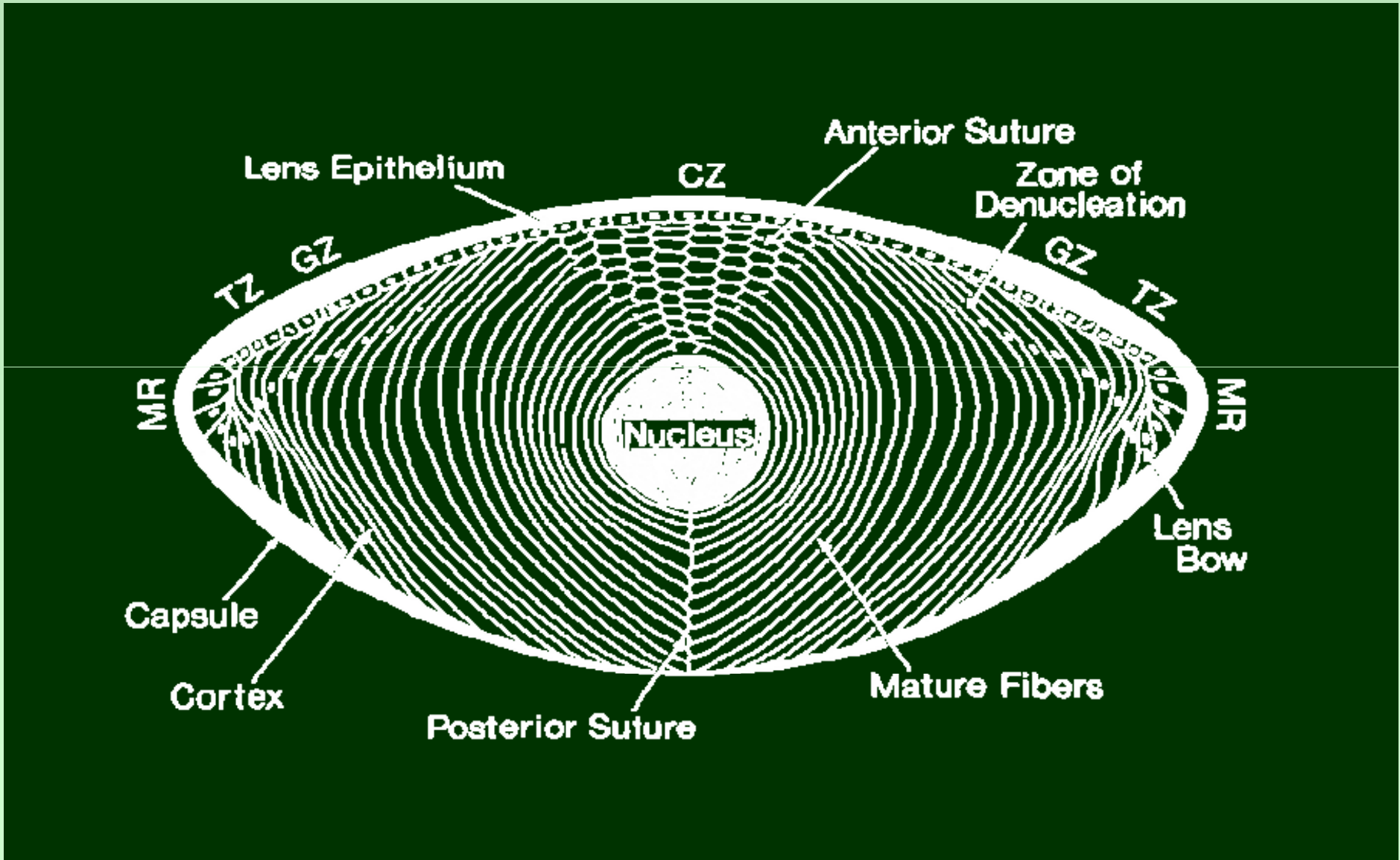


Cataract Risk at Low-to-Moderate Doses: (Not) Seeing is Believing

**Late Health Effects Conference
6 May 2009**

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Radiation Effects Research Foundation**



Courtesy of N. Kleiman, Columbia University



ICRP Guidance on Cataract Induction

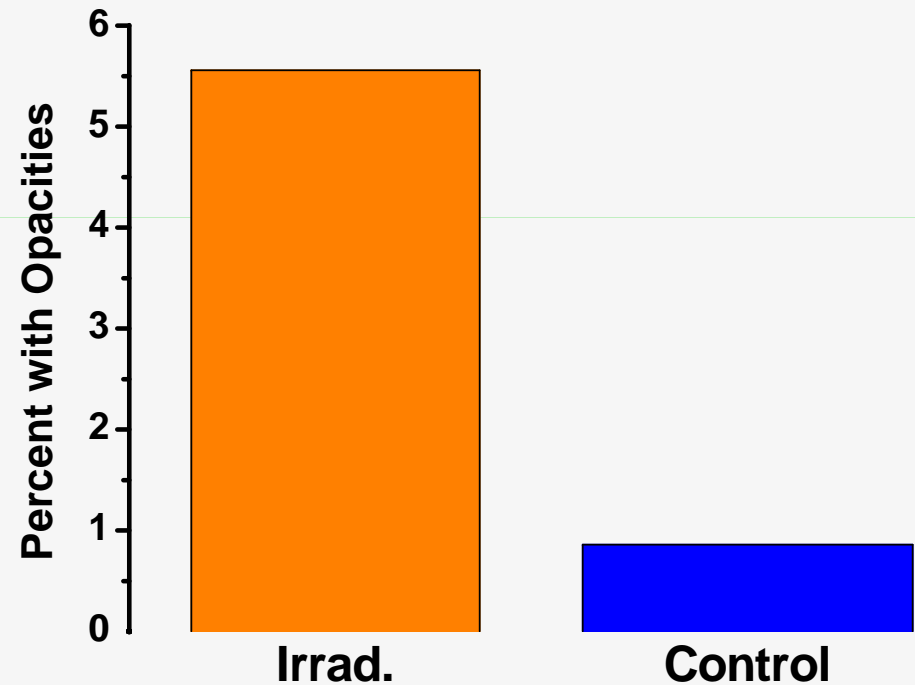
	Brief Exposures (Sv)	Fractionated / Protracted (Sv)	Annual Dose Rate (Sv)
Detectable Opacities	0.5 – 2	5	> 0.1
Visual Impairment	5	> 8	> 0.15

