SEGMENTED POISSON MODELS

Enrique Vidal, Roberto Pastor-Barriuso, Marina Pollán, Gonzalo López-Abente

Enviromental and Cancer Epidemiology Unit, National Centre of Epidemiology, Carlos III Institute of Health. Madrid, Spain.

CIBERESP, Spain

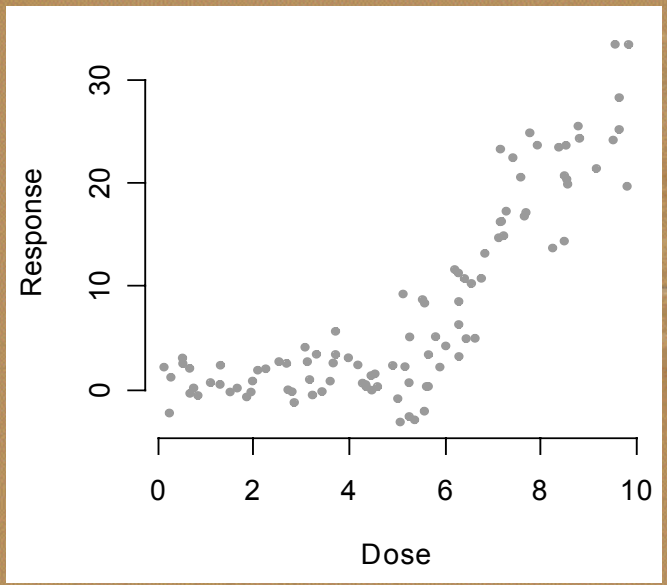
BACKGROUND

There are many situations in which threshold effects could be supposed to explain dose-response relationship

@ Diabetes

@ Mortality trends

@ Physics



We need tools to deal with dose-response analyses

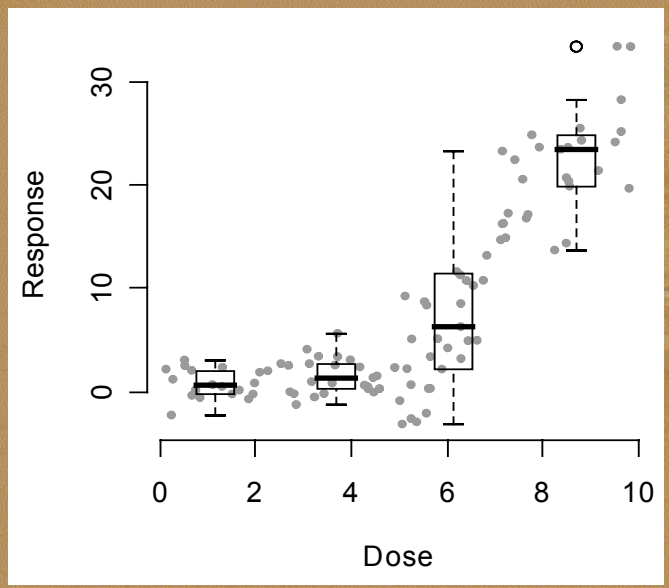
BACKGROUND

Standard dose-response analyses provide flexible tools to describe the overall shape of the relationship

* Categorical Analyses

* Non Parametrical Regressions

* Splines



BUT identification of change points is subjective

We need to test existence & location of possible change points

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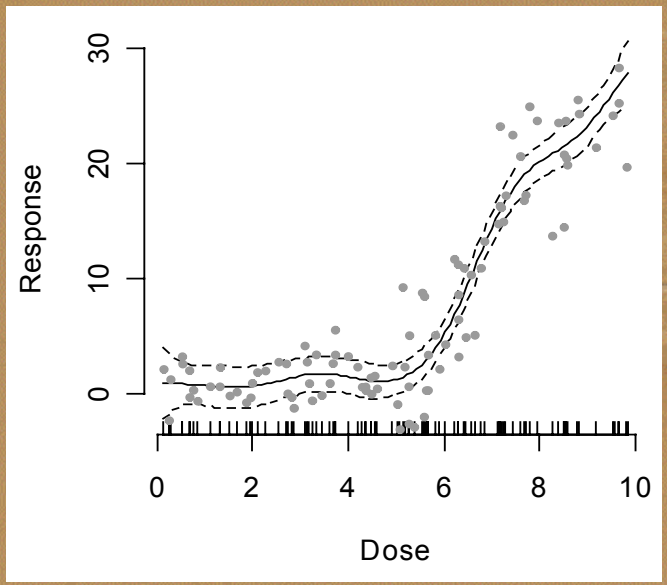

