Interactive RadioEpidemiologic Program (IREP) Update

Timothy D. Taulbee, PhD, CHP

Daniel Stancescu, PhD

Division of Compensation Analysis and Support (DCAS)

Advisory Board on Radiation and Worker Health (ABRWH) Meeting
Augusta, Georgia| August 16, 2023

Preview of the IREP Update

- Proposing to change Probability of Causation (PC) procedure, not the cancer risk models nor any dose reconstructions
- Update will correct a negative bias in IREP that is observed in some claims thus generally increasing the Probability of Causation
- Update ensures no claims are being incorrectly denied compensation when the Probability of Causation is close to 50%
- Update likely only impacts a few claims (2-4) with a Probability of Causation (PC) greater than 49.5%

Overview

- Background - Probability of Causation
- Quantile Computation Methods
- Potential Computation Impact on Claims
- IREP Update – New Probability of Causation Procedure
- Expected Programmatic Impact

Background – Probability of Causation

Probability of Causation Rule - (42 CFR § 81)

- *Guidelines for Determining the Probability of Causation Under the Energy Employees Occupational Illness Compensation Program Act of 2000*; Final Rule

- Rule promulgates EEOICPA's "at least as likely as not" standard
  - *Is there at least a 50-50 chance that a worker's cancer was caused by occupational radiation exposure (rather than by something else)?*

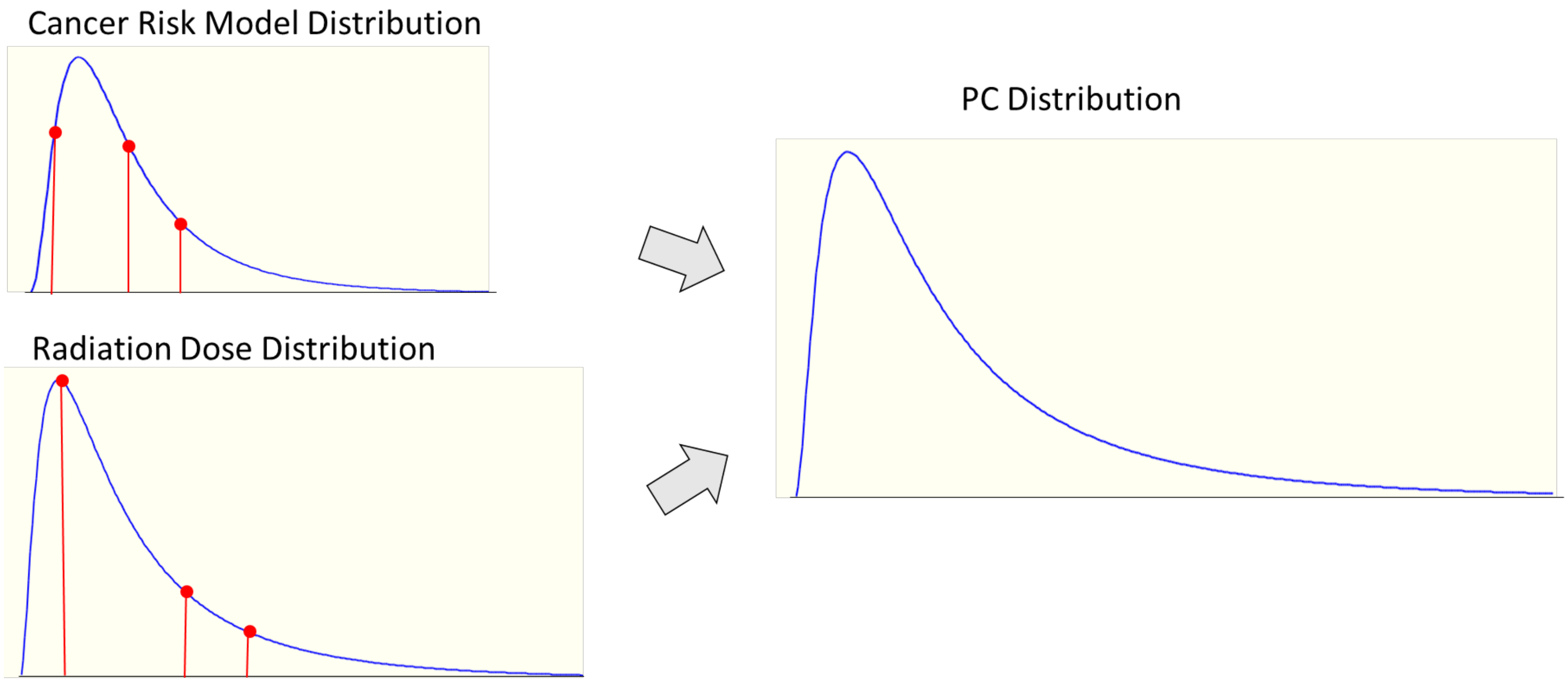
Probability of Causation

- Frequently abbreviated as "PC" or "PoC," refers to the proportion of disease in a given population that would not have occurred absent the exposure of interest

$$PC = \frac{RadRisk}{RadRisk + BasRisk}$$

- *RadRisk* = the risk of an individual's cancer due only to occupational radiation exposure
- *BasRisk* = the baseline (background) risk of that cancer

