Statistical Risk Benchmarking in Environmental Risk Assessment

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Chair, GIDP in Statistics

Statistics GIDP

Statistics is an <u>interdiscipline</u>: the broad array of problems to which statistical methods can be applied is vast. For instance, consider

Benchmark Risk Analysis.

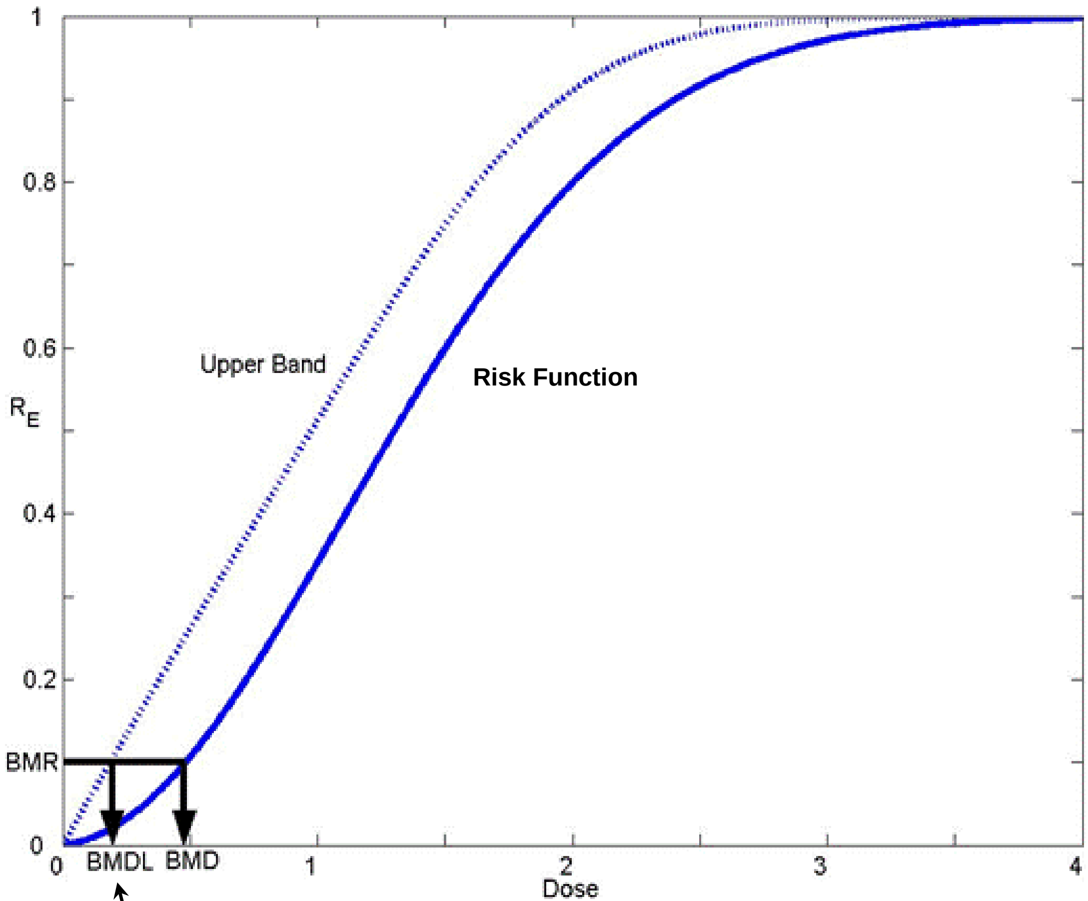
Benchmark analysis attempts to give risk assessors guidance on when the risk of some adverse stimulus moves from acceptable to unacceptable levels.

Benchmark Dose

In Benchmark Risk Analysis:

- **A Benchmark Risk (BMR) value is set, above which risks are felt to exceed acceptable levels.**
- **A function that represents the risk effect, $R_E(x)$, is fit to dose-response data on the adverse outcome.**
- **We set $R_E(x)$ = BMR and solve for x: the (smallest positive) solution is the Benchmark Dose, BMD.**

BMD and BMDL



A 100(1 – α)% lower confidence limit on BMD is the **Benchmark Dose Lower Limit**, BMDL.

