Towards continuous domain models in Spatial Epidemiology

Garyfallos Konstantinoudis; Dominic Schuhmacher; Haavard Rue; Ben Spycher

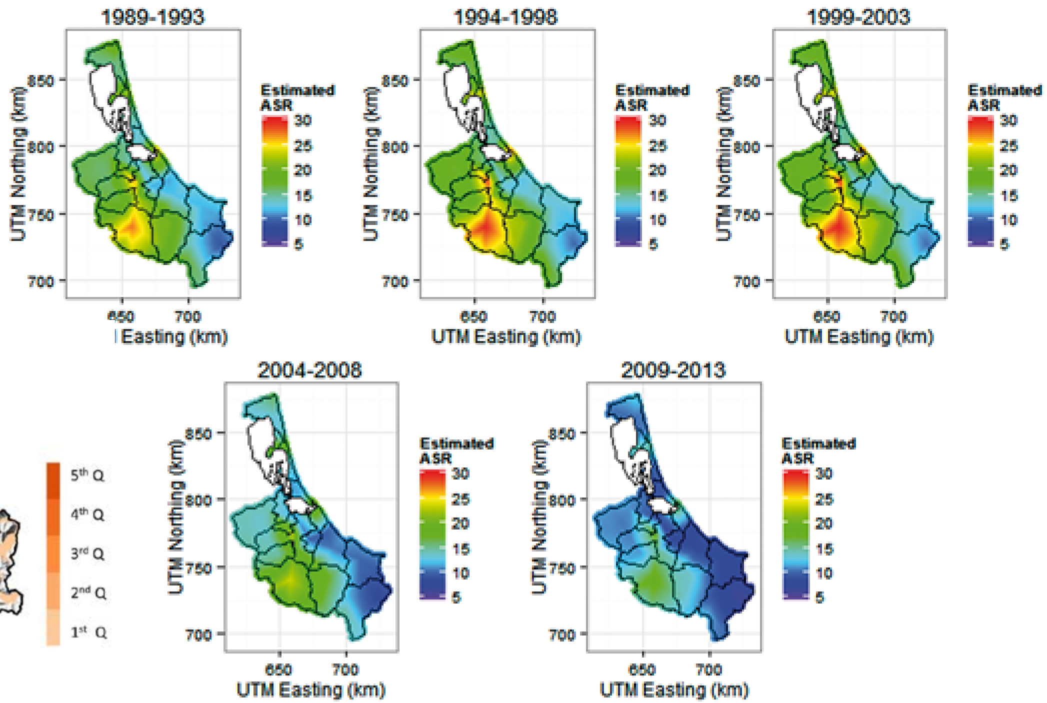
Institute of Social and Preventive Medicine ISPM
University of Bern

29 August 2018

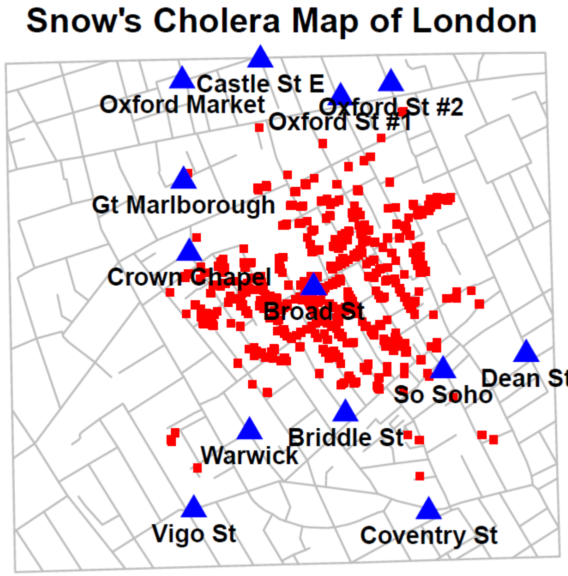
Geographical Analysis in Spatial Epidemiology

