

US EPA ARCHIVE DOCUMENT



HSRB MEETING AEATF II MOP STUDY 28 October, 2010

Extra Statistical Slides
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Statistical Models for UE

- $X = \text{Unit Exposure} = \text{UE} = \text{Exposure} / \text{Lb AI}$
- $Y = \ln X$
- Empirical: $Y = \ln \text{GM} + \text{Error}$, Errors i.i.d, mean 0
- SRS Lognormal: $Y = \ln \text{GM} + \text{Error}$, Errors i.i.d Normal
- Mixed: $Y = \ln \text{GM} + \text{Cluster} + \text{Error}$
 - Cluster $\sim N(0, V_c)$
 - Error $\sim N(0, V_w)$
 - $V = V_c + V_w$
 - Intra-cluster correlation $\text{ICC} = V_c / V$
- For fitted dermal exposure mixed models, $\text{ICC} = 0$
- Thus SRS Lognormal = Mixed for dermal exposures.

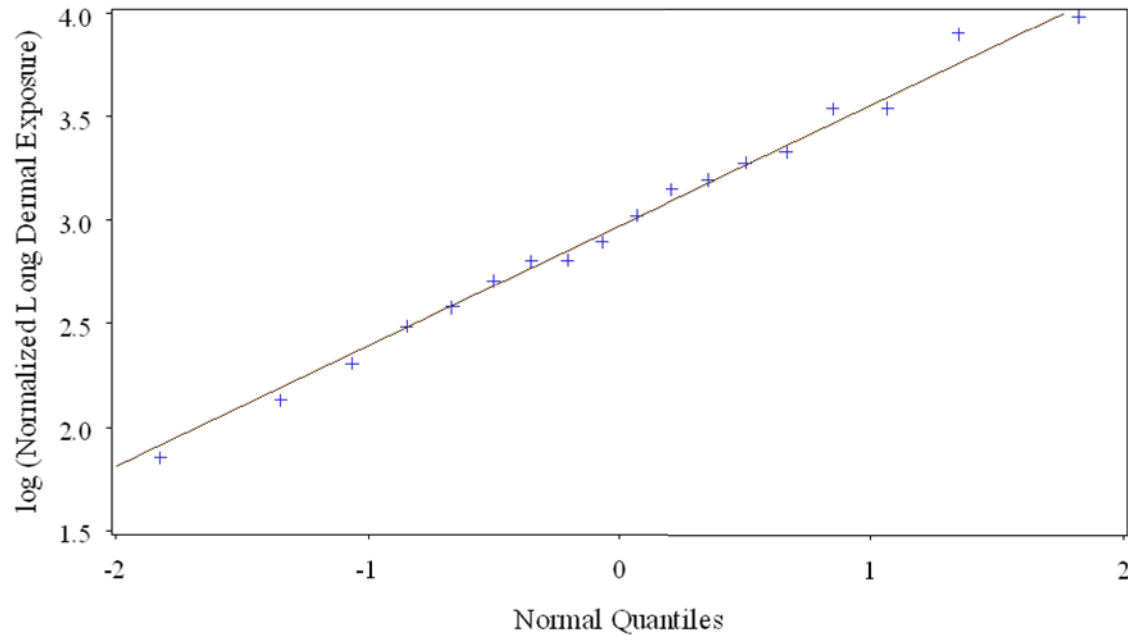
Mixed Model

- PARAMETERS:
- Arithmetic Mean = $AM(X) = \exp(\ln GM) \exp(V/2)$
- Geometric Mean = $GM(X) = \exp(\ln GM)$
- Geometric Standard Deviation = $GSD(X) = \exp(\sqrt{V})$
- 95th Percentile (X) = $\exp(\ln GM) \exp(1.96 \sqrt{V})$