ICRP 60 (1991) and ICRP 103 (2007)



X-ray Treatment for Tinea Capitis

- Median age at irradiation ~7.5 years
- Median age at blinded slit-lamp examination ~17 years
- Mean dose to the eye ~0.5 Gy
- Posterior subcortical opacities (#detected/#examined)
 - 13/234 – Irradiated
 - 2/232 – Control
- Age-adjusted Odds Ratio = 5.9 (95% CI: 1.4, 23.6)



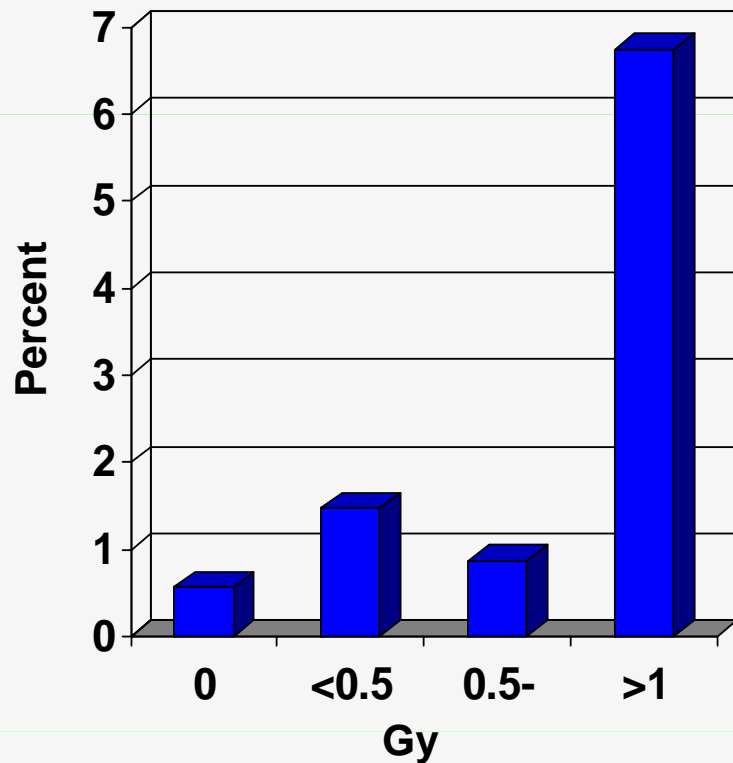
(Albert R et al. *Arch Env Health*, 1968; 17:919-34)



Dose-Response for Lens Opacities after Radium Plaques for Hemangioma in Infancy

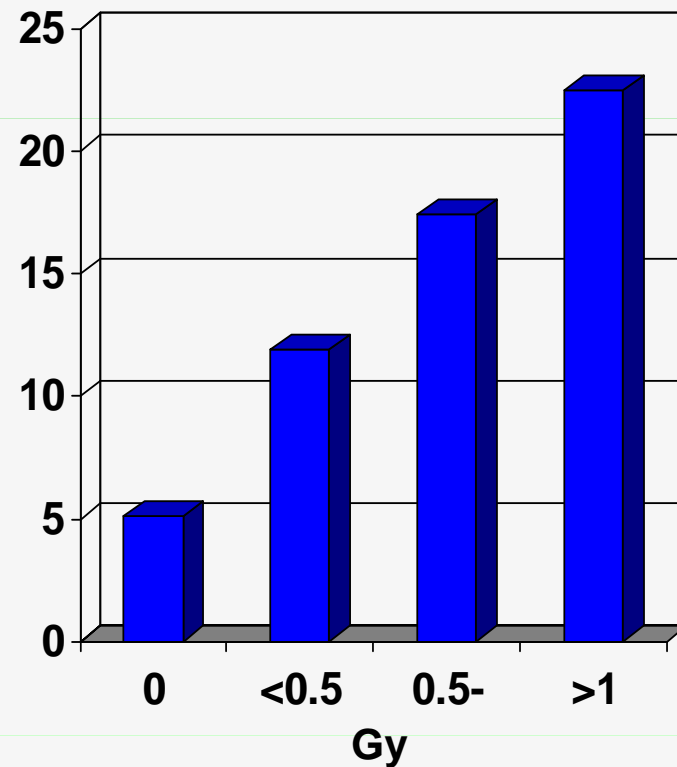
Posterior Subcapsular

$OR_{1Gy} = 1.49$ (CI: 1.1-2.1)



Posterior Subcapsular + Cortical

$OR_{1Gy} = 1.50$ (CI: 1.1-2.0)



Hall P, et al. *Radiat Res*, 1999; 152:190-95



Low Dose-Rate Gamma Irradiation from Radiocontaminated Buildings, Taiwan: Clinical Examination for Lens Opacities

- For those of **ages <20y** (n=61):
 - Mean dose **~170 mGy**. Dose range 1-1200 mGy.
 - Dose-response association for minor lenticular opacities: **OR at 1 Gy = 1.18 (95% CI: 1.02, 1.36)**
- Saw no association for those of ages 20-40 or >40.

