Presenter Disclosures

Sensitivity Analysis to Quantify the Impact of Outcome Misclassification on Health Risk Models: A Simulation Approach

1. **The following personal financial relationships with commercial interests relevant to this presentation existed during the past 24 months:**

   No relationships to disclose

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Sensitivity Analysis to Quantify the Impact of Outcome Misclassification on Health Risk Models: A Simulation Approach

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U.S. Transuranium and Uranium Registries

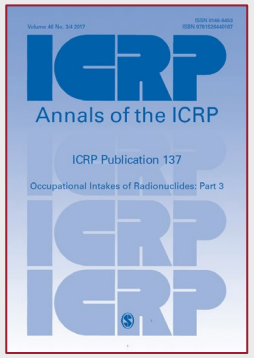
Mission:

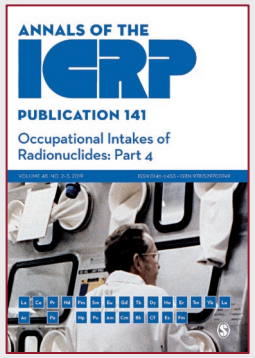
- To follow up occupationally exposed workers by **studying the biokinetics and tissue dosimetry of the actinides**
- To refine dose assessment methods **in support of reliable epidemiological studies**, radiation risk assessment, and regulatory standards for **radiological protection** of workers and general public

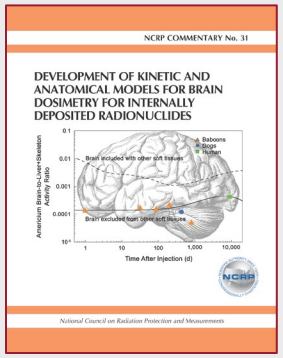
Registrants:

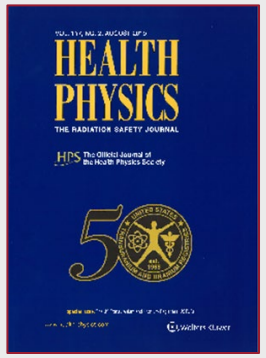
- Former nuclear workers with **documented exposures** to actinide elements (plutonium, americium, and uranium)
- **Volunteered to donate** their organs, tissues, or entire bodies for **postmortem research**

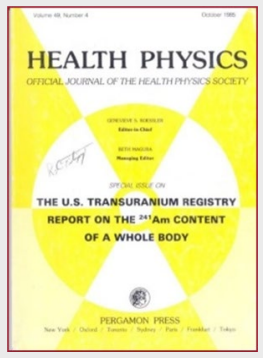
In Support of Epidemiological Studies





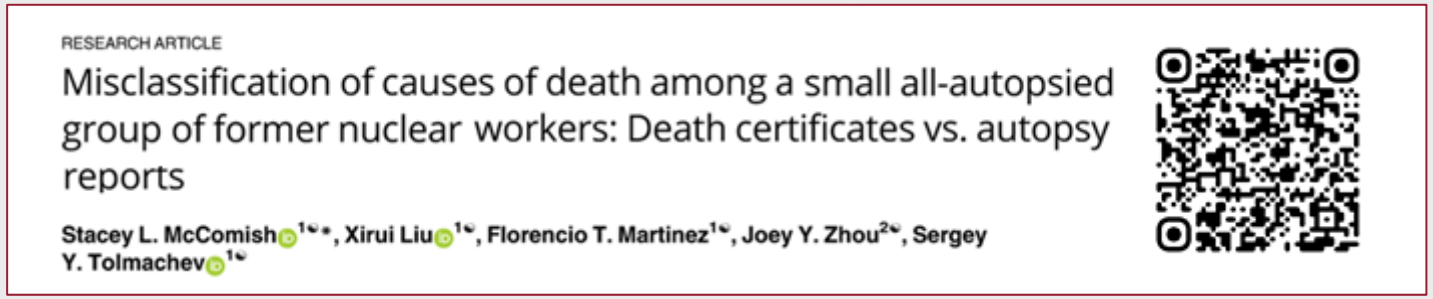






Biokinetic model improvement → Better radiation dose assessment

Death certificate misclassification study → Better health outcome assessment


RESEARCH ARTICLE

Misclassification of causes of death among a small all-autopsied group of former nuclear workers: Death certificates vs. autopsy reports

