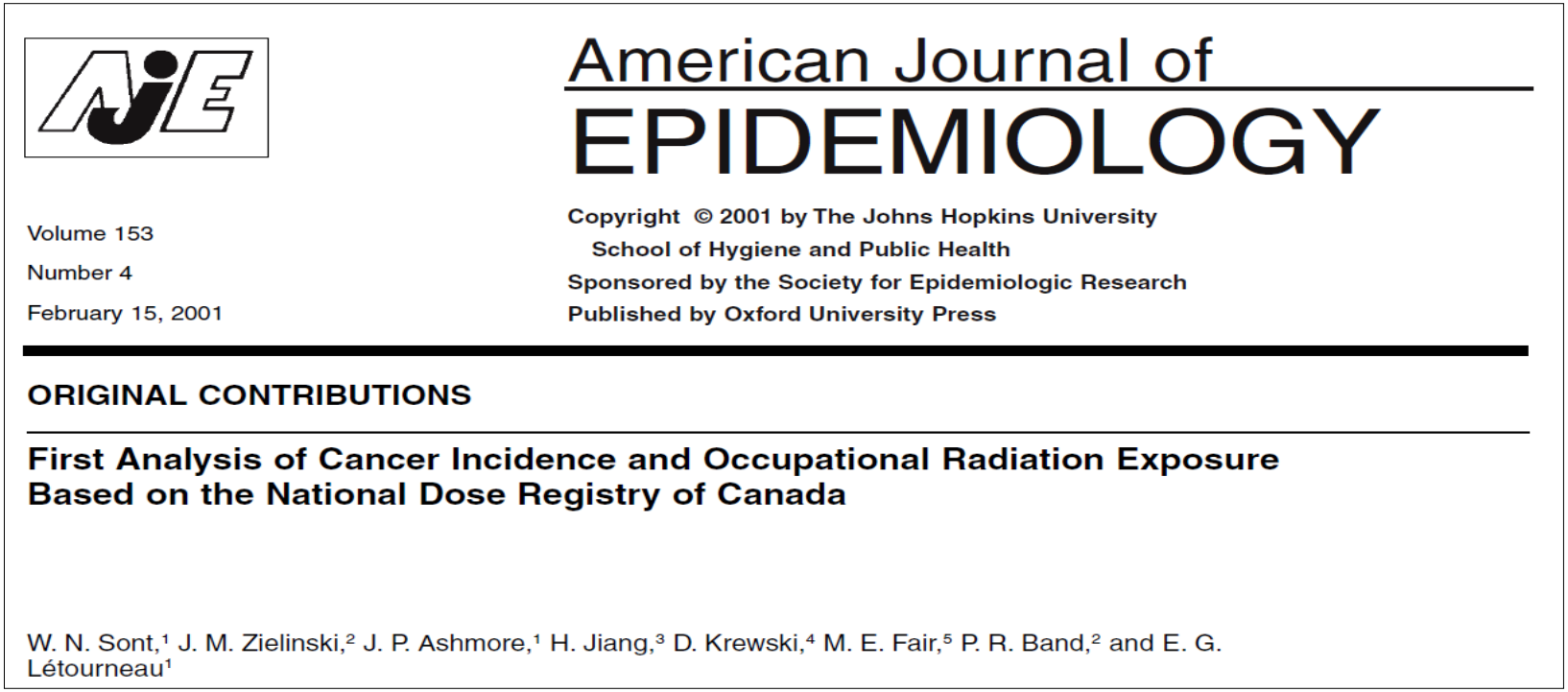
First Analysis of Mortality and Occupational Radiation Exposure based on the National Dose Registry of Canada

J. P. Ashmore,[1] D. Krewski,[2,3] J. M. Zielinski,[2] H. Jiang,[4] R. Semenciw,[2] and P. R. Band[2]

- 206, 620 workers (105,456 males and 101,164 females) monitored between 1951 and 1983
- Average cumulative dose 6.3 mSv
- Mortality follow-up 1951-1987
- 5,426 deaths; 1,632 cancer deaths


25
20
15
10
5
0
-5
-10
-15
ERR/Sv for males
All causes
All cancers
Lung cancer
All cancers except lung
Leukemia
Infectious diseaes
Endocrine diseases
Circulatory diseases
Respiratory diseases
Genito-urinary
Accidents

National Dose Registry of Canada



American Journal of
EPIDEMIOLOGY

Volume 153
Number 4
February 15, 2001

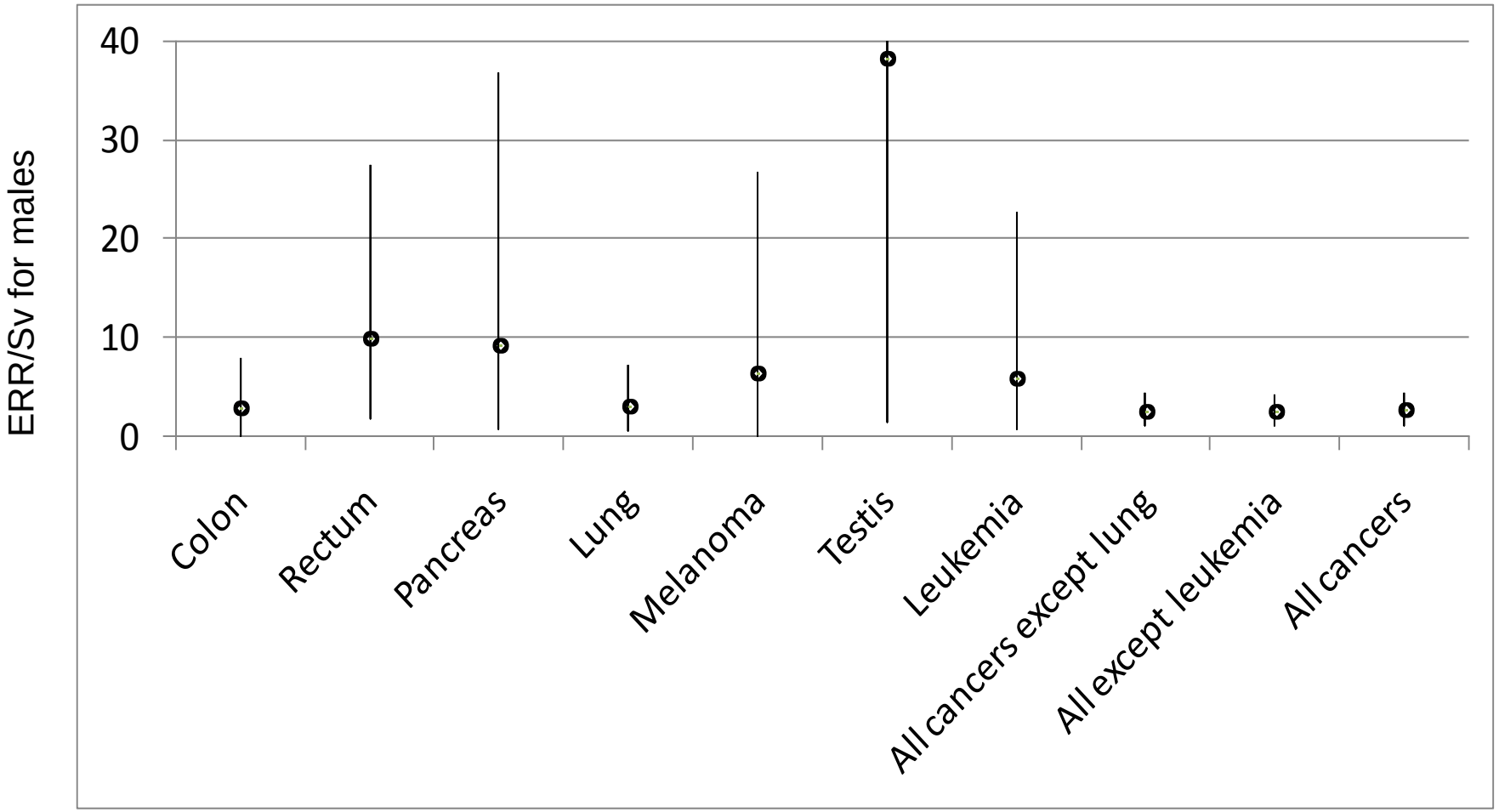
Sponsored by the Society for Epidemiologic Research
Published by Oxford University Press

ORIGINAL CONTRIBUTIONS

First Analysis of Cancer Incidence and Occupational Radiation Exposure Based on the National Dose Registry of Canada

W. N. Sont,[1] J. M. Zielinski,[2] J. P. Ashmore,[1] H. Jiang,[3] D. Krewski,[4] M. E. Fair,[5] P. R. Band,[2] and E. G. Létourneau[1]

- 191,333 workers (95,643 males and 95,690 females) monitored between 1969 and 1983
- Cancer incidence data for the period 1969-1988
- 3,737 cancer cases


ERR/Sv for males
40
30
20
10
0
Colon
Rectum
Pancreas
Lung
Melanoma
Testis
Leukemia
All cancers except lung
All except leukemia
All cancers

Decreases in Occupational Exposure to Ionizing Radiation among Canadian Dental Workers

• Jan M. Zielinski, PhD •
• Michael J. Garner, MSc •
• Daniel Krewski, PhD •
• J. Patrick Ashmore, PhD •
• Pierre R. Band, MD •
• Martha E. Fair, MSc •
• Huixa Jiang, PhD •
• Ernest G. Letourneau, MD •
• Robert Semenciw, MSc •
• Willem N. Sont, PhD •

J Can Dent Assoc 2005; 71(1):29–33

- 42,175 dental workers (9,051 males and 33,124 females)
- Study period 1951-1987 for mortality and 1969-1987 for cancer incidence
- 558 deaths from all causes and 656 incident cases of cancer