Carcinogenicity Example: Aflatoxin B_1

- **The Benchmark Method was originally designed for toxicity testing; e.g., risk assessors use the BMDL as a "point of departure" from the dose-response fit to assess the risk of cancer induction.**

- **EXAMPLE: Hepatocellular tumors in rodents after exposure to Aflatoxin B_1 (dose, x, in µg/kg/day):**

x = dose	0	.04	.2	.6	2	4
Y = cancer cases	0	2	1	4	20	28
N = rodents tested	18	22	22	21	25	28

Technical Details: Aflatoxin B_1

- **Data are proportions, Y_i / N_i; dose is x_i, $i = 0,\ldots,I$**
- **Assume $Y_i \sim$ indep. Bin.(N_i, π_i).**
- **Use "Extra Risk" function**

$$R_E(x) = \{\pi(x) - \pi(0)\}/\{1 - \pi(0)\}$$

- **Apply "multistage model"**

$$\pi(x) = 1 - \exp\{-\beta_0 - \beta_1 x - \beta_2 x^2\}$$

- **Upper 95% conf. band on $R_E(x)$ over $0 \le x \le 4$ is**

$$1 - \exp\{-.0331x - .3845x^2 - x(0.260 - 0.291x + 0.121x^2)^{1/2}\}$$

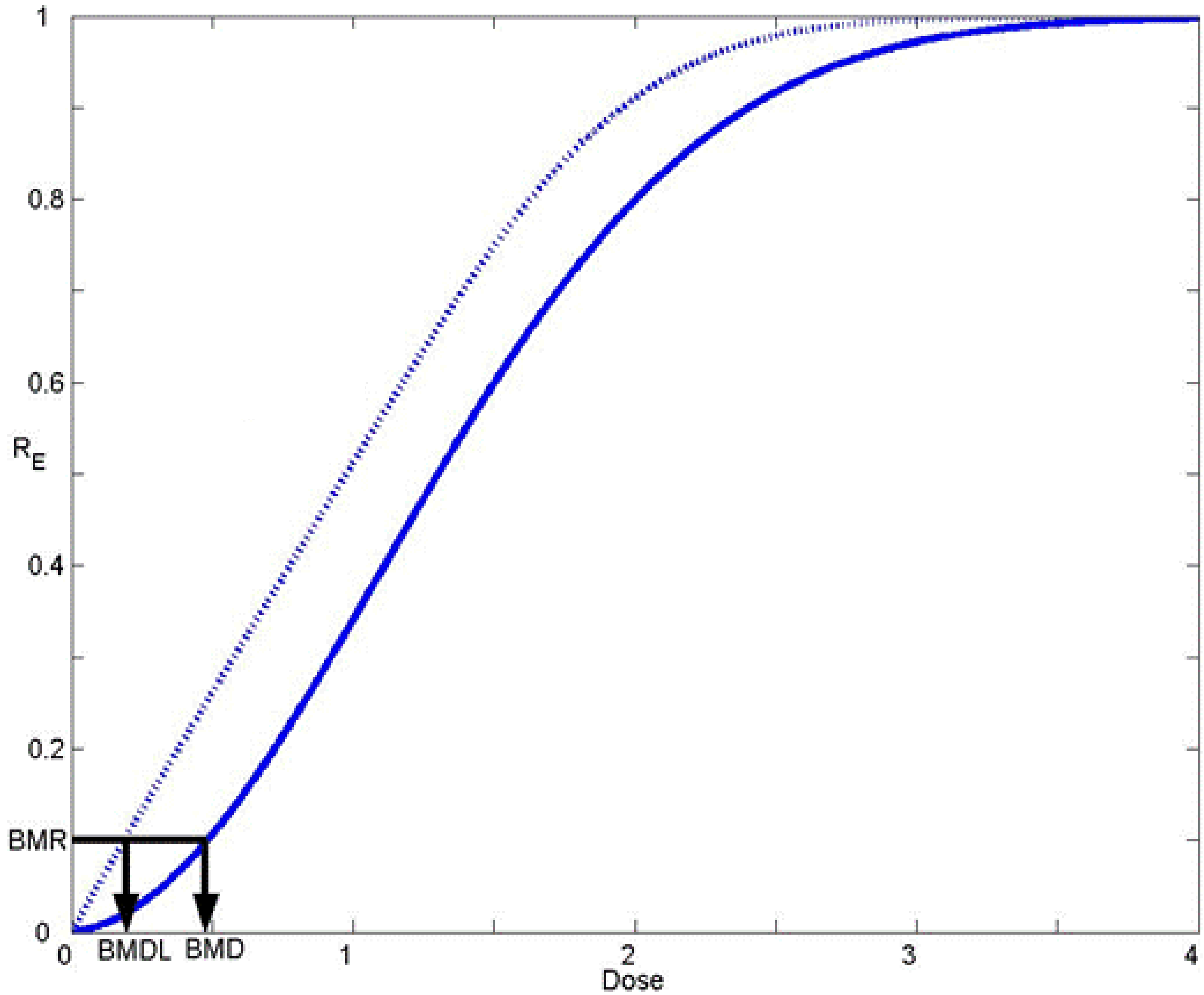
Aflatoxin B_1 BMD/BMDL at BMR = 10%

BMR = 0.10

⇒ BMD_{10} = 0.482

$BMDL_{10}$ = 0.187

(µg/kg/day).



Translational Benchmark Analysis

- **The Benchmark Method can be *translated* to non-cancer risk settings with great efficiency!**
- **EXAMPLE: Urban vulnerability to terrorism.**
  - → **"Dose" is a weighted index using social, built-environment, and geo-physical urban measures.**
  - → **Risk outcome is casualty vulnerability of a city to terrorist attack.**
  - → **Goal is to visualize the Benchmark pattern:**