(Chen W-L, et al. *Radiat Res*, 156:71-, 2001)

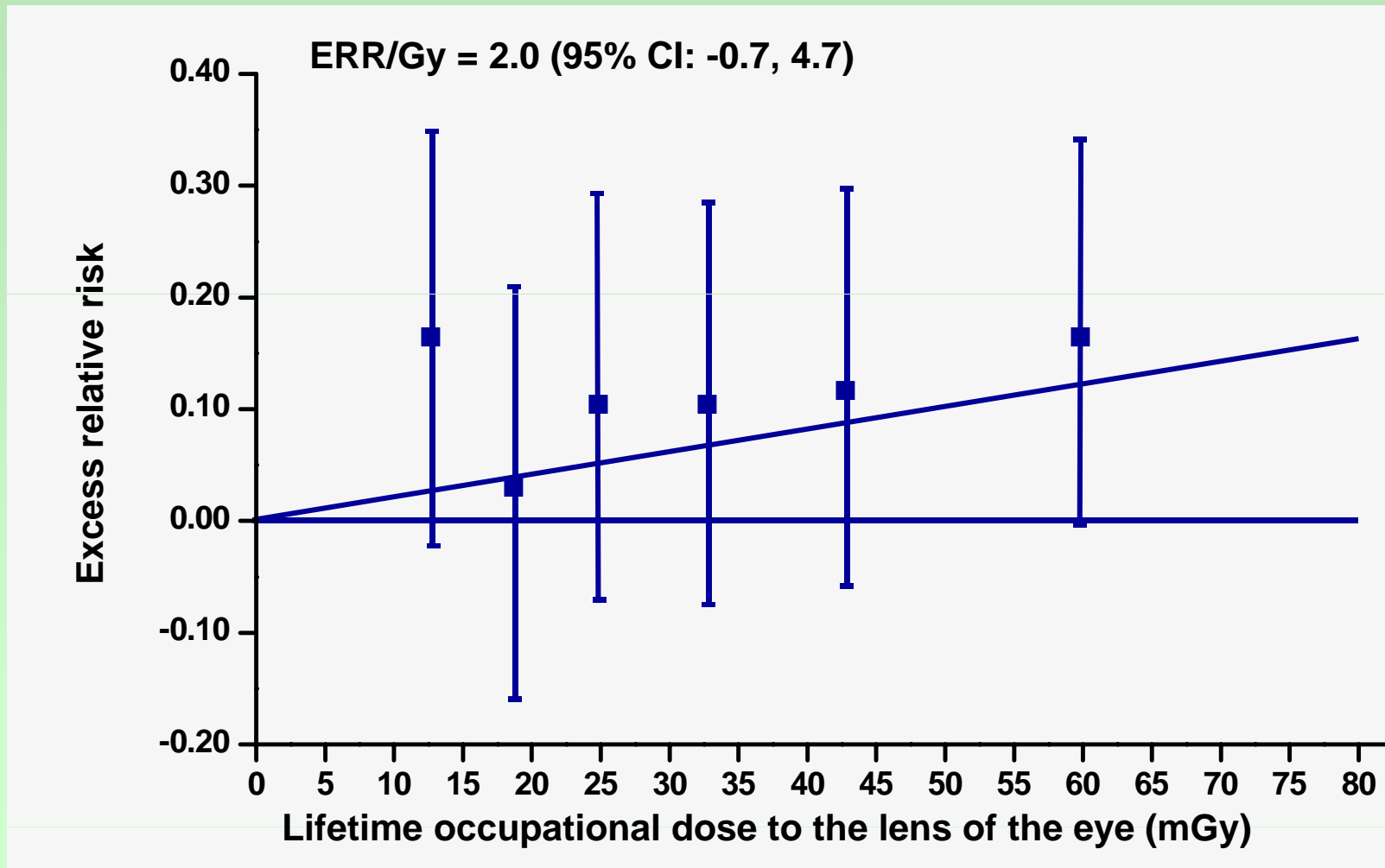


U.S. Radiologic Technologist Study

- **N = 35,700** workers, ages 24-44, followed up for ~20y.
 - **2,380 cataracts**, including 650 cataract extractions
 - Cataract assessment based on self reports
- Median lens dose from occupational exposure = **28 mGy** (highest dose group ~60 mGy)

