Dosimetry for Epidemiologic Studies of Nuclear Workers

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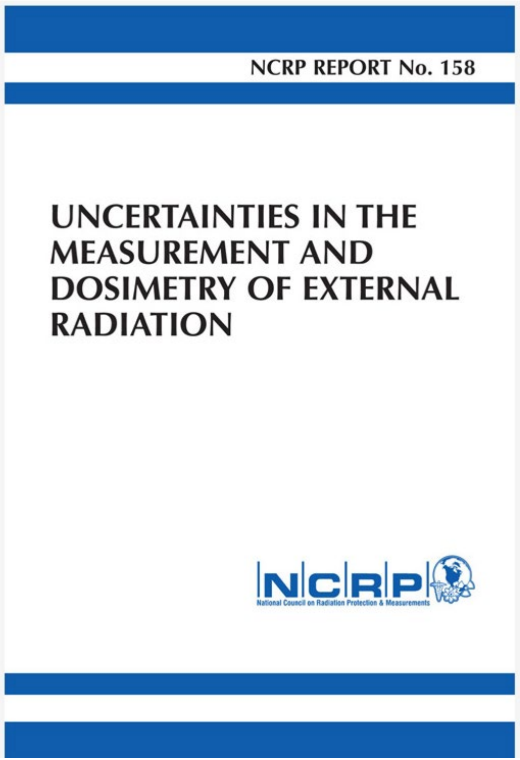
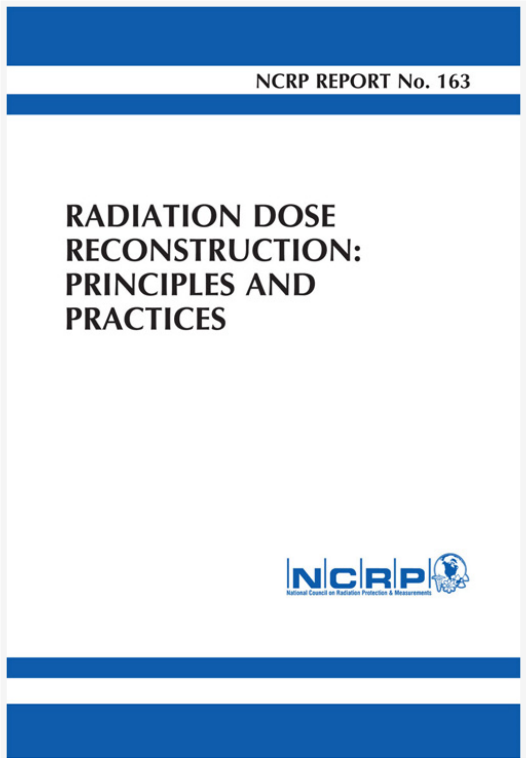
Suggested References





Occupational Exposure to Ionizing Radiation:

Nuclear Workers (BEIR VII):

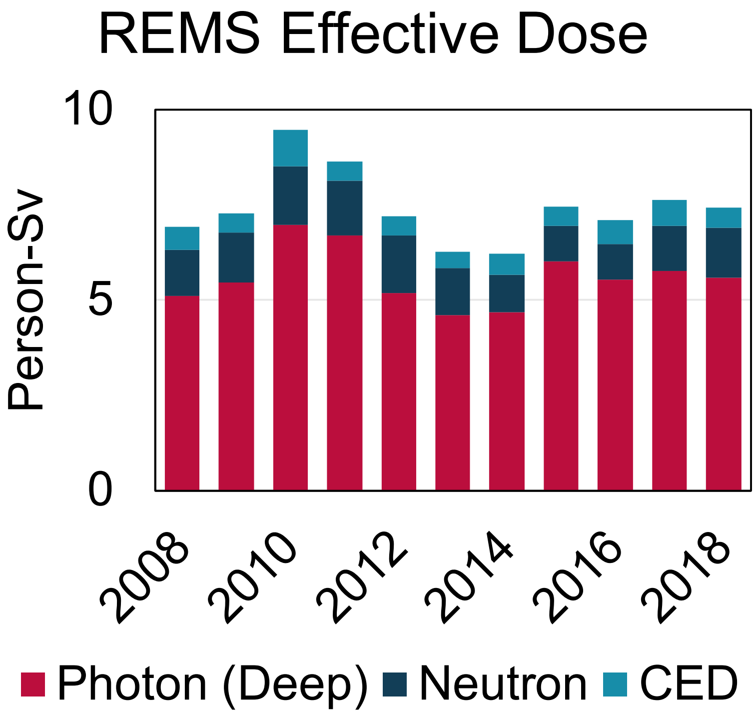
- Commercial nuclear power
- Nuclear weapons manufacture
- Enrichment and reprocessing of nuclear fuel
- Reactor research