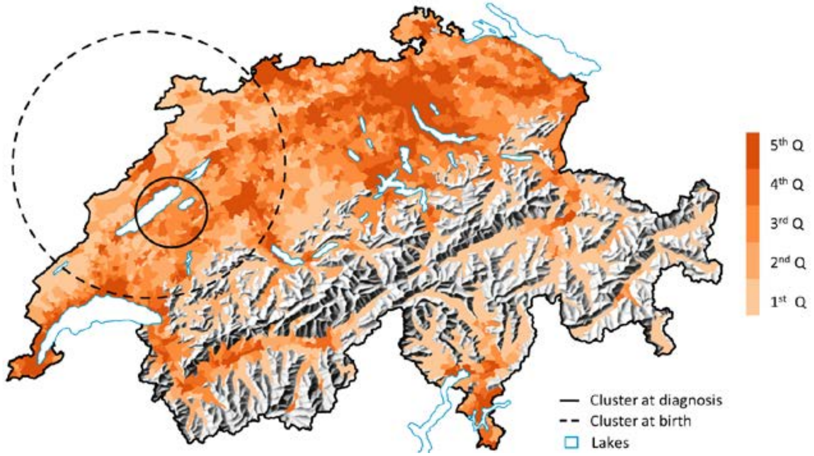
- > Generate hypotheses
- > Identify hotspots of environmental contamination
- > Target areas for health interventions

Cervix cancer incidence in Thailand



Zhao Health Policy and Planning 2017





Konstantinoudis et al 2018 Cancer Causes and Control

Motivation

UNIVERSITÄT BERN

- Childhood leukaemia: 5.4 per 100,000 person years
- Leukaemia clusters: Sellafield, Woburn Fallon
- Putative environmental risk factors

EXCLUSIVE

Nineteen children living within 20 miles of the Sellafield nuclear plant have developed leukaemia, a cancer affecting their blood and bone marrow. In a few weeks' time their parents will begin proceedings to sue British Nuclear Fuels for compensation. If they win, it will make legal history. Four of these families have told their story exclusively to the Observer Magazine. Report by Alison Whyte and Annabel Ferriman. Photographs by Christopher Pillitz

SELLAFIELD AND THE SUFFERING CHILDREN

Fallon, Nevada's deadly legacy

In a small town once plagued by childhood cancer, some families still search for answers.

Sierra Crane-Murdoch | March 9, 2014 | *From the print edition* | PRINT | SHARE

Gary Ridenour, a Fallon doctor, has teamed up with April Brune's attorney, Alan Levin, to uncover environmental causes of cancer. But they're at odds with town and state officials, who have accused them of spreading false information.
Max Whittaker/Prime

1 2 3 4 5 6 7 8 9 10 View Gallery

One night in May 2008, in a modest ranch house in central Nevada, Ryan Brune woke with a headache. He had complained about the pain earlier that week, but his doctor said it was migraines. This time, he couldn't sleep, and so his mother,

Previous studies

UNIVERSITÄT BERN

- Areal data: Besag York Mollié (BYM) model
  - Besag *Ann Inst Statist Math* 1991
  - Acute Leukaemia in France (Faure *Eur J Cancer Prev* 2009), Childhood leukaemia and Type 1 Diabetes in Yorkshire (Manda et al. Eur J Epidemiol 2009)

- Precise data: Log Gaussian Cox process (LGCP)
  - Møller et al. *Scand J Stat* 1998
  - Cancer mapping: Lung cancer in Spain (Diggle et al. Stat Sci 2013), Colon and rectum in Minesota (Liang et al. Ann Appl Stat 2008)
    - none for childhood cancers.

- Simulation studies:
  - Lung and stomach cancer (Li et al. *J R Stat Soc C-Appl* 2012)
  - Syphilis (Li et al. *Methods in Medical Research* 2012)

Aims

UNIVERSITÄT BERN

Does LGCP on point data provide additional benefit over the BYM model on areal data when:

- **Aim 1**: Quantifying the risk in space
- **Aim 2**: Identify high-risk areas

Methods: Data Availability

- Cases
  - Swiss Childhood Cancer Registry (SCCR)
  - >90% coverage since 1985
  - Precise location

