Epidemiologic Studies of Radiation Cataract Risk

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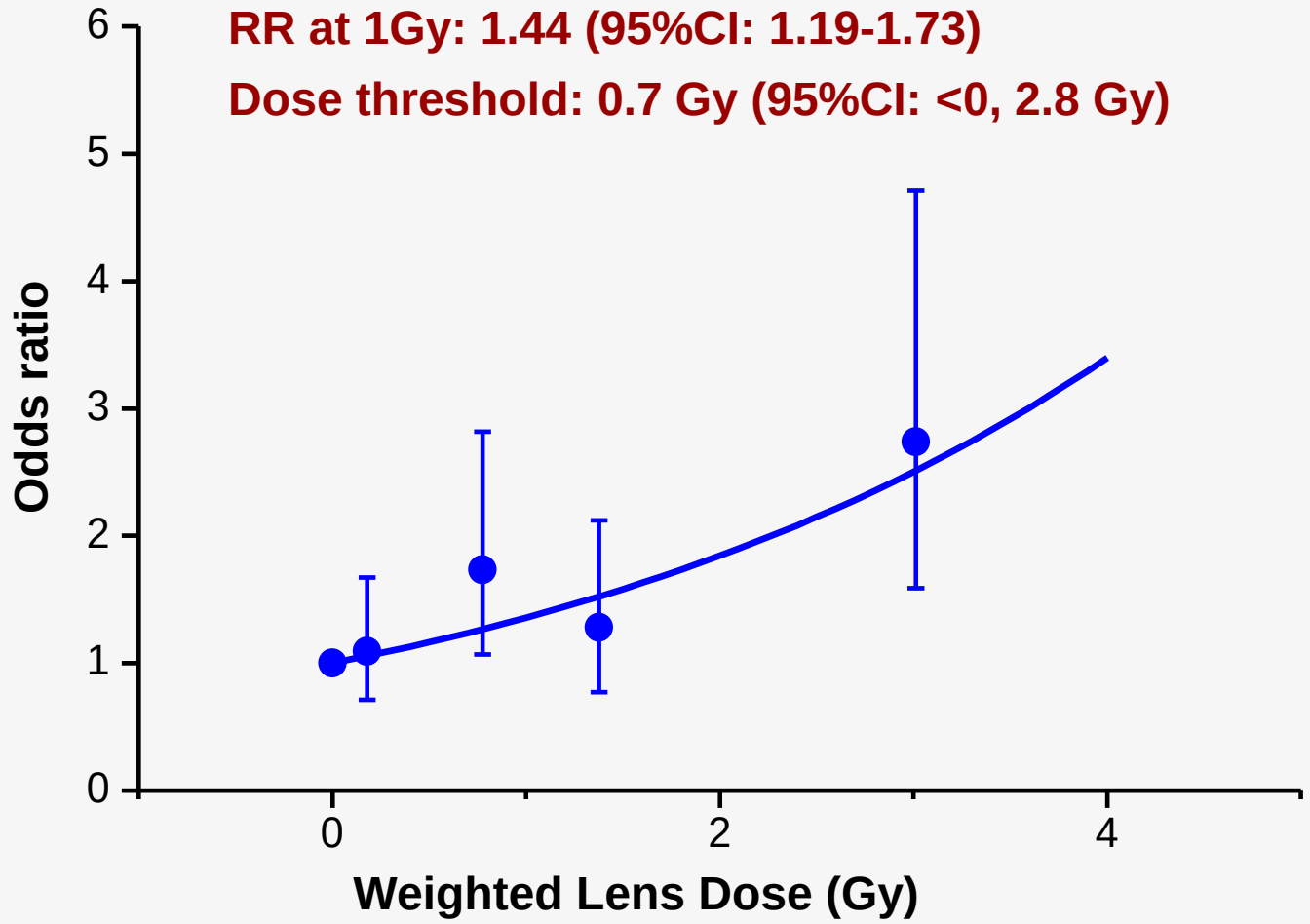
Overview of Presentation