Other Radiation Workers

- Chornobyl Liquidators
- Medical workers (e.g., radiologists, nuclear medicine, radiological technicians)
- Airline crews
- Uranium miners/millers
- Atomic veterans

Nuclear Workers

- ~ 1M workers worldwide
- Mid-1940s to present
- Exposed mostly to high energy photons (300 keV to 3 MeV)
- Personal monitoring data available



Nuclear Worker Epi Studies (2008-2017):

Study Population	Period	No. Exposed Workers	Average dose[1]	Study Reference
Korean NW	1984-2004	79,679	6	Ahn et al 2008
UKNRRW	1946-2001	174,541	25	Muirhead et al 2009
Korean NPW	1978-2005	16,236	20	Jeong et al 2010
Rocketdyne NW	1948-1999	5,801	14	Boice et al 2011
Japanese NW	1957-2002	200,583	12	Akiba and Mizuno 2012
Canadian NW	1956-1994	45,316	22	Zablotska et al 2014
German NPW	1966-2008	8,972	30	Merzenich et al 2014
US NW	1944-2005	119,195	20	Schubauer-Berigan et al 2015
INWORKS	1944-2005	308,297	21 mGy (colon)	Richardson et al 2015
			16 mGy (RBM)	Leuraud et al 2015
French NW	1950-2004	59,004	26	Leuraud et al 2017

1. Penetrating whole-body equivalent dose from low-LET radiation (mSv), unless otherwise indicated.

Occupational Radiation Studies: Utility in Risk Assessment

Advantages:

- Direct estimation of the effects from protracted low-dose exposure
- Individual measurements generally preferred in dose-response analyses

Limitations:

- Usually underpowered
- Potential for unmeasured confounding
- Healthy worker effects
- Dose error is not taken into account in most studies.

BEIR VII (NRC 2006): … *the committee concluded that the occupational studies are currently* ***<u>not suitable for projection of population-based risk.</u>***

Study Design and Dose Reconstruction

EPI Study Needs:	Dose Reconstruction Effects
Sufficient size (person-years): • Large number of exposed workers • Long observation period accounting for latency	Adding person-years increases the complexity
Detailed information on factors that can modify or confound the effect	More information on "factors" means: • Assessing multiple exposure scenarios and pathways • Estimating concomitant exposures to other agents
Accurate and precise analysis variables	Individual dose estimates with assessment of error

Two Common Designs

Cohort:

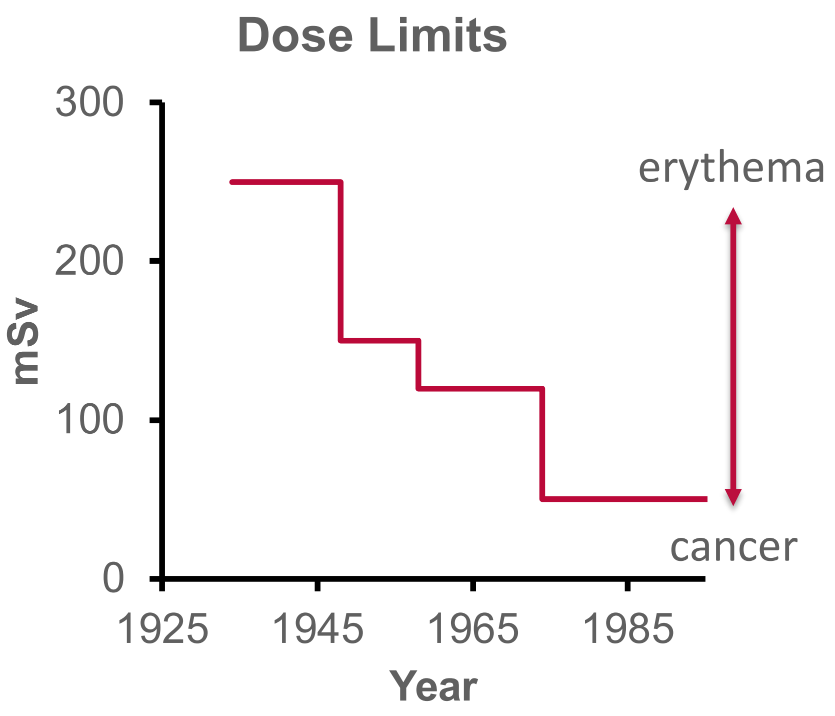
- Large study population
- Multiple targets tissues
- Summary doses:
  - Annual external dose
  - Sparse data on internal dose
- Limited data for uncertainty analysis