- Population
  - Census (1990, 2000, 2010 onwards)
  - Precise location

- Geographical units in Switzerland
  - 26 Cantons
  - 2353 municipalities

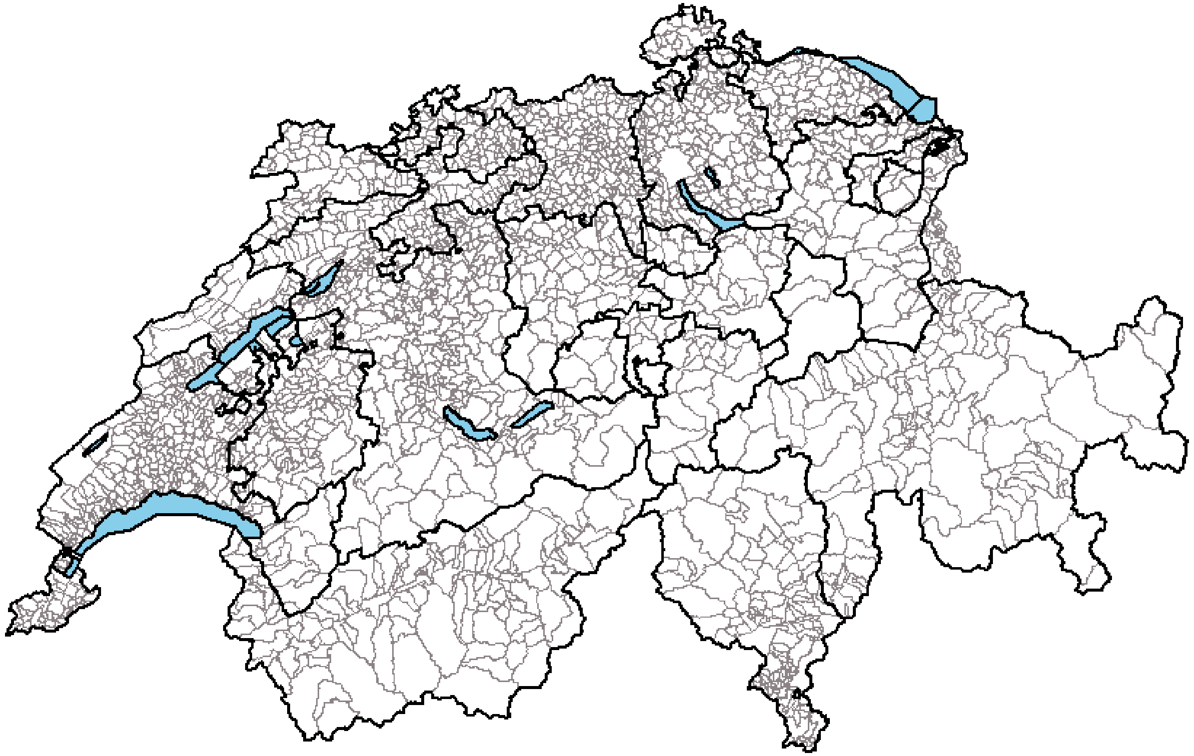


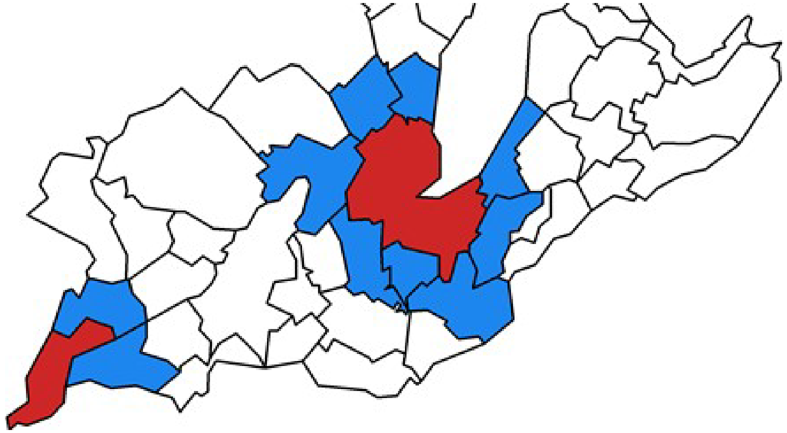
Figure. Geographical units in Switzerland