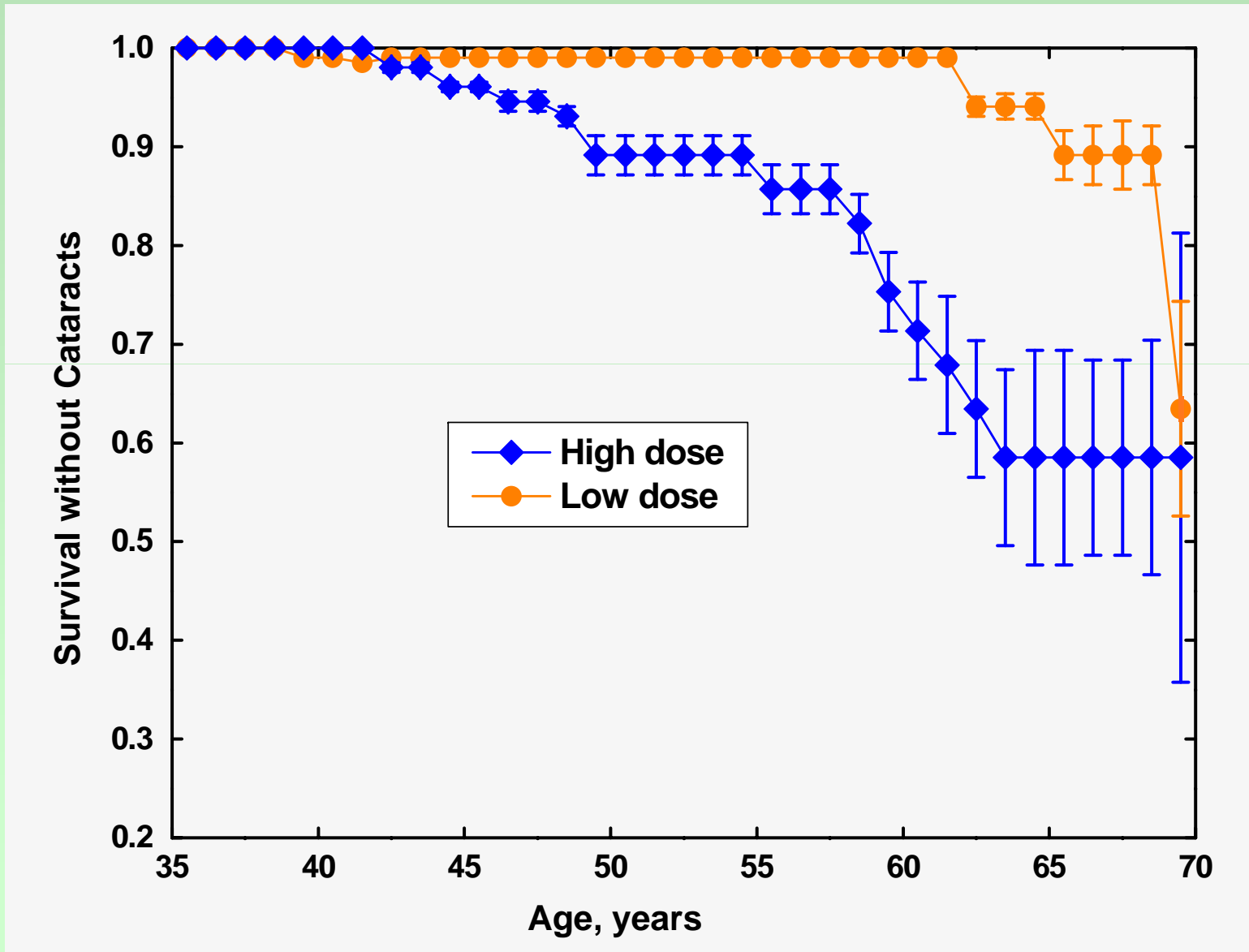
(Chodick, et al. *Am J Epidemiol*, 168:620-, 2008)