Stacey L. McComish[1*], Xirui Liu[1], Florencio T. Martinez[1], Joey Y. Zhou[2], Sergey Y. Tolmachev[1]

Unique Data and Material Resource

Work history

Medical records

Smoking history†

Tissue analysis results

Bioassay measurements

Radiation exposure records

Industrial hygiene records†

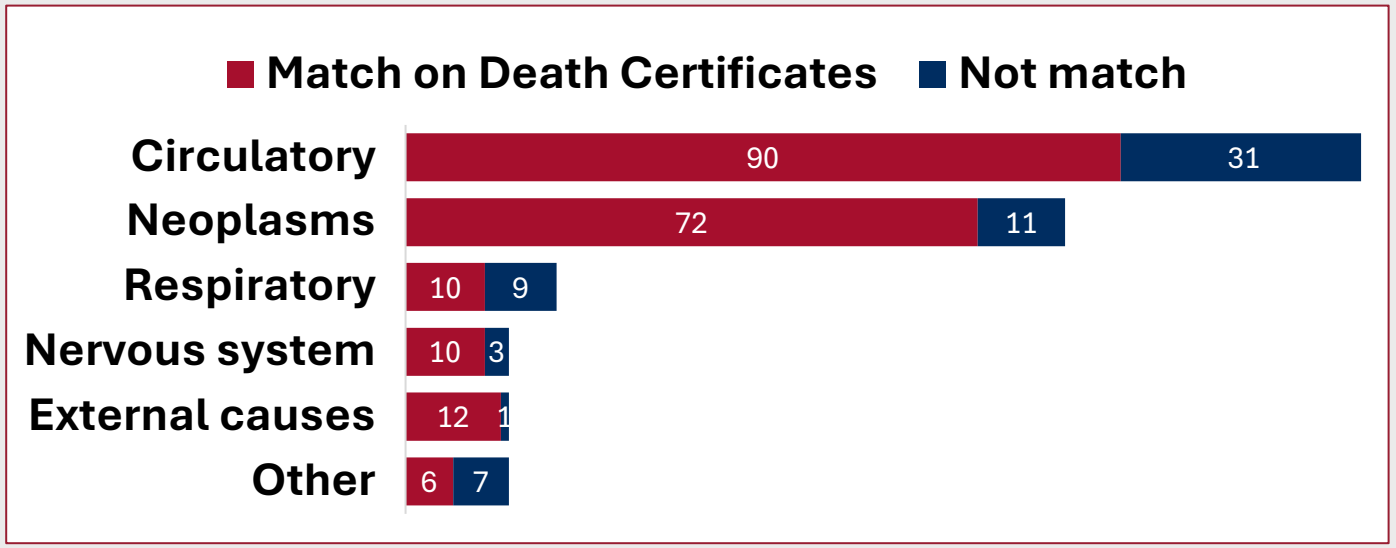
† Self reported

Cause of Death Misclassification

Underlying cause of death on				Match status
Death certificate		Autopsy report		
Description	ICD-10	Description	ICD-10	
Malignant neoplasm of colon	**Neoplasm**	… death is attributed to complications of metastatic moderately differentiated adenocarcinoma of the bowel	**Neoplasm**	**Match**
Pneumonia	Respiratory disease	… died as the result of extensive spread of a bronchogenic carcinoma	**Neoplasm**	**Not match** **Under**-misclassification of **Neoplasm** (false negative)
Malignant neoplasm of bronchus and lung	**Neoplasm**	Autopsy revealed adult respiratory distress syndrome in both lungs. No tumor was found in hilar, paratracheal, or mediastinal lymph nodes	Respiratory disease	**Not match** **Over**-misclassification of **Neoplasm** (false positive)

Over and Under Misclassification Rates

Top 5 disease category	Circulatory	**Neoplasms**	Respiratory	Nervous system	External causes
Over-misclassification rate	12%	**4%**	6%	2%	1%
Under-misclassification rate	26%	**13%**	47%	23%	8%



