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Impact of Outcome Misclassification on Radiation Health Risk Models

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Who We Are: USTUR

The United States Transuranium and Uranium Registries:

- a research program designed to study the **biokinetics, tissue dosimetry**, and possible **biological effects** of **actinides** in the human body
- contribute occupational **radiation protection standards** and **support epidemiological studies**

USTUR Registrants:

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



What We Have: Unique Data



Work history



Medical records



Smoking history [†]



Tissue analyses results



Radiation exposure records



Bioassay measurements



Chemical exposure records [†]

[†] self-reported



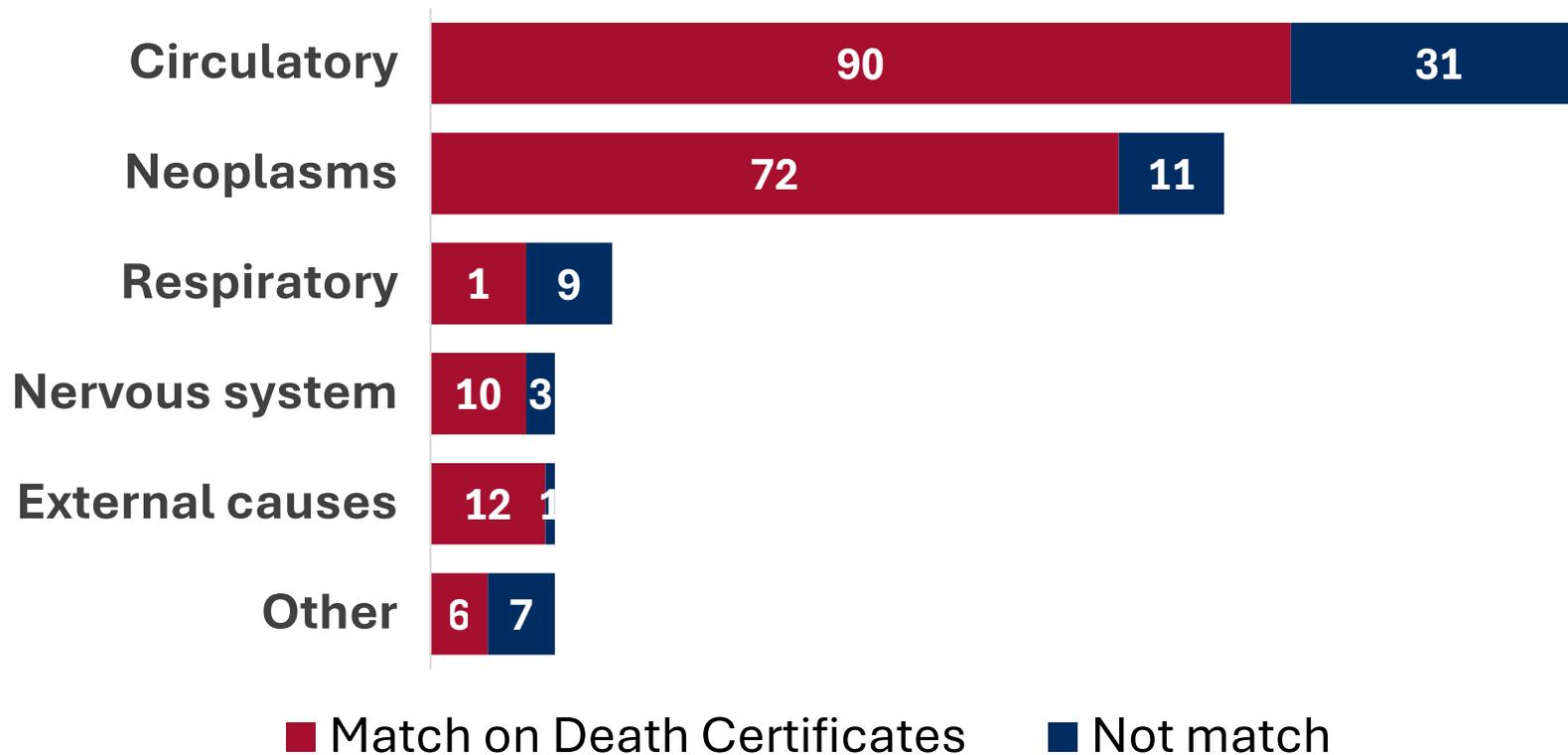
Previous Study: Cause of Death

Underlying cause of death on		Match Status
Death certificate	Autopsy report	
Metastatic carcinoma	He died as a result of metastatic carcinoma of urogenital origin	Match
Chronic kidney disease	Cause of death is heart failure secondary to massive renal failure	Match