Dose-Response for Total-Cataract Risk from Occupational Exposure



Chodick G, et al. *Am J Epidemiol*, 168:620-, 2008

Cataracts in Astronauts, by Radiation Dose



Cucinotta, *Radiat Res*, 156:460-6, 2001

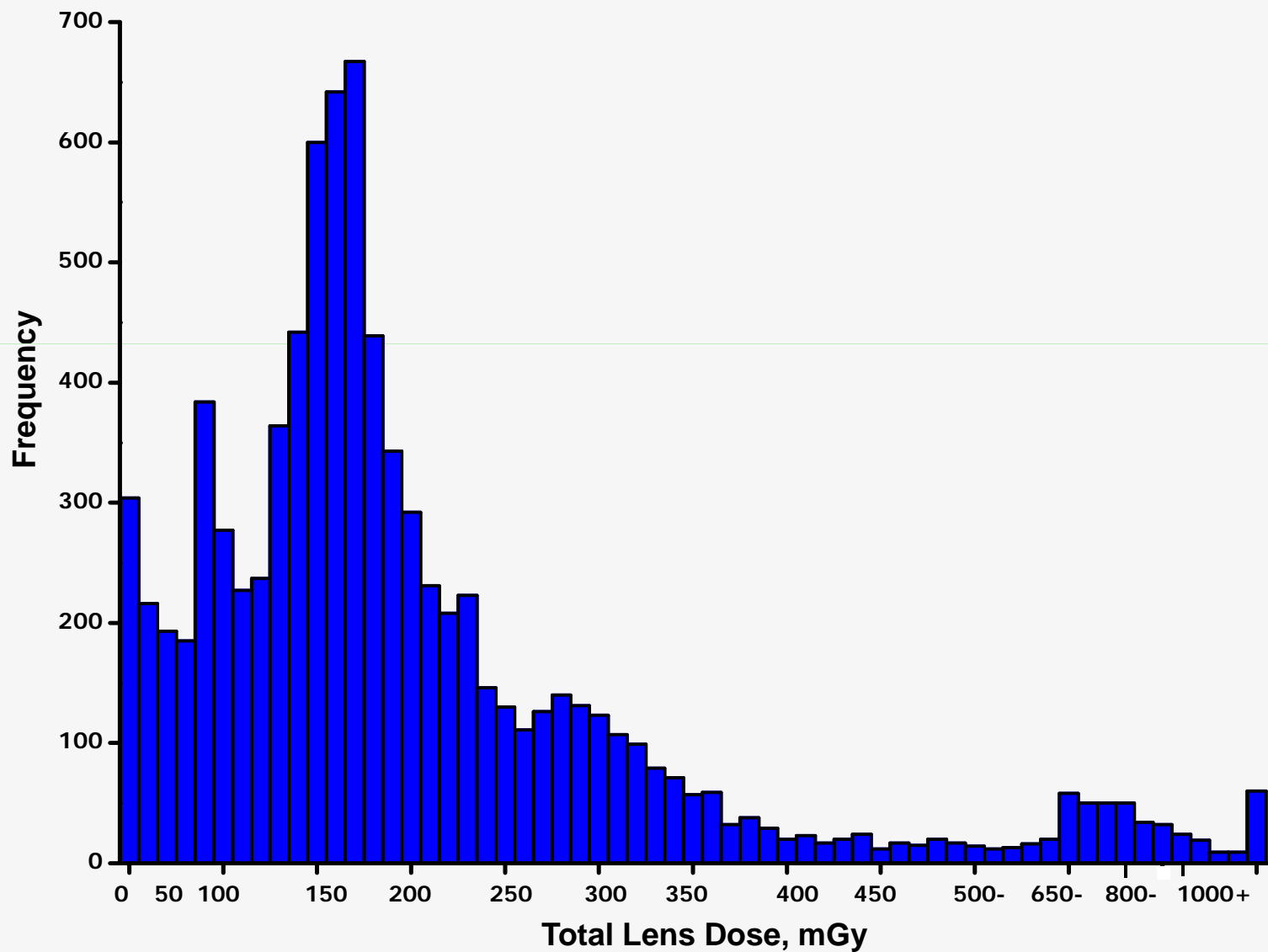


Chernobyl Clean-up Workers

- Subject selection criteria:
8,607 clean-up workers during 1986-87
- Individual estimates of lens doses, but doses mostly estimated and not measured. Median dose of 123 mGy.
- Blinded, standardized ophthalmologic exams 12 and 14 y after exposure. 90% ages 35-54y at exam.
- Analyses adjusted for age, smoking, diabetes, UVR exposure, corticosteroid use, clinic where examined, etc.

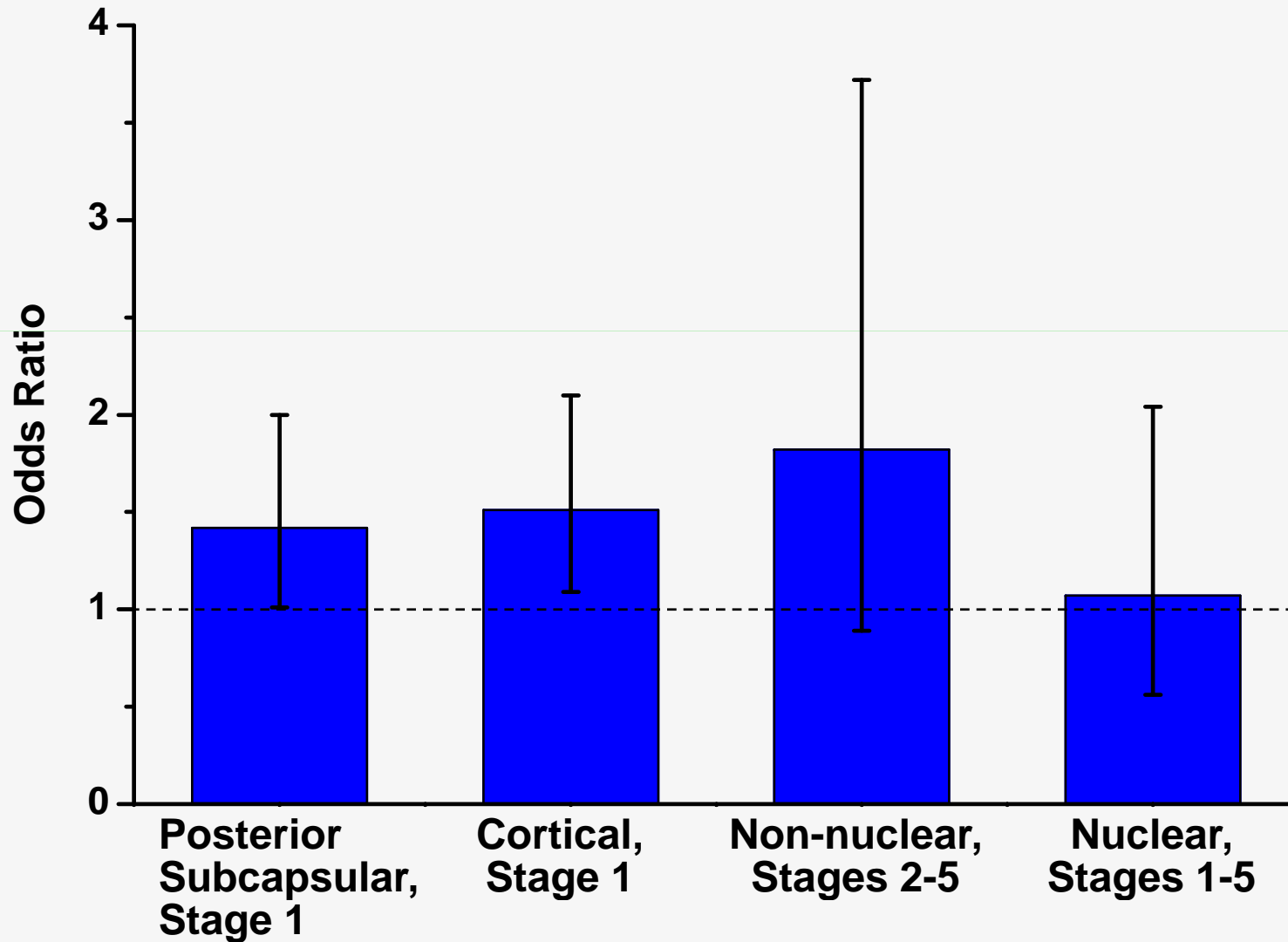
(Worgul, *Radiat Res*, 167:233-43, 2007)