Nested Case-Control:

- Smaller study population
- One target tissue
- Individual measurements:
  - Quarterly, monthly, biweekly dosimeter measurements
  - Bioassay and *in vivo* measurements
- Detailed uncertainty analysis possible.

Nuclear Worker Dosimetry Practices

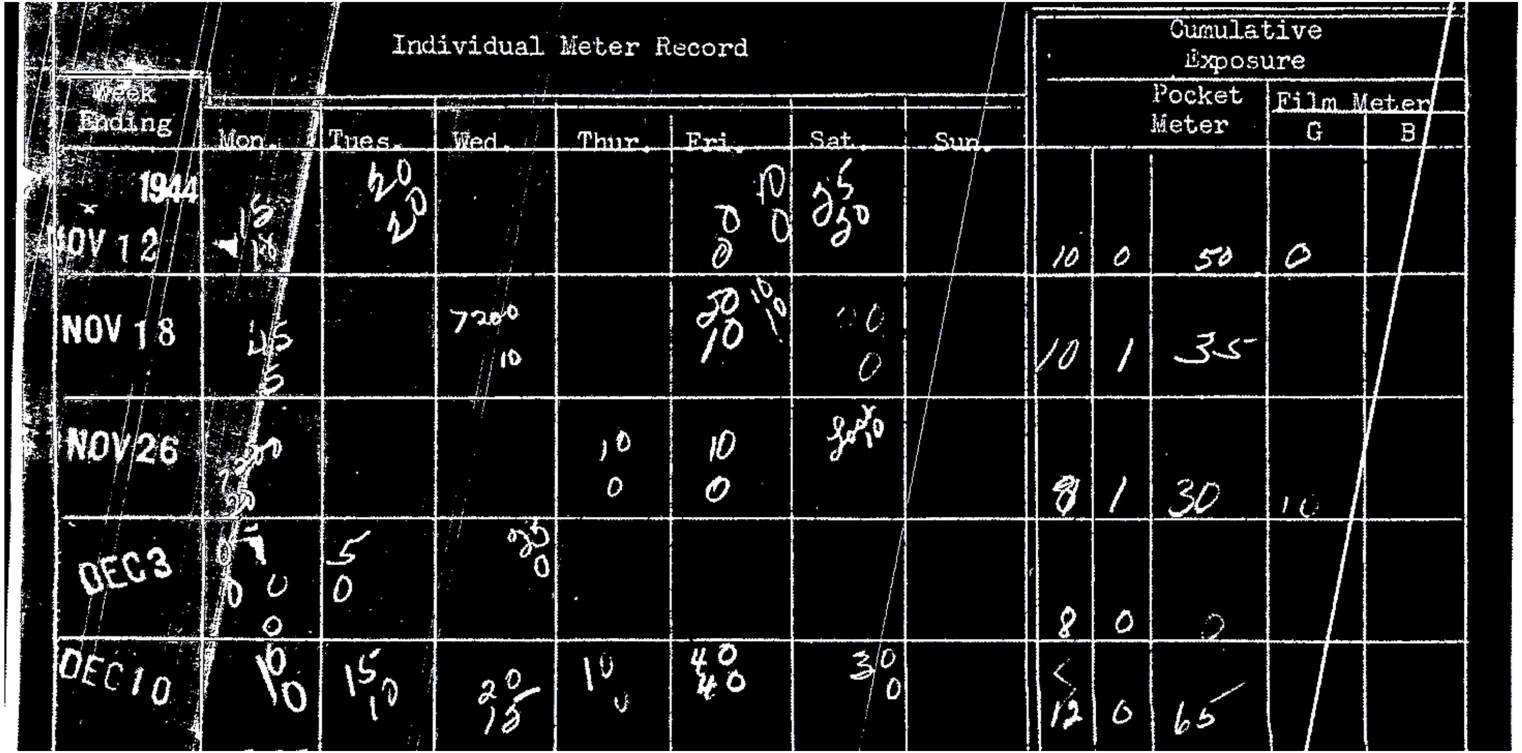
- Dosimetry designed for worker protection, not research.
- Regulatory requirements affect workplace monitoring.
- Safe work practices are informed by research.
- **Dose error becomes smaller over time.**