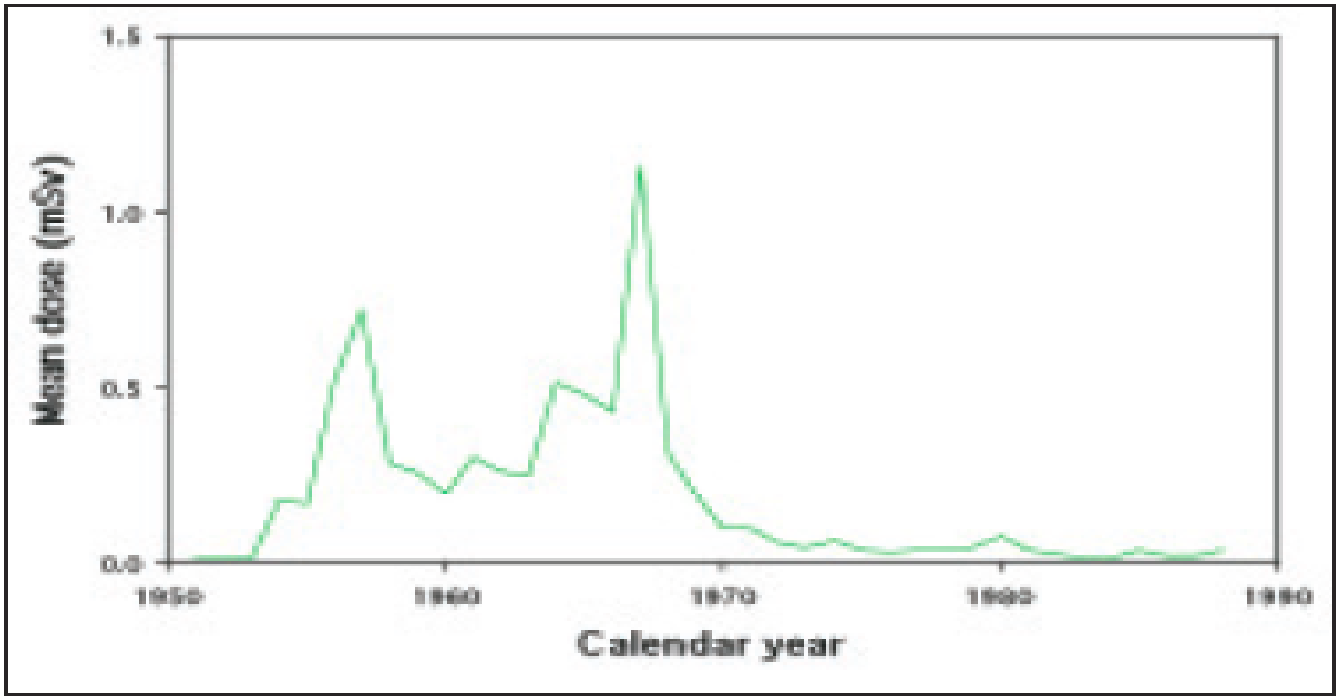


Figure 2: *Mean annual radiation dose received by dental workers in the National Dose Registry between 1951 and 1987.*

Average annual exposure to Canadian dental workers has decreased markedly in recent decades

Radiation Hormesis

DRCA: Database of Radiogenic Caner in Animals

Journal of Toxicology and Environmental Health, Part B, 15:186–209, 2012

ISSN: 1093-7404 print / 1521-6950 online
DOI: 10.1080/10937404.2012.659136

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DATABASE OF RADIOGENIC CANCER IN EXPERIMENTAL ANIMALS EXPOSED TO LOW DOSES OF IONIZING RADIATION

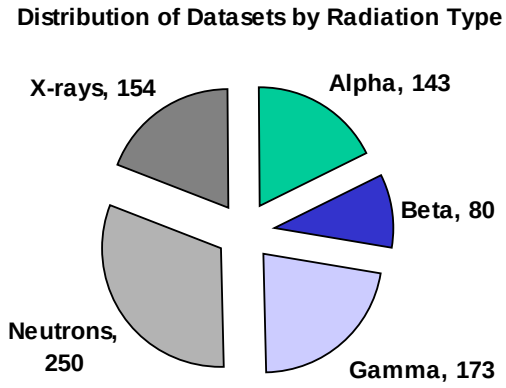
Philippe Duport[1], Huixia Jiang[2], Natalia S. Shilnikova[2], Daniel Krewski[2,3], Jan M. Zielinski[3,4]

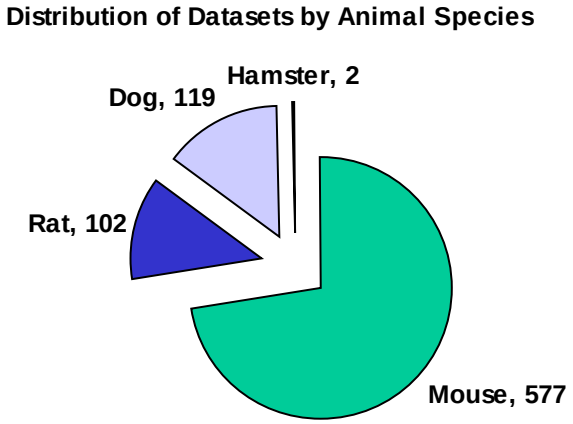
[1]Institute of the Environment, University of Ottawa, Ottawa, Ontario, Canada
[2]McLaughlin Centre for Population Health Risk Assessment, University of Ottawa, Ottawa, Ontario, Canada
[3]Department of Epidemiology and Community Medicine, Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada
[4]Environment Health Science and Research Bureau, Health Canada, Ottawa, Ontario, Canada

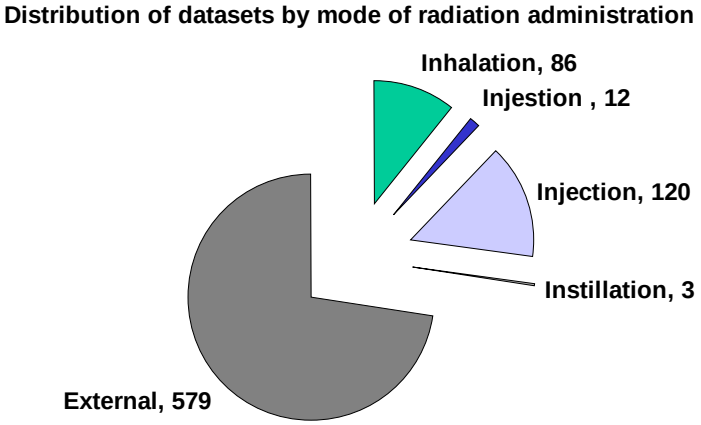
Characteristics of the Database

A comprehensive database contains data from 262 experiments:

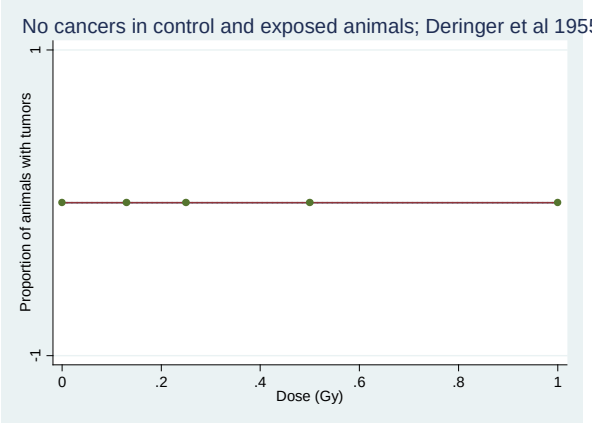
- 800 datasets on the incidence of specific tumours;
- 87,982 exposed animals;
- 37,111 control animals.

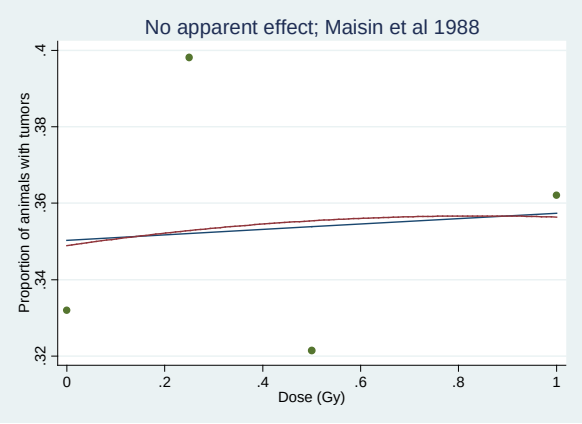


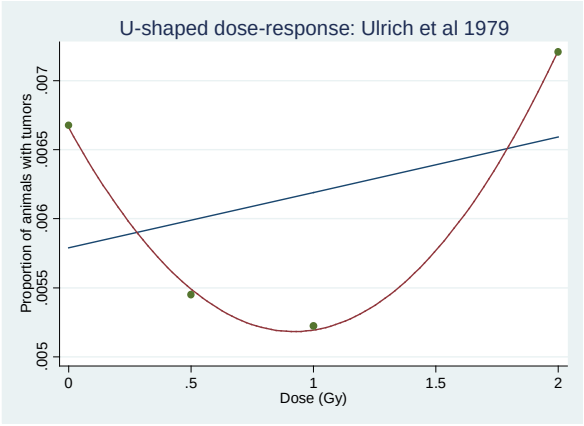


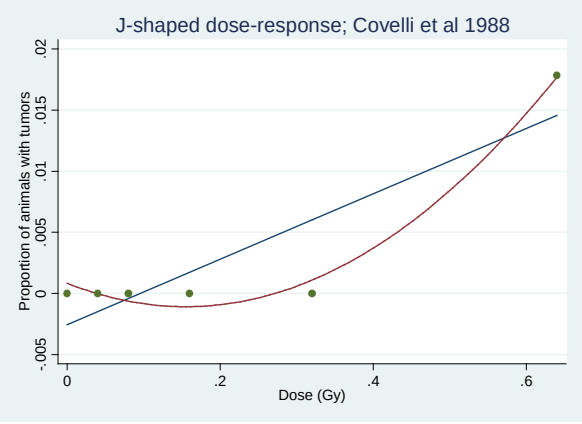


Examples of Dose-Response with No Evidence of an Effect or a Decrease in Cancer Incidence at Low Doses