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Stacey L. McComish[1☯]*, Xirui Liu[1☯], Florencio T. Martinez[1☯], Joey Y. Zhou[2☯], Sergey Y. Tolmachev[1☯]

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☯ These authors contributed equally to this work.
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Misclassification Impact: USTUR Data

	Data		Results		
	Radiation dose, Sv (exposure)	Diagnosed cancer death (outcome)	Odds ratio	95% CI	*p*-value
Non-misclassified	Cumulative external	on **autopsy report**	0.36†	(0.05, 2.77)	0.326
Misclassified	Cumulative external	on **death certificate**	0.53†	(0.07, 4.04)	0.540

† Odds ratio less than 1 likely due to bias in recruitment process

Consistent with general belief

- Misclassification **always weakens the association between risk factors and health outcomes**
- **Correcting** such misclassification will **make the association stronger**

Misclassified outcome yields odds ratio **toward the null**

Neither shows a significant association

Misclassification Impact Quantification

	Data		Results		
	Radiation dose, Sv (exposure)	Diagnosed cancer death (outcome)	Odds ratio	95% CI	*p*-value
Non-misclassified	Cumulative external	on **autopsy report**	0.36†	(0.05, 2.77)	0.326
Misclassified	Cumulative external	on **death certificate**	0.53†	(0.07, 4.04)	0.540

† Odds ratio less than 1 likely due to bias in recruitment process

Only examine one possible misclassification scenario

- Do **other possible misclassification scenarios** exist?
- Does the impact in other misclassification scenarios **also follow the general belief**?
- Can we **quantify the impact** when the results contradict the general belief?

Methods: Misclassification Simulation

	Data		Results		
	Radiation dose, Sv (exposure)	Diagnosed cancer death (outcome)	Odds ratio	95% CI	*p*-value
Non-misclassified	Cumulative external	on **autopsy report**	0.36	(0.05, 2.77)	0.326
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Initial dataset

- **Radiation dose** as the independent variable
- **Cancer death** as the dependent variable
- Represents an ideal **non-misclassified scenario**

Misclassification simulation

- Randomly change X%† of non-cancer deaths to cancer deaths (**over-misclassification**)
- Randomly change Y%† of cancer deaths to non-cancer deaths (**under-misclassification**)

