Nuclear worker studies that inform low dose risk assessment: Example of the International Nuclear Workers Study (INWORKS)

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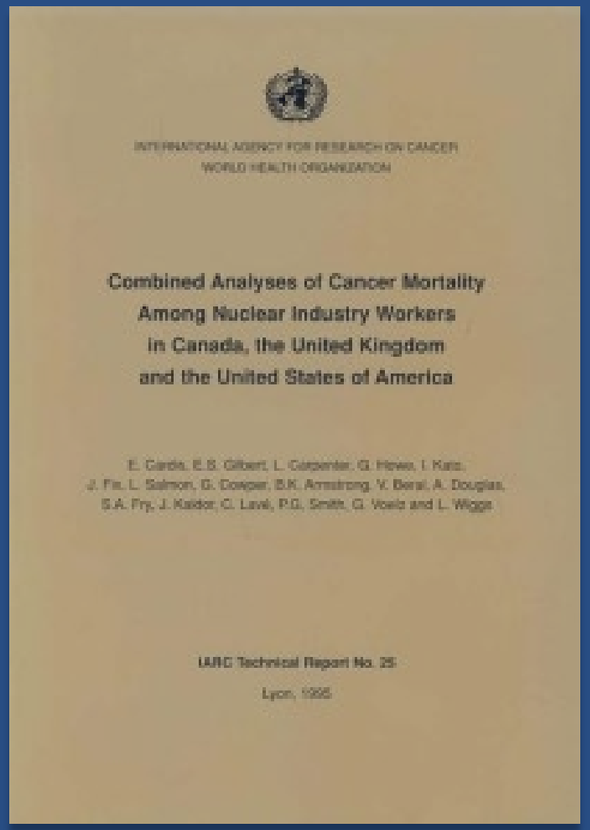
Recent cohort studies: occupational radiation dose and solid cancer

Country, Population (Author, Year)	Mean dose (mGy)	No. cancers	ERR Gy^{-1} (95% CI)
Australia, nuclear workers (Habib, et al. 2005)	6.1	17	13.40 (-6.0, 119)
US, Navy nuclear submariners (Friedman-Jimenez et al. 2022)	5.7	492	5.20 (-3, 18)
S Korea, NPP workers (Jeong, Jin et al. 2010)	19.7	96	2.06 (-1.91, 9)
France, Uranium process workers (Zhivin et al. 2016)	0.8	406	1.60 (-4.3, 7.5)
S Korea, diagnostic medical radiation workers (Lee et al. 2021)	7.2	3,220	1.50 (-2.0, 5.1)
Japan, nuclear workers (Furuta, et al. 2022)	11.0	7,929	1.22 (0.24, 2.26)
Spain, nuclear workers (Cardis, Vrijheid et al. 2007)	25.5	25	1.02 (-11.9, 13.9)
China diagnostic x-ray workers (Sun, et al. 2016)	40.6	1,643	0.87 (0.48, 1.45)
US, medical radiologic workers (Boice, et al. 2022)	14.6	3,191	0.70 (-0.1, 1.5)
Chornobyl clean-up workers, Russia (Kashcheev, et al. 2015)	132.0	2,442	0.58 (0.002, 1.25)
INWORKS (Richardson et al. 2023)	20.9	28,089	0.52 (0.27, 0.77)
Germany, Uranium process, Germany (Kreuzer, et al. 2015)	26.0	434	0.26 (-2.47, 2.99)
Mayak workers, Russia (Sokolnikov, et al. 2015,. 2017)	354.0	1,825	0.16 (0.07, 0.26)
Canada, Port Hope uranium process (Zablotska, et al. 2013)	134.0	225	0.12 (-0.74, 0.98)
US, NPP workers (Boice, et al. 2022)	43.7	8,445	0.10 (-0.3, 0.5)
US, Rocketdyne workers (Boice, et al. 2011)	13.5	651	-0.2 (-1.8, 1.7)
Sweden, nuclear workers (Cardis, et al. 2007)	6.1	190	-0.58 (-7.65, 6.49)
Belgium, nuclear workers (Engels, et al. 2005)	26.6	87	-0.59 (-7.42, 6.24)
Germany, NPP workers (Merzenich, et al. 2014)	29.5	115	-1.00 (-4, 1)
Canada, nuclear workers (Zablotska, et al. 2014)	21.6	324	-1.20 (-4.79, 2.39)