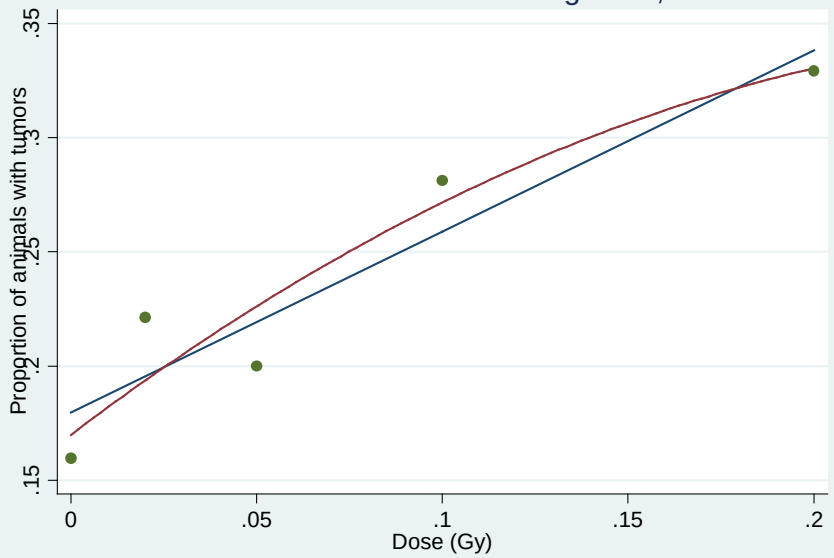




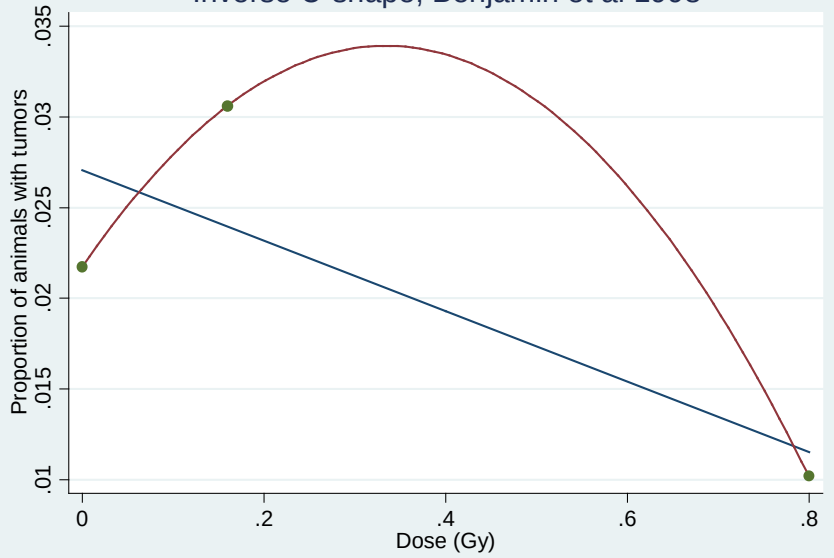


Examples of Dose-Response with Some Evidence of a Radiation Effect at Low Doses

Cancer incidence increases with increasing dose; Ulrich et al 1984



Inverse U-shape; Benjamin et al 1998



Numbers of Datasets with Various Dose-Response Shapes

Type of dose-response	Number of datasets (%)
U-shape	245
J-shape	98
No apparent effect	127
No cancers in exposed and control animals	42
Total with no evidence of an effect or a decrease in cancer incidence at low doses	512 (64%)
Increase in cancer incidence with dose	214
Inverse U-shaped	74
Total with some evidence of a radiation effect at low doses	288 (36%)
Total	800 (100%)

Meta-analysis of the DRCA: What is the Empirical Evidence for Radiation Hormesis?

Journal of Toxicology and Environmental Health, Part B, 15:210–231, 2012

ISSN: 1093-7404 print / 1521-6950 online
DOI: 10.1080/10937404.2012.659140

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A META-ANALYSIS OF EVIDENCE FOR HORMESIS IN ANIMAL RADIATION CARCINOGENESIS, INCLUDING A DISCUSSION OF POTENTIAL PITFALLS IN STATISTICAL ANALYSES TO DETECT HORMESIS

Kenny S. Crump[1], Philippe Duport[2], Huixia Jiang[3], Natalia S. Shilnikova[3], Daniel Krewski[3,4], Jan M. Zielinski[4,5]

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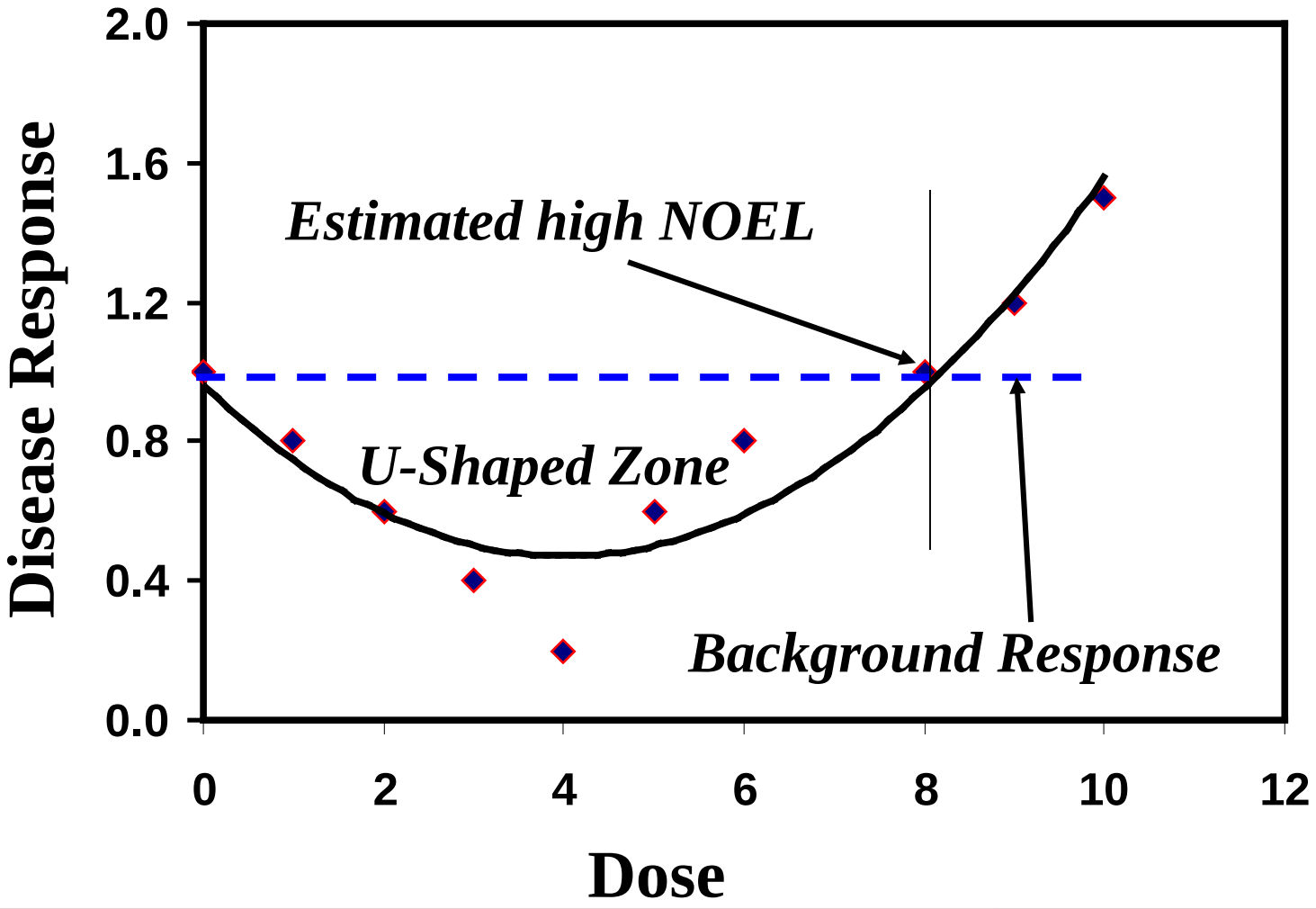
[2]International Centre for Low Dose Radiation Research, Institute of the Environment, University of Ottawa, Ottawa, Ontario, Canada
[3]McLaughlin Centre for Population Health Risk Assessment, University of Ottawa, Ottawa, Ontario, Canada
[4]Department of Epidemiology and Community Medicine, Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada
[5]Environment Health Science and Research Bureau, Health Canada, Ottawa, Ontario, Canada

Defining a U-Shaped Dose-response Relationship (Hunt-Bowman Quadratic Model Below NOEL)