Summary statistics

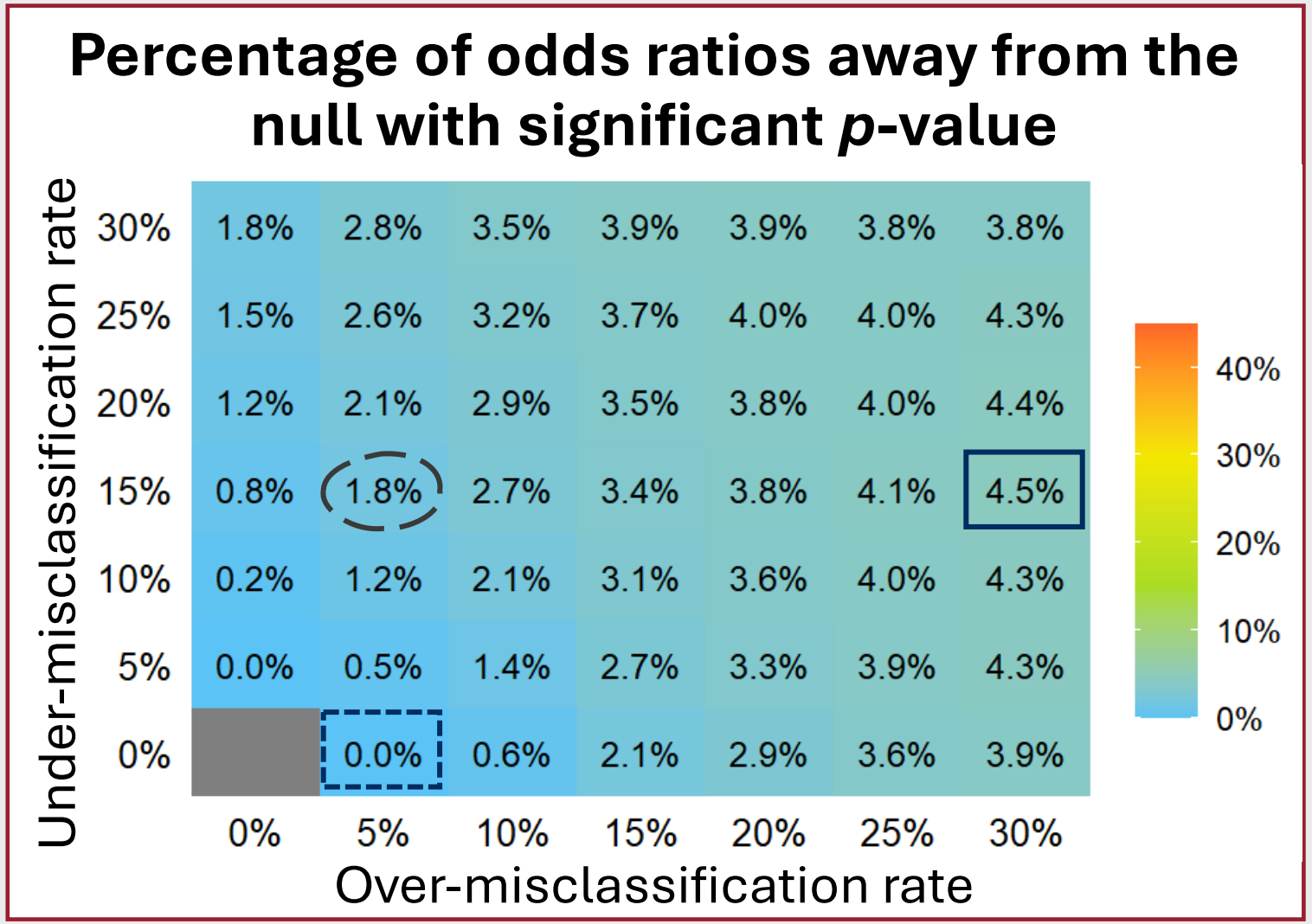
- Calculate the **odds ratio** and ***p*-value** for each simulated dataset
- **Compare** misclassified results to the non-misclassified result

† Various rate combinations ranging from 0-30% will be tested for quantification.

Xirui Liu | xirui.liu@wsu.edu I American Public Health Association 2025 Annual Meeting, November 5, 2025