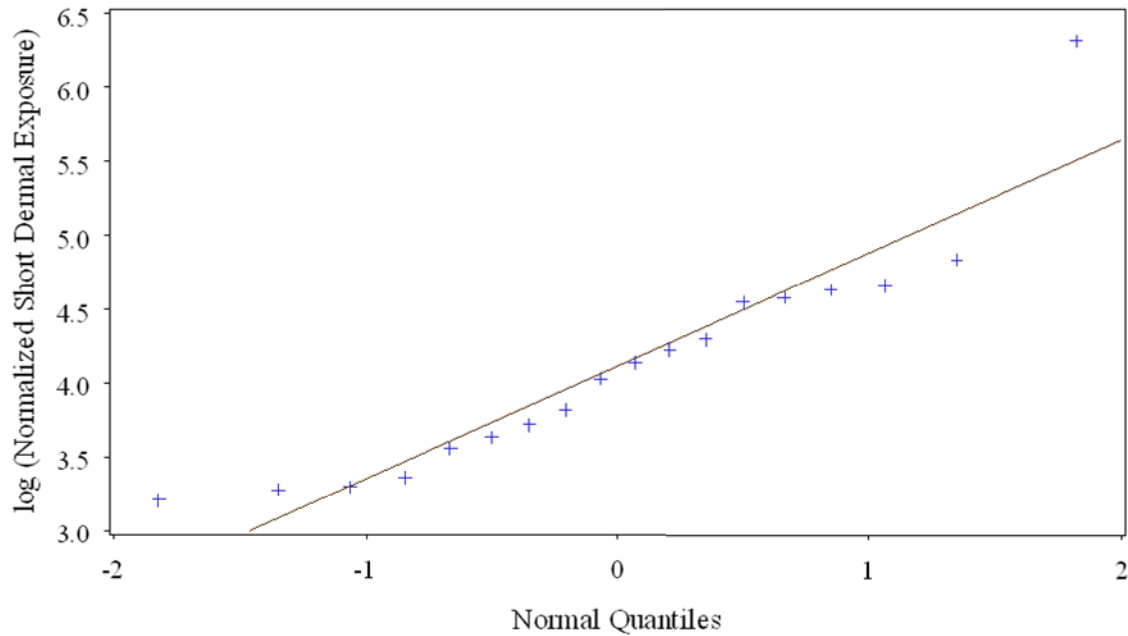
Fold Relative Accuracy

- E.g., for $AM(X) = \exp(\ln GM) \exp(V/2)$
- Step 1. Fit mixed model
- Step 2. 10,000 bootstrap simulations:
 - Simulate 18 exposure values from fitted mixed model
 - Refit mixed model
 - Compute $AM(X)$ for each simulation (10,000 values)
- Step 3. 95% confidence interval = $(T_{2.5}, T_{97.5})$
 - $T_{2.5}$ = 2.5th percentile of simulated $AM(X)$ values
 - $T_{97.5}$ = 97.5th percentile of simulated $AM(X)$ values
- Fold Relative Accuracy = $fRA_{95} = \max(T_{97.5}/AM(X), AM(X)/T_{2.5})$
- Study design benchmark: $fRA_{95} \leq 3$
- Estimate $AM(X)$ within a factor of 3.

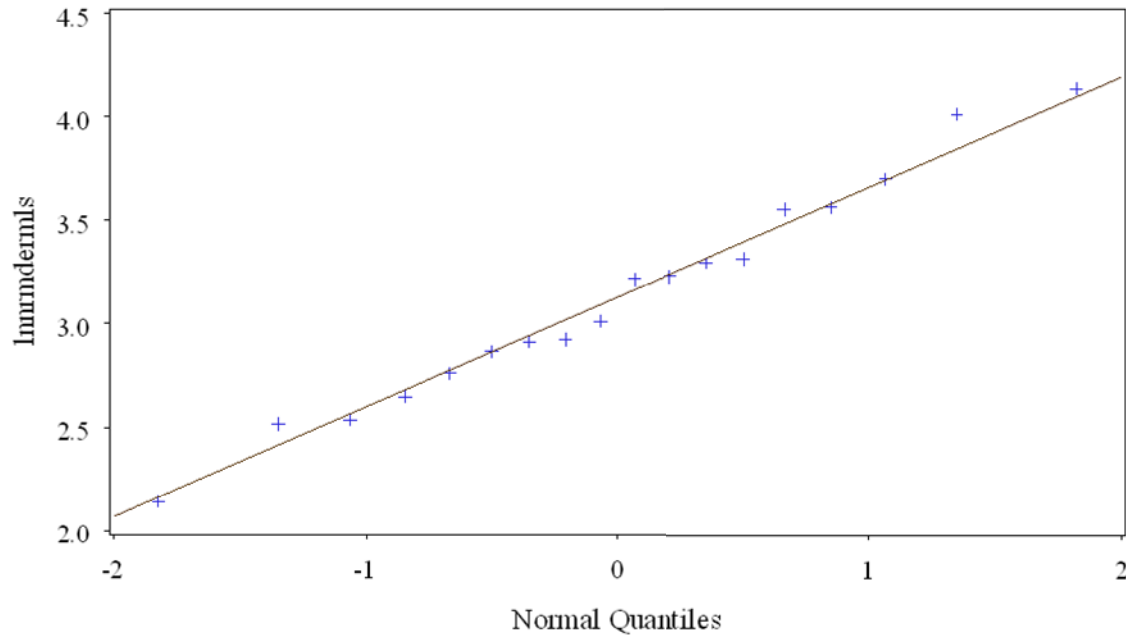
**Quantile plot normalized long dermal exposure data with a lognormal distribution
Normalized by Pounds Active Ingredient Handled**