- Selected epidemiologic studies of radiation and cataract
- Summary of dose-response risk estimates
- Comparison of dose-response threshold estimates
- Radiation risk of “significant” cataracts
- Studies of interventional cardiology workers
- Radiation and cataract: Unresolved questions

Selected Epidemiologic Studies of Radiation and Cataract

Studies of Opacities in Atomic Bomb Survivors:
Adult Health Study (AHS)

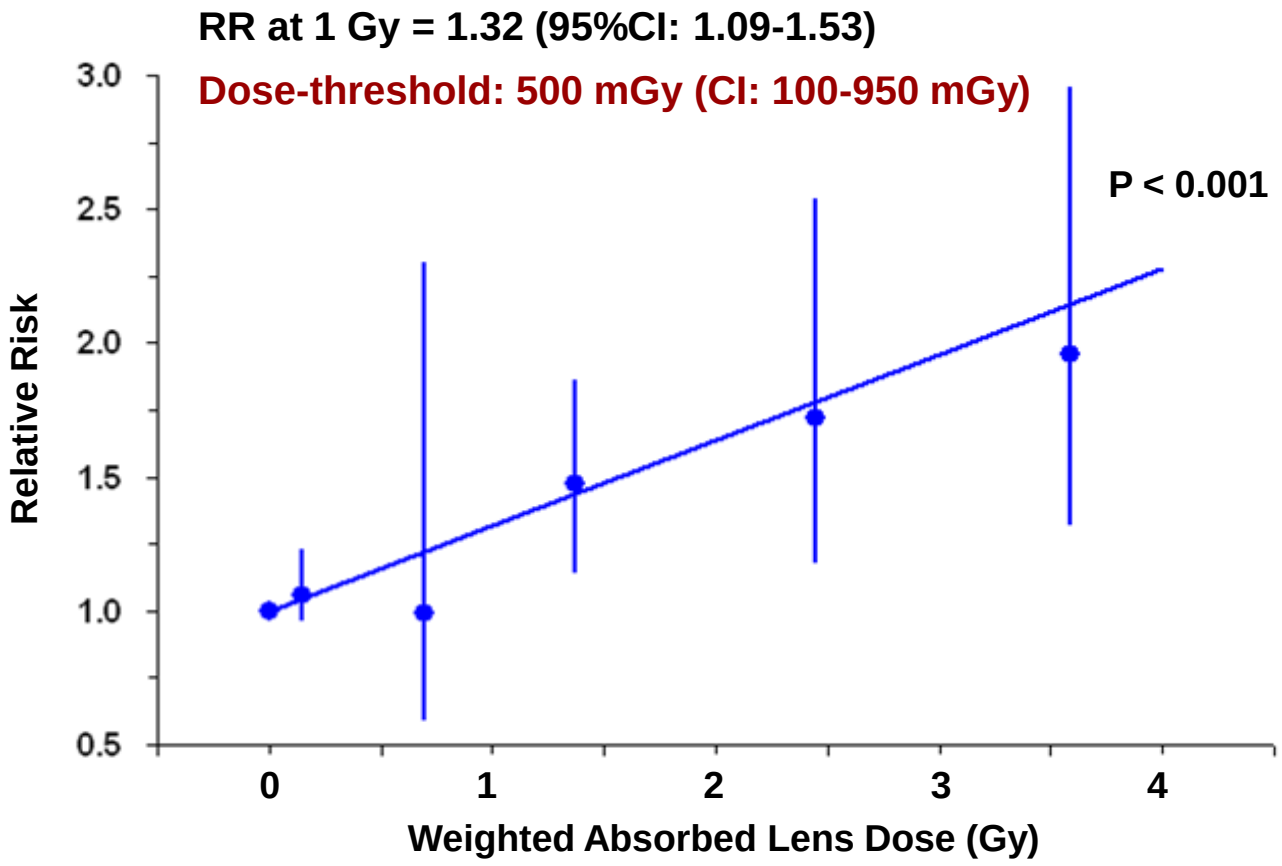
AHS Ophthalmologic Exam: Dose Response for Posterior Subcapsular Opacities



242 with PSCs, 873 examined. Adjusted for age, sex and various cataract risk factors.
Screening 55 y after exposure; 68% ages ≤13 at exposure.