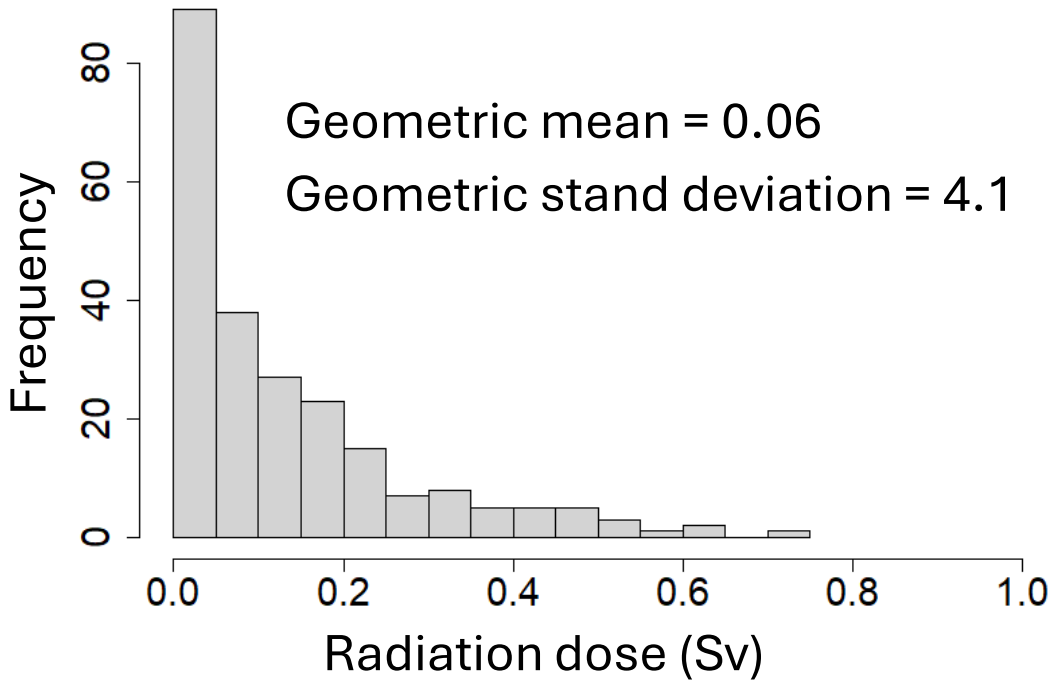
Results: USTUR Data

Initial dataset	
Radiation dose	Worksite
Death diagnose	Autopsy
Sample size	229
Odds ratio	0.36
95% CI	(0.05, 2.77)
p-value	0.326

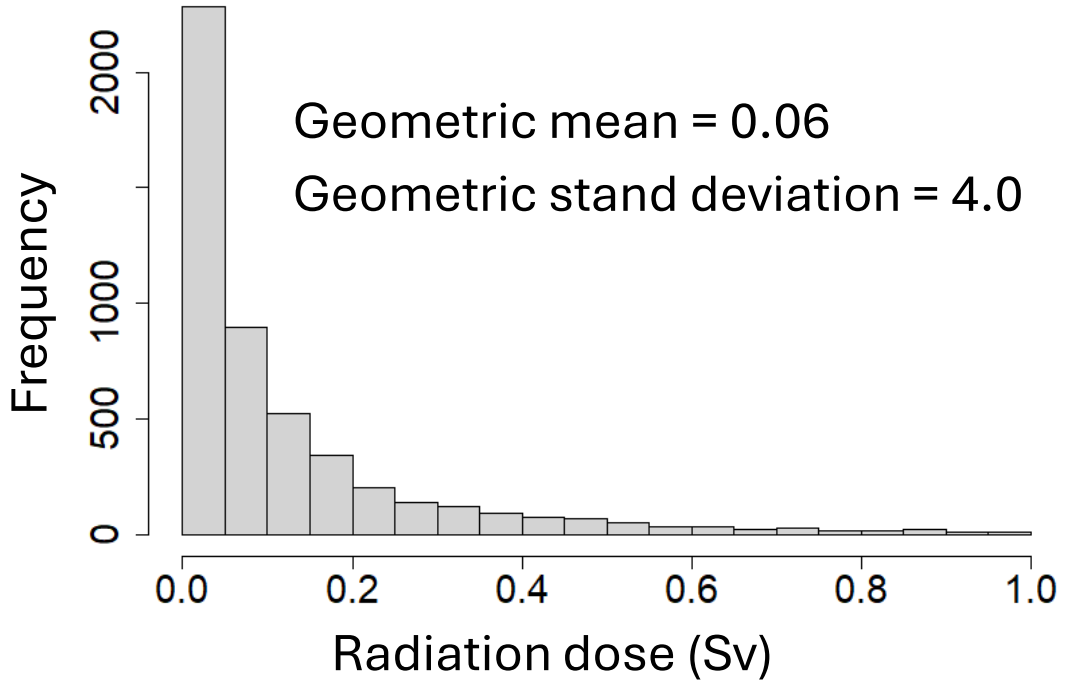


Methods: Increase of Sample Size

USTUR dose distribution
(*n* = 229)