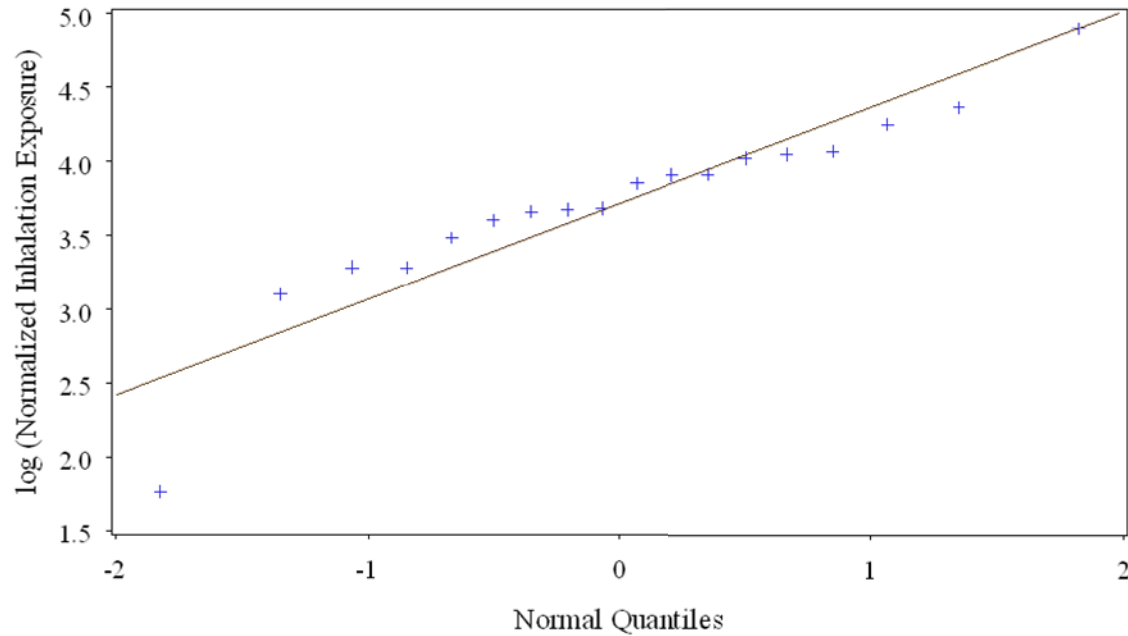
**Quantile plot normalized short dermal exposure data with a lognormal distribution
Normalized by Pounds Active Ingredient Handled**



Quantile plot normalized long short dermal exposure data with a lognormal distribution
 Normalized by Pounds Active Ingredient Handled



**Quantile plot normalized inhalation exposure data with a lognormal distribution
Normalized by Pounds Active Ingredient Handled**



Normalized Long Dermal Exposure

u = empirical, s = SRS lognormal, m = mixed

Parameter	Estimate	Lower Bound (95% confidence)	Upper Bound (95% confidence)	Fold Relative Accuracy (95% confidence)
GSDs	1.8	1.5	2.2	1.2
GSDm	1.8	1.5	2.2	1.2
ICC	0.0	0.0	0.4	
GMs	19.5	14.9	25.7	1.3
GMm	19.5	14.9	25.7	1.3
AMs	22.8	17.1	30.9	1.4
AMu	23.1	17.3	31.2	1.3
AMm	23.1	17.4	31.4	1.4
P95s	53.7	33.2	109.6	2.0
P95u	50.8	33.1	76.2	1.5
P95m	50.8	33.3	77.3	1.5