Pneumonia	... died as the result of extensive spread of a bronchogenic carcinoma	Not match Over-misclassification of Respiratory disease (false positive)
Phlebitis and thrombophlebitis of deep vessels	Death is attributed to bilateral pulmonary thromboli due to deep venous thrombosis arising as a result of metastatic bladder adenocarcinoma	Not match Under-misclassification of Neoplasm (false negative)



Previous Study: Misclassification

Top 5 Categories on Autopsy Reports



Paper published:
PLoS One (2024)

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



Does Misclassification Impact?

	Data sources		Calculated results		
	Dose	Outcome	Odds ratio	95% CI	p-value
Non-misclassified	Cumulative external doses	Cancer cause of death on autopsy reports	0.36	(0.05, 2.77)	0.326
Misclassified	Cumulative external doses	Cancer cause of death on death certificates	0.53	(0.07, 4.04)	0.540

General belief:

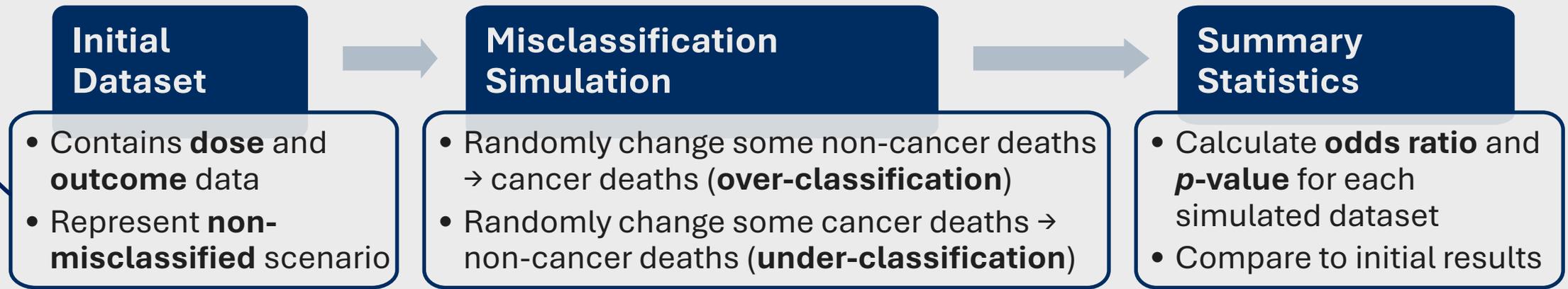
- misclassification **always weakens** study results
- **correcting** misclassification will make results **stronger**

