



Understanding Inaccuracy in Point Estimate Toxicity Reference Values

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June 2010





Starting Point

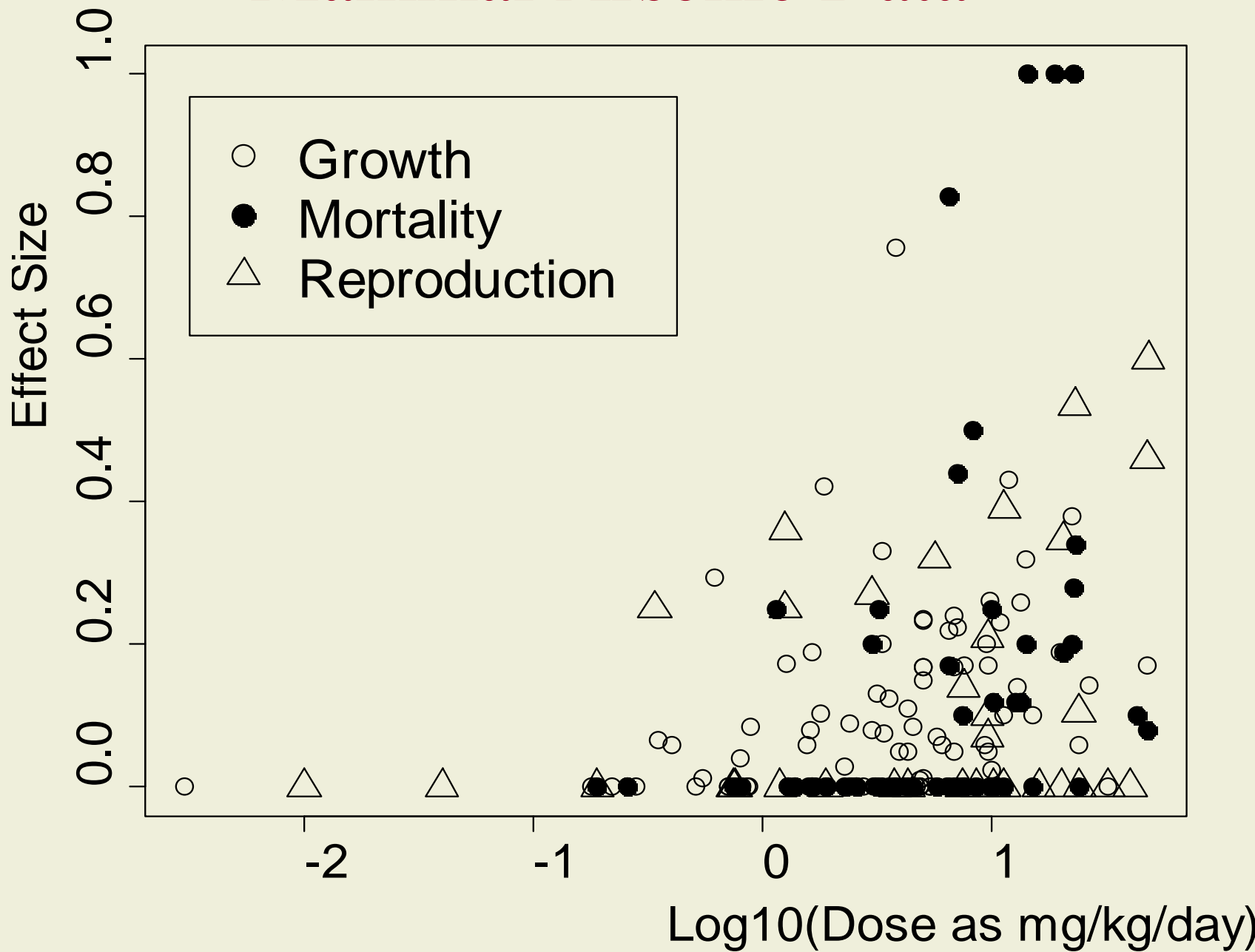
- Allard, P., A. Fairbrother, B.K. Hope, R.N. Hull, M.S. Johnson, L. Kapustka, G. Mann, B. McDonald, and B.E. Sample. 2010. Recommendations for the development and application of wildlife toxicity reference values. *Int Environ Assess Manage* 6:28–37.