(Minamoto, *Int J Radiat Biol*, 80:339-, 2004; Nakashima, *Health Phys*, 90:154-,2006)

Radiation Dose and Cataract-Surgery Incidence, 1986-2005 (Adult Health Study)



(Adjusted for gender, age at exposure, attained age, & diabetes)

6,066 study subjects; 1,028 with cataract surgery. (Neriishi et al, *Radiol*, 265:167-, 2012)
Mean age at exposure, 20y; at surgery, 74y (range 48-94y).

Atomic Bomb: Adult Health Study (AHS) Cataract Studies – Critique

Strengths

Opacity Screening

- Used standard LOCS-II cat. scoring
- Blinded ophthalmologic evaluation & systematic review of slit-lamp photos

Cataract Surgery

- Addresses vision-impairing cataracts (VICs).
- Good statistical power - >1000 surgeries

Both Studies

- Doses fairly accurate & wide range.
- Long follow-up
- Evaluated/adjusted for many cat. risk factors – e.g., age, sex, diabetes, smoking, corticosteroids.

Limitations

Screening

- Relatively few high grade opacities, e.g., ~4% of PSCs potentially "vision impairing"
- Young age at exposure

Cataract Surgery

- Limited sensitivity/specificity as surrogate for VICs
- No information on cat. location
- Uncertainties in cat. ascertainment

Both Studies

- High dose rate only
- Early time since expos. and younger adult ages not included.

(Minamoto, *Int J Radiat Biol*, 80:339-, 2004; Nakashima, *Health Phys*, 90:154-, 2006; Neriishi, *Radiol*, 265:167-, 2012)