NIOSH-IREP propagates the uncertainty using Monte Carlo methods to compute the Probability of Causation

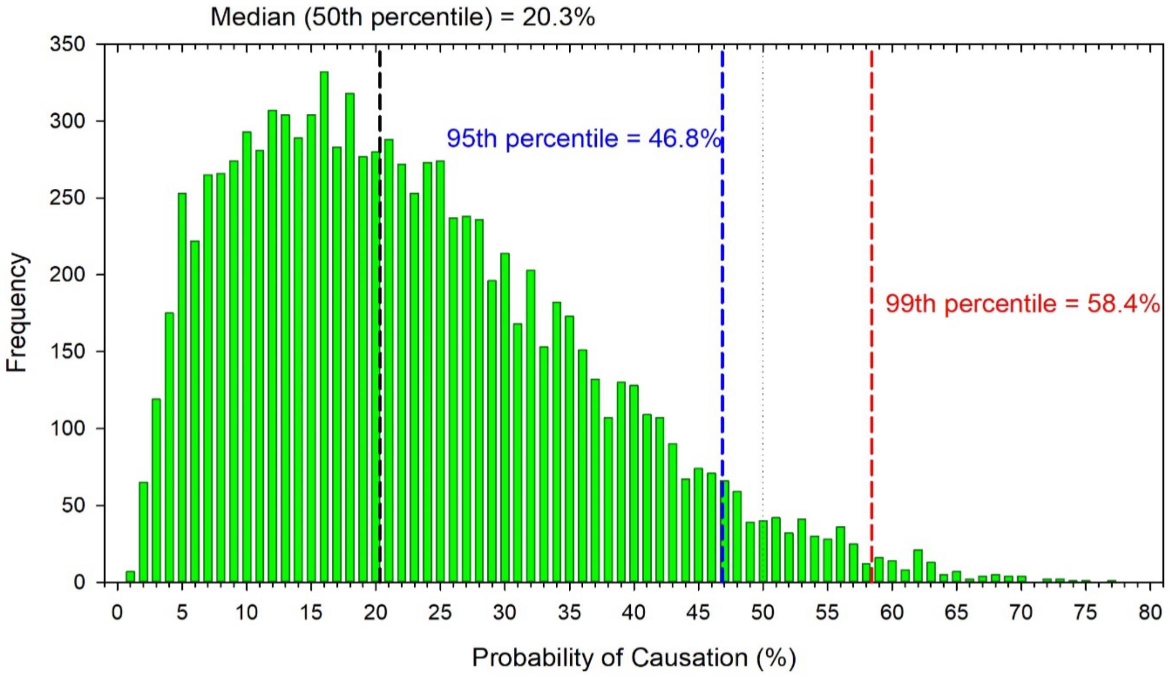


Probability of Causation Distribution

- EEOICPA requires the calculation of PC, expressed as a percentage (e.g., a PC of 0.5 is expressed as 50%).
- "At least as likely as not" standard means the claim is compensable if PC ≥50% at the upper 99th percent confidence interval (credibility limit) of the PC *(42CFR§81.2)*
- Upper 99th percentile of PC is calculated within the NIOSH-IREP software program *(42CFR§81.10)*

Example PC Credibility Limits

- *Male, age 20y at first exposure, exposed to 1 rem of photons (E>250 keV) each year for 30 years. Diagnosed with liver cancer at age 65. (n = 10000 PC simulations)*



Procedure to Update NIOSH-IREP *42CFR§81.12*

- NIOSH may periodically revise NIOSH-IREP to
  - *Add, modify, or replace cancer risk models*
  - *Improve modeling uncertainty*
  - *Improve functionality and user interface of NIOSH-IREP*
- NIOSH will submit substantive changes of NIOSH-IREP to the Advisory Board on Radiation and Worker Health (ABRWH) for review and address any recommendations from the Board's review before completing and implementing the change
- NIOSH will also inform the public of proposed changes and address relevant public comments through Federal Register Notices

Quantile Computation Methods

Sample Quantile Definitions

- Hyndman and Fan (1996) presented nine sample quantile definitions with a goal of standardization
- Currently there is ***No*** standard definition of a percentile, however there are multiple definitions currently in use
- Probabilistic modeling and risk analysis software packages such as Crystal Ball, @Risk, Analytica, and Model Risk (Vose) have different methods implemented to compute percentiles
- Statistical Software Packages (SAS and R) have multiple methods available with one method being the default.