Nuclear Worker Dosimetry

Timeframe	Dosimeter	Characteristics
<1944	Paired pencil-type ion chambers (pocket meters)	Unreliable, tendency to overestimate dose.
1944 – early 1950s	Two-element film badge	Improved reliability; still tendency to overestimate dose.
1950s – early 1970s	Multi-element film badge (mixed radiation fields)	Reliable, monthly processing in late 1950s improves sensitivity
1970s – late 1980s	TLD	Improved precision and reliability
Late 1980s on	TLD with laboratory accreditation	Tissue equivalency and Hp(10) standardized by the mid 1990s

Common Early Dosimetry Record (film and pocket meter)



Week Ending	Mon.	Tues.	Wed.	Thur.	Fri.	Sat.	Sun.			Pocket Meter	Film Meter G	Film Meter B
1944 NOV 12	15 18	20 20			0 0 10 0	25 20		10	0	50	0	
NOV 18	15 5		7200 10		20 10 10 10	10 0		10	1	35		
NOV 26	[illegible]			10 0	10 0	[illegible]		8	1	30	10	
DEC 3	0 0 0 0	5 0	25 0					8	0	[illegible]		
DEC 10	10 10	15 10	20 15	10 0	40 40	30 0		12	0	65		

Common Sources of Dose Uncertainty

- Random and systematic error in measurements
- Incomplete exposure histories
- Undetected dose
- Notional dose assignments

Typical Sources of Systematic Error in Measured Dose

- Radiation factors (source and field)
  - Energy, geometry (wearing), and dose dependence
- Exposure environment
  - Material uniformity
  - temperature, humidity, light, shock

- Laboratory error
  - Calibration (representativeness of exposure conditions)
    - In-air vs. on-phantom (backscatter)
    - Calibration source and geometry
  - Analytical procedures
    - Dosimetry processing
    - Monitoring frequency
    - Dose interpretation

Sources of Systematic Error: Unadjusted Dose

Source	Description	Common Correction
Unadjusted Dose	Recorded dose poorly describes **absorbed dose to target tissues**.	Adjust measurements to account for radiological, laboratory, and environmental sources of error. Example: INWORKS (Thierry-Chef et al, 2015)