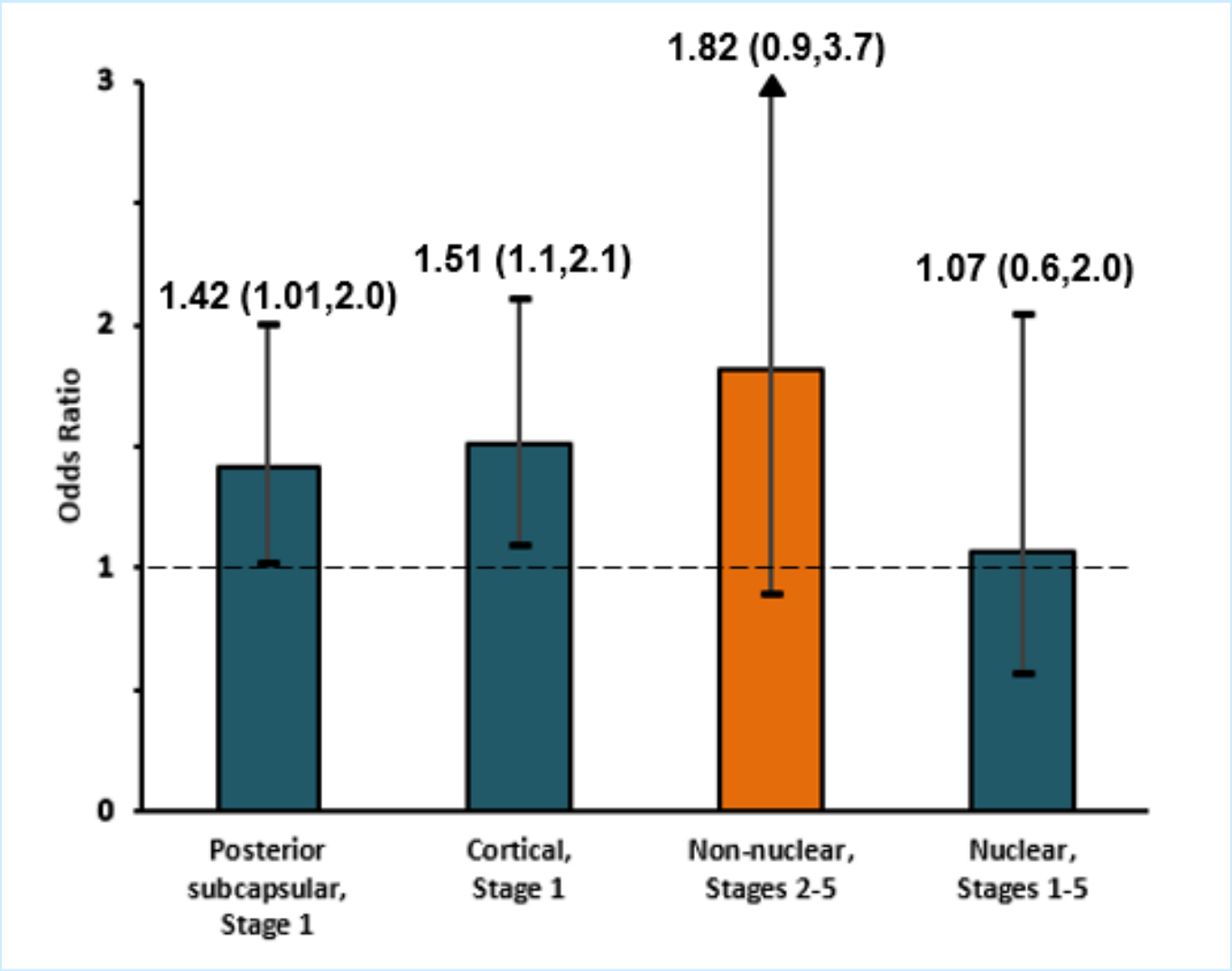
Opacities in Chernobyl Clean-up Workers

Chernobyl Clean-up Workers: Dose Assessment Issues

- Official gamma doses (whole body) mostly estimated. Only 14% had measurements.
- Official estimates based on:
  - Time & motion studies,
  - Projected task dose estimates, or
  - Group dosimetry (1 dosimeter for group of workers)
- Corrected lens dose estimates: official doses calibrated against EPR measurements of tooth enamel.
- Beta doses: Substantial at some worksites. Not measured by standard dosimeters. Estimated ratios of beta/gamma lens doses, but substantial uncertainties.