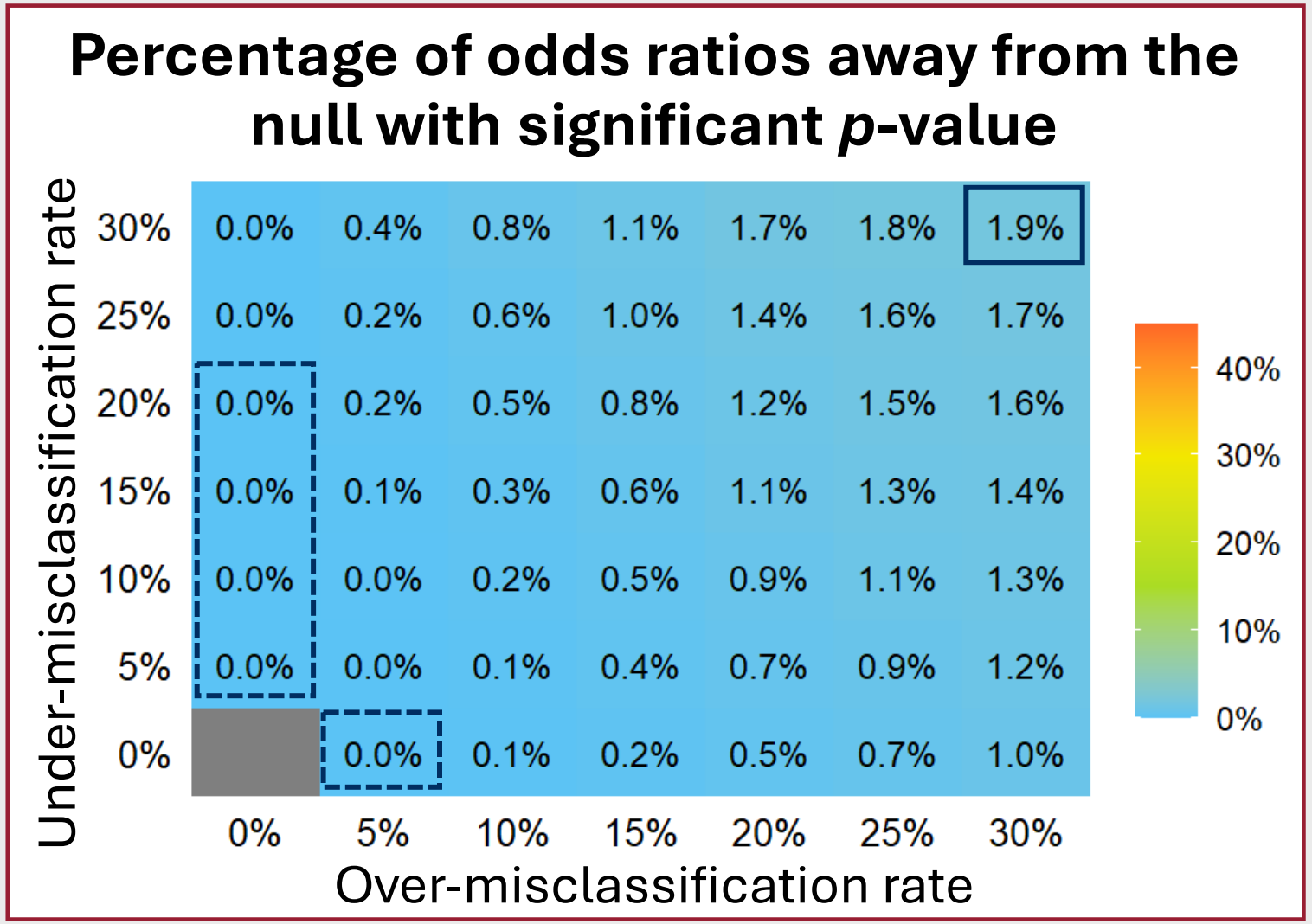


Simulated dose distribution
(*n* = 5,000)