Frequency Distribution of Workers' Lens Doses



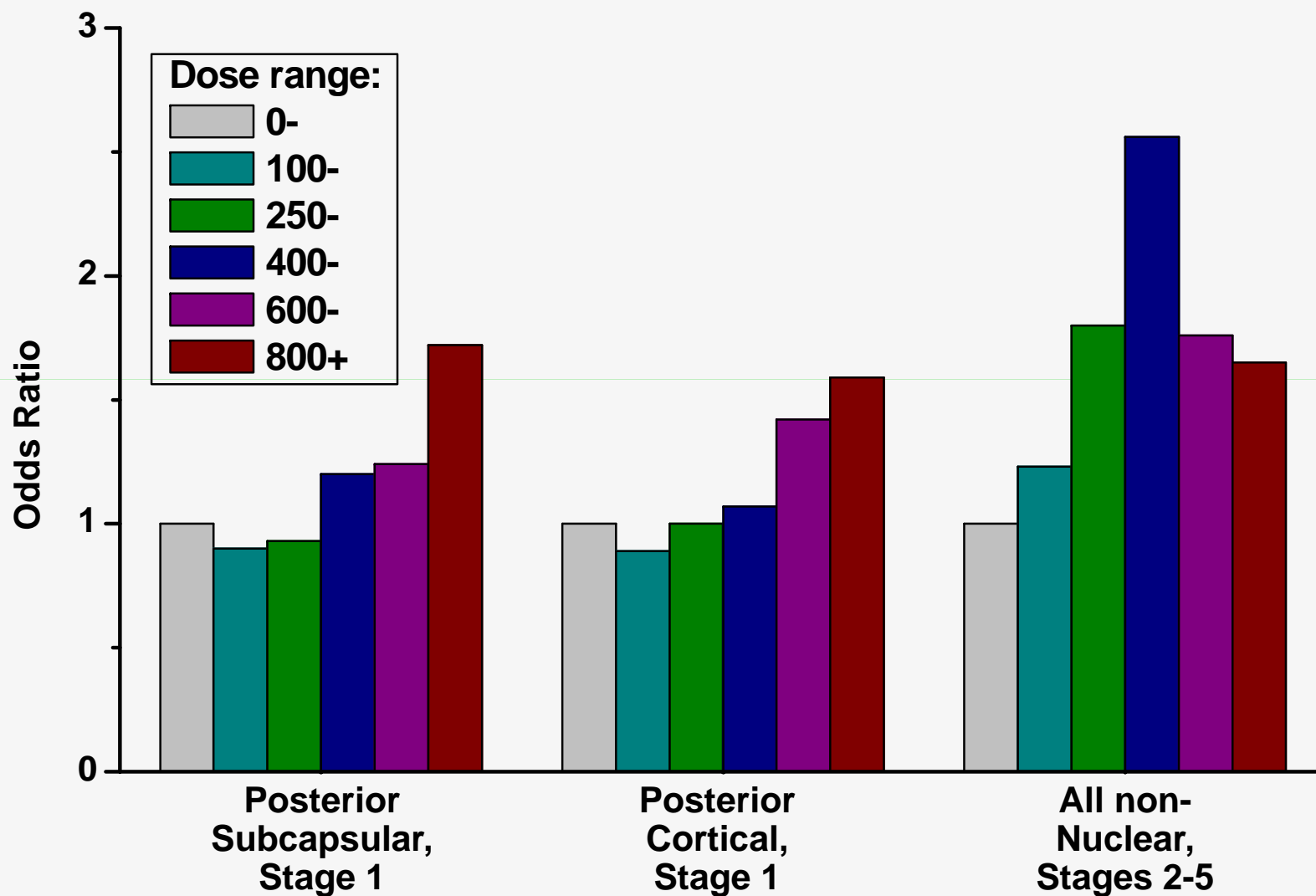
(Chumak, *Radiat Res*, 167:606, 2007)