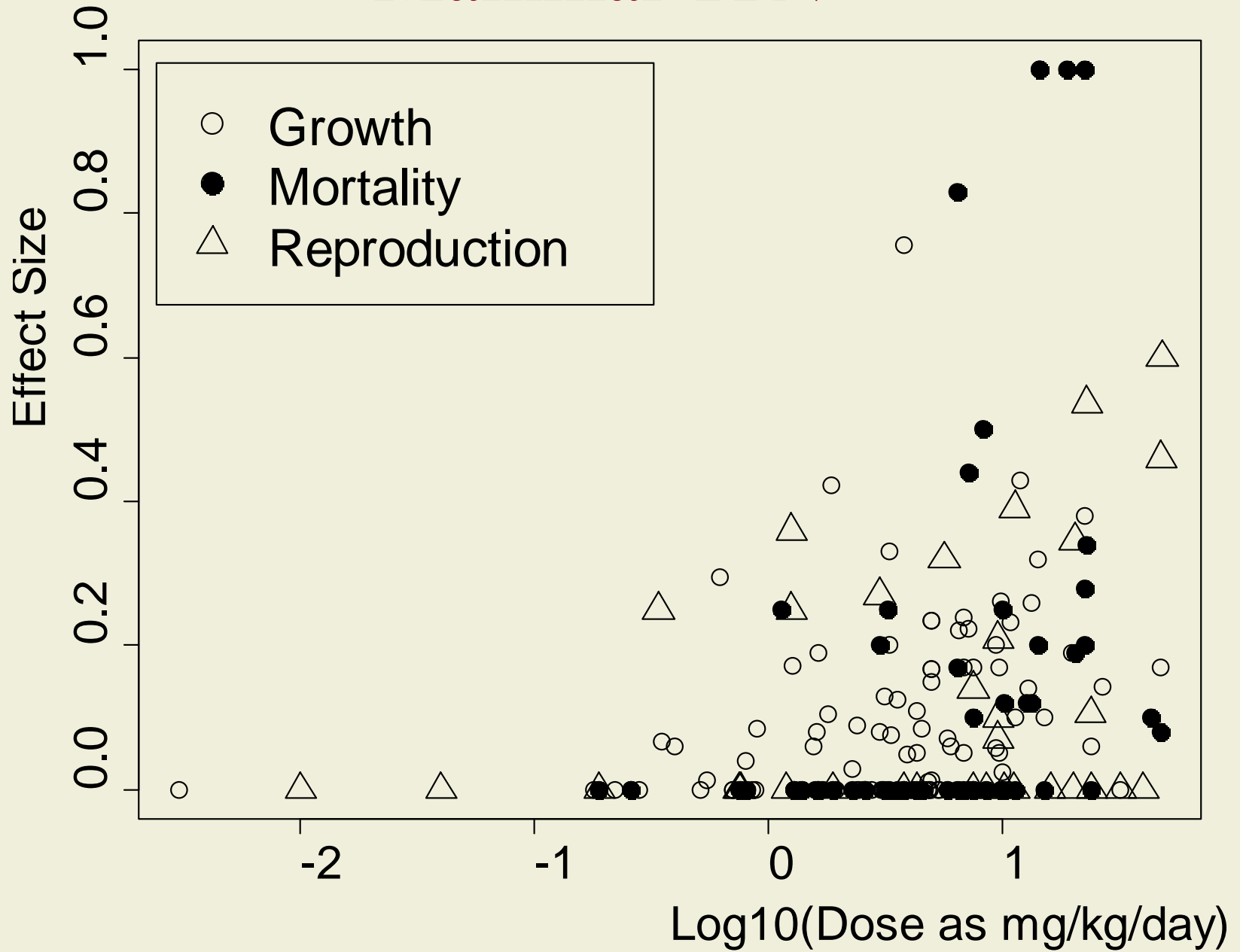
(Selected) Recommendations of Allard et al. (2010):

- ED_x – based TRVs associated with a particular effect level x are preferable to TRVs based on NOAELs / LOAELs
- Risk assessors should compile available data and try to understand underlying dose-response relationships, even if the dose-response curve itself will not be used explicitly
- Extrapolation among species is acceptable (and appropriate given data limitations), but extrapolation across taxonomic Classes is not recommended.