International Nuclear Workers Study (INWORKS)



INTERNATIONAL AGENCY FOR RESEARCH ON CANCER
WORLD HEALTH ORGANIZATION

Combined Analyses of Cancer Mortality
Among Nuclear Industry Workers
in Canada, the United Kingdom
and the United States of America

E. Gardis, E.S. Gilbert, L. Carpenter, G. Howe, I. Kato,
J. Fix, L. Salmon, G. Cowper, B.K. Armstrong, V. Beral, A. Douglas,
S.A. Fry, J. Kaldor, C. Lavé, P.G. Smith, G. Voelz and L. Wiggs

IARC Technical Report No. 25

Lyon, 1995

IRSN
INSTITUT
DE RADIOPROTECTION
ET DE SÛRETÉ NUCLÉAIRE

Public Health England

National Institute for Occupational Safety and Health
NIOSH

National cohort	UK NRRW	US combined cohort
n = 60 697	n = 147 872	n = 101 363

Employed 1+ year and monitored for external exposure to radiation (via dosimeters)

- CEA civil
- Orano
- EDF

- UK Atomic Energy Authority
- British Nuclear Fuels plc
- British Energy Generation and Magnox Electric Ltd
- Atomic Weapons Establishment
- Ministry of Defence

- Hanford Site
- Idaho National Lab
- Oak Ridge National Lab
- Portsmouth Naval Shipyard
- Savannah River Site