Odds Ratio and 95% Confidence Intervals at 1 Gy for Types of Opacities



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

Odds Ratios by Dose Response for Types of Opacities



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

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

Chernobyl Cleanup Workers: Cataract Dose Threshold

Type of Opacity	Dose-effect threshold, Gy (95% CI)
Posterior subcapsular, Stage 1	0.35 (0.19-0.66)
Posterior Cortical, Stage 1	0.34 (0.18-0.51)
Stage 1-5 non-nuclear cataract	0.50 (0.17-0.69)

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

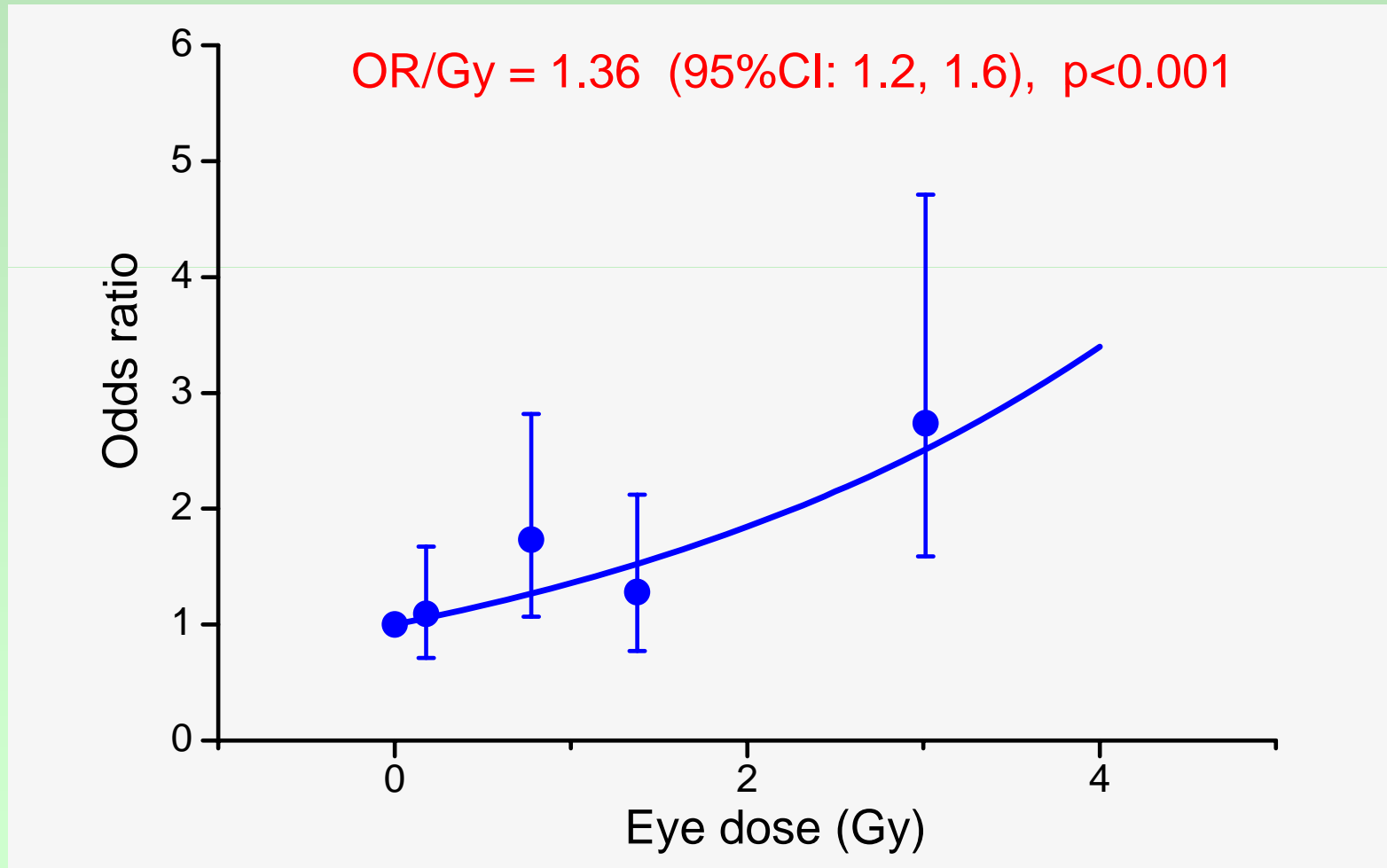
Japanese Atomic Bomb Survivors: Adult Health Study (AHS), Lens Opacities and Surgically Removed Cataracts

Minamoto A, et al. *Int J Radiat Biol* 80:339-345; 2004.

Nakashima E, et al. *Health Phys* 90:154-160; 2006.

Neriishi K, et al. *Radiat Res* 168:404-408; 2007.