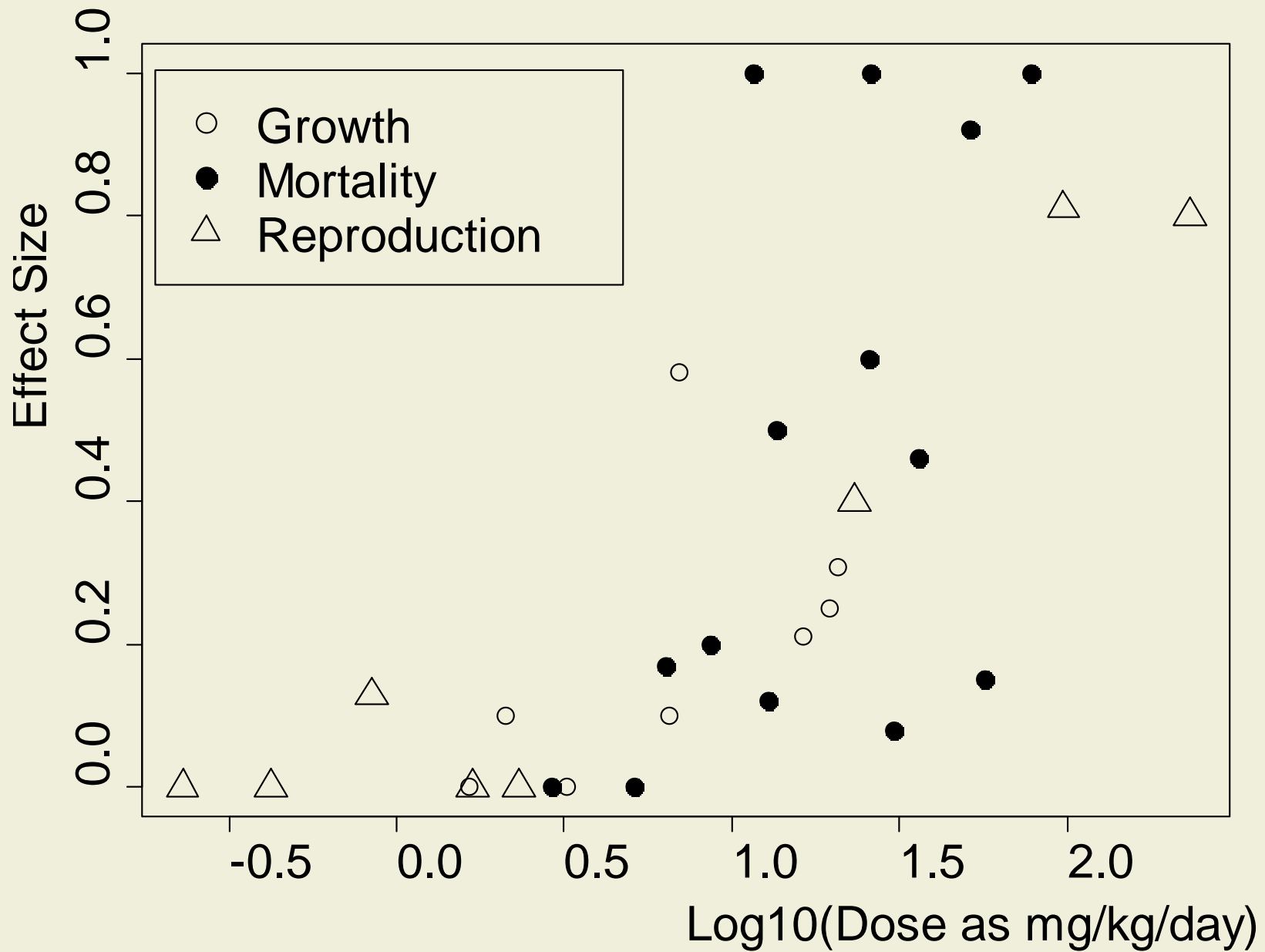
Mammal Arsenic Data



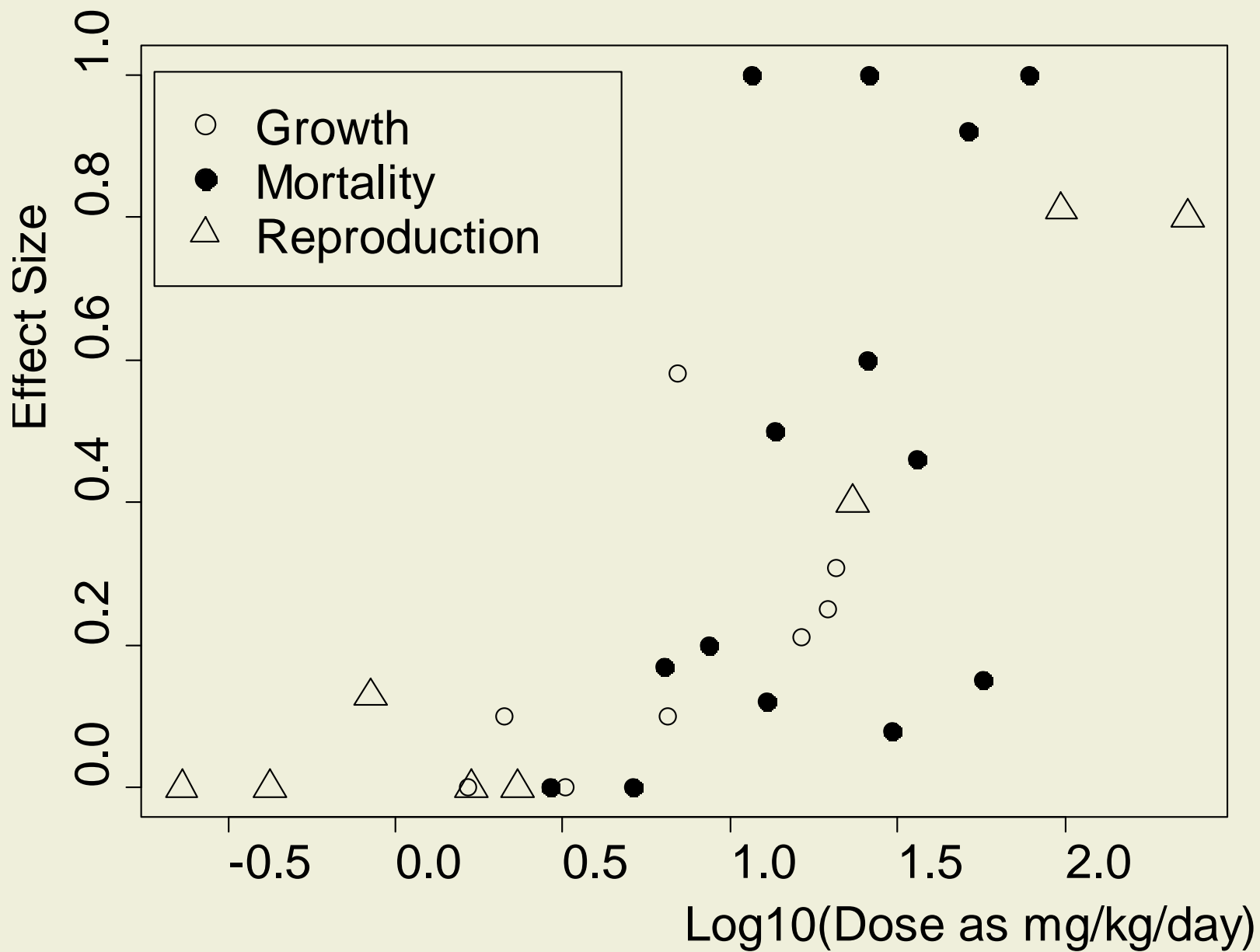
Mammal TRV



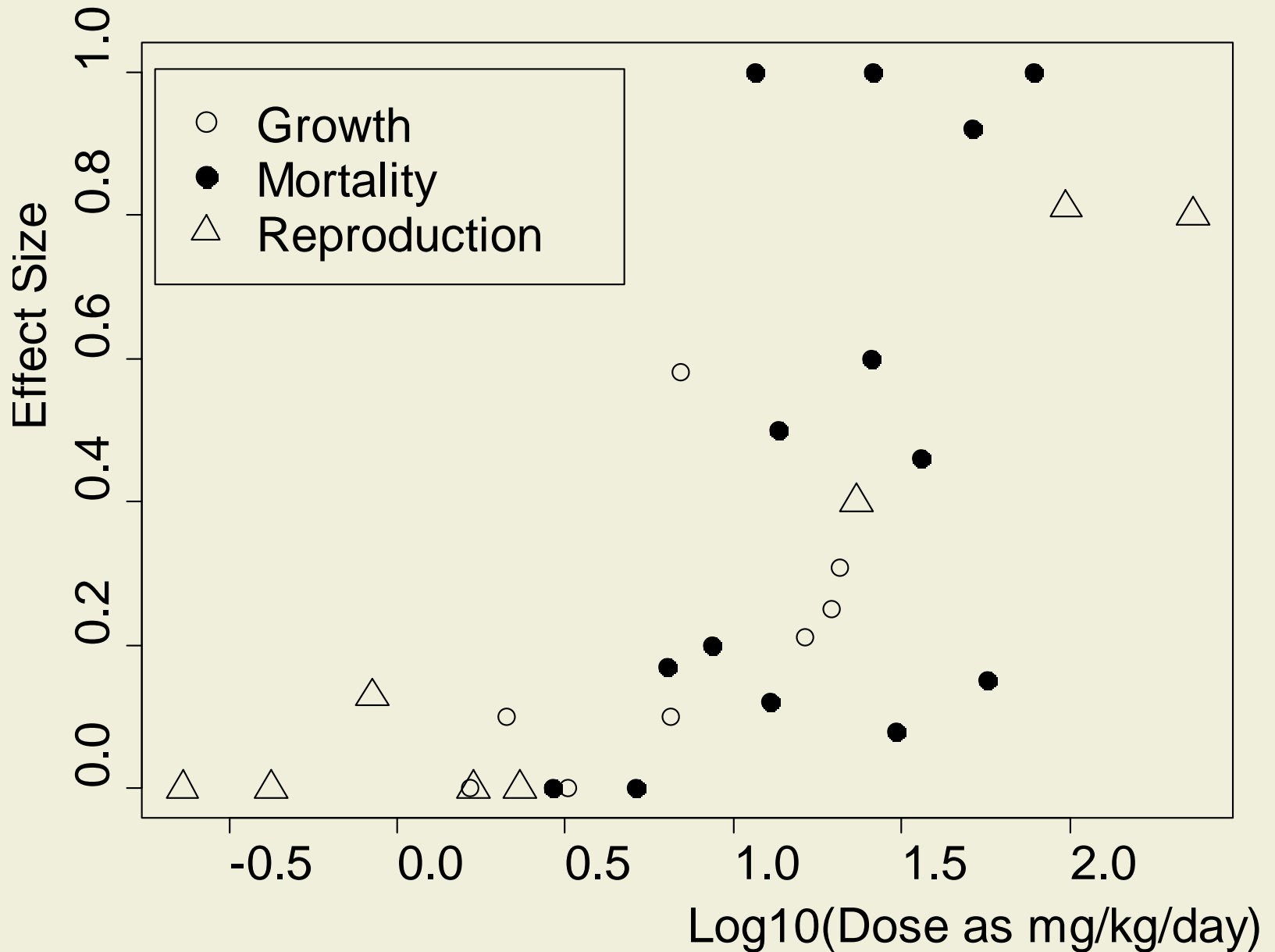
Bird Data



Bird TRV



Bird Dose-Response Fits



Comparison

	Mammal	Bird
ED ₂₀ as highest dose below which 20% ES not exceeded	0.28 mg/kg/d	6.51 mg/kg/d
ED ₂₀ from best-fit dose-response curve	10.5 (<u>37-fold higher</u>)	4.92 (<u>lower!</u>)



Conclusions

- TRVs based on usual methods (e.g.,) may be conservative when data set is large, but not necessarily when data are sparse.
- Plotting dose-response data provides, at a minimum, qualitative understanding of potential conservatism (or lack thereof) in a point estimate TRV
- Mortality not necessarily less sensitive than sublethal endpoints





Data Set Details

- Raw data from original studies compiled
- Separate data sets for mammals and birds
- Studies of all durations allowed
- Oral route of exposure only; no data based on intramuscular injection, etc.
- No allometric scaling to account for differences among species
- Statistical significance not a criterion for including data
- Separate dose-response curves for mortality, growth, reproduction

Effect Size as the Endpoint

- All 3 endpoints converted to “effect size” relative to control
- Advantages: (a) can combine data for different specific endpoints (e.g., brood size and fetal mortality); (b) can compare effect sizes among the 3 endpoint groups easily; (c) easy to interpret if effect size is used as criterion for acceptability
- Disadvantage: can't directly relate results to population level

$$\text{effect_size} = \frac{\text{control} - \text{treatment}}{\text{control}}$$



Derivation of Point Estimate TRV

- Highest dose below which effect size x not exceeded
- The data point does not have to be statistically significant, but should not come from a study where there is a data point showing response $< x$ at a higher dose
- Applied to all three endpoints, and the lowest among the three is taken as the TRV