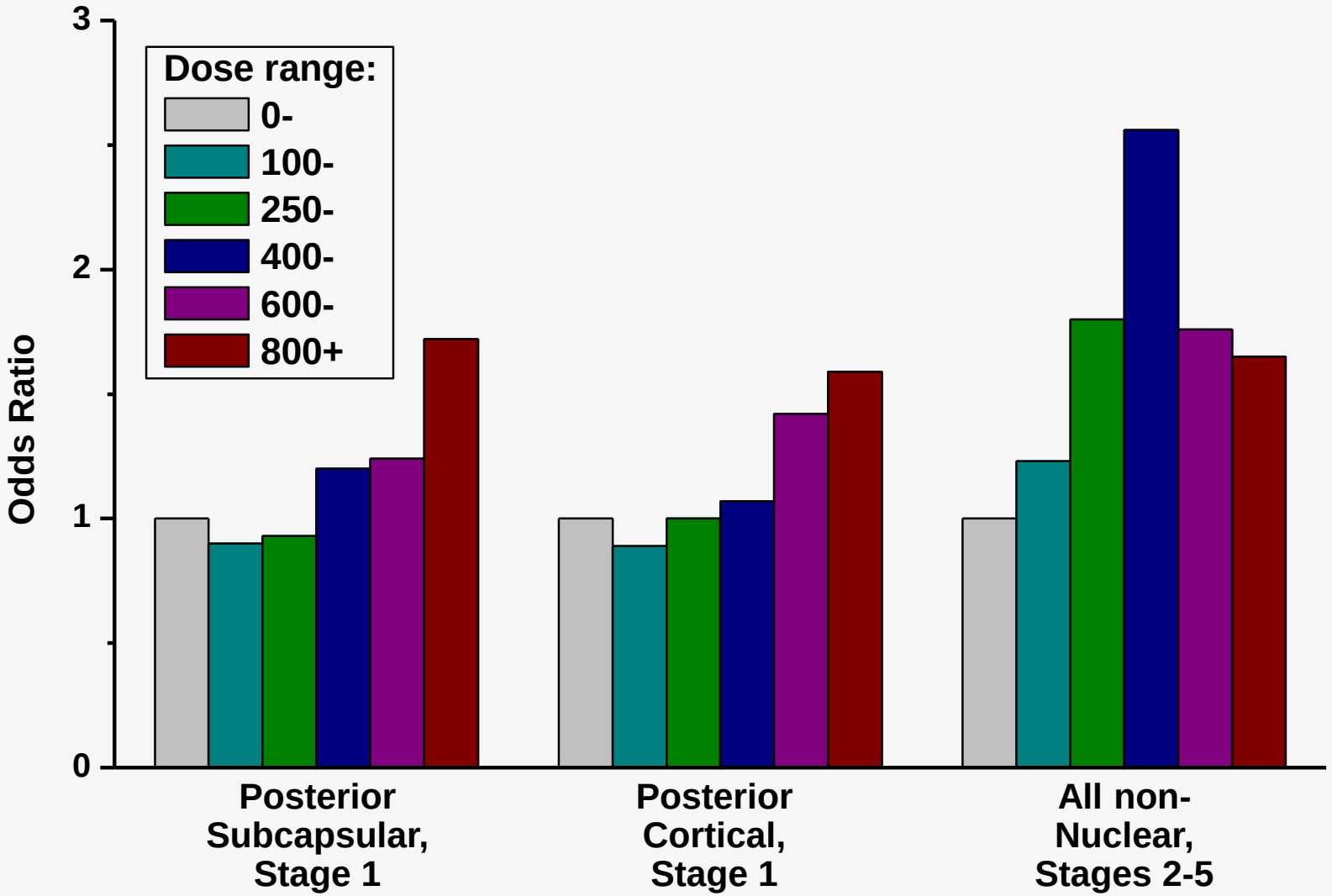
(Chumak, *Radiat Res*, 167:606-14, 2007)

Chernobyl Clean-up Workers: Odds Ratios and 95% CI at 1 Gy for Various Types of Opacities



8,600 workers; 90% <55 y old at exam. (Worgul, *Radiat Res*, 167:233-43, 2007)

Chernobyl Clean-up Workers: Dose-Response Odds Ratios for Types of Opacities



Analyses adjusted for: clinic, age, smoking, diabetes, etc.

(Worgul, *Radiat Res*, 167:233-43, 2007)