Select Examples of Sample Quantile Definitions

Method	Software	Description
Type 1	*Nearest rank method*	Inverse of empirical cumulative distribution function
Type 2	SAS (default)	Same as Type 1 but with averaging at discontinuities
Type 3		The Observation numbered closest to *Np*
Type 4	@Risk, Crystal Ball	Linear interpolation of the empirical distribution function (EDF)
Type 5		Piecewise linear function where the knots are the values midway through the steps of the EDF
Type 6	Excel (PERCENTILE.EXC)	Linear interpolation of the expectations of the order statistics for the uniform distribution [0,1]
Type 7	R (default), Analytica (IREP)	Linear interpolation of the modes for the order statistics for the uniform distribution [0,1]

Comparison of Different Methods

- Sample from a Simple Lognormal Distribution
  - Geometric Mean (GM)= 3
  - Geometric Standard Deviation (GSD) = 6
  - **Theoretical 99% = 193.808**
  - RLH: Random Latin Hypercube
  - MLH: Median Latin Hypercube

Method Comparison with Increasing Sample Size (1 of 2)

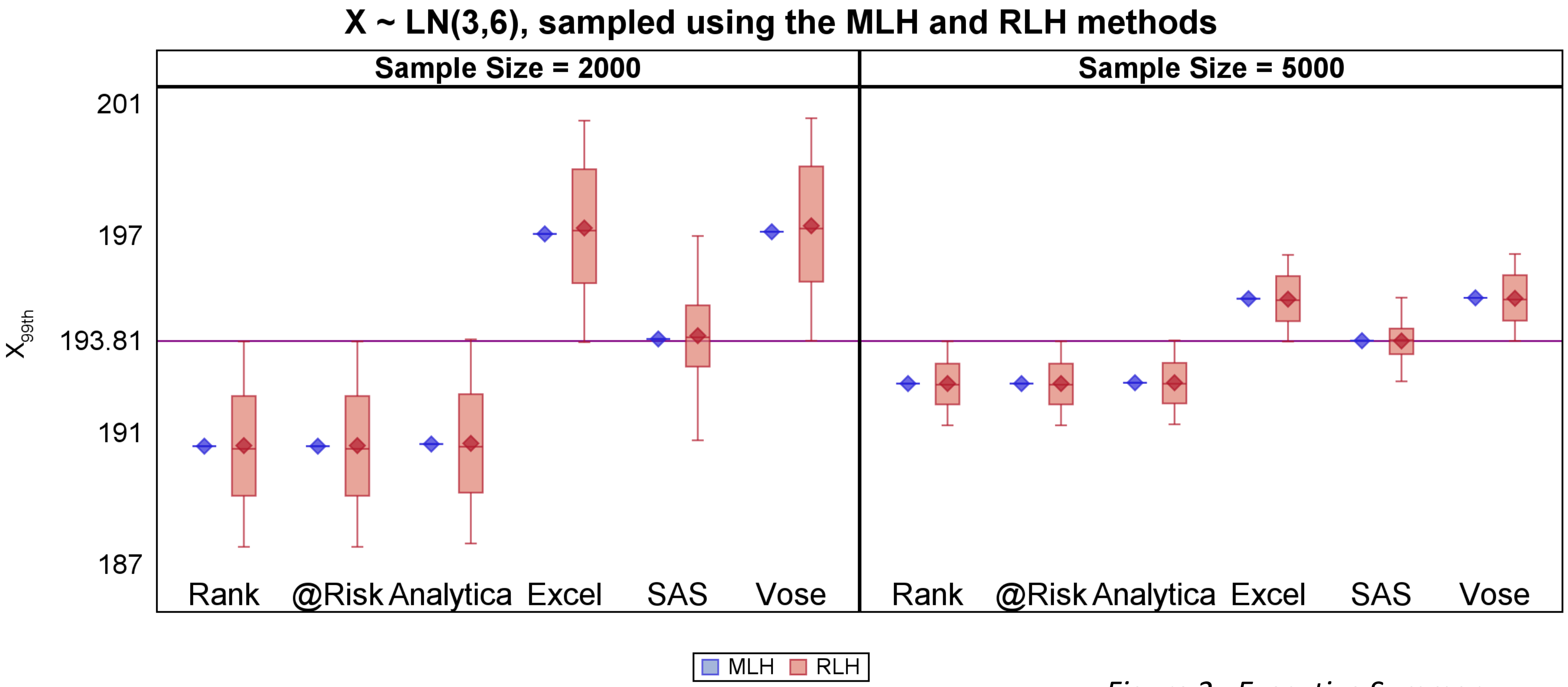


Figure 2: Executive Summary

Method Comparison with Increasing Sample Size (2 of 2)