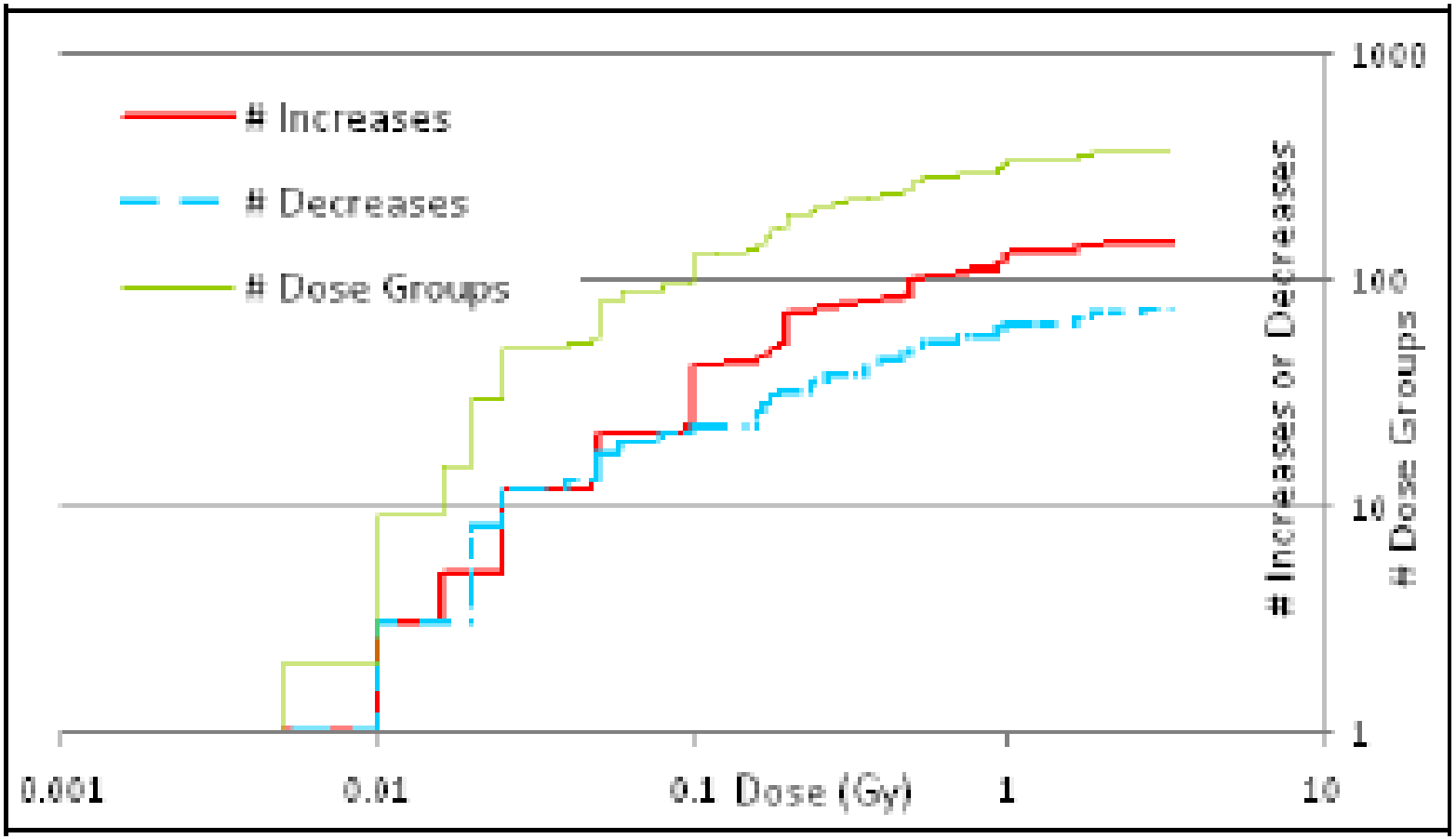


Examine Empirical Evidence for Hormesis

Under the hypothesis of hormesis, an excess of decreased tumour responses at low doses would be expected: *the DRCA provides an opportunity to compare the observed number of decreases and increases in tumour response at low doses*

Compare Increases and Decreases in Risk at Low Doses

D: Neutron



Similar results for A: Alpha; B: Beta; C: Gamma; and E: X-ray

Conclusions from Meta-analysis

- The meta-analysis of this large database of radiation tumourigenesis experiments in animals provides limited evidence of hormesis

- This finding should not be interpreted as providing strong evidence against the hypothesis of radiation hormesis, since the power to detect a hormetic effect in the currently available animal carcinogenicity literature is limited by the moderately small number of studies with data points in the low dose range

Occupational Exposure to Radon

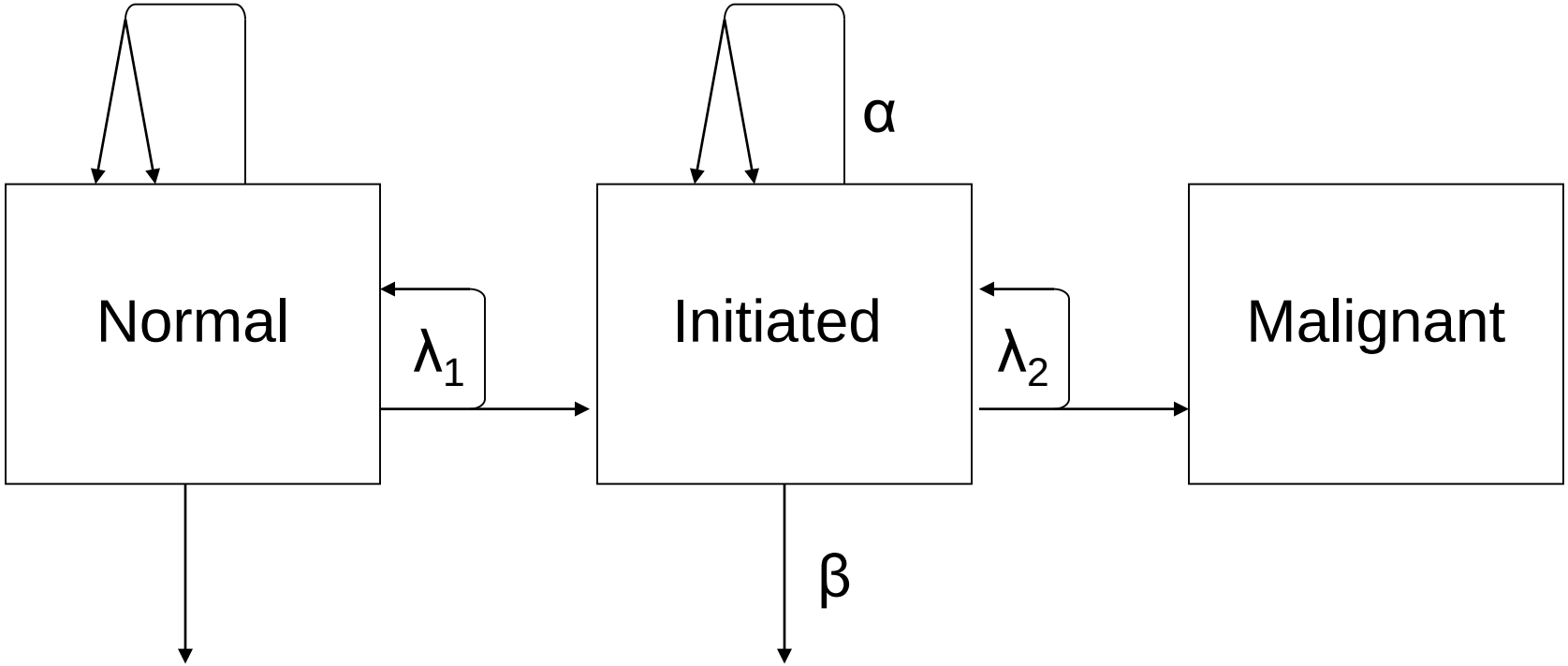
Modeling Lung Cancer Risks in Colorado Uranium Miners Exposed to Radon

Radon, Cigarette Smoke, and Lung Cancer: A Re-analysis of the Colorado Plateau Uranium Miners' Data

Suresh H. Moolgavkar,[1] E. Georg Luebeck,[1] Daniel Krewski,[2] and Jan M. Zielinski[2]

S. H. Moolgavkar, G. Luebeck, D. Krewski, and J. M. Zielinski. Radon, cigarette smoke, and lung cancer: a reanalysis of the Colorado plateau uranium miners' data. *Epidemiology 4:204-217, 1993*.

Two-stage Clonal Expansion Model of Carcinogenesis



Model Parameters to be Estimated

Mutation Rates

$$\lambda_1 = \nu(d_s, d_r) = a_0 + a_s d_s + a_r d_r$$

$$\lambda_2 = \mu(d_s, d_r) = b_0 + b_s d_s + b_r d_r$$

Promotion

$$\delta = (\alpha - \beta)(d_s, d_r) = c_0 + c_{s1}(1 - \exp[-c_{s2} d_s]) + c_{r1}(1 - \exp[-c_{r2} d_r])$$

and β/α = constant

Parameter	Estimate	Standard Error
$a_0=b_0$	$1.11*10^{-7}$	$2.14*10^{-8}$
a_s	$1.44*10^{-8}$	$5.70*10^{-9}$
a_r	$2.51*10^{-8}$	$1.44*10^{-8}$
c_0	$1.10*10^{-1}$	$7.41*10^{-3}$
c_{s1}	$4.93*10^{-2}$	$9.28*10^{-3}$
c_{s2}	$1.67*10^{-1}$	$8.15*10^{-2}$
c_{r1}	$4.16*10^{-1}$	$6.42*10^{-2}$
c_{r2}	$7.09*10^{-2}$	$1.82*10^{-2}$
β/α	$9.93*10^{-1}$	$1.80*10^{-3}$

No effect of radon or smoking on the second stage ($b_s=b_\gamma=0$)

Interaction Between Radon and Tobacco Smoke In Colorado Uranium Miners Data

Radon[a] WLM/m	Tobacco[b] Cigarette/day	Relative Risk for Radon	Relative Risk For Tobacco	At Age=60 Combined
1.0	10	1.3	5.3	6.4
1.0	30	1.3	10.0	12.0
1.0	40	1.3	11.6	14.1
50.0	10	12.3	5.3	26.6
50.0	30	12.3	10.0	44.1
50.0	40	12.3	11.6	52.0

a. Exposure to radon between 30 and 40 years of age
b. Cigarette smoking between 25 and 60 years of age

Application of Two-stage Model to the National Dose Registry of Canada

Journal of Toxicology and Environmental Health, Part A, 69:1013–1038, 2006

ISSN: 1528–7394 print / 1087–2620 online
DOI: 10.1080/00397910500360202

Taylor & Francis

BIOLOGICALLY BASED ANALYSIS OF LUNG CANCER INCIDENCE IN A LARGE CANADIAN OCCUPATIONAL COHORT WITH LOW-DOSE IONIZING RADIATION EXPOSURE, AND COMPARISON WITH JAPANESE ATOMIC BOMB SURVIVORS

William D. Hazelton[1], Suresh H. Moolgavkar[1], Stanley B. Curtis[1], Jan M. Zielinski[2], J. Patrick Ashmore[3], Daniel Krewski[4]

[1]Fred Hutchinson Cancer Research Center, Seattle, Washington, USA
[2]Healthy Environments and Consumer Safety Branch, Health Canada, Ottawa, Ontario, and Department of Epidemiology and Community Medicine, Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada
[3]Radiation Protection Bureau, Health Canada, Ottawa, Ontario, Canada
[4]Department of Epidemiology and Community Medicine, Faculty of Medicine, University of Ottawa, Ottawa, Ontario, and McLaughlin Centre for Population Health Risk Assessment, University of Ottawa, Ottawa, Ontario, Canada

Useful in describing temporal patterns of exposure and risk, and in demonstrating compatibility with atomic bomb survivors

Residential Exposure to Radon

Early Large-scale Case-control Study

American Journal of Epidemiology
Vol. 140, No. 4
Printed in U.S.A.

