



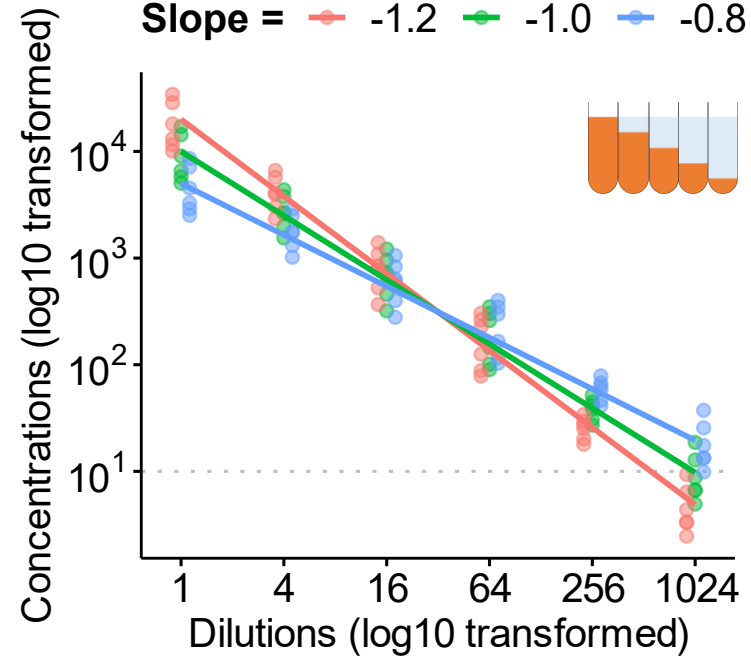
Biological assays linearity demonstration by dose-proportionality model using an equivalence framework with links to clinical outcomes

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¹. GSK Vaccine R&D Biostatistics ; ². 4Clinics

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- Clinical studies outcomes (e.g., fold increase) rely on laboratory assay measurements

- Assay linearity = ability to provide measurements directly proportional to the amount of analyte in the sample

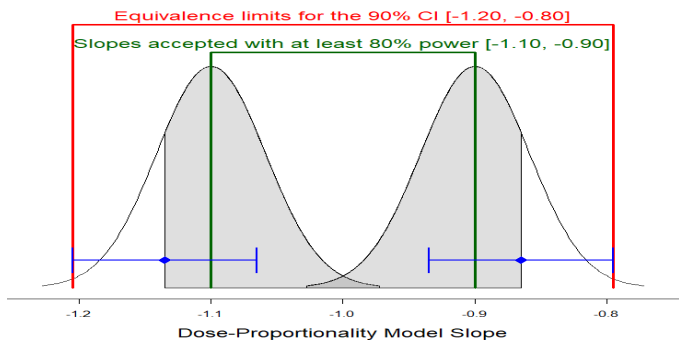
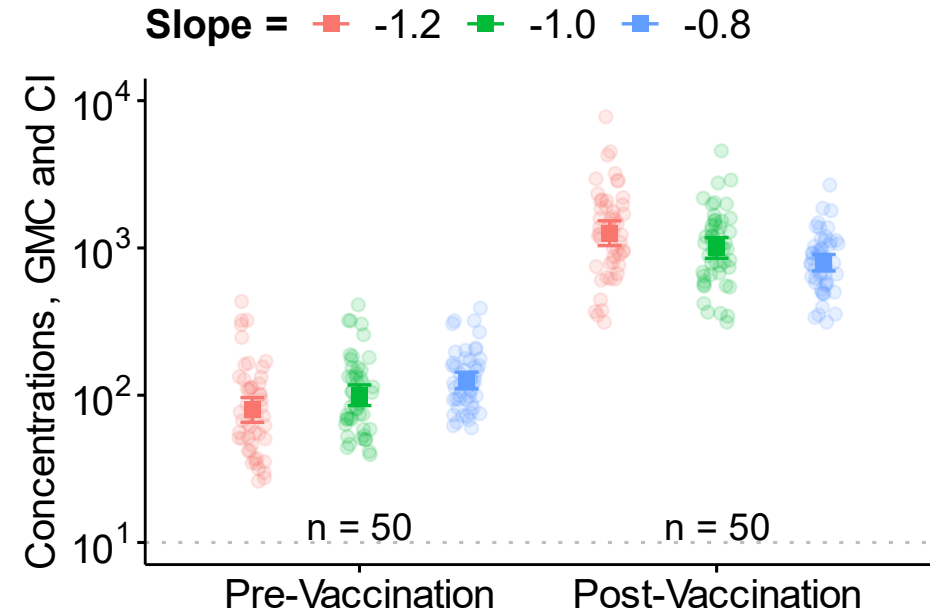
- True amount of analyte often unknown → Deduced by independent dilutions

- Dose-proportionality model
 $\log_{10}(\text{Concentrations}_j) \sim N(\beta_0 + \beta_1 \log_{10}(\text{Dilution}_j), \sigma_j^2)$

- Equivalence approach
 $H_1: \beta_1 \in [L, U]$ with $L < -1 < U$

- Equivalence limits set to accept slopes within the equivalence range with $\geq 80\%$ power, given the expected slope estimate sampling distribution

- Impact on clinical fold:
 $E(\hat{\Delta}_{Post/Pre}) = \Delta_{Post/Pre}^{-\beta_1}$



Slope	Biased 2-fold	Relative bias	Biased 4-fold	Relative Bias	Biased 10-fold	Relative Bias
-0.80	1.74	0.87	3.03	0.76	6.31	0.63
-0.90	1.87	0.93	3.48	0.87	7.94	0.79
-1.00	2.00	1.00	4.00	1.00	10.00	1.00
-1.10	2.14	1.07	4.59	1.15	12.59	1.26
-1.20	2.30	1.15	5.28	1.32	15.85	1.58