BUT identification of change points is subjective

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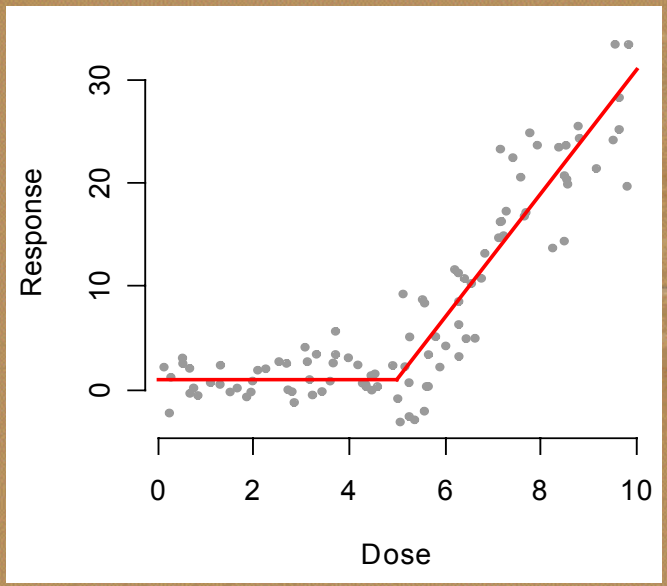
BACKGROUND

One choice could be linear joinpoint regression

+ It tests existence of joinpoints

+ It's already implemented

- It assumes an abrupt transition



May be smooth transitions will be more plausible in many biological settings

AIM

It would be desirable to find a model that

assess changes in response trends related to a dose variable

tests existence and location of change points

allows a gradual transition at the change point

could be implemented in R code

MODEL

We propose a Segmented Poisson Model with

Poisson variance for aggregated counts

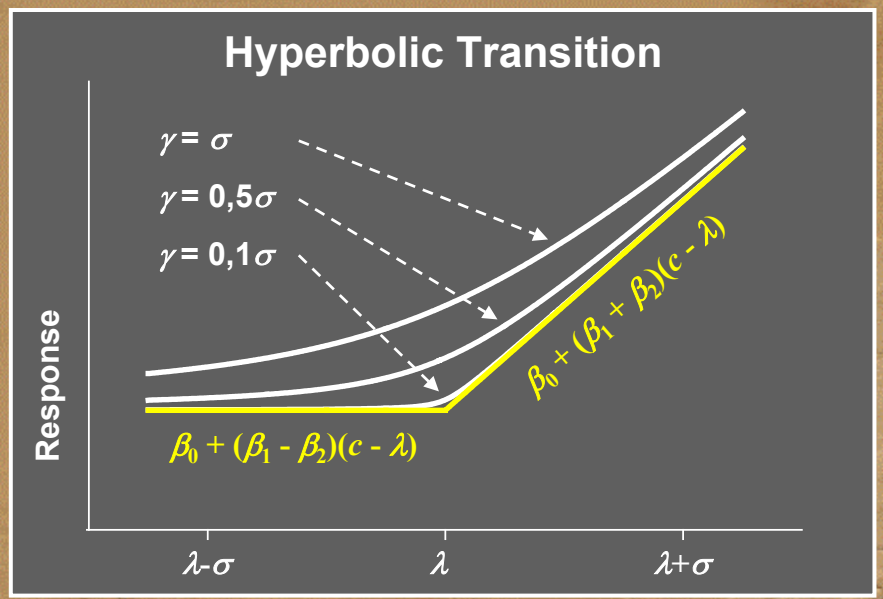
Free dispersion parameter for extra variance (small areas)

2 intersecting straight lines for differential dose-response

Hyperbolic transition function for smoothness at the change point

and a log link function

$$\log[E(d)/n] = \alpha_i Z_i + \beta_0 + \\ + \beta_1 (c-\lambda) + \beta_2 \sqrt{(c-\lambda)^2 + \gamma^2}$$



ESTIMATION

For change point and transition parameter fixed, the function is lineal in β so

existence is tested performing a grid search over the dose variable, and applying improved Bonferroni corrections for multiple search to a likelihood ratio test

location is estimated by searching around de ML knot of the above grid. Its CI is approximated by cubic spline interpolation over the knots

Once the existence and location of the change point has been assed, the final model is fitted to obtain the corresponding slopes

FUNCTION

Input

- Data, as data frame
- Outcome variable, as character
- Dose variable, as character
- Covariates (offset), as formula

Output

- Change Point existence test
- Change point location point & interval estimates
- Slopes below & above change point

EXAMPLES

[1] Renal cancer mortality

Response: Deaths by municipalities in Spain (1994-2003)

Dose: Distance to he nearest metallurgical facilities (EPER)

Covariables: Expected cases (offset), age, sex, socio-eco. ind.