ORIGINAL CONTRIBUTIONS

Case-Control Study of Residential Radon and Lung Cancer in Winnipeg, Manitoba, Canada

E. G. Létourneau,[1] D. Krewski,[1,2] N. W. Choi,[3,4] M. J. Goddard,[1] R. G. McGregor,[1] J. M. Zielinski,[1] and J. Du[3]

750 cases-control pairs
in city with highest radon levels in Canada
with multiple one year integrated radon measurements in all homes

TABLE 4. Odds ratios for residential radon exposure and lung cancer based on cumulative radon exposure in all residences occupied: Winnipeg, Manitoba, Canada, 1992

Area monitored and cumulative radon exposure (Bq/m³-years)	All participants				At least 75% coverage*			
	No. of cases	No. of controls	OR†,‡	95% CI†	No. of cases	No. of controls	OR	95% CI
5–30 years before enrollment in the study								
Bedroom								
0–1,800	92	84	1.0		51	38	1.0	
1,801–3,600	488	453	0.97	0.63–1.48	93	102	0.61	0.31–1.22
3,601–7,200	118	153	0.84	0.51–1.39	64	68	0.76	0.37–1.56
≥7,201	40	48	1.00	0.69–1.46	19	19	1.56	0.92–2.66
Basement								
0–2,800	108	93	1.0		52	44	1.0	
2,801–5,600	494	487	0.82	0.55–1.22	109	115	0.76	0.42–1.37
5,601–11,200	106	113	0.85	0.51–1.41	49	46	0.90	0.43–1.89
≥11,201	30	45	0.60	0.42–0.86	17	22	1.03	0.65–1.62

Large case-control study with extensive exposure monitoring fails to identify lung cancer risk

Residential Radon and Lung Cancer

ORIGINAL ARTICLE

Epidemiology (2005), V16, pp. 137-145

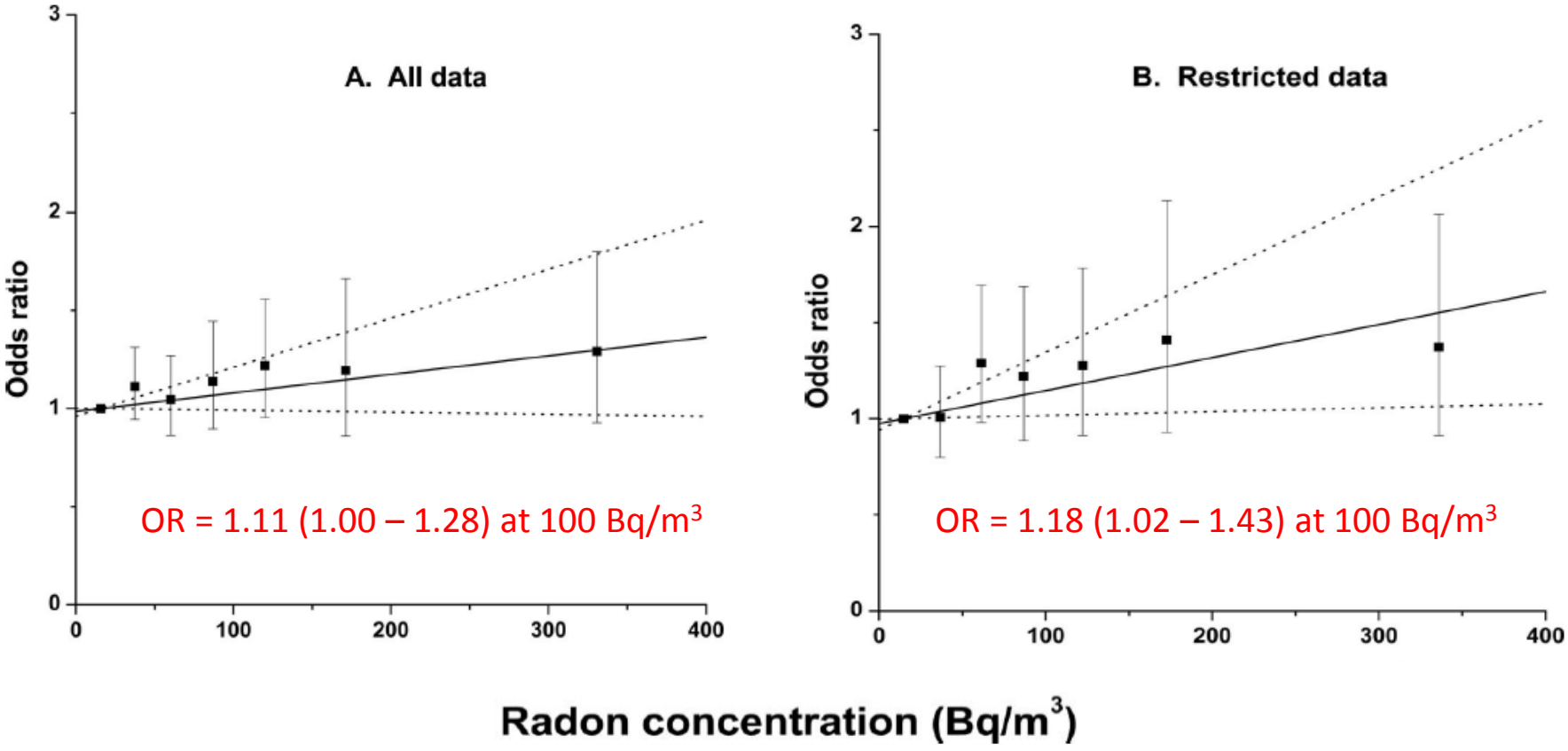
Residential Radon and Risk of Lung Cancer

A Combined Analysis of 7 North American Case-Control Studies

Daniel Krewski,[*] Jay H. Lubin,[†] Jan M. Zielinski,[‡] Michael Alavanja,[§] Vanessa S. Catalan,[‖] R. William Field,[**¶] Judith B. Klotz,[††] Ernest G. Létourneau,[‡‡] Charles F. Lynch,[¶] Joseph I. Lyon,[§§] Dale P. Sandler,[‖‖] Janet B. Schoenberg,[††] Daniel J. Steck,[¶¶] Jan A. Stolwijk,[***] Clarice Weinberg,[†††] and Homer B. Wilcox[††]*

Combining data from multiple studies identifies lung cancer risk

Exposure-response Relationships for Radon and Lung Cancer



Reducing measurement error increases lung cancer risk estimate

Large-scale Cohort Study of Residential Radon

Published OnlineFirst January 6, 2011; DOI:10.1158/1055-9965.EPI-10-1153

Cancer Epidemiology, Biomarkers & Prevention

Research Article

Radon and Lung Cancer in the American Cancer Society Cohort

Michelle C. Turner[1,2], Daniel Krewski[2,3,4], Yue Chen[3], C. Arden Pope III[5], Susan Gapstur[6], and Michael J. Thun[6]

811,961 participants in American Cancer Society CPS-II Study, With radon exposure based on county level radon surveys

Table 3. Adjusted HRs (95% CIs) for lung cancer mortality in relation to mean county-level residential radon concentrations (LBL; Bq/m^3) at enrollment (1982), follow-up 1982–1988, CPS-II cohort, United States

Radon concentration (Bq/m^3)	Lung cancer deaths	Person-years	Death rate[a]	Minimally adjusted HR (95% CI)[b]	Fully adjusted HR (1) (95% CI)[c]	Fully adjusted HR (2) (95% CI)[d]
Categorical						
<25	856	1,062,216.23	77.79	1.00	1.00	1.00
25-<50	1,312	1,767,001.74	75.59	0.97 (0.89–1.06)	0.96 (0.88–1.04)	1.01 (0.90–1.13)
50-<75	632	863,881.31	74.09	0.96 (0.86–1.06)	1.00 (0.90–1.10)	1.03 (0.89–1.19)
75-<100	274	428,430.94	64.47	0.82 (0.72–0.94)	0.90 (0.79–1.03)	0.97 (0.82–1.16)
100-<150	332	526,638.30	62.49	0.80 (0.70–0.90)	0.97 (0.85–1.10)	1.15 (0.95–1.39)
150-<200	53	62,903.34	83.53	1.07 (0.81–1.41)	1.27 (0.96–1.68)	1.53 (1.10–2.13)
≥200	34	42,084.48	82.20	1.07 (0.76–1.50)	1.24 (0.88–1.75)	1.38 (0.95–2.00)
P_{trend}[e]				*0.006*	*0.44*	*0.02*
EPA guideline value						
<148	3,396	4,631,071.50	73.31	1.00	1.00	1.00
≥148	97	122,084.84	80.82	1.10 (0.90–1.34)	1.24 (1.02–1.52)	1.34 (1.07–1.68)
Continuous						
per 100 Bq/m^3	3,493	4,753,156.34	73.49	0.88 (0.80–0.96)	1.03 (0.94–1.13)	1.15 (1.01–1.31)

Ecologic measure of radon, adjusting for individual smoking habits, confirms residential radon lung cancer risk

Comparison of Radon Risk Estimates

Study Population	Odds/Hazard Ratio (95% CI)	Adjusted Odds Ratio (95% CI)
Occupational Cohort Studies		
Underground Miners (NRC, 1999)	1.12 (1.02 – 1.25)	
Residential Case-control Studies		
North American Residential (Krewski et al., 2005, 2006)	1.11 (1.00 – 1.28)	1.18 (1.02 - 1.43)
European Residential (Darby et al., 2005)	1.08 (1.03 – 1.16)	1.16 (1.05 – 1.31)
Chinese Residential (Lubin et al., 2004)	1.33 (1.01 – 1.36)	
Residential Cohort Studies		
North American Residential (Turner et al., 2011)	1.15 (1.01 – 1.31)	