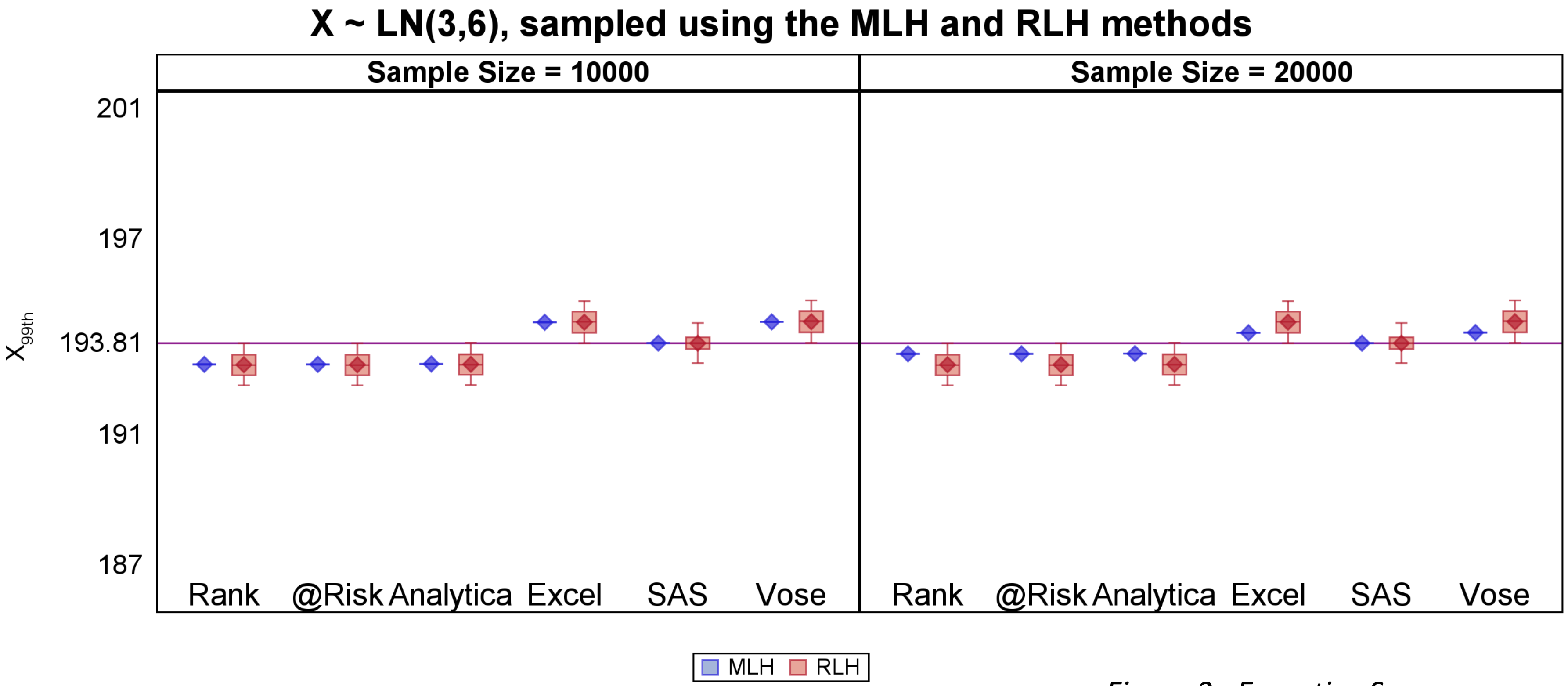


Figure 2: Executive Summary

Convergence as the sample size increases

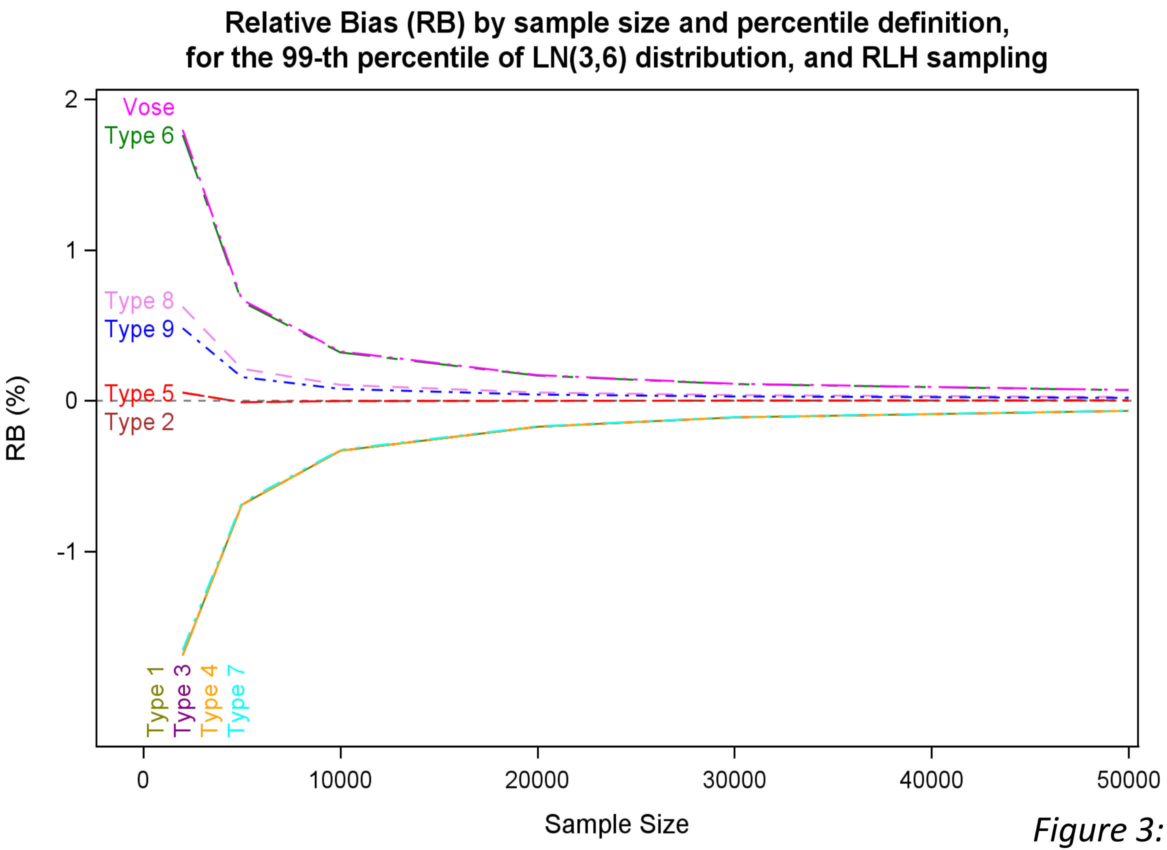


Figure 3: Executive Summary

Summary of Method Evaluation

- At low number of iterations (small sample size), relative bias can be 1% to 2% for individual distributions
- Type 2 (SAS) appears to be least impacted by sample size
- Type 4 (@Risk) and Type 7 (Analytica-IREP) appear to have a negative bias at small sample sizes
- Type 6 (Excel) and VOSE appear to have a positive bias at small sample sizes
- All methods converge to the same value as sample size increases

Potential Computational Impact on Claims

Potential Impact on Claims

- IREP uses the Analytica statistical engine and can result in a negative bias at the 99th percentile
- The bias is more pronounced when:
  - Large dose uncertainty
    - Dose distribution has a large Geometric Standard Deviation (GSD)
  - Large number of IREP input exposures
- These can translate into a Probability of Causation (PC) distribution with a longer tail with larger distance between PC realizations

PC Number of Iterations

- PC @ 99^{th} %
  - *n=2000, PC = 50.41%*
  - *n=10000, PC = 49.66%*
  - *n=20000, PC = 49.81%*
  - *n=30000, PC = 49.99%*
- Overall goal is to improve the modeling uncertainty at the 99^{th} percentile of the PC