Risk < 25%

25% < Risk < 50%

Risk > 50%

Placed-Based BMI/BMIL at BMR = 50%

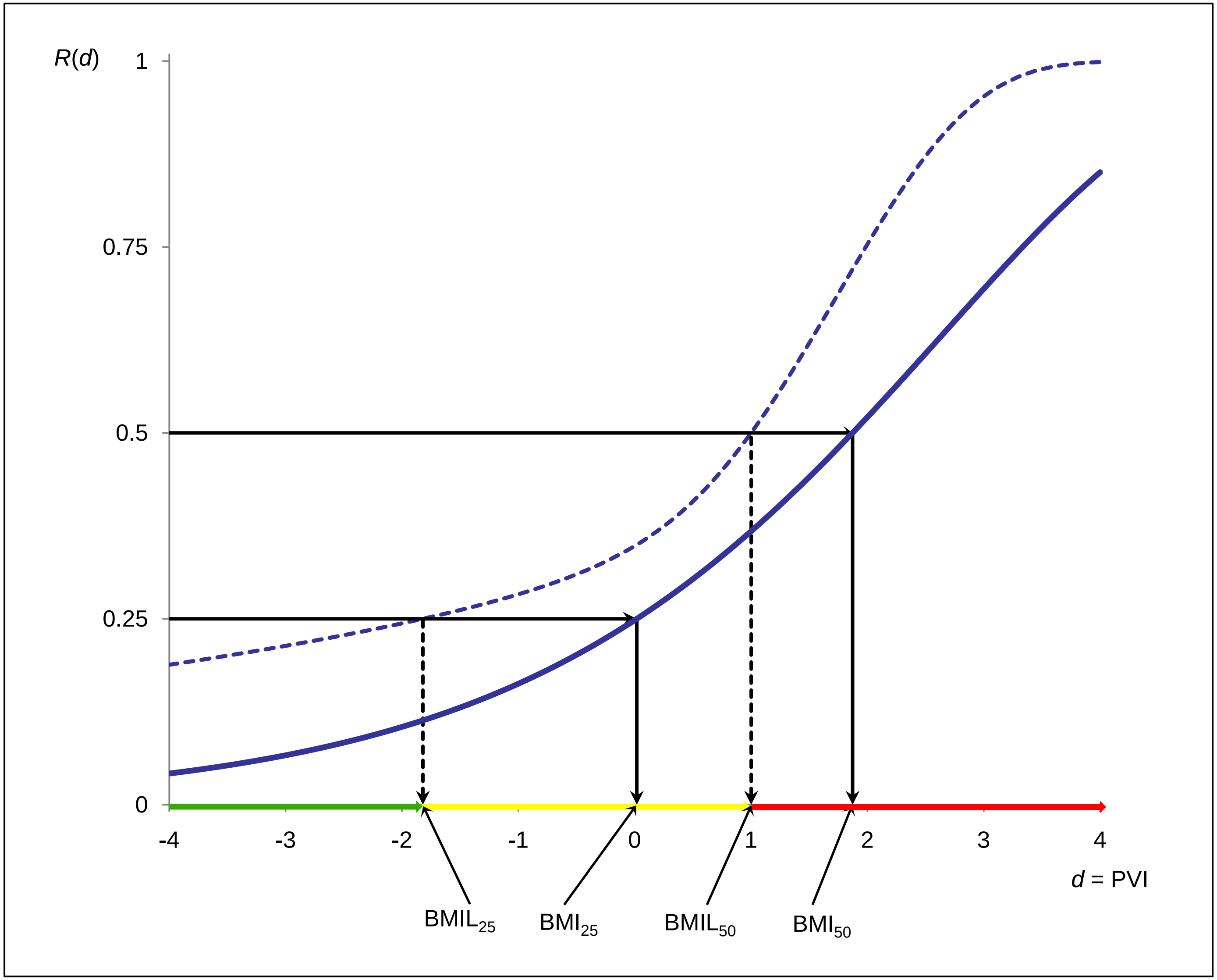
BMR = 0.50

$\Rightarrow$ **BMI$_{50}$ = 1.873**

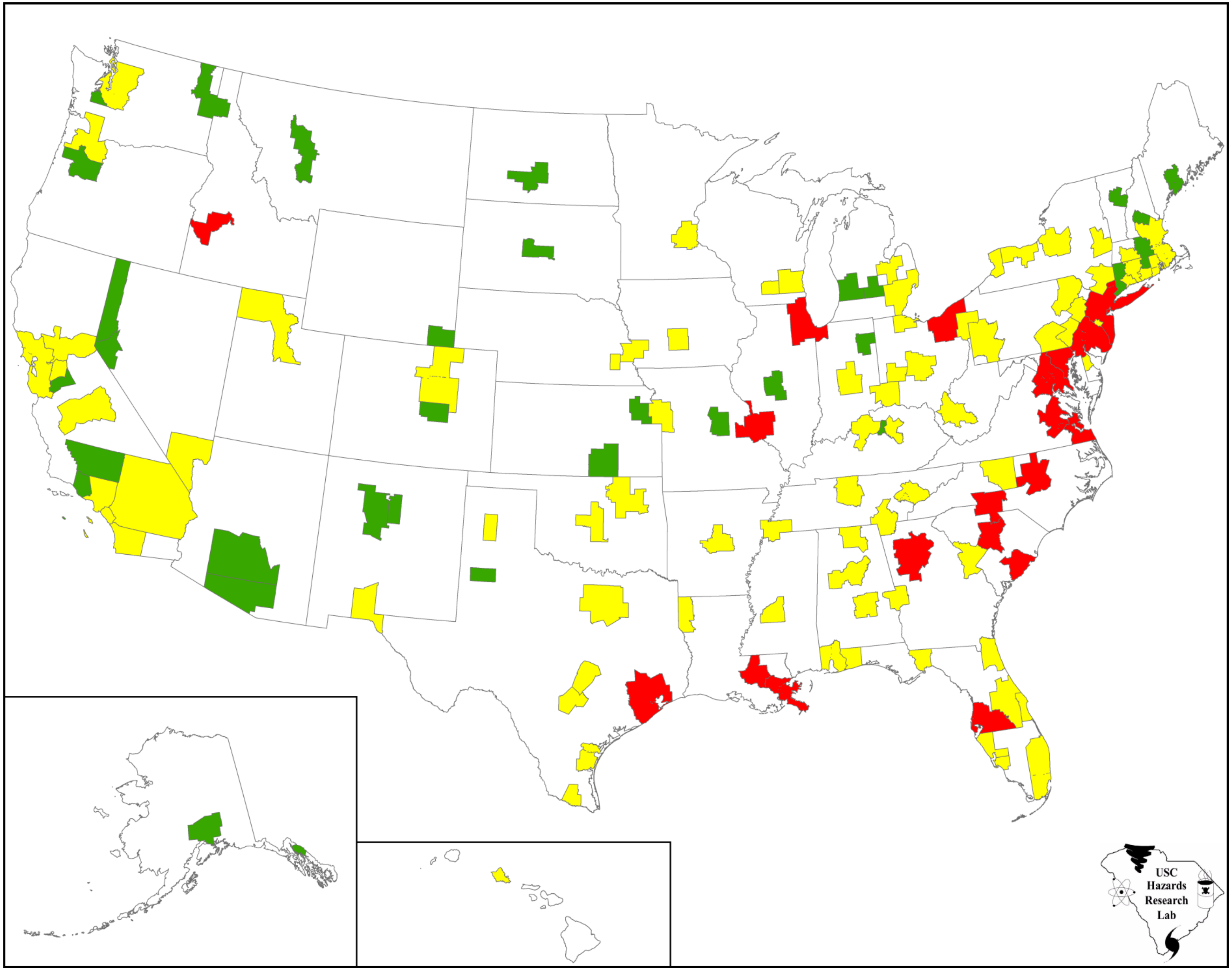