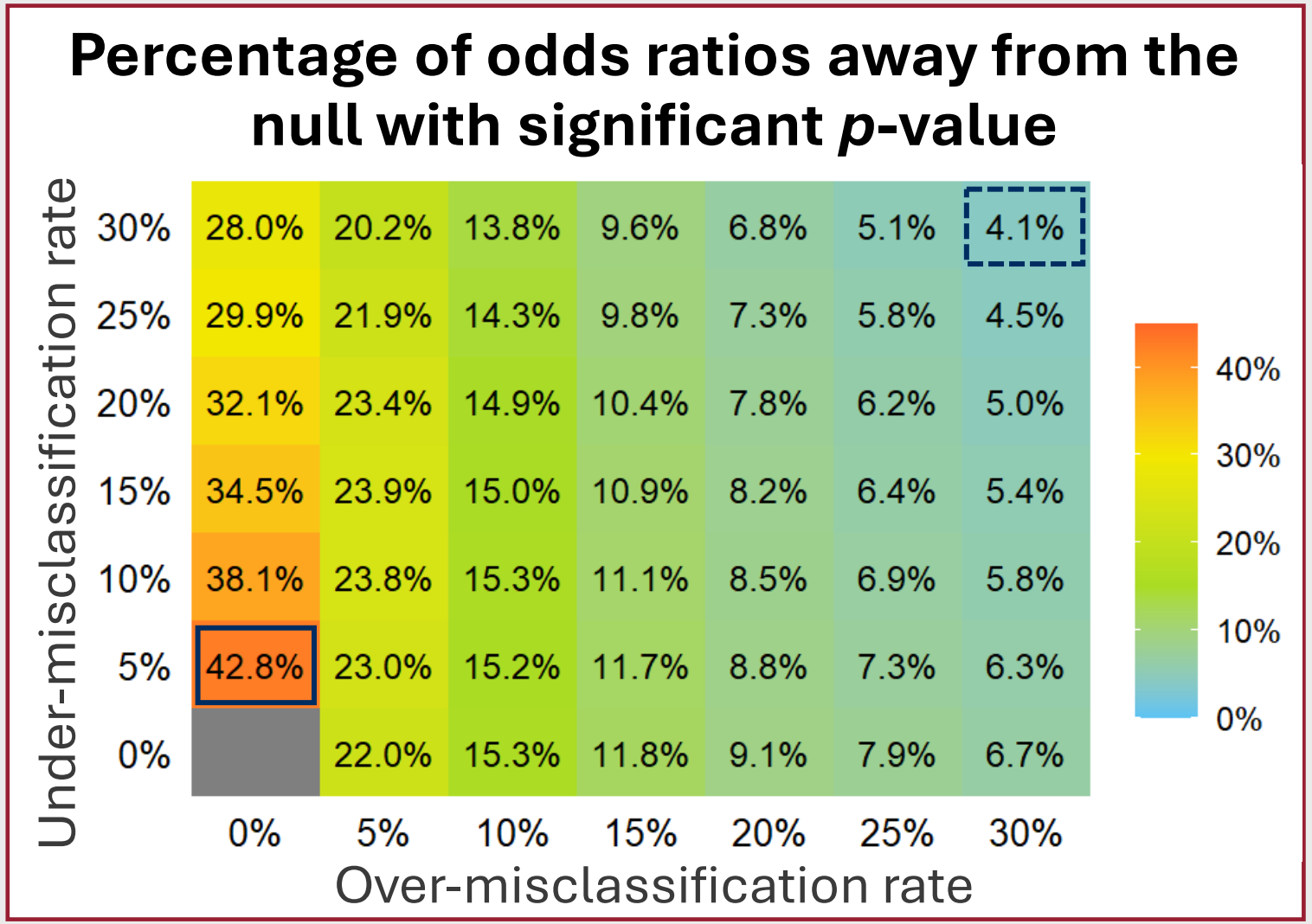
Results: Non-significant Lowest Effect Scenario

Initial dataset	
Radiation dose	Simulated
Death diagnose	Simulated
Sample size	5,000
Odds ratio	**1.0001**
95% CI	**(0.67, 1.49)**
p-value	**0.996**



Results: Non-significant Borderline Scenario

Initial dataset	
Radiation dose	Simulated
Death diagnose	Simulated
Sample size	5,000
Odds ratio	**1.47**
95% CI	**(0.99, 2.17)**
p-value	**0.0501**



Summary

General belief:

- Misclassification always weakens the association between risk factors and health outcomes
- Correcting such misclassification will make the association stronger

Conclusion: General belief is not always true for individual studies

- Non-differential misclassification can significantly **move the odds ratio away from the null** in a non-trivial percentage of cases
- This effect could be even **more substantial** under **low misclassification rates**


Thank you! :)