Chernobyl Clean-up Worker Cataract Study – Critique

Strengths

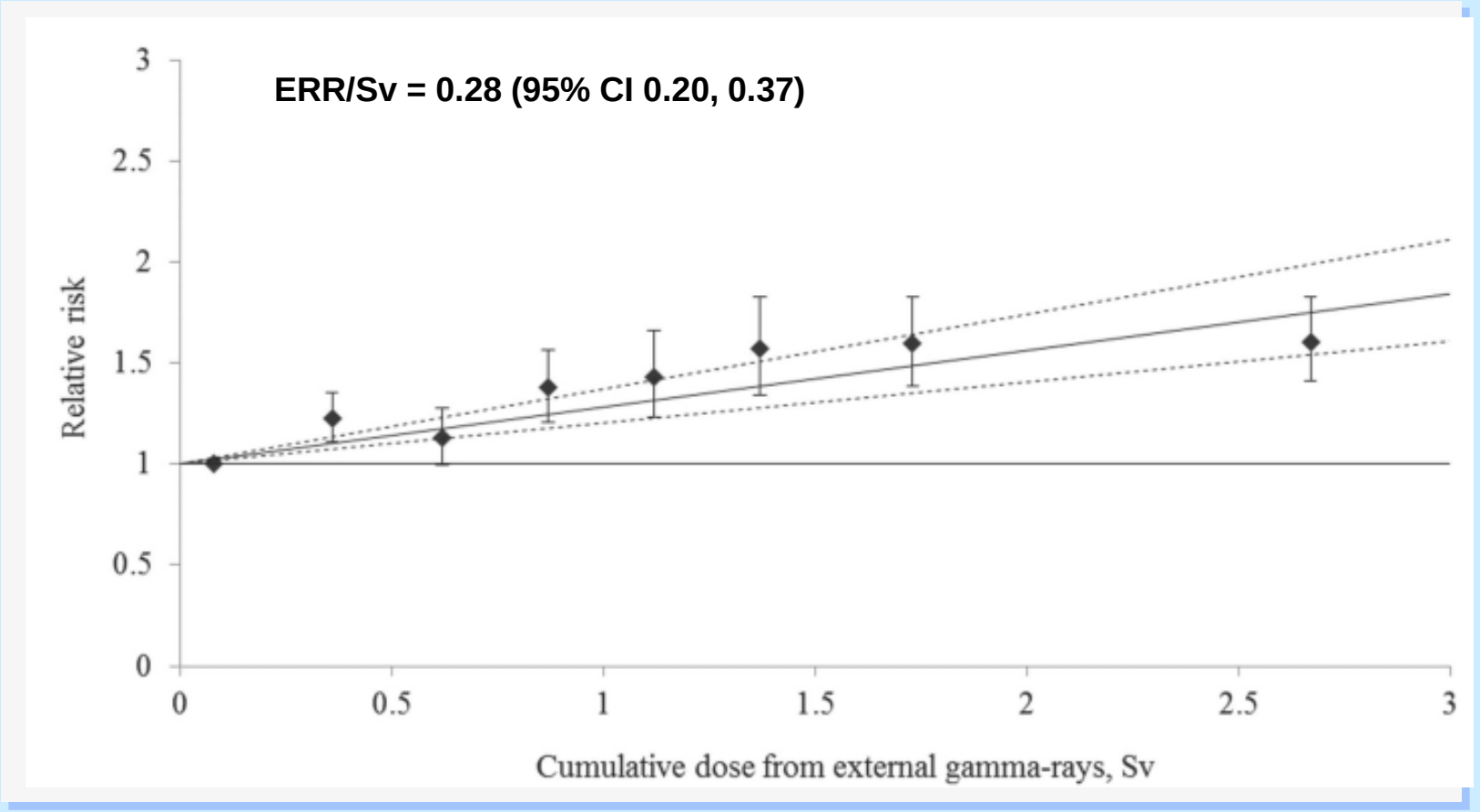
- Mostly low dose rates
- Individual gamma and beta dose estimates were derived
- Blinded ophthalmologic evaluation of large cohort
- Evaluated/adjusted for a number of cataract risk factors

Limitations

- Relatively few measured doses; substantial individual dose uncertainties
- In estimating individual doses, used worker reports for details on types and locations of clean-up work.
- Scoring variation by examiner (but adjusted for)
- Relatively few higher grade opacities

(Worgul, *Radiat Res*, 167:233-43, 2007; Chumak, *Radiat Res*, 167:606-14, 2007)

Mayak Nuclear Workers: Dose-Response for 'Senile Cataract' Incidence, 1948-2008



Senile cataracts in 4159 of 21,060 workers. Mean Hp(10) gamma dose 0.54 Gy in males, 0.46 Gy in females.
(Azizova et al, PLoS One, 10:e0164357, 2016)