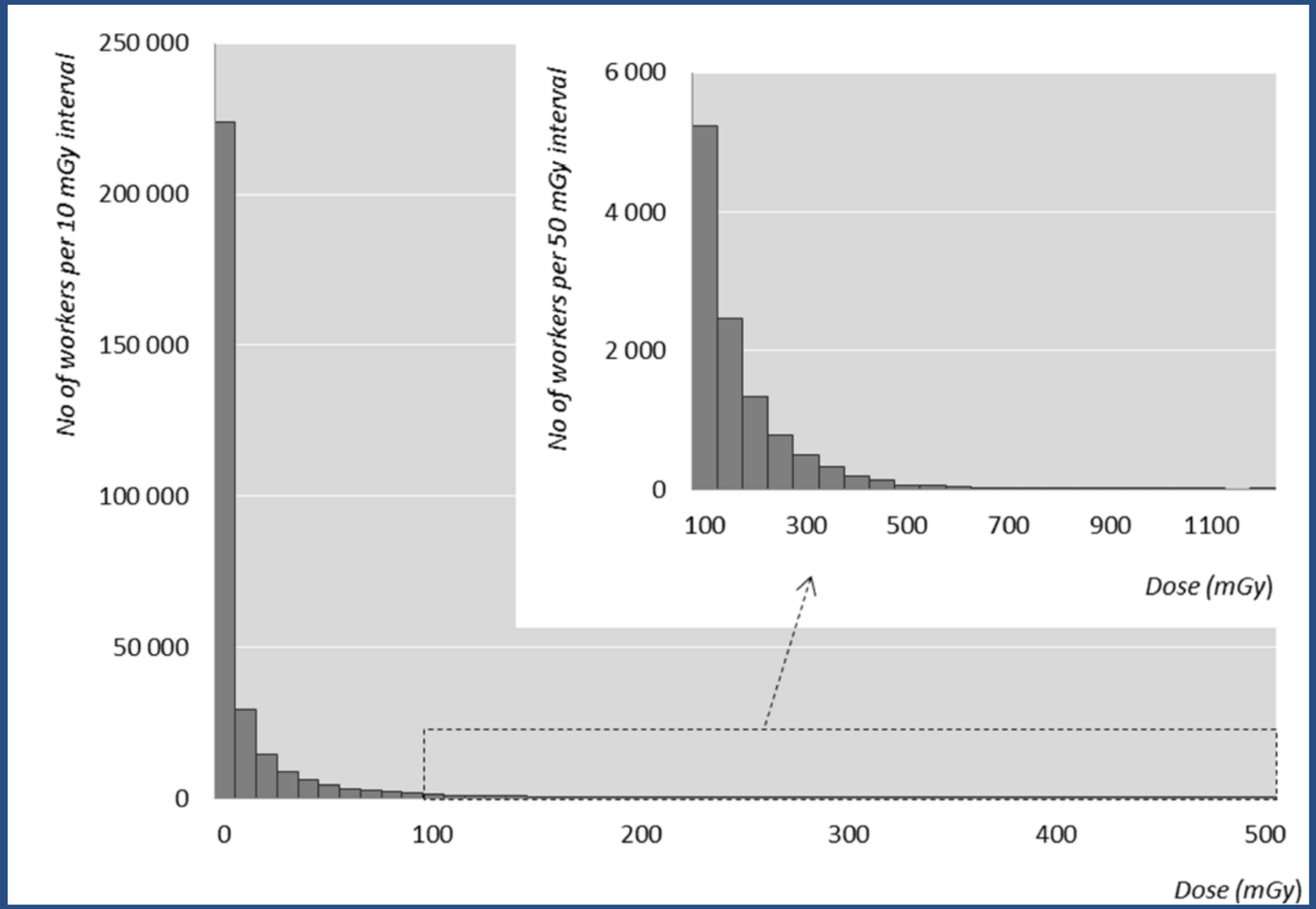
309 932 workers

International Nuclear Workers Study (INWORKS)

Characteristics of INWORKS cohorts: 1944-2016

Calendar years of follow-up	1944-2016
Workers	309,932
Person-years (millions)	10.72
males	9.24
females	1.48
Deaths (all causes)	103,553
All cancer	31,009
Solid cancer	28,089
Solid cancer other than lung	19,823
Average duration of follow-up (years)	34.6
Average age at end of follow-up (years)	65.9
Average cumulative dose (mGy)	20.9

International Nuclear Workers Study (INWORKS)



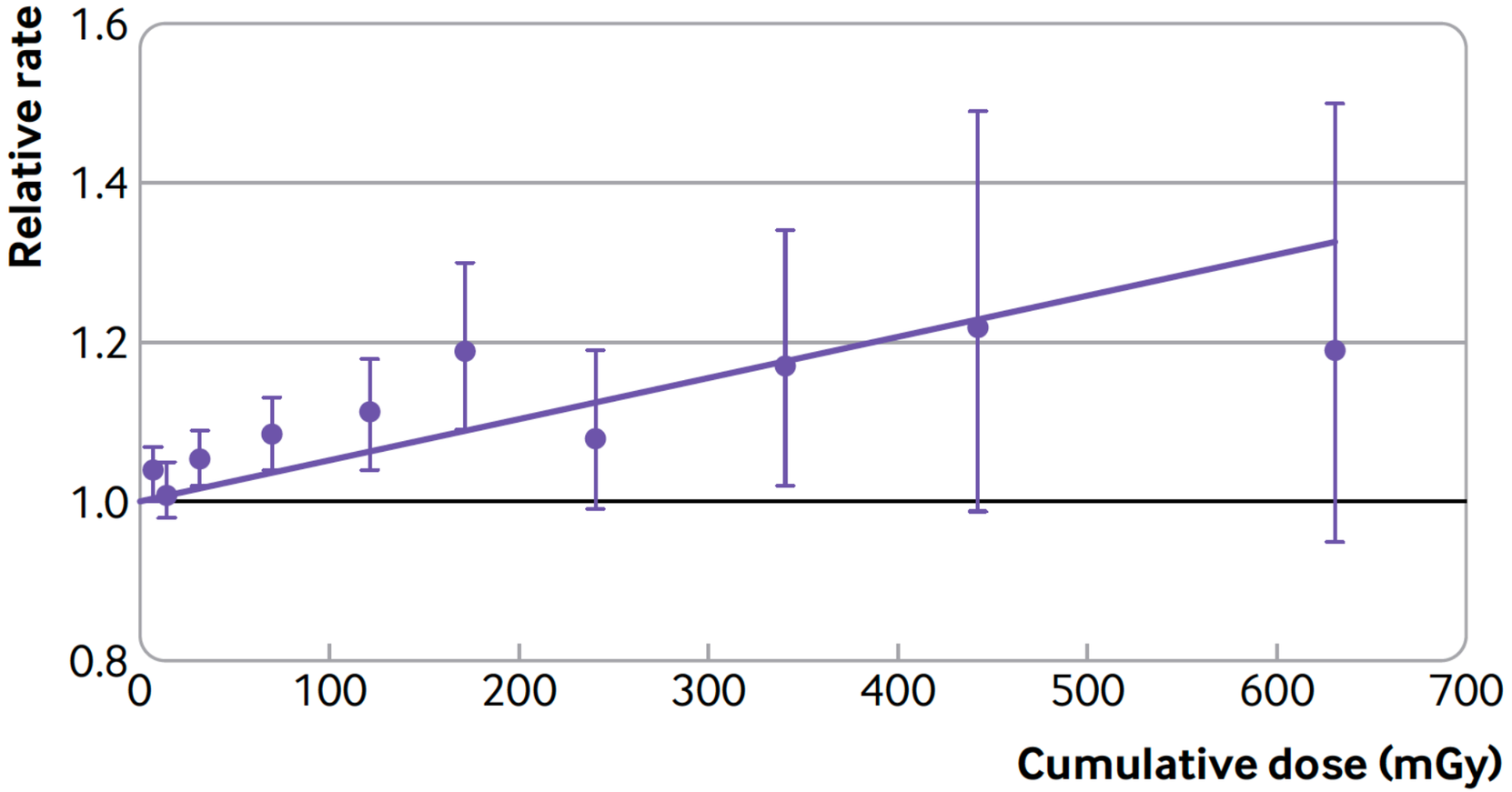
Distribution of cumulative red bone marrow doses