✓ **True for this study**



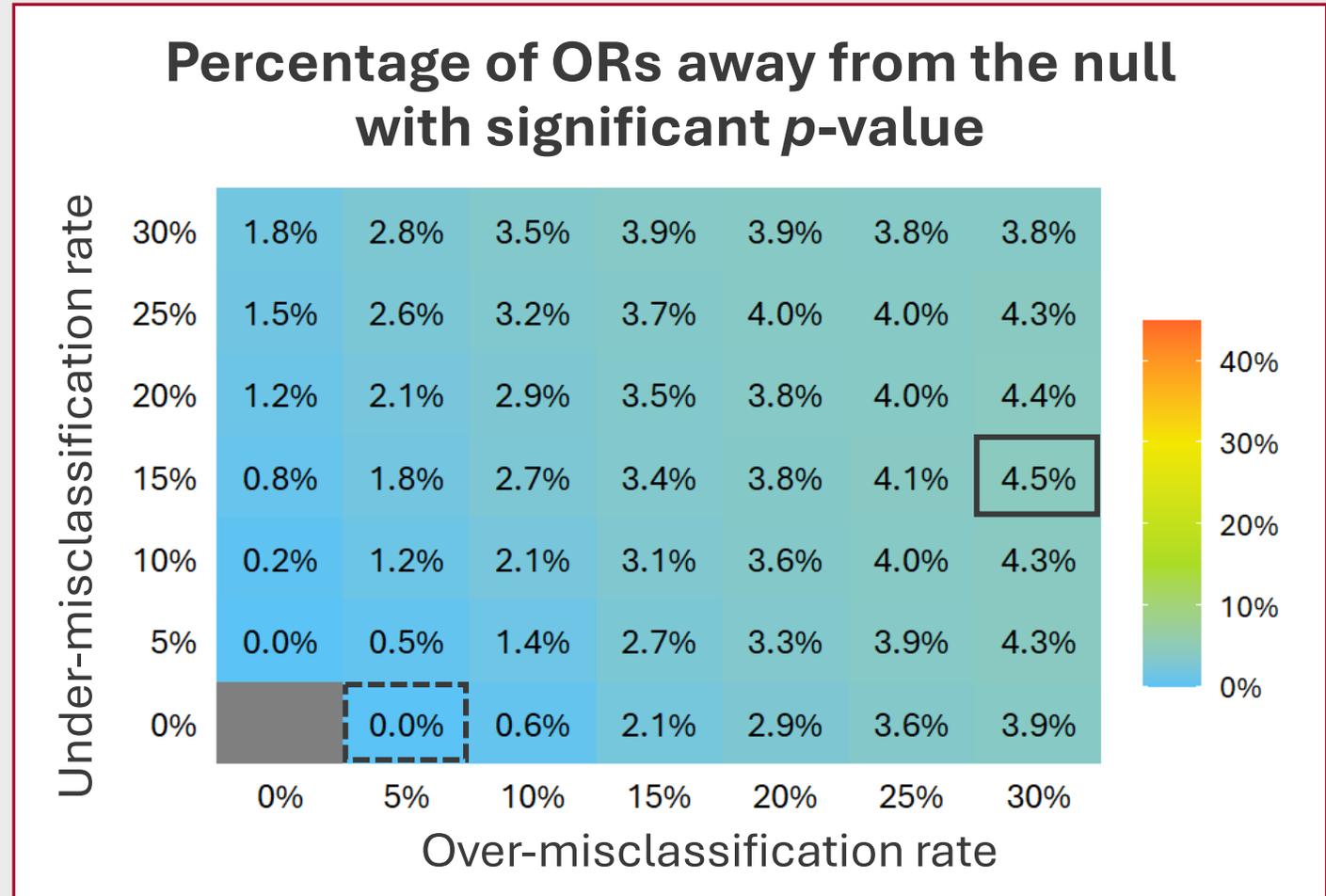
Could Misclassification Impact?

	Data sources		Calculated results		
	Dose	Outcome	Odds ratio	95% CI	p-value
Non-misclassified	Cumulative external doses	Cancer cause of death on autopsy reports	0.36	(0.05, 2.77)	0.326
Misclassified	Cumulative external doses	Cancer cause of death on death certificates	0.53	(0.07, 4.04)	0.540