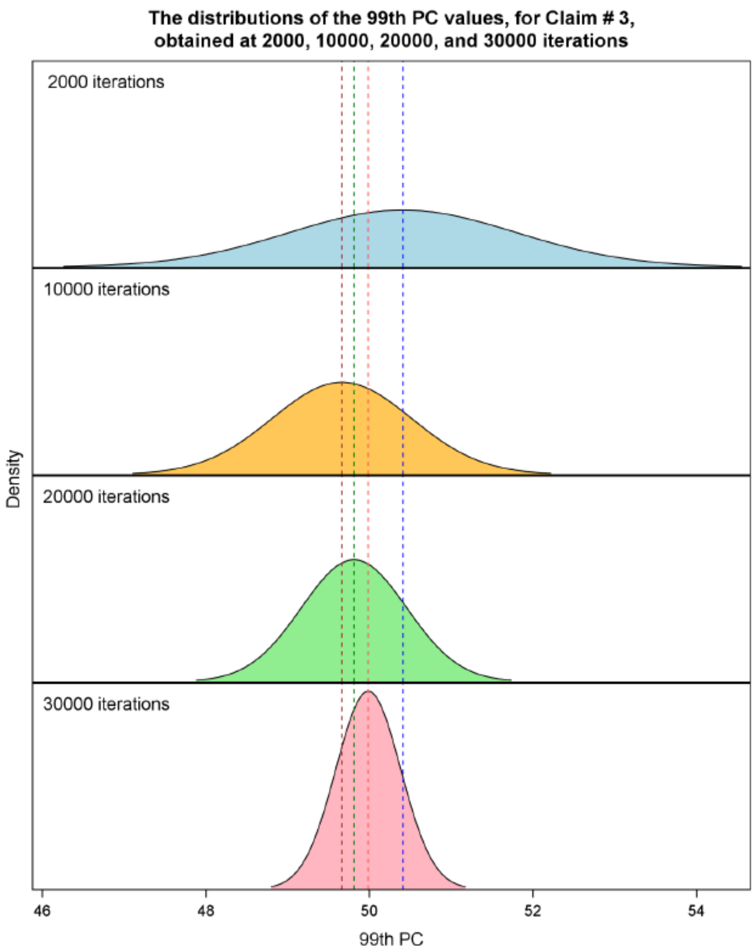


Figure 12: Executive Summary

Current Methodology – 30 runs