$$B_i = \frac{D_{recorded}}{D_{true}}$$

Bias factor from source *i*

$$B_{final} = \prod_{i=1}^{n} B_i$$

Total bias

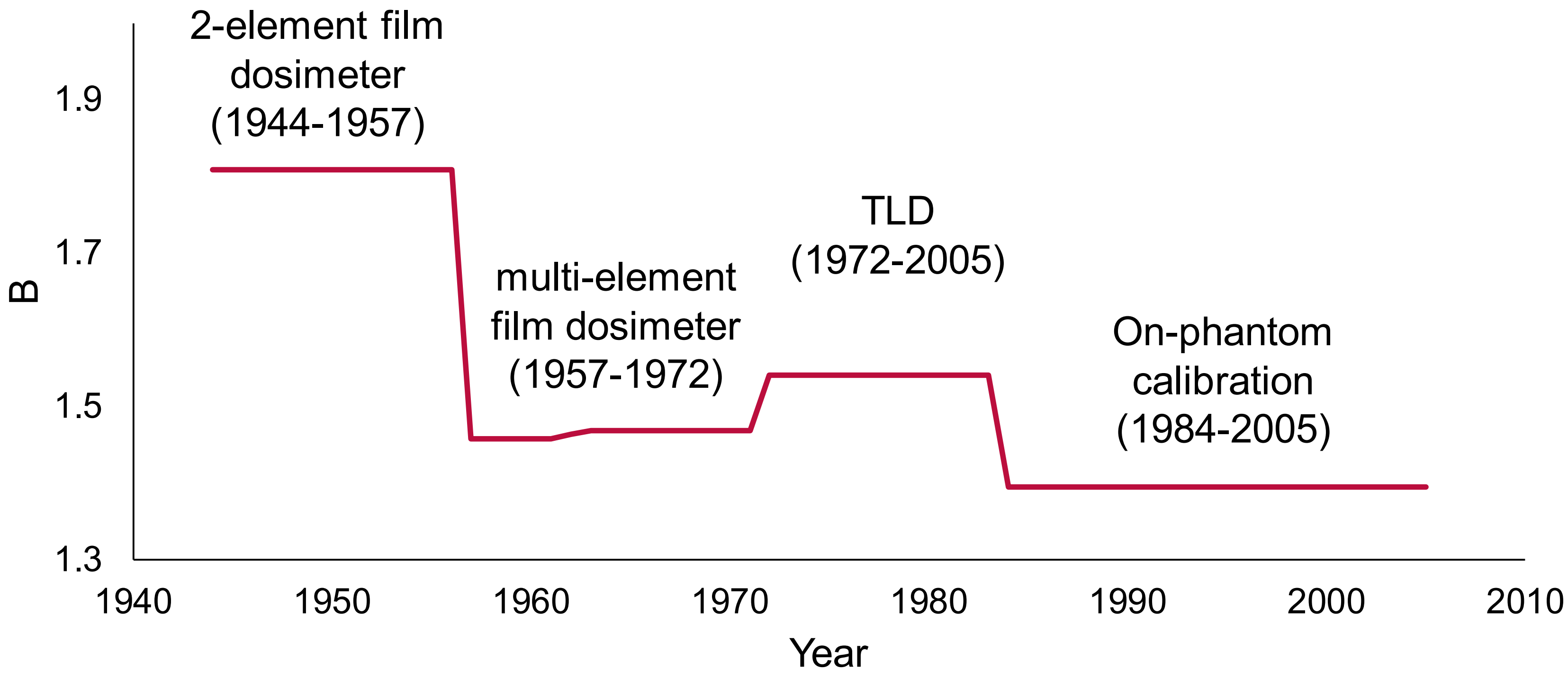
$$K_i = GSD^{1.96} = e^{1.96\sigma_i}$$

Uncertainty in B_i

$$\mathrm{K} = e^{1.96\sqrt{\sum_{i=1}^{n}\sigma^2}}$$

Total Uncertainty *(single measure)*

INWORKS RBM Bias Factors (Hanford 1944-2005, males)



INWORKS Effective Bias Factors for Cumulative Dose

			$H_P(10)$			RBM			Colon		
Country	**N**	**Record**	**D**	**B**	**Δ%**	**D**	**B**	**Δ%**	**D**	**B**	**Δ%**
France	59003	16.1	18.4	0.9	14.4	11.6	1.4	-27.8	12.6	1.3	-21.7
UK	147866	27.5	28.7	1.0	4.6	18.2	1.5	-33.9	19.9	1.4	-27.7
US	101428	23.2	24.0	1.0	3.4	15.2	1.5	-34.5	16.7	1.4	-28.2
ALL	308297	23.9	25.2	0.9	5.5	15.9	1.5	-33.3	17.4	1.4	-27.1

On average, badge dose overestimates absorbed dose to RBM by about 30%

Systematic Error: BDL Dose

Source	Description	Common correction
Below Detection Limit (BDL) doses	Exposures below the detection threshold of the dosimetry system are not accounted for in dose estimates.	Adjust recorded dose to account for BDL doses by substitution or distribution fitting.