Methods: Model description

- BYM model on municipalities

$$\log(Y_i) = \log(M_i) + \beta_0 + u_i + v_i \ ,$$

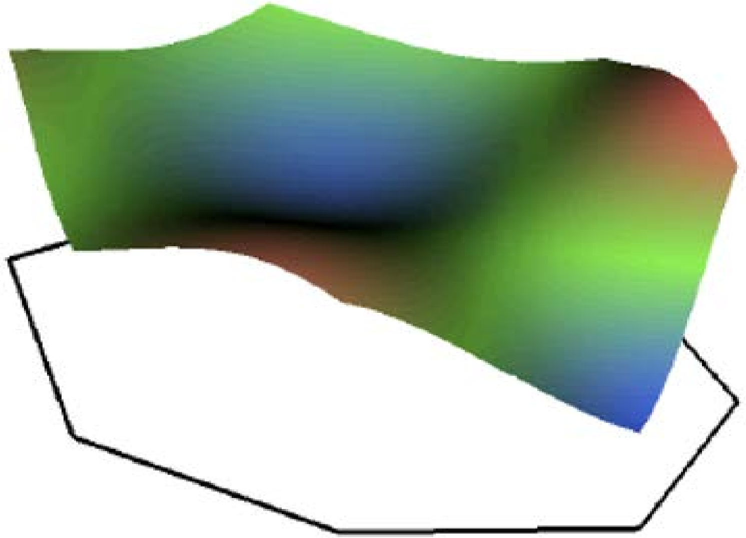
$$u_{i|-i} \sim N\left(\frac{\sum w_{ij} u_j}{\sum w_{ij}}, \frac{\sigma_1^2}{\sum w_{ij}}\right), v_i \sim N(0, \sigma_2^2), \ \mathrm{i} = 1, \dots, \mathrm{m}$$



- LGCP model

$$\log[\mathrm{Y(s)}] = \log[M(s)] + \ \beta_0 + u(s)$$

$u(s) \sim GRF(0, \kappa), \kappa(|h|) = \sigma^2 \rho_\nu(|h|/\phi)$, $\rho_\nu(\cdot)$ is Matèrn



- Inference with Integrated Nested Laplace Approximation (INLA)

Methods: Data Simulation

> Canton of ZH (168 municipalities)

> N = 205,242 (15%) children

> Leukaemia incidence 1985-2015 (n = 334)