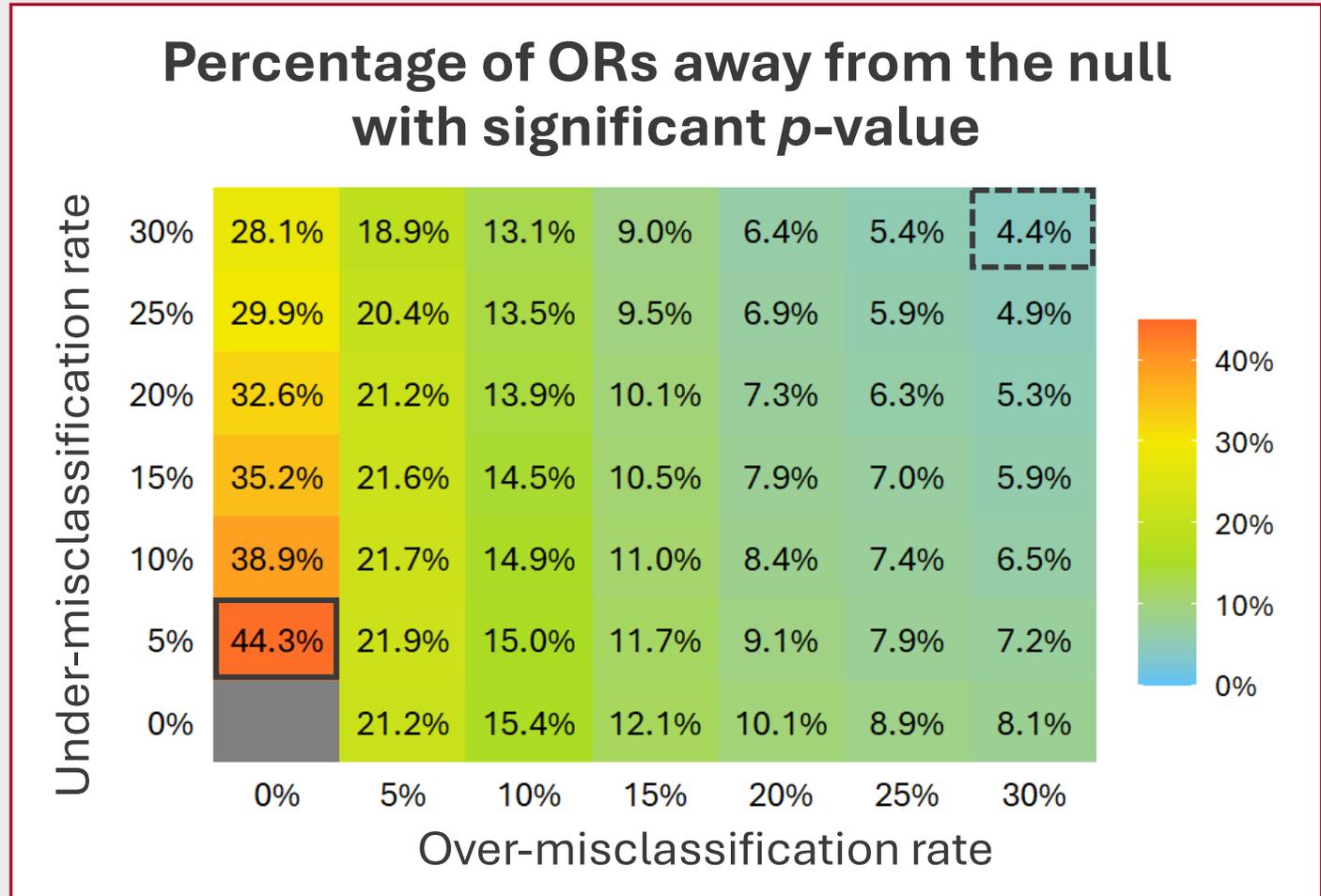
Simulation Study: Potential Impact

Initial dataset source	
Dose	USTUR records
Outcome	USTUR AR
Initial dataset info	
Sample size	229
Odds ratio	0.36
95% CI	(0.05, 2.77)
<i>p</i> -value	0.326