Radon risk estimates highly consistent across diverse studies

Exposure to Non-ionizing Radiation

Sources of Diagnostic Exposure to Non-ionizing Radiation

- Electromagnetic fields
  - Magnetic resonance imaging (MRI)
  - Transcranial magnetic stimulation (TMS)
  - RF identification (RFID)
  - Wireless signal transfer
  - Radar for vital functions
  - Radar imaging or MW tomography
  - Electromagnetic (EM) movement tracking
  - Volumetric EMF phase-shift spectroscopy (VEPS)
  - Microwave-induced thermo-acoustic echography
- Optical radiation
- Ultrasound

ICNIRP statement on diagnostic devices using non-ionizing radiation. Health Phys. 112(3):305–321; 2017

INTERPHONE

WHO INTERPHONE Study

Eur J Epidemiol
DOI 10.1007/s10654-007-9152-z

NEW STUDY

The INTERPHONE study: design, epidemiological methods, and description of the study population

Elisabeth Cardis · Lesley Richardson · Isabelle Deltour · Bruce Armstrong · Maria Feychting · Christoffer Johansen · Monique Kilkenny · Patricia McKinney · Baruch Modan · Siegal Sadetzki · Joachim Schüz · Anthony Swerdlow · Martine Vrijheid · Anssi Auvinen · Gabriele Berg · Maria Blettner · Joseph Bowman · Julianne Brown · Angela Chetrit · Helle Collatz Christensen · Angus Cook · Sarah Hepworth · Graham Giles · Martine Hours · Ivano Iavarone · Avital Jarus-Hakak · Lars Klaeboe · Daniel Krewski · Susanna Lagorio · Stefan Lönn · Simon Mann · Mary McBride · Kenneth Muir · Louise Nadon · Marie-Elise Parent · Neil Pearce · Tiina Salminen · Minouk Schoemaker · Brigitte Schlehofer · Jack Siemiatycki · Masao Taki · Toru Takebayashi · Tore Tynes · Martie van Tongeren · Paolo Vecchia · Joe Wiart · Alistair Woodward · Naohito Yamaguchi

Interphone Study Results

Published by Oxford University Press on behalf of the International Epidemiological Association

International Journal of Epidemiology 2010;1–20
doi:10.1093/ije/dyq079

Brain tumour risk in relation to mobile telephone use: results of the INTERPHONE international case–control study

The INTERPHONE Study Group*

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*List of members of this study group is available in the Appendix.

Interphone Study Results

	Meningioma			Glioma			
Cumulative call time with no hands-free devices (h)[b]							
Never regular user	1147	1174	1.00	1042	1078	1.00	
<5 h	160	197	0.90 (0.69–1.18)	141	197	0.70	(0.52–0.94)
5.0–12.9	142	159	0.82 (0.61–1.10)	145	198	0.71	(0.53–0.94)
13–30.9	144	194	0.69 (0.52–0.91)	189	179	1.05	(0.79–1.38)
31–60.9	122	145	0.69 (0.51–0.94)	144	196	0.74	(0.55–0.98)
61–114.9	129	162	0.75 (0.55–1.00)	171	193	0.81	(0.61–1.08)
115–199.9	96	155	0.69 (0.50–0.96)	160	194	0.73	(0.54–0.98)
200–359.9	108	133	0.71 (0.51–0.98)	158	194	0.76	(0.57–1.01)
360–734.9	123	133	0.90 (0.66–1.23)	189	205	0.82	(0.62–1.08)
735–1639.9	108	103	0.76 (0.54–1.08)	159	184	0.71	(0.53–0.96)
⩾1640	130	107	1.15 (0.81–1.62)	210	154	1.40	(1.03–1.89)

Interphone Study Conclusions

"[1] Overall, no increase in risk of glioma or meningioma was observed with the use of mobile phones. [2] There were suggestions of an increased risk of glioma at the highest exposure levels, but biases and errors prevent a causal interpretation. [3] The possible effects of long-term heavy use of mobile phones require further investigation."

The INTERPHONE Study Group. Int. J. Epidmiol. 35 (453):464, 2011.

Journal of Exposure Science and Environmental Epidemiology (2009) 19, 369–381

www.nature.com/jes

Recall bias in the assessment of exposure to mobile phones

MARTINE VRIJHEID[a,b], BRUCE K. ARMSTRONG[c], DANIEL BÉDARD[d], JULIANNE BROWN[c], ISABELLE DELTOUR[a], IVANO IAVARONE[e], DANIEL KREWSKI[d], SUSANNA LAGORIO[f], STEPHEN MOORE[c], LESLEY RICHARDSON[a], GRAHAM G. GILES[g], MARY MCBRIDE[h], MARIE-ELISE PARENT[i], JACK SIEMIATYCKI[j] AND ELISABETH CARDIS[a,b]

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[g]*Cancer Epidemiology Centre, The Cancer Council Victoria, Melbourne, Victoria, Australia*
[h]*B.C. Cancer Agency, Vancouver, British Columbia, Canada*
[i]*INRS-Institut Armand-Frappier, Université du Québec, Laval, Quebec, Canada*
[j]*University of Montreal, Montreal, Quebec, Canada*

Table 5. Ratio of self-reported to operator-recorded mobile phone use.

	Cases			Controls			*P* for difference cases/controls*
	N	Ratio[a]	95% confidence interval	*N*	ratio	95% confidence interval	
Number of calls							
Overall	212	0.81	0.71, 0.93	296	0.81	0.73, 0.91	0.82
Up to 1 year before interview	176	0.91	0.77, 1.06	274	0.84	0.75, 0.94	0.27
Excluding Australia	133	0.98	0.83, 1.15	183	0.91	0.79, 1.05	0.43
By country							
Australia	79	0.60	0.47, 0.76	113	0.68	0.58, 0.79	0.61
Canada	54	0.89	0.70, 1.13	77	0.95	0.76, 1.19	0.84
Italy	79	1.04	0.84, 1.29	106	0.88	0.73, 1.07	0.19
		$P^* < 0.001$			$P^* = 0.02$		
Cumulative duration of calls							
Overall	212	1.40	1.18, 1.67	295	1.39	1.21, 1.60	0.76
Up to 1 year before interview	176	1.55	1.27, 1.89	273	1.42	1.23, 1.65	0.34
Excluding Australia	133	1.51	1.21, 1.87	183	1.42	1.18, 1.72	0.60
By country							
Australia	79	1.24	0.92, 1.66	112	1.33	1.09, 1.62	0.94
Canada	54	1.30	0.98, 1.73	77	1.83	1.37, 2.43	0.20
Italy	79	1.67	1.22, 2.27	106	1.19	0.92, 1.53	0.09
		$P^* = 0.23$			$P^* = 0.10$		

Journal of Exposure Science and Environmental Epidemiology (2006), 1–14

www.nature.com/jes

The effects of recall errors and of selection bias in epidemiologic studies of mobile phone use and cancer risk

MARTINE VRIJHEID[a], ISABELLE DELTOUR[a], DANIEL KREWSKI[a,b], MARIE SANCHEZ[a] AND ELISABETH CARDIS[a]

[a]*International Agency for Research on Cancer, Lyon, France*
[b]*McLaughlin Centre for Population Health Risk Assessment, University of Ottawa, Ottawa, Ontario, Canada*

This paper examines the effects of systematic and random errors in recall and of selection bias in case–control studies of mobile phone use and cancer. These sensitivity analyses are based on Monte–Carlo computer simulations and were carried out within the INTERPHONE Study, an international collaborative case–control study in 13 countries. Recall error scenarios simulated plausible values of random and systematic, non-differential and differential recall errors in amount of mobile phone use reported by study subjects. Plausible values for the recall error were obtained from validation studies. Selection bias scenarios assumed varying selection probabilities for cases and controls, mobile phone users, and non-users. Where possible these selection probabilities were based on existing information from non-respondents in INTERPHONE. Simulations used exposure distributions based on existing INTERPHONE data and assumed varying levels of the true risk of brain cancer related to mobile phone use. Results suggest that random recall errors of plausible levels can lead to a large underestimation in the risk of brain cancer associated with mobile phone use. Random errors were found to have larger impact than plausible systematic errors. Differential errors in recall had very little additional impact in the presence of large random errors. Selection bias resulting from underselection of unexposed controls led to J-shaped exposure–response patterns, with risk apparently decreasing at low to moderate exposure levels. The present results, in conjunction with those of the validation studies conducted within the INTERPHONE study, will play an important role in the interpretation of existing and future case–control studies of mobile phone use and cancer risk, including the INTERPHONE study. *Journal of Exposure Science and Environmental Epidemiology* advance online publication, 14 June 2006; doi:10.1038/sj.jes.7500509

Keywords: *mobile phones, recall bias, measurement error, selection bias, sensitivity analyses, Monte–Carlo simulations, case–control studies.*