at 10,000 iterations

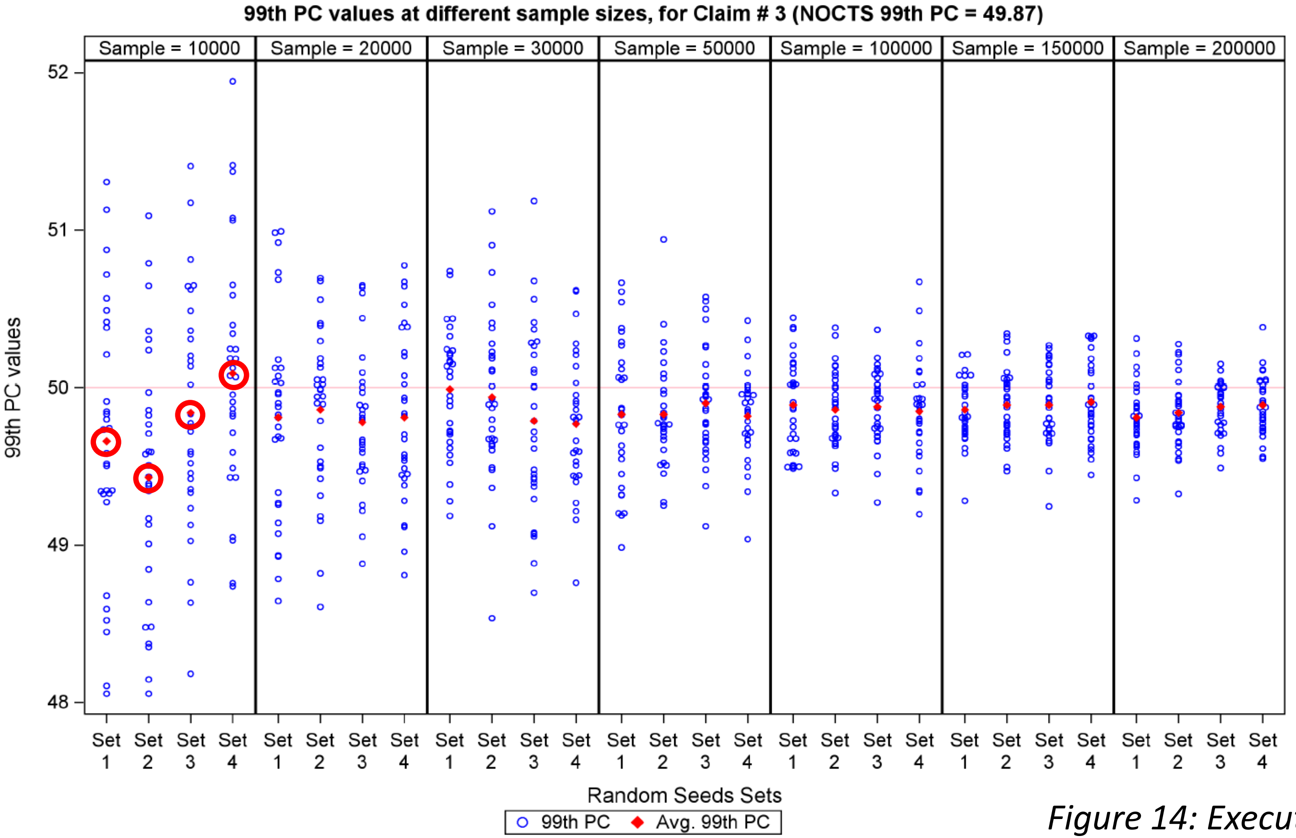
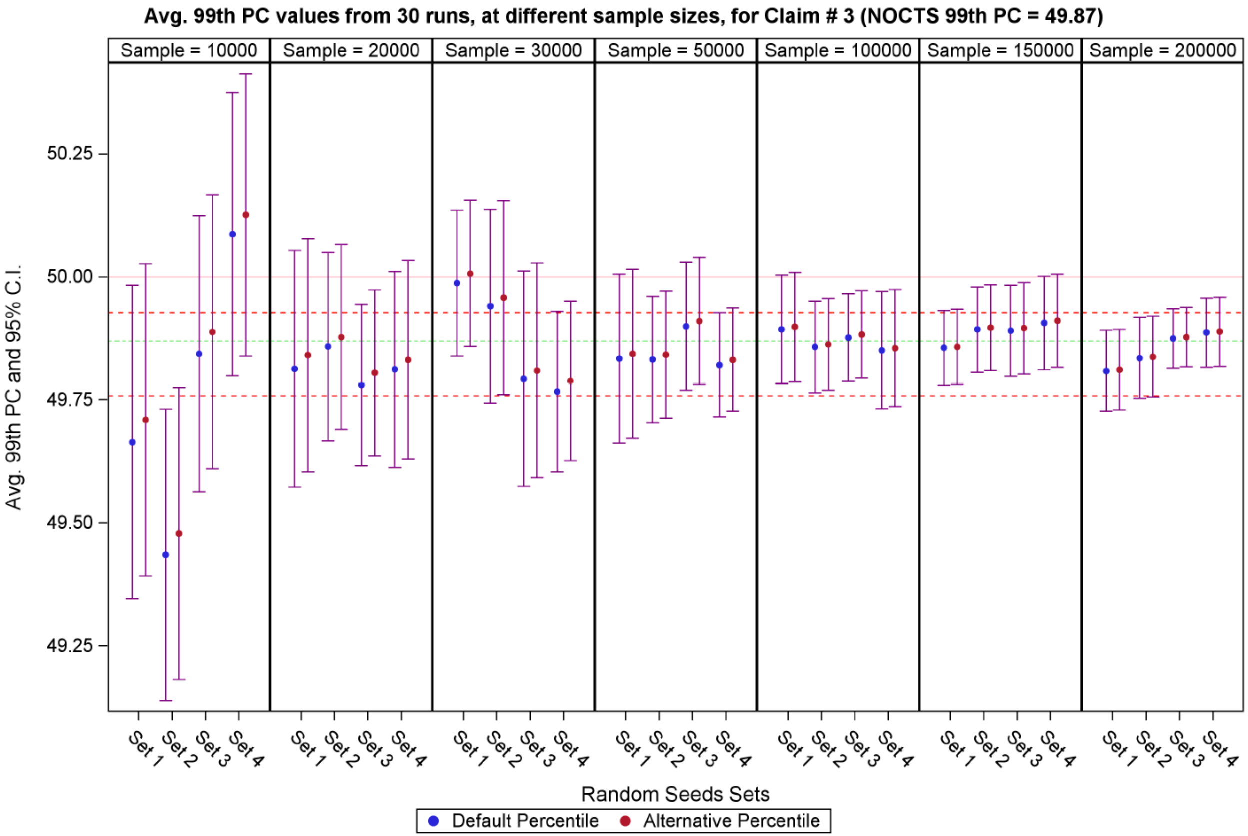