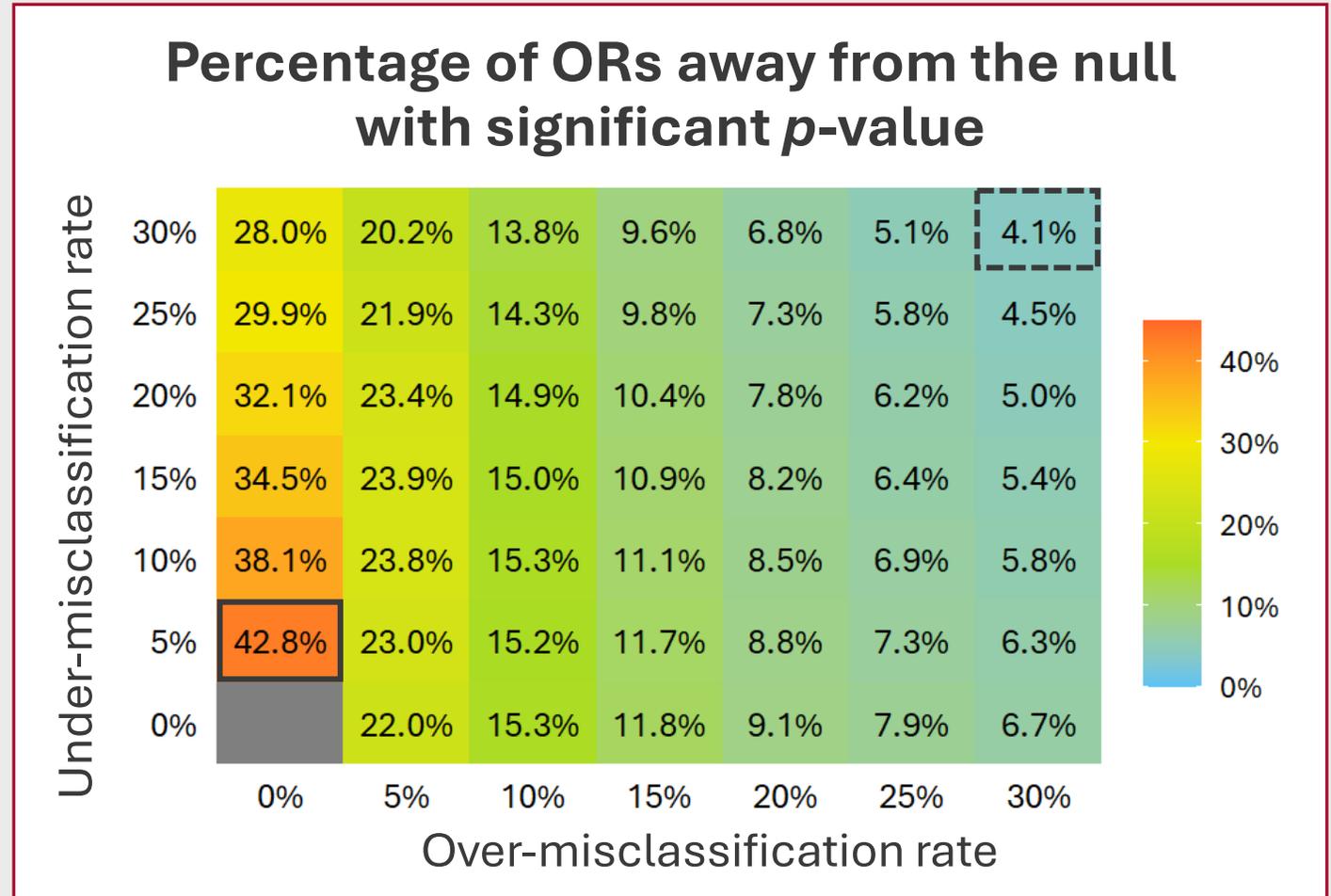
Worst Scenario: Maximum Impact

Initial dataset source	
Dose	USTUR records
Outcome	Generated
Initial dataset info	
Sample size	229
Odds ratio	8.27
95% CI	(0.99, 68.3)
p-value	0.05001



Sample Size: Larger Dataset Validation

Initial dataset source	
Dose	Generated
Outcome	Generated
Initial dataset info	
Sample size	5,000
Odds ratio	1.473
95% CI	(0.99, 68.3)
<i>p</i> -value	0.05001



Summary



General belief:

- misclassification **always weakens** study results
- **correcting** misclassification will make results **stronger**

Conclusion: **general belief not always true for individual studies**

- misclassification **can artificially strengthen** dose-response associations
 - !! even change **non-significant** results to **significant**
- **non-trivial probability** of such impact occurs at typically **low misclassification rates**





Thank you! :)