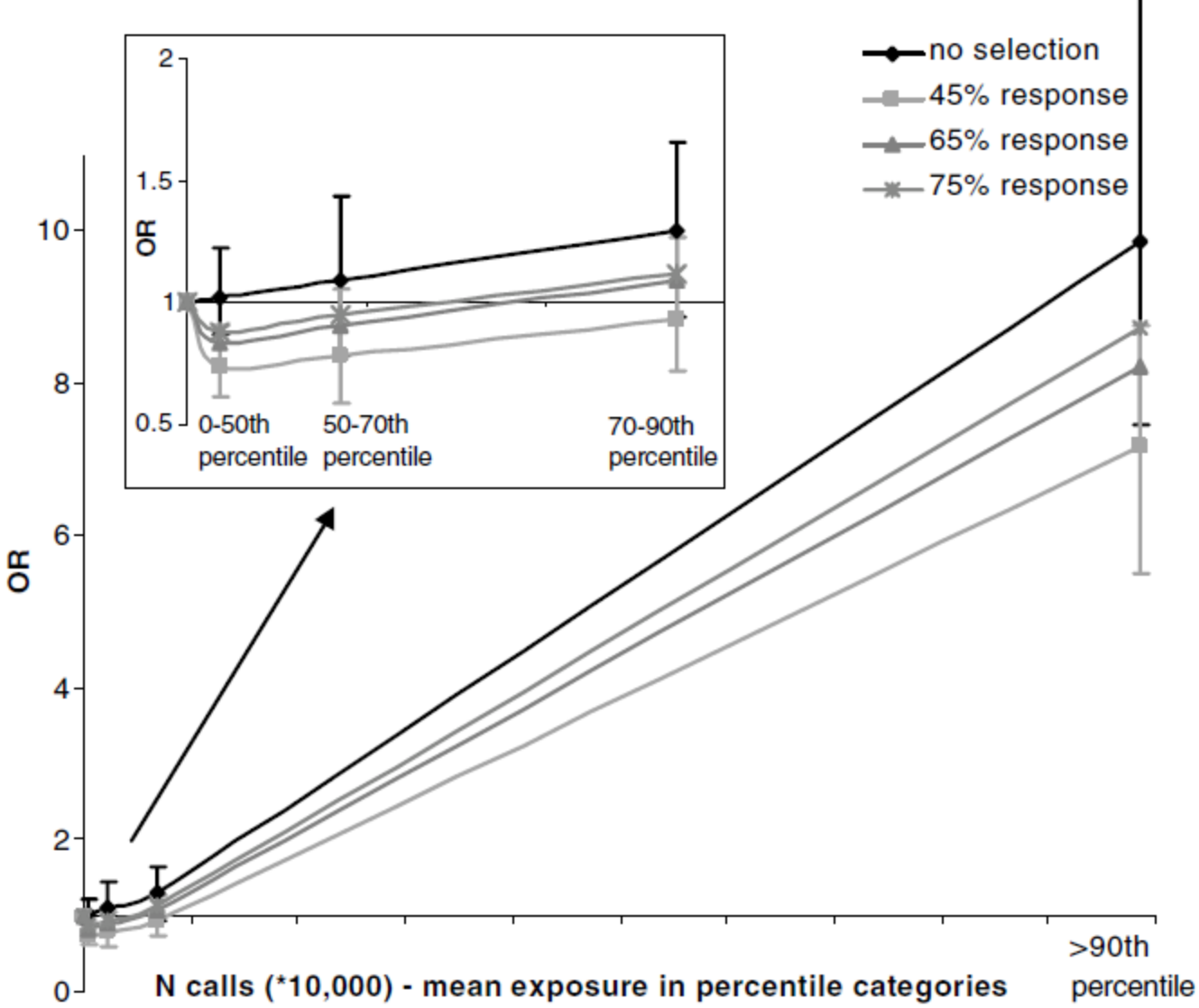


Figure 1. J-shaped exposure–response relationship in the case of underselection of unexposed controls, based on 64% users among participants, 50% among non-participants. (see Table 7 for values of the ORs).

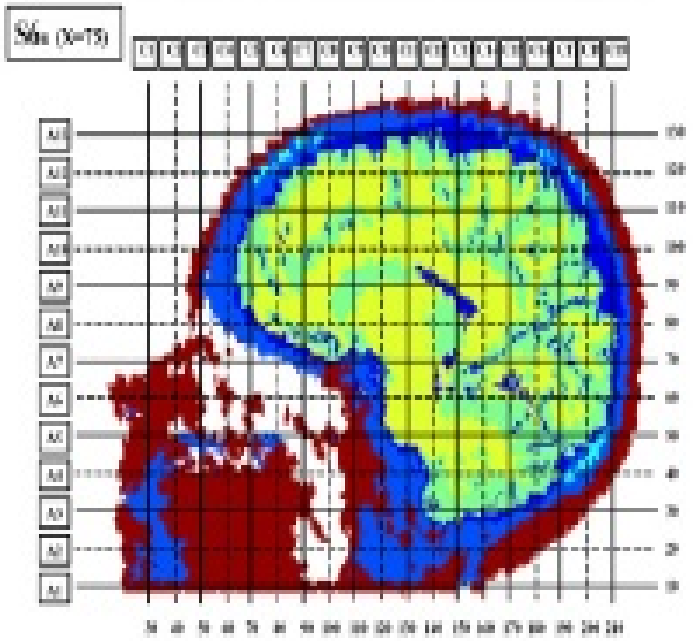
Risk of brain tumours in relation to estimated RF dose from mobile phones: results from five Interphone countries

E Cardis,[1] B K Armstrong,[2] J D Bowman,[3] G G Giles,[4,5] M Hours,[6] D Krewski,[7] M McBride,[8] M E Parent,[9] S Sadetzki,[10,11] A Woodward,[12] J Brown,[2] A Chetrit,[10] J Figuerola,[1] C Hoffmann,[11,13] A Jarus-Hakak,[10] L Montestruq,[6] L Nadon,[9] L Richardson,[14] R Villegas,[1] M Vrijheid[1]

Table 2 ORs for brain tumours with level of total cumulative specific radio frequency energy (total cumulative specific energy) (in joules per kilogram)*

	Subjects with tumour centre estimated by a neuroradiologist or computer algorithm†			Only subjects with tumour centre estimated by a neuroradiologist		
	Cases	Controls	OR (95% CI)	Cases	Controls	OR (95% CI)
Glioma						
Never regular user	196	617	1.00	117	361	1.00
<76.7	67	265	0.76 (0.53 to 1.09)	36	150	0.84 (0.51 to 1.36)
76.7–	68	227	0.94 (0.66 to 1.35)	43	128	1.00 (0.62 to 1.60)
284.1–	60	207	0.80 (0.54 to 1.18)	39	102	1.15 (0.69 to 1.90)
978.9–	57	197	0.89 (0.61 to 1.30)	34	99	0.92 (0.55 to 1.53)
3123.9+	103	207	1.35 (0.96 to 1.90)	57	86	1.66 (1.03 to 2.67)
Meningioma						
Never regular user	294	643	1.00	156	396	1.00
<76.7	103	261	0.90 (0.67 to 1.21)	51	150	0.86 (0.57 to 1.29)
76.7–	71	199	0.74 (0.53 to 1.04)	47	127	0.95 (0.62 to 1.44)
284.1–	56	233	0.56 (0.39 to 0.80)	29	136	0.53 (0.32 to 0.87)
978.9–	62	209	0.72 (0.51 to 1.02)	23	117	0.55 (0.32 to 0.93)
3123.9+	88	251	0.90 (0.66 to 1.24)	35	114	1.01 (0.63 to 1.62)

*Analyses based on unconditional logistic regression stratified on age, sex and region and adjusted for education and timing of interview.
†Centre is as estimated by a neuroradiologist when available or as estimated by computer algorithm otherwise.



Multiple Bias Modeling in INTERPHONE

Table 5: Conditional Logistic and Bias-Adjusted Odds Ratios for Phone Use by Tumor Type, INTERPHONE study, Canada (Montreal, Ottawa, Vancouver), 2001-2004

Tumor type and exposure metric	No. of Cases	No. of Controls	OR[a]	95% CI	Bias Modelling: Adjustment for bias due to recall error [b] OR	95% limits	Adjustment for selection bias [b] OR	95% limits	Adjustment for recall and selection biases, with random error OR	95% limits
GLIOMA										
Reference level [c]	89	339	1.0		1.0		1.0		1.0	
Regular use	81	314	1.0	0.7, 1.5	NA[d]	NA	1.1	1.0, 1.2	1.1	0.7, 1.6
Cumulative hours										
<40	14	77	0.9	0.4, 1.7	0.8	0.7, 0.9	1.0	0.7, 1.3	0.9	0.4, 1.8
40-558	35	163	0.7	0.4, 1.2	0.7	0.6, 0.8	0.8	0.6, 1.0	0.8	0.4, 1.4
559+	32	74	2.0	1.2, 3.4	2.0	1.8, 2.1	2.3	1.9, 2.8	2.2	1.3, 4.1
MENINGIOMA										
Reference level [c]	52	339	1.0		1.0		1.0		1.0	
Regular use	42	314	1.3	0.8, 2.0	NA	NA	1.4	1.2, 1.6	1.4	0.8, 2.2

F Momoli, J Siemiatycki, ML McBride, M.-É. Parent, L Richardson, D Bedard, R Platt, M Vrijheid, E Cardis, D Krewski; Probabilistic multiple-bias modelling applied to the Canadian data from the INTERPHONE study of mobile phone use and risk of glioma, meningioma, acoustic neuroma, and parotid gland tumors. *Am J Epidemiol* 2017 kwx157. doi: 10.1093/aje/kwx157

MOBI-KIDS

Use of Cellular Telephones by Children and Young Adults

frontiers in PUBLIC HEALTH

METHODS ARTICLE
published: 23 September 2014
doi: 10.3389/fpubh.2014.00124

The MOBI-Kids study protocol: challenges in assessing childhood and adolescent exposure to electromagnetic fields from wireless telecommunication technologies and possible association with brain tumor risk

Siegal Sadetzki[1,2], Chelsea Eastman Langer[3,4,5], Revital Bruchim[1], Michael Kundi[6], Franco Merletti[7], Roel Vermeulen[8], Hans Kromhout[8], Ae-Kyoung Lee[9], Myron Maslanyj[10], Malcolm R. Sim[11], Masao Taki[12], Joe Wiart[13], Bruce Armstrong[14], Elizabeth Milne[15], Geza Benke[11], Rosa Schattner[11], Hans-Peter Hutter[6], Adelheid Woehrer[16], Daniel Krewski[17,18], Charmaine Mohipp[19,20], Franco Momoli[21,22], Paul Ritvo[23], John Spinelli[24], Brigitte Lacour[25,26], Dominique Delmas[25], Thomas Remen[25], Katja Radon[27], Tobias Weinmann[27], Swaantje Klostermann[27], Sabine Heinrich[27], Eleni Petridou[28], Evdoxia Bouka[28], Paraskevi Panagopoulou[28], Rajesh Dikshit[29], Rajini Nagrani[29], Hadas Even-Nir[1], Angela Chetrit[1], Milena Maule[7], Enrica Migliore[30], Graziella Filippini[31], Lucia Miligi[32], Stefano Mattioli[33], Naohito Yamaguchi[34], Noriko Kojimahara[34], Mina Ha[35], Kyung-Hwa Choi[36], Andrea 't Mannetje[37], Amanda Eng[37], Alistair Woodward[38], Gema Carretero[3,4,5], Juan Alguacil[39,40], Nuria Aragones[41,42], Maria Morales Suare-Varela[42,43], Geertje Goedhart[8], A. Antoinette Y. N. Schouten-van Meeteren[44,45], A. Ardine M. J. Reedijk[45] and Elisabeth Cardis[3,4,5]*