Figure 14: Executive Summary

Current Methodology – Confidence Interval



95% C.I. for the 99th PC value is based on a sample size of 5,000,000

Figure 15: Executive Summary

IREP Update – Change to PC Procedure

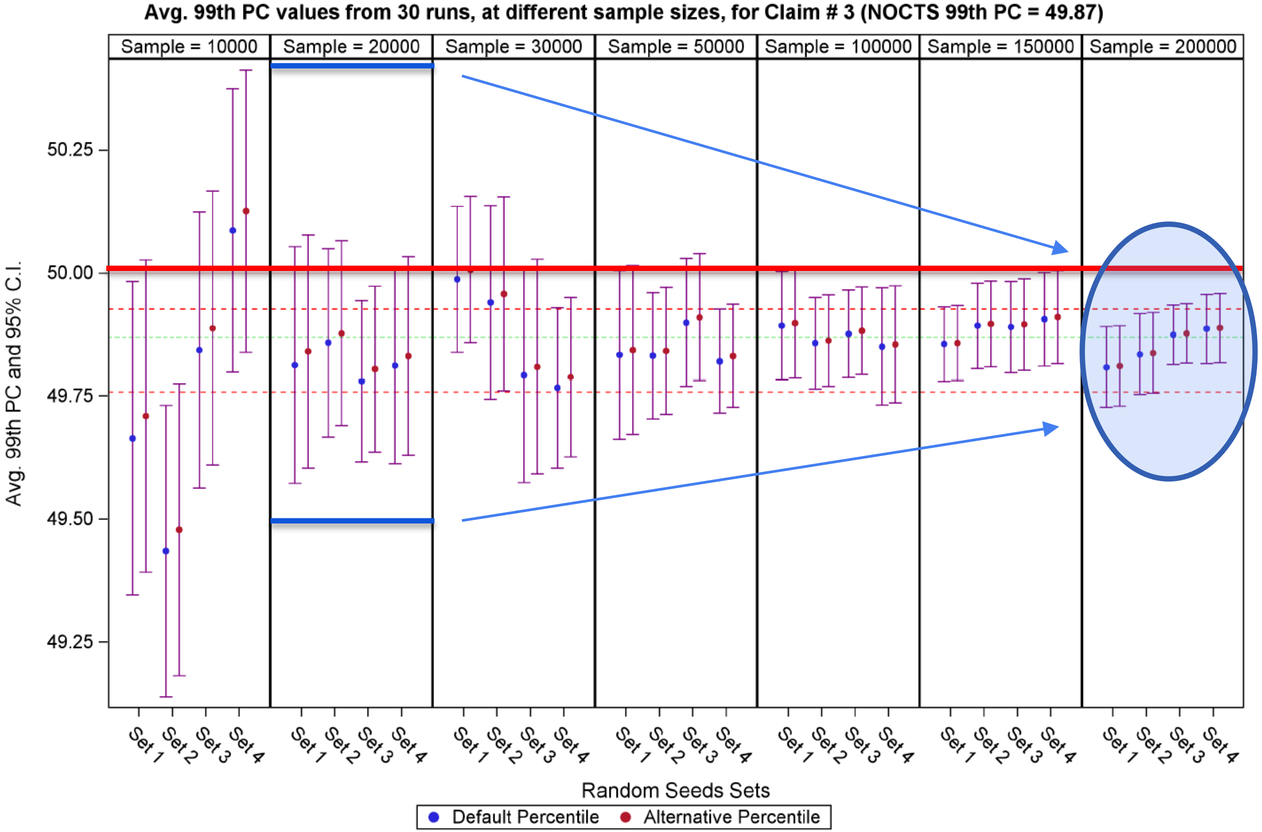
IREP Update Changes (version 6.0)