Summary of Dose-Response Risk Estimates

Comparison of Estimated Dose-Response Slopes for Posterior Subcapsular (PSC) and Cortical Opacities

Studies and Opacity Endpoints *	RR at 1 Gy (95% CI)
Swedish hemangioma, PSC opacities (Hall '99)	1.5 (1.1, 2.1)
A-bomb, "PSC changes" (Otake '92)	1.6 (1.5, 1.8)
A-bomb, PSC opacities (Nakashima '06)	1.4 (1.2, 1.7)
Chernobyl workers, Grade 1 PSC (Worgul '07)	1.4 (1.0, 2.0)
China, industrial radiographers, PSC (Lian '15)	1.1 (<1, 1.8)
Swedish hemangioma, Cortical opacities (Hall '99)	1.4 (1.1, 1.7)
A-bomb, Cortical opacities (Nakashima '06)	1.3 (1.1, 1.5)
Chernobyl workers, Grade 1 Cortical opacities (Worgul '07)	1.5 (1.1, 2.1)
China, indust. radiogr., Cortical opacities (Lian '15)	1.2 (0.96, 1.4)

* All the studies assessed opacity prevalence.

Comparison of Dose-Effect Slopes for Mixed/Undefined Cataract Types

Studies and Opacity/Cataract Endpoints	RR at 1 Gy (95% CI)
Taiwan, Contaminated buildings, Minor opacities [A,$,*]	1.1 (1.0, 1.2)
Techa River residents, All cataracts [B]	1.4 (0.6, 2.5)
Mayak workers, "Senile cataracts" [C]	1.3 (1.2, 1.4)
U. S. Radiation technologists, All cataracts [D]	3.0 (<1, 5.7)
Chernobyl, All non-nuclear opacities, Stages 1-5 [E]	1.6 (1.2, 2.3)
A-Bomb, Axial opacities [F]	1.3 (1.1, 1.5)
A-bomb, All-cataract incidence [G]	1.06 (1.01, 1.11)
U.S. Radiation technologists, Cataract surgery [D]	2.5 (<1, 7.4)
A-bomb, Cataract surgery incidence [H]	1.3 (1.1, 1.5)

[A] Hsieh '10; [B] Mikryukova '17; [C] Azizova '16; [D] Chodick '08; [E] Worgul '07; [F] Otake '92; [G] Yamada '04; [H] Neriishi '12.

* Studies of opacity prevalence unless noted otherwise; [$] For subgroup examined at <20 years old; had no excess risk on LOCS-III scale, or for those ≥ 20 years.

Comparison of Dose-Response Thresholds

Estimated Dose-Response Thresholds in Lens Opacity Studies (PSC, Cortical, Undefined, "Significant")

Studies and Opacity/Cataract Endpoints	Threshold, Gy (95% CI)
A-bomb, PSC opacity prevalence [A]	0.7 (<0, 2.8)*
Chernobyl, PSC, Grade 1 prevalence [B]	0.4 (0.2, 0.7)
Chernobyl, Cortical, Grade 1 prevalence [B]	0.3 (0.2, 0.5)
A-bomb, Cortical opacity prevalence [A]	0.6 (<0, 1.2)*
Chernobyl, All non-nuclear prevalence, Stages 1-5 [B]	0.5 (0.2, 0.7)
A-bomb, 1949-1964 studies [C]	1.8 (1.3, 2.2)
A-bomb, Axial opacity prevalence, 1963-64 [D,$]	1.4 (<0, 1.8)
A-bomb, PSC (LOCS-II ≥ 2) [A]	0.3 (<0, 1.6)*
A-bomb, Cataract surgery incidence [E]	0.5 (0.1, 1.0)

[A] Nakashima '06, [B] Worgul '07, [C] Schull '92, [D] Otake '96, [E] Neriishi '12; * 90% CI
[$] Axial opacities, probably primarily a mix of PSC and nuclear opacities.