Radius	RR	Times n	decay
1km	2	1	Step
5km	5	5	Smooth
10km	-	10	Flat

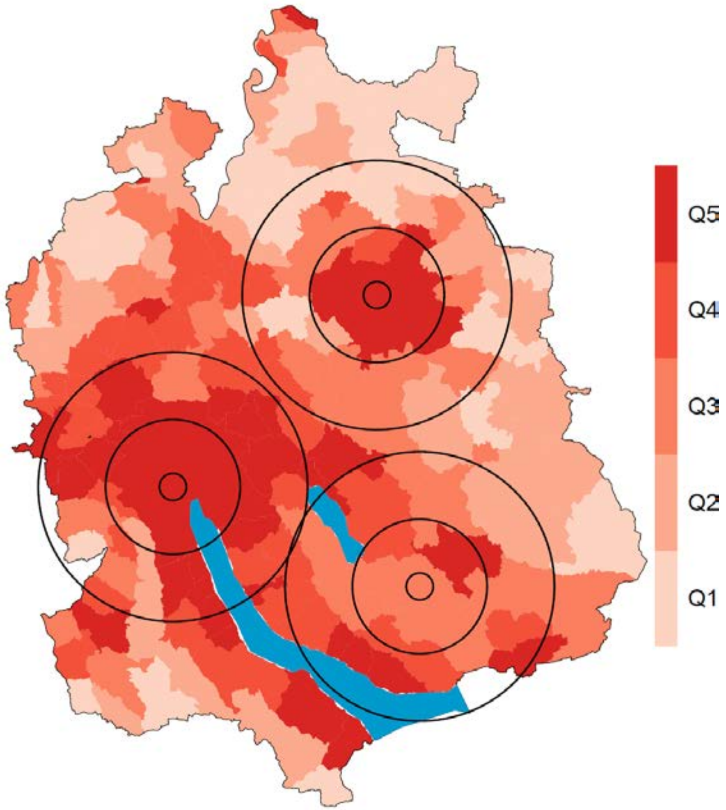


Figure. Quintiles of population density

Simulation Metrics

UNIVERSITÄT
BERN

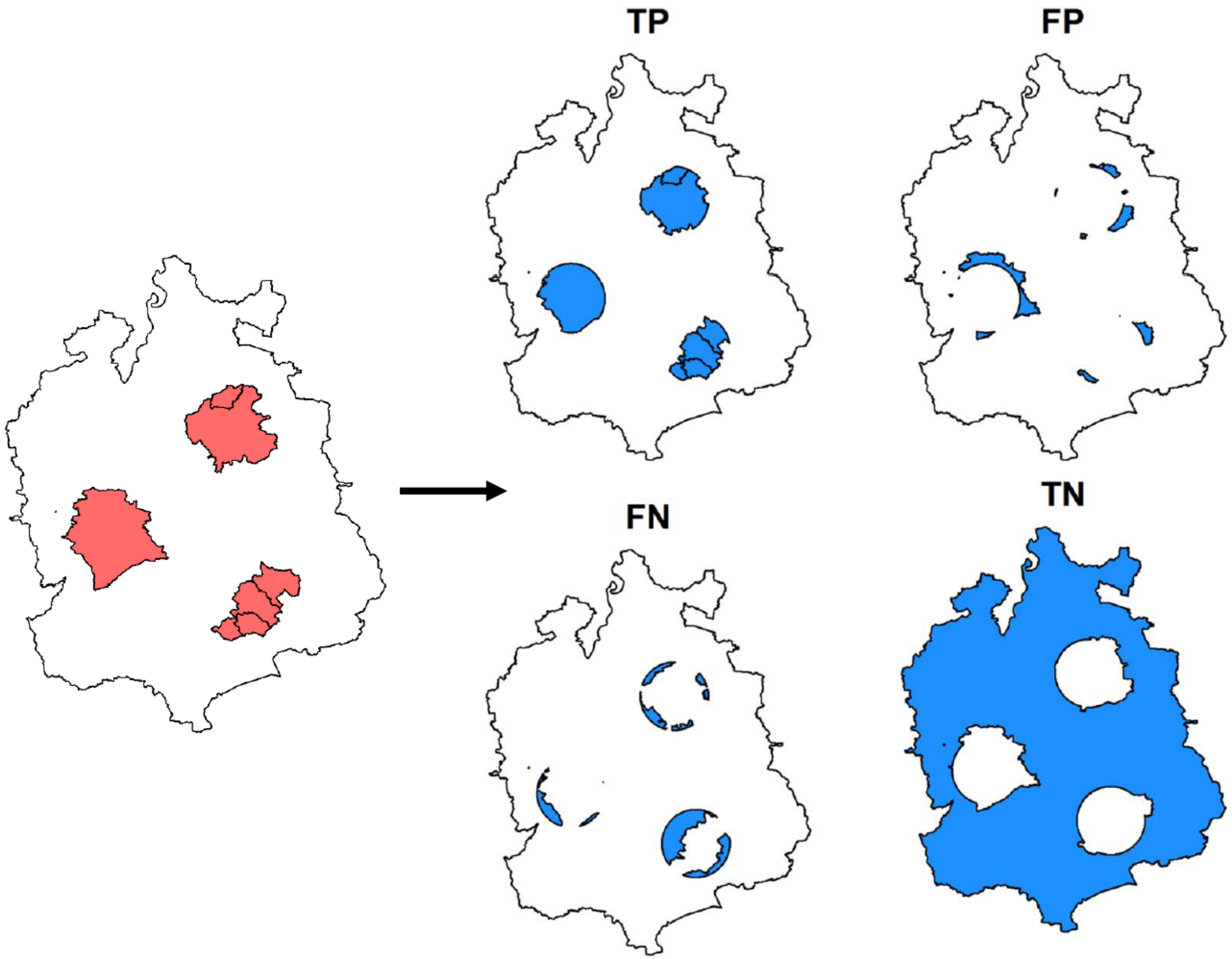
> Root mean integrated square error (RMISE):

$$RMISE = \left\{ E\left[\int w(s) \left(\hat{R}(s) - R(s) \right)^2 ds \right] \right\}^{1/2}$$