- Current IREP (v5.9)
  - Maximum number of iterations is 10,000
- **New IREP** (v6.0)
  - Maximum number of iterations is 20,000
- Current IREP_EE (v5.9)
  - Averages 30 runs at 10,000 iterations for final PC
- **New IREP_EE** (v6.0)
  - Capability for either 30 or 300 runs at 20,000+ iterations

Proposed Probability of Causation (PC) Procedure

PC Value	IREP Version	Current Procedure (# of Iterations)	Proposed Procedure (# of Iterations)
<45% or > 52%	IREP	2,000	20,000
45% to 52%	IREP-EE	30 runs @ 10,000	30 runs @ 20,000
49.5% to 50.5%	IREP-EE	30 runs @ 10,000	300 runs @ optimal # of iterations (20,000 – 70,000+)

Improving the Modeling Uncertainty



95% C.I. for the 99th PC value is based on a sample size of 5,000,000

Similar to 300 runs @ 20000+ iterations

Figure 15: Executive Summary

IREP Predictive Tool for Claims 49.5% to 50.5% PC

- New tool that evaluates the width of the confidence interval (CI) based on the claim uncertainty distributions
- IREP Predictive Tool will be run by NIOSH/ORAU to determine the optimal number of iterations
- The tool rapidly conducts 300 runs using only 1,000 iterations and then applies a power function to predict the optimal number of iterations in order to achieve a CI of less than 0.1
- Final PC will be the average of 300 runs at the optimal number of iterations

Expected Programmatic Impact

Expected Programmatic Impacts

- Overall IREP 6.0 should have minimal programmatic impact
- Greater precision in the PC value will be achieved
- Probability of Causation run times will increase as the number of iterations increases (computer power changes over time)
- Slightly more complicated evaluation process when the PC value is near the 50% (49.5% to 50.5%)
- Additional computational time increase will be minimized with the use of the IREP Predictive Tool to optimize number of iterations

Program Evaluation Report (PER) (1 of 2)

- All PC calculations for claims between 45% to <50% will be re-evaluated using the new PC procedure
- Minimal impact on claims in this region as we have been using 30 runs at 10,000 iterations for many years (since 2006)
- Relatively few claims with PC's in the 49.5% to 50.5% range
- ***PRELIMINARY*** Evaluation of using 2019 data is that 2-4 claims may exceed 50% PC
- Considering programmatically over 50,000+ claims evaluated to date 2-4 claims is approximately 0.008%

Program Evaluation Report (PER) (2 of 2)

- PER will be initiated once we implement IREP 6.0; however, this will take some time due to current IT constraints
  - (i.e. require contractor to querying claims and current inability to batch process IREP claims)
- Dose Reconstructions do not have to be redone; this is purely a PC calculation of already completed Dose Reconstructions
- Subcommittee on Procedure Review (SPR) will likely review the PER when it is completed
- Target implementation is September 2023

Summary

- Proposing to change Probability of Causation procedure, not the cancer risk models nor any dose reconstructions
- Increasing the number of iterations in IREP will correct a negative bias in IREP observed with some claims thus generally increasing the Probability of Causation
- Increasing the number of iterations also improves the modeling uncertainty by decreasing the width of the Confidence Interval (CI), thus ensuring that claims close to 50% will be properly evaluated

References

- Stancescu D., Comparison of Several Percentile Definitions, DCAS, October 2022.
- Stancescu D., Effect of Alternative Percentile Definition on PC Values, DCAS, July 2023.
- Stancescu D., Increasing the Accuracy of the 99th PC values, DCAS, July 2023.
- Stancescu D., Percentile Definitions Comparison, Effect on PC values, and Increasing Accuracy of PC Values - Executive Summary, July 2023

Questions?