Radiation Risk of "Significant" Cataract, Grades ≥2 or Cataract Surgery

Study and Endpoint	RR @ 1 Gy (95% CI)	Mean Dose, mGy
Chernobyl clean-up; non-nuclear, grades 2-5 [A]	1.8 (0.9, 3.7)	166
China, industrial radiographers; PSC, LOCS-III ≥2 [B]	1.1 (<1, 1.8)	77
China, industrial radiogr.; Cortical, LOCS-III ≥3 [B]	1.2 (0.96, 1.4)	77
U.S. radiologic technologists; cataract surgery [C]	2.5 (<1, 7.4)	28
A-bomb; cataract surgery [D]	1.3 (1.2, 1.5)	0.5 Gy
U.S. Childhood Cancer Survivors; cataract surgery [E]	1.8 (1.3, 2.4)	2.2 Gy
Childhood cancer patients with radiotherapy; cataract surgery [F]	2.0 (1.1, 2.9)	2.6 Gy
U.S. radiologic techs, nuclear medicine; cataract surg. [G]	1.1 (1.0, 1.2) *	Ever nuc. med.
^{131}I treatment for thyroid cancer; cataract surgery [H]	0.9 (0.6, 1.3) * 1.1 (0.6, 1.9)	3.7-7.3 GBq >7.3 GBq
CT examinations; cat. surgery or cat. prescription [I,$]	1.6 (0.9, 2.9) *,$ 2.1 (1.1, 4.1)	1-2 CTs ≥5 CTs

[A] Worgul '07, [B] Lian '15, [C] Chodick '08, [D] Neriishi '12, [E] Chodick '16, [F] Allodji '16, [G] Bernier '18, [H] Lin '16, [I] Yuan '13;
* RR for group, not RR @ 1 Gy; $ Implausible result—probable bias in study.

Does Age at Exposure Modify the Radiation Risk of Cataract?

Dose-Response for Posterior Subcapsular Cataracts and Cataract Surgery in A-bomb Adult Health Study

PSC Prevalence

Age at Exposure (y)	Odds Ratio @ 1 Gy (95% CI)
0-9	1.6 (1.3, 2.1)
10-19	1.3 (1.0, 1.7)
≥ 20	0.9 (0.5, 1.5)
(Age trend p = 0.02)	

(Nakashima et al, *Health Phys*, 90(2):154-, 2006;

Cataract Surgery Incidence

Age at Exposure (y)	Relative Risk @ 1 Gy (95% CI)
10	1.61
20	1.32
30	1.15
(Age trend p = 0.006)	

Neriishi et al, *Radiol*, 265:167-, 2012)

Studies of Interventional Cardiology Workers

Approximate Risk Estimates from Cataract Studies of Interventional Cardiology Workers

	Reconstructed Mean Dose (Gy)	Number Examined	Estimated RR at 1 Gy (95% CI) *
Colombia & Uruguay (Vano '10)	6.0 [C] 1.5 [N]	58 52	1.4 (1.1-1.9) 1.5 (<1-2.8)
Argentina (Vano '13)	5.7 [C] 2.2 [N]	54 69	2.1 (1.4-3.8) 2.9 (1.6-5.6)
Malaysia (Ciraj-Bjelac '10)	1.1 [C,A] 0.64 [N,A]	56 11	5.3 (1.5-20) 7.3 (1.3-32)
Malaysia (Ciraj-Bjelac '12)	1.1 [C] 1.8 [N]	30 22	2.4 (1.2-5.0) 1.7 (1.0-3.2)
France (Jacob '13)	0.42 [C]	106	7.9 (1.7-26)

[A] Median dose; [C] Cardiologists; [N] Nurses/technicians. * Assuming linearity.

Radiation and Cataract: Unresolved Questions

- How large is the dose threshold?
- Are the risks and dose thresholds the same for acute (single moderate/high) exposures and cumulative small exposures at low dose rates?
- Are the risks and dose thresholds the same for minor lens opacities and for clinically significant (vision-impairing) cataracts?

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