Normalized Short Dermal Exposure

u = empirical, s = SRS lognormal, m = mixed

Parameter	Estimate	Lower Bound (95% confidence)	Upper Bound (95% confidence)	Fold Relative Accuracy (95% confidence)
GSDs	2.1	1.7	2.8	1.3
GSDm	2.1	1.7	2.8	1.3
ICC	0.0	0.0	0.4	
GMs	61.3	43.1	87.7	1.4
GMm	61.3	43.1	87.7	1.4
AMs	89.0	54.2	121.7	1.6
AMu	82.1	55.0	124.3	1.5
AMm	82.1	55.1	125.5	1.5
P95s	551.2	123.0	591.2	4.5
P95u	215.4	122.7	366.6	1.8
P95m	215.4	123.6	373.2	1.7

Normalized Long/Short Dermal Exposure

u = empirical, s = SRS lognormal, m = mixed

Parameter	Estimate	Lower Bound (95% confidence)	Upper Bound (95% confidence)	Fold Relative Accuracy (95% confidence)
GSDs	1.7	1.4	2.0	1.2
GSDm	1.7	1.4	2.0	1.2
ICC	0.0	0.0	0.4	
GMs	22.8	17.9	29.3	1.3
GMm	22.8	17.9	29.3	1.3
AMs	26.1	20.1	34.0	1.3
AMu	26.3	20.2	34.5	1.3
AMm	26.3	20.3	34.6	1.3
P95s	62.4	37.1	110.5	1.8
P95u	54.7	37.0	79.3	1.5
P95m	54.7	37.2	80.3	1.5

Normalized Inhalation Exposure

u = empirical, s = SRS lognormal, m = mixed

Parameter	Estimate	Lower Bound (95% confidence)	Upper Bound (95% confidence)	Fold Relative Accuracy (95% confidence)
GSDs	1.9	1.5	2.7	1.4
GSDm	2.0	1.5	3.1	1.5
ICC	0.5	0.0	0.8	
GMs	40.9	22.2	75.3	1.8
GMm	40.9	22.2	75.3	1.8
AMs	48.2	26.0	95.9	2.0
AMu	50.5	26.4	97.7	1.9
AMm	52.4	27.0	105.7	2.0
P95s	133.9	53.9	327.0	2.5
P95u	119.0	53.4	263.5	2.2
P95m	130.0	54.8	317.5	2.4

Regression Test for Proportionality

- $\text{Ln}(\text{Exposure}) = \text{Intercept} + \text{Slope} \times \text{Ln}(\text{AI}) \{+ \text{Cluster}\} + \text{Error}$
 - Simple Linear (no cluster effect) or Mixed model
- $\Rightarrow \text{Exposure} \propto \text{AI}^{\text{Slope}}$
- $\text{Slope} = 1 \Leftrightarrow \text{Exposure} \propto \text{AI}$ Proportionality
- $\text{Slope} = 0 \Leftrightarrow \text{Exposure} \propto 1$ Independence
- Compute 95% Confidence interval for slope (Lower, Upper)
- If (Lower, Upper) includes 1, not 0 Assume Proportionality
- If (Lower, Upper) includes 0, not 1 Assume Independence
- Study design benchmark: Test has 80% power to distinguish slope = 1 from slope = 0
 - Using CMA data, designed so that expected confidence interval width = 1.4

Confidence Intervals for Slope

Exposure Route	Clothing	Model	Estimate	Lower	Upper	Confidence Interval Width
Dermal (mg)	Long pants and long sleeves	Mixed	0.71	-0.08	1.51	1.59
	Short pants and short sleeves	Mixed	1.06	0.00	2.13	2.13
		Mixed excluding MW-02	0.94	0.16	1.71	1.55
	Long pants and short sleeves	Mixed	0.63	-0.09	1.34	1.43
	None	Mixed	1.00	-0.10	2.11	2.22
		Mixed excluding MW-02	0.89	-0.02	1.80	1.81
Inhalation ($\mu\text{g}/\text{m}^3$)		Mixed	-0.03	-0.49	0.44	0.93
		Simple Linear	-0.20	-0.84	0.44	1.29
Dermal (mg)	Any	Repeated Measure	0.78	0.09	1.46	1.37

Repeated Measure Model

- From physical considerations, expect same slopes for all dermal
- Repeated Measure Model:
- $\ln(\text{dermal exposure}) =$
Intercept (Clothing) + Slope \times $\ln(\text{AI})$ + Cluster + Error
- Same slope, different intercepts
- $\text{Cov}(\text{Error}) = C$: errors for same worker are correlated
- Fitted to all long, short, and long/short clothing data
 - Failed to converge for complete set of dosimeters, socks, face/neck, hands
- 95% confidence interval for slope includes 1, not 0
- \Rightarrow Proportionality for Dermal