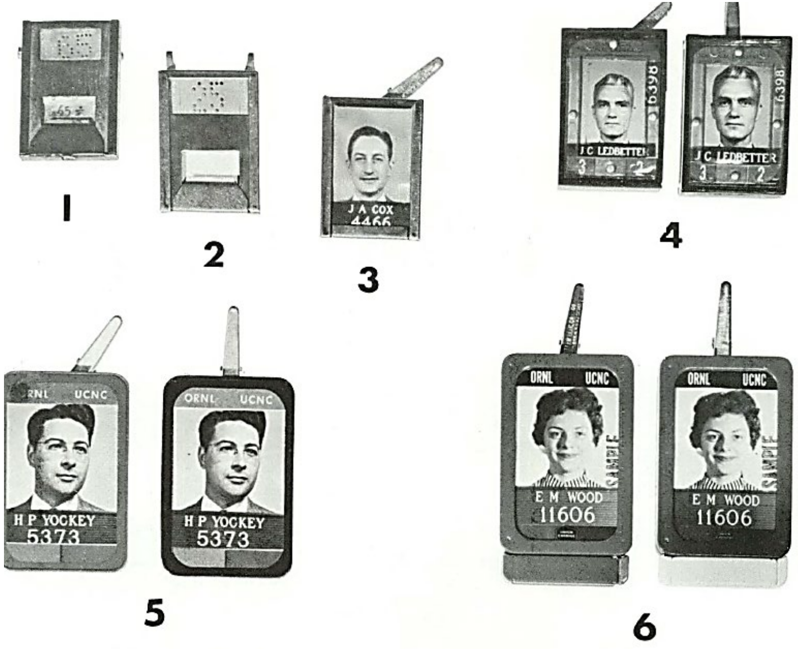
Typical Dosimeter Sensitivity

Era	Limit of Detection (mSv)	Monitoring Frequency	Maximum Annual Missed Dose (mSv)
1940s-1960s	0.30	Weekly	15.6
1960s-1970s	0.10	Biweekly, monthly, quarterly	2.6, 1.2, 0.4
1970s-2000s	0.05	Monthly, quarterly	0.6, 0.2
2000s	0.01	quarterly	0.04

- Most studies have not indicated a strong bias in dose-response from BDL doses (e.g., Muirhead et al 2009; Telle-Lamberton et al 2007; Kubale et al 2005)
- Error is largest for exposures prior to 1960 (e.g., Frome et al 1997).

BDL Doses: ORNL (1943-1956) example

- Film badge monitoring weekly, minimum sensitivity 0.3 mSv.
- After adjustment:
  - 50% increase in mean cumulative dose (10.8 to 16.3 mSv, Watkins et al 1997)
  - 22% decrease in cancer risk per Sv after adjusting for BDL doses (Frome et al 1997).