International Nuclear Workers Study (INWORKS)

ERR per Gy = 0.52
90%CI [0.27 – 0.77]

Poisson regression stratified by country, age, sex, birth cohort, socioeconomic status, duration employed, neutron monitoring. 10 year lag assumption.

Relative rate of solid cancer mortality by categories of cumulative dose, and fitted line. INWORKS, 1944-2016



SOME MAJOR STUDIES: ASSOCIATIONS BY CAUSE

	Leukemia excl CLL ERR per Gy (95% CI) [cases]	Solid cancer ERR per Gy (95% CI) [cases]	Ischemic heart disease ERR per Gy (95% CI) [cases]
INWORKS (Richardson et al. 2023; Leuraud et al. 2015; Gillies et al. 2016)	2.96 (1.17 to 5.21)[a] [531]	0.52 (0.27 to 0.77)[a] [28,089]	0.17 (0.00 to 0.36)[a] [17,279]
Mayak workers (Preston, et al. 2017; Azizova 2010)	0.11 (-0.20 to 0.50) [90]	0.16* (0.07 to 0.26) [1,825]	0.07 (-0.02 to 0.15) [577]
NPP workers (Boice, et al. 2022)	1.50 (-0.01 to 3.10)[a] [311]	0.10 (-0.30 to 0.50) [8,445]	-0.10 (–0.60 to 0.40) [5,410]

* Solid excl lung, liver, bone

[a] 90% CI

UNSCEAR Report on Cancer Epi

What we have is:

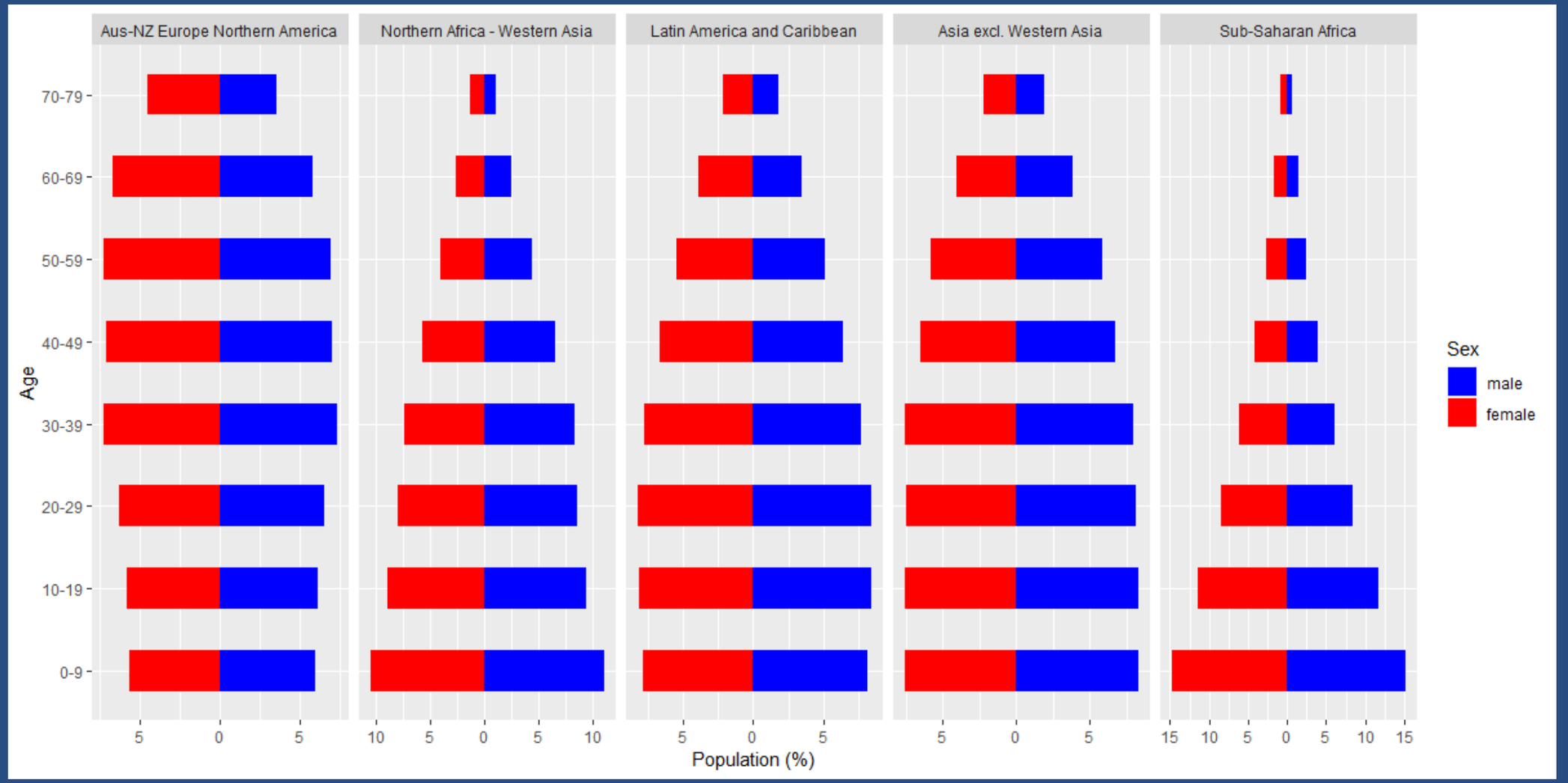
Model for (Relative) Rate, expressed as events per person-year, which varies as a function of age, sex, time since exposure, dose

What we want is:

Risk - the probability that a disease will develop in a person within a specified time period, expressed as the number of events divided by size of the population at risk

Target populations

Australia, Europe, New Zealand, North America	Northern Africa – Western Asia	Latin America and the Caribbean	Asia excluding Western Asia	Sub-Saharan Africa



Occupational Exposure Scenario

UNSCEAR 2019 : Cumulative risk of all solid cancers mortality for United States workers exposed to a total dose of 100 mGy of low-LET radiation delivered from ages 30 to 45.

Illustrative values for estimated excess solid cancer deaths per 10,000 workers by age 65 years

<u>Excess Relative Rate model</u>
LSS - 6.4 (4.0, 9.8) per 10,000 workers
INWORKS - 11 (3.1, 19.3) per 10,000 workers

<u>Excess Absolute Rate model</u>
LSS - 12 (8.1, 18) per 10,000 workers
INWORKS - 11 (−1.1, 25) per 10,000 workers

Conclusions

Over the last 20 years there have been many low dose studies.

- New studies yield results with greater precision than earlier studies.
- Positive associations reported between protracted low dose external exposures and solid cancer and leukemia mortality

Risk assessments

- Assess coherence Life Span Study and nuclear worker study findings
- Examine influence of target populations
- Describe importance of model and transportability assumptions