> ROC curves

– Exceedance probabilities, i.e $\Pr\left[Y(s) > \frac{n}{N} \right] > \alpha,$ for $\alpha = 0, 0.05, \dots, 1$

– area based sensitivity and Specificity

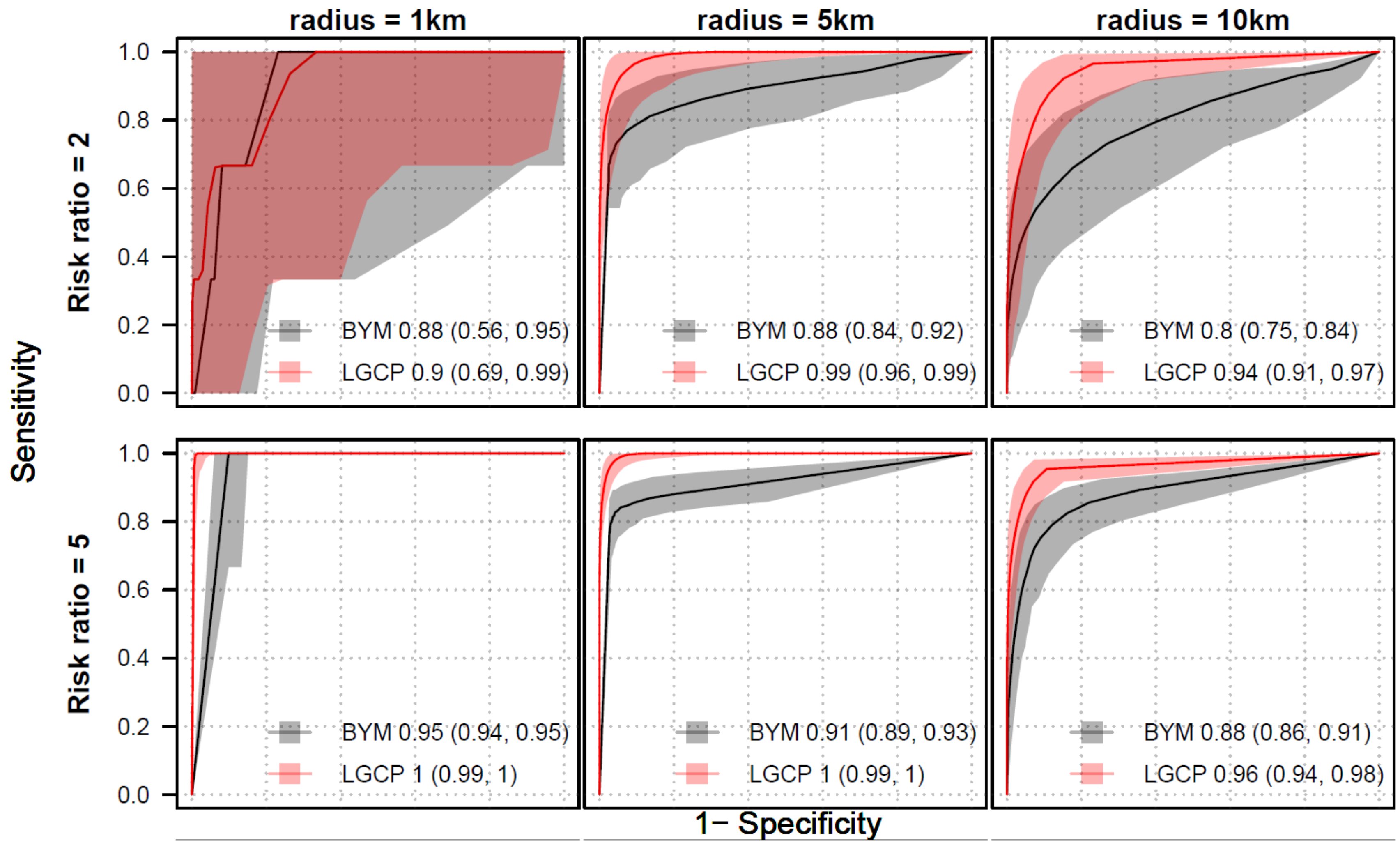


Results: RMISE, 5n

UNIVERSITÄT BERN