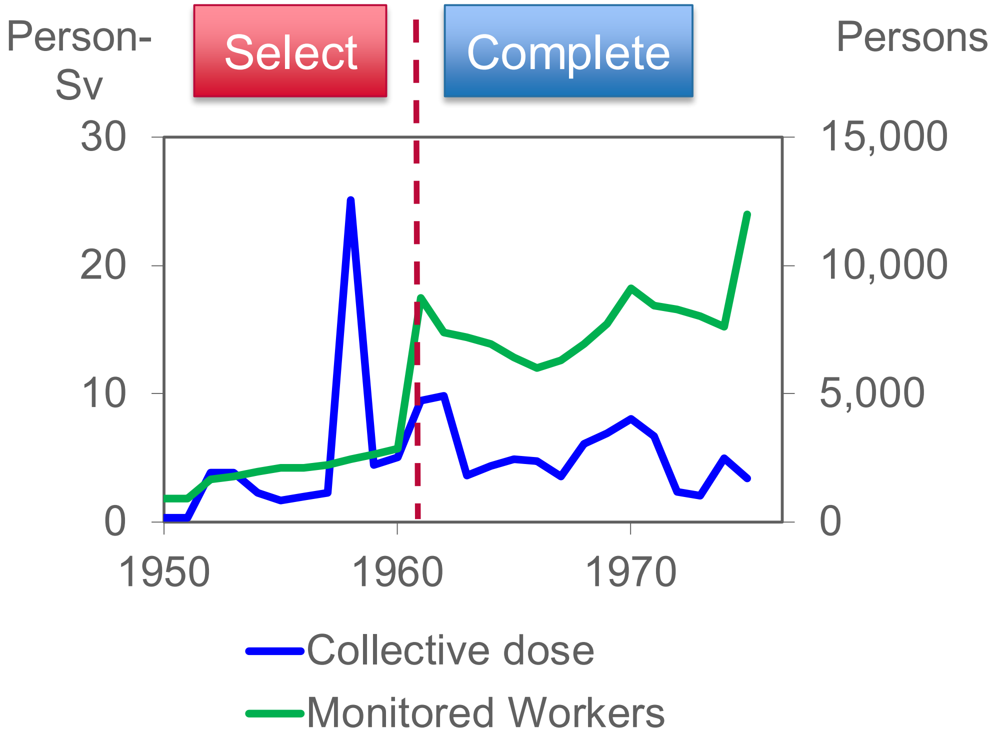


Systematic Error: Missing Dose

Error	Description	Typical sources	Common correction
Incomplete exposure history	Dose accrued by a worker that is not included in the dose of record.	Compliance monitoring Radiation work in other facilities Work-related X-rays Exposures below the detection threshold of the dosimeter.	Coworker models Search multiple databases Develop WRX exposure model based on equipment, procedures, and job assignment

Compliance Monitoring (Y12 Example)

- Select (1947-1960): workers who could exceed 3 mSv/qtr.
- 70% increase in mean cumulative dose (Watkins et al 1997)
- 48% decrease in cancer ERR/Sv (Frome et al 1997).



Random Error

Source	Description	Potential effect on dose-response	Common correction
Classical error	Natural variation in dose measurements	Loss of power. Attenuates dose dose-response.[1]	Adjust dose-response models using regression calibration or MLE
Berkson	Error that occurs when the mean for a group is substituted for the individual dose within the group.	Loss of power. Berkson error results in little bias	None

Other Errors

Source	Description	Potential effect on dose-response	Common correction
Shared error	Correlations in errors between individuals, groups, or time.	Increased variance (wider CIs) Possible bias from misspecification of mean.	Examine multiple realizations of dose by Monte Carlo simulation
Differential Error	Systematic error that is differentially distributed by case status	Bias in either direction and can lead to spurious associations	Keep exposure assessors blinded to case status

Measurements for most nuclear workers:

- Are comparable through time and across facilities, thus appear suitable for epidemiologic purposes.
- Reasonably approximate personal equivalent dose, but may need adjustment to estimate organ absorbed dose.
- Are less reliable at low exposures and during earlier years of operation.
- Includes limited information on internal contamination and neutrons, but these sources likely contribute little to total worker dose.

Dose Error and Dose-Response

- The effect depends on the magnitude, the error structure, and if shared or independent. In general:
  - Random error reduces power and can attenuate the dose-response.
  - Systematic error that is non-differential can affect the slope but is unlikely to cause a spurious response.
  - Differential error can cause a spurious dose-response; however, this error is unlikely in most NW studies.
- Dose error is more likely to mask a true dose-response than lead to a spurious one (Gilbert 2009).

Question #1

- Standards for protection against occupational ionizing radiation exposure (i.e., dose limits) are based on cancer risks projected from nuclear worker studies.
- A. True
- B. False

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- Standards for protection against occupational ionizing radiation exposure (i.e., dose limits) are based on cancer risks projected from nuclear worker studies.
- A. True
- **B. False**

Question #2

- Studies examining the effects of dose error on risk estimates in nuclear worker studies have found:
  - A. Little evidence of a strong bias in risk estimates from dose error.
  - B. a decrease in estimate precision (i.e., wide confidence intervals) after accounting for dose error.
  - C. Dose error is more likely to mask a true dose-response than lead to a spurious one.
  - D. All of the above.

Question #2

- Studies examining the effects of dose error on risk estimates in nuclear worker studies have found:
  - A. Little evidence of a strong bias in risk estimates from dose error.
  - B. A decrease in estimate precision (i.e., wide confidence intervals) after accounting for dose error.
  - C. Dose error is more likely to mask a true dose-response than lead to a spurious one.
  - **D. All of the above.**

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