BMIL$_{50}$ = 1.001

BMI$_{25}$ = 0.018

BMIL$_{25}$ = –1.820



Placed-Based Vulnerability to Terrorism

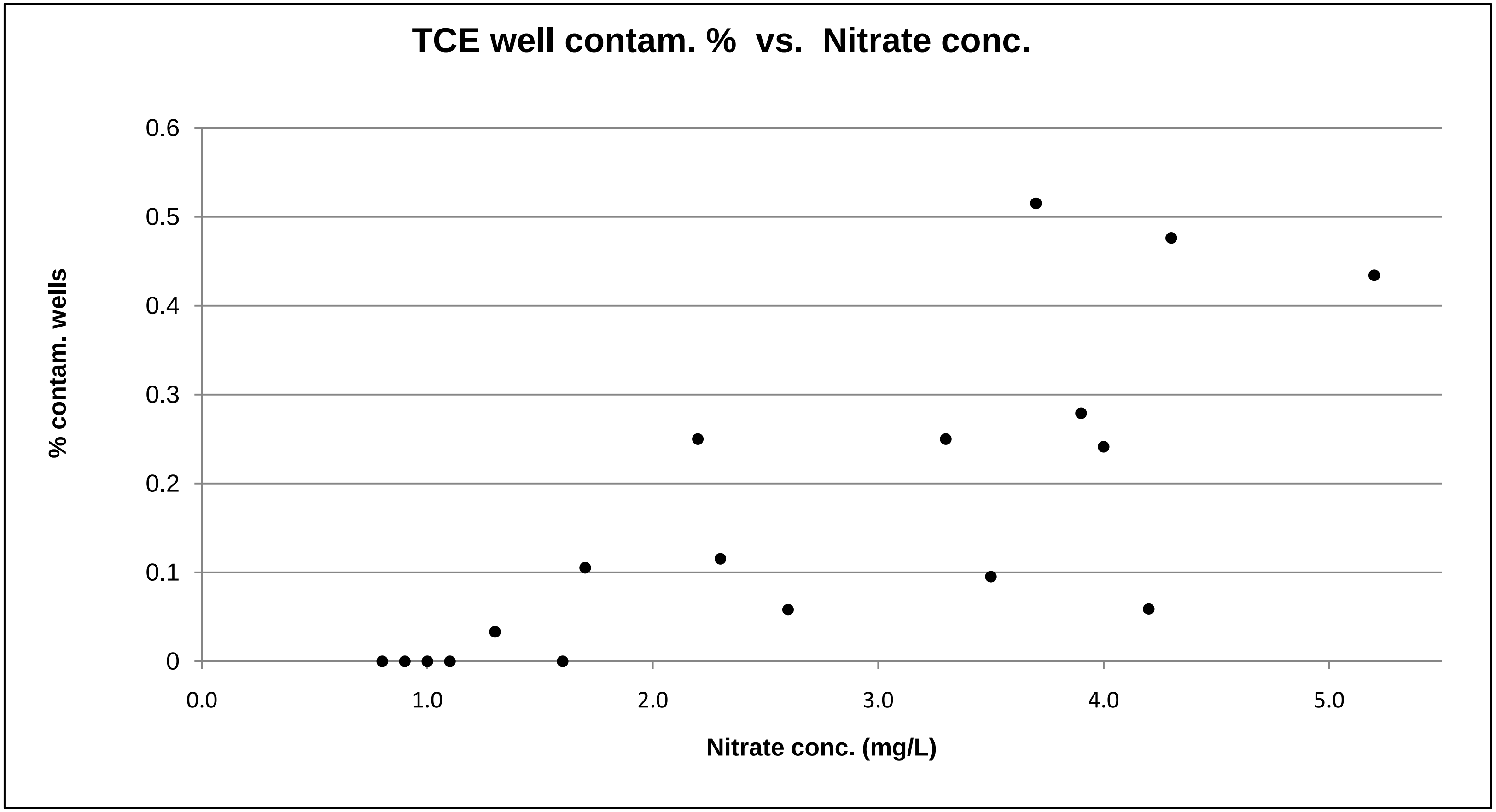


Translational Benchmark Analysis

- **The Benchmark Method can be *translated* to non-cancer risk settings with great efficiency!**
- **EXAMPLE: TCE contamination of groundwater wells as related to x = Nitrate concentration (in mg/L):**

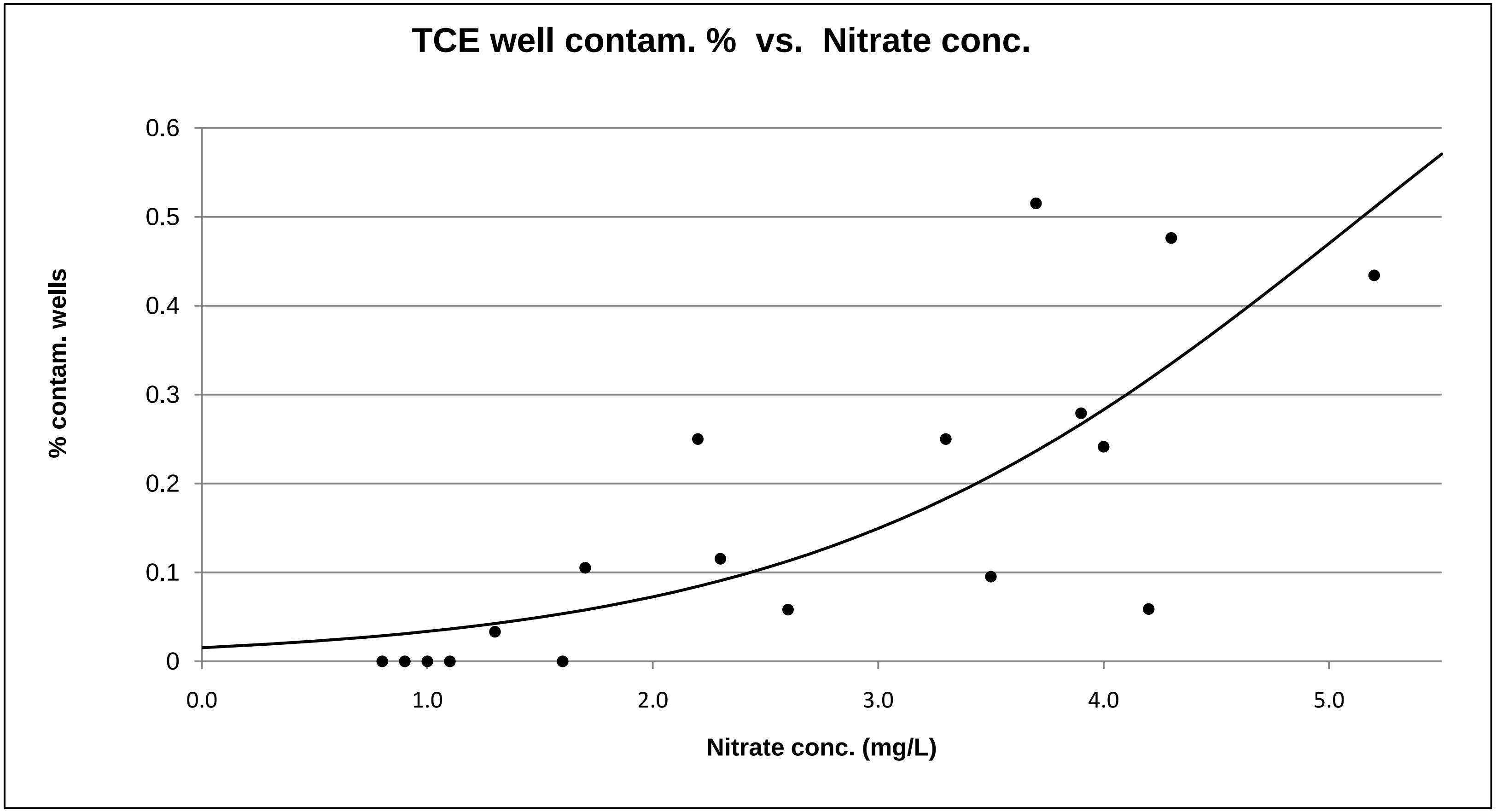
x	0.8	0.9	1.0	...	2.6	3.3	...	4.3	5.2
Y	0	0	0	...	5	8	...	20	33
N	59	22	17	...	86	32	...	42	76

TCE Well Contamination – logit model fit



Source: Eckhardt, D. A., Flipse, W. J., and Oaksford, E. T. (1989). Relation between land use and ground-water quality in the upper glacial aquifer in Nassau and Suffolk Counties, Long Island. Water-Resources Investigations Report number 86-4142. U.S. Geological Survey, Syosset, NY.

TCE Well Contamination – logit model fit



Logistic regression model fit: P[Contam. Well] = 1/{1 + exp(4.166 - 0.809x)}

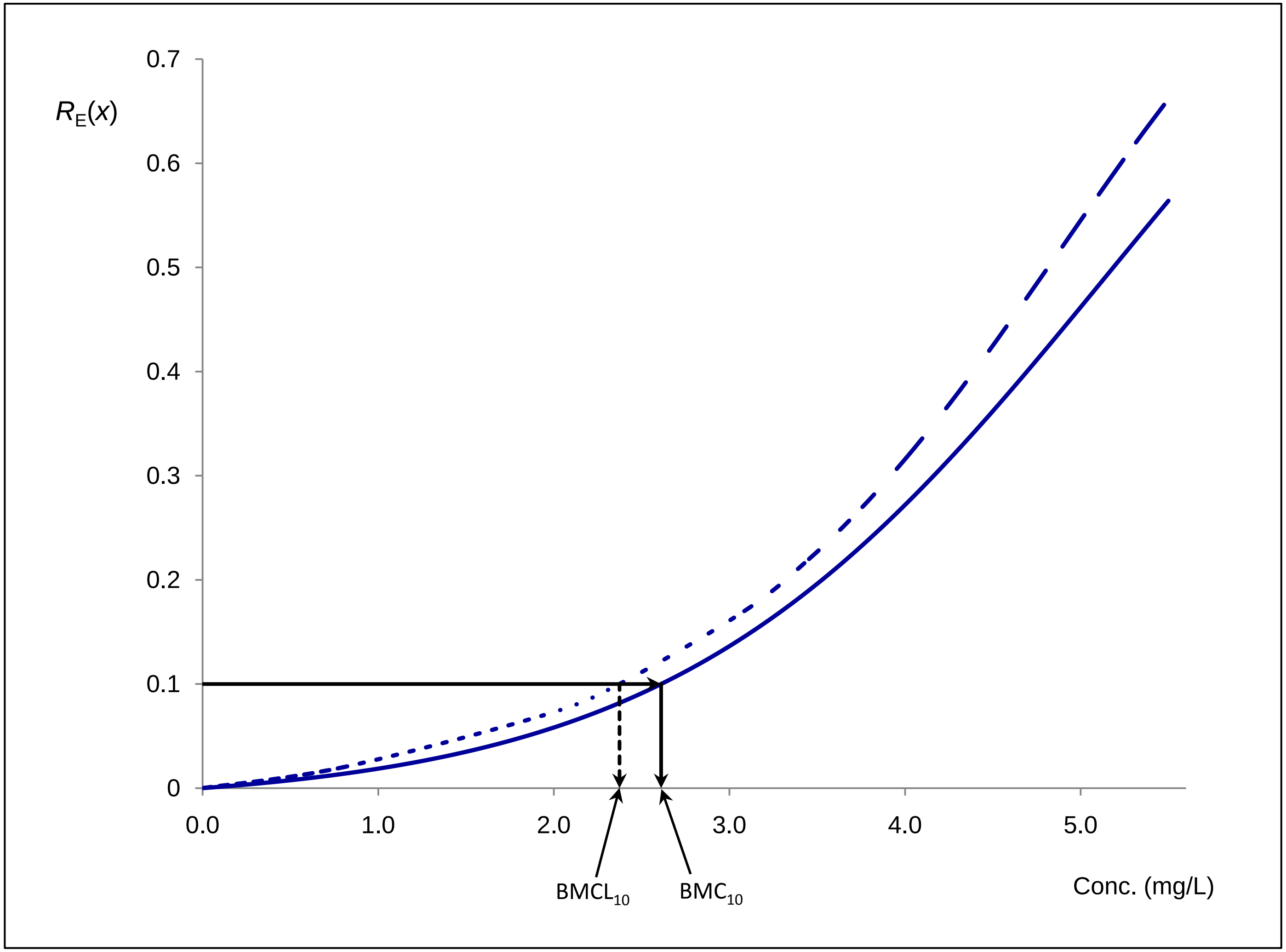
Nitrate BMC/BMCL at BMR = 10%

BMR = 0.10

⇒ BMC_{10} = 2.611

$BMCL_{10}$ = 2.374

(mg/L).



Recent Publications

Piegorsch, W.W., West, R.W., Pan, W., and Kodell, R.L. (2005). Simultaneous confidence bounds for low-dose risk assessment with non-quantal data. *Journal of Biopharmaceutical Statistics* 15, 17-31.

Piegorsch, W.W., Cutter, S.L., and Hardisty, F. (2007). Benchmark analysis for quantifying urban vulnerability to terrorist incidents. *Risk Analysis* 27, 1411-1425.

West, R.W., Nitcheva, D.K., and Piegorsch, W.W. (2009). Bootstrap methods for simultaneous benchmark analysis with quantal response data. *Environmental and Ecological Statistics* 16, 63-73.

Piegorsch, W.W. (2010). Translational benchmark risk analysis. *Journal of Risk Research* 13, 653-667.