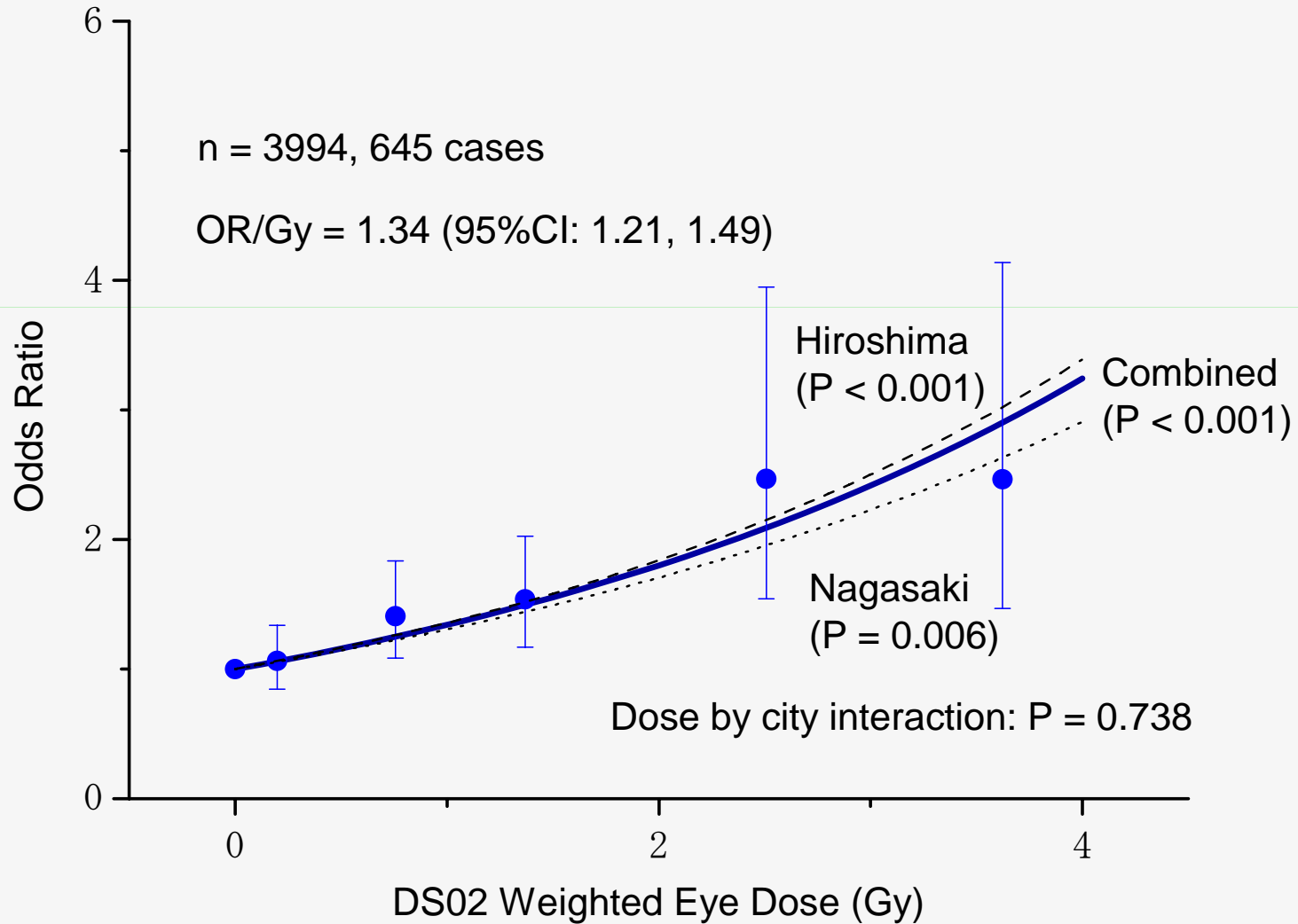
AHS Ophthalmologic Screening: Posterior Subcapsular Opacities



(Minamoto, *Int J Rad Biol*, 80:339, 2004)



Prevalence of Surgically Removed Cataracts by Dose



(Neriishi, Nakashima et al, 2008, Unpub)



Cataract Dose-Threshold Estimates

Study	Dose-Threshold Estimate (CI), Gy	Cataract Endpoint	Comments
Ra-224 – Ankylosing spondylitis (Chmelevsky, 1988)	0.025 – 0.16	Mostly extractions	Alpha dose, Lens doses uncertain, Apply RBE of 20??
Chernobyl cleanup workers (Worgul, 1997)	0.35 (0.19-0.66) → 0.34 (0.18-0.51) → 0.50 (0.17-0.69) →	Stage 1, PSC Stage 1, Cortical Stages 1-5, Non-nuclear	Gamma+Beta, Protracted, Young adult ages, Doses uncertain
A-bomb survivors (Nakashima 2006; Neriishi, 2007; Nakashima, 2009, Unpub)	0.7 (<0-2.8) → 0.6 (<0-1.2) → 0.0 (<0-0.7) → 0.4 (<0-0.8) →	Screening, PSC Screening, Cortical Extracted, preval. Extracted, incid.	Late ages at exam, 55y after irradiation; ages 0– ~35y at irradiation.



Radiation and Cataract: Unresolved Issues

- What is the dose threshold and degree of risk for opacities following highly fractionated or protracted exposure?
- What is an appropriate estimate of the dose threshold for the induction of vision-impairing cataracts? How does this impact regulations?
- How often do minor opacities grow to become vision-impairing cataracts?
- Degree to which age at exposure affects radiogenic cataract risk?
- What biological mechanisms mediate the development of radiation cataracts?



Radiation and Cataract: Addressing Mechanisms

- At RERF we are implementing a protocol to collect cataract tissue samples from ophthalmologists for persons in our Life Span Study (so that we have dose estimates) – K. Neriishi
 - Cryopreserve specimens – several per month
 - Collaborations with radiobiologists to conduct mechanistic studies in the future.
-
- Study of polymorphisms in *ATM* gene and susceptibility to radiation-induced cataract – K. Neriishi



Thank you