[2] Breast cancer incidence:

Response: New cases from 16 (of the 50) Spanish registers

Dose: Year of diagnosis (1970-2004)

Covariables: Person-years (offset), register

RESULTS

[1] Renal cancer mortality

It does exist a change point (p-value < 0.002), located at 5 Km (CI 95% 3 13 Km) away from the point source

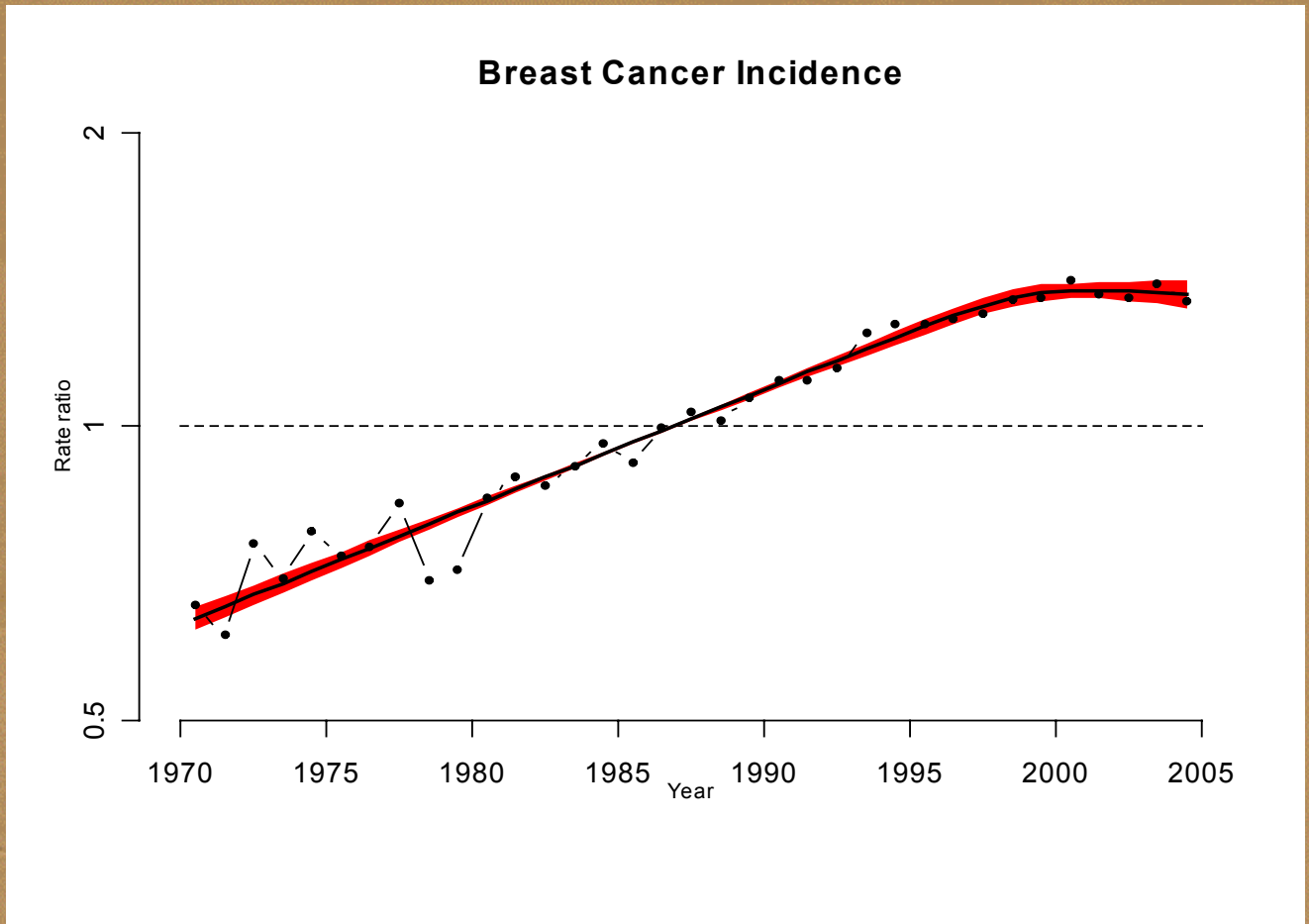
Significant decrease of renal cancer mortality with further distance bellow change point, no trend above it

[2] Breast cancer incidence:

It does exist a change point (p-value < 10^{-10}), happening in year 1999 (CI 95% 1996 2001)

Breast cancer incidence increased in Spain (2.8% per year) during the 70s, 80s &90s and levelled in the XXI century

RESULTS


Breast Cancer Incidence
Rate ratio
2
1
0.5
1970
1975
1980
1985
1990
1995
2000
2005
Year

THANK YOU