Risk Communication

Media Messages on Interphone

CELL PHONES LINKED TO CANCER HEADLINES

-- Ten-year worldwide study links mobile phone use to cancer - The Daily Mail

-- Study links mobile phone use to brain tumours - Scotsman

-- Heavy mobile users risk cancer - Time Online

-- Study can't rule out brain cancer link to mobiles - The Sydney Morning Herald

-- Landmark study set to show potential dangers of heavy mobile phone use - The Telegraph

-- Heavy use of cell phones may increase tumour risk: study - The Globe and Mail

CELL PHONE CANCER RISK INCONCLUSIVE HEADLINES

-- Study: Cell phone-brain cancer link inconclusive - AP

-- WHO study has no clear answer on phones and cancer - Reuters

-- INTERPHONE finds no increased risk of brain cancer from mobile phone use - Wire Up Date

-- Largest cellphone-cancer study to date clarifies little - arstechnica

-- 10-year Cell Phone Cancer Study Proves Nothing but a Major Waste of Time - Digital Trends

-- Phone-cancer link 'inconclusive' - BBC

-- Study finds no link in cell phone use, brain tumors - CNN

BEST BALANCED ARTICLE

-- Cell Phones and Cancer: a Study's Muddled Findings TIME

http://www.textually.org/textually/archives/2010/05/026019.htm

The Sunday Edition | April 25, 2010: MediaPhiles - God and the Media, The Living Heart of the Lake, An Air of Uncertainty Over Cell Phones

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An Air of Uncertainty Over Cell Phones

Michael Enright was in conversation with Dr. Magda Havas is a professor of Environmental Studies at Trent University. Henry Lai is a medical researcher from the University of Washington and Frank Gilbert is the President of Lakehead University in Thunder Bay, Ontario. All three were in our Thunder Bay studio.

An Air of Uncertainty Over Cell Phones - Dr. Daniel Krewski

Most of the medical community disagrees with the three researchers we just heard.

Dr. Daniel Krewski is in that majority . He is the director of the McLaughlin Centre for Population Health Risk Assessment at the University of Ottawa and professor of epidemiology and community medicine at the University.

He is one of Canada's leading scientists responsible for the Interphone study.When the study finally comes out, it is expected to be the definitive word on cellphone use and cancer.

http://www.cbc.ca/thesundayedition/2010/04/april-25-2010.html

Risk Perception

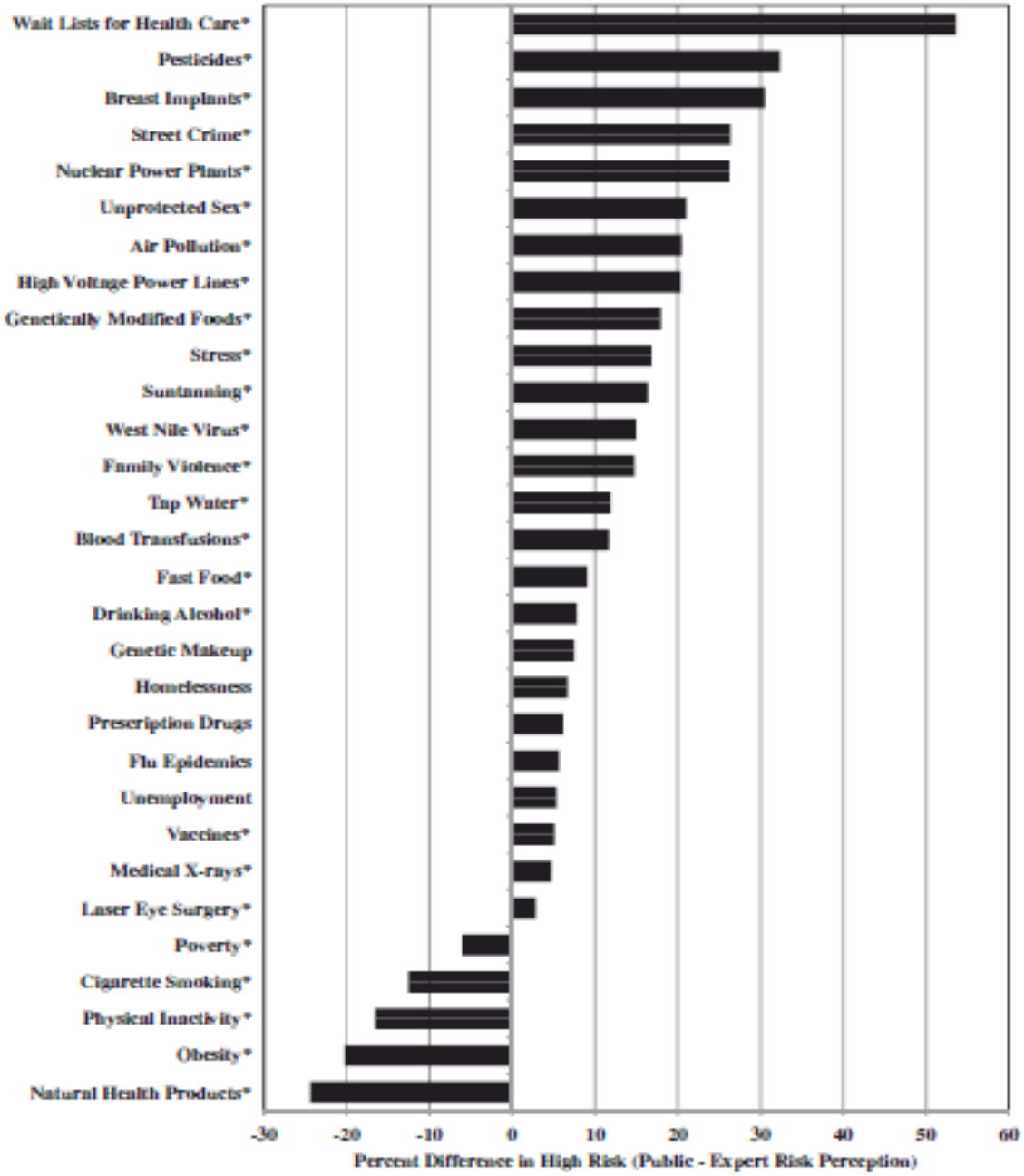
Journal of Risk Research
2012, 1–25, iFirst Article

Routledge
Taylor & Francis Group

Expert vs. public perception of population health risks in Canada

Daniel Krewski[a,b,c]*, Michelle C. Turner[a,d], Louise Lemyre[a,e] and Jennifer E.C. Lee[f]

[a]*McLaughlin Center for Population Health Risk Assessment, Institute of Population Health, University of Ottawa, Ottawa, Canada;* [b]*Department of Epidemiology and Community Medicine, Faculty of Medicine, University of Ottawa, Ottawa, Canada;* [c]*Risk Sciences International, Ottawa, Canada;* [d]*Faculty of Graduate and Postdoctoral Studies, University of Ottawa, Ottawa, Canada;* [e]*Faculty of Social Sciences, School of Psychology, GAP-Santé Research Unit, University of Ottawa, Ottawa, Canada;* [f]*Faculty of Social Sciences, GAP-Santé Research Unit, University of Ottawa, Ottawa, Canada*


Wait Lists for Health Care*
Pesticides*
Breast Implants*
Street Crime*
Nuclear Power Plants*
Unprotected Sex*
Air Pollution*
High Voltage Power Lines*
Genetically Modified Foods*
Stress*
Suntanning*
West Nile Virus*
Family Violence*
Tap Water*
Blood Transfusions*
Fast Food*
Drinking Alcohol*
Genetic Makeup
Homelessness
Prescription Drugs
Flu Epidemics
Unemployment
Vaccines*
Medical X-rays*
Laser Eye Surgery*
Poverty*
Cigarette Smoking*
Physical Inactivity*
Obesity*
Natural Health Products*
-30
-20
-10
0
10
20
30
40
50
60
Percent Difference in High Risk (Public - Expert Risk Perception)

Risk Decision Making

Application of Principles of Risk Decision Making in Different Risk Contexts

Risk Context	Risk Decision Principle									
	P1. Risk-based Decision Making	P2. Precautionary Principle	P3. Balancing Risks and Benefits	P4. Cost-effectiveness	P5. Acceptable Risk	P6. Zero Risk	P7. Equity	P8. Stakeholder Engagement	P9. Openness and Tranparency	P10. Flexibility
RC1. Air Pollution										
RC2. Radon										
RC3. Artificial Sweeteners										
RC4. Climate Change										
RC5. Ebola										
RC6. Chemotherapeutic Agents										
RC7. Tsunami										
RC8. Terrorism										
RC9. Prion Disease										
RC10. Pandemic Influenza										

Legend: Highly relevant; Somewhat relevant; Largely irrelevant; Universally relevant

Different risk decision principles more relevant in different risk contexts

Conclusions

1. Human exposure to ionizing and non-ionizing radiation, both natural and anthropogenic, occurs under many circumstances
2. Medical applications of radiation, for both diagnosis and treatment, can be beneficial for the patient
3. Because radiation has been associated with potential health risks, including cancer, even at low doses, it is important that radiation risks be well-characterized
4. Radiation risk assessment is well-supported by a rich body of evidence derived from epidemiological, toxicological, and other sources
5. Exposure-response modeling can be used to better understand exposure-response relationships for radiation
6. Fundamental principles of risk assessment and risk management can inform risk decision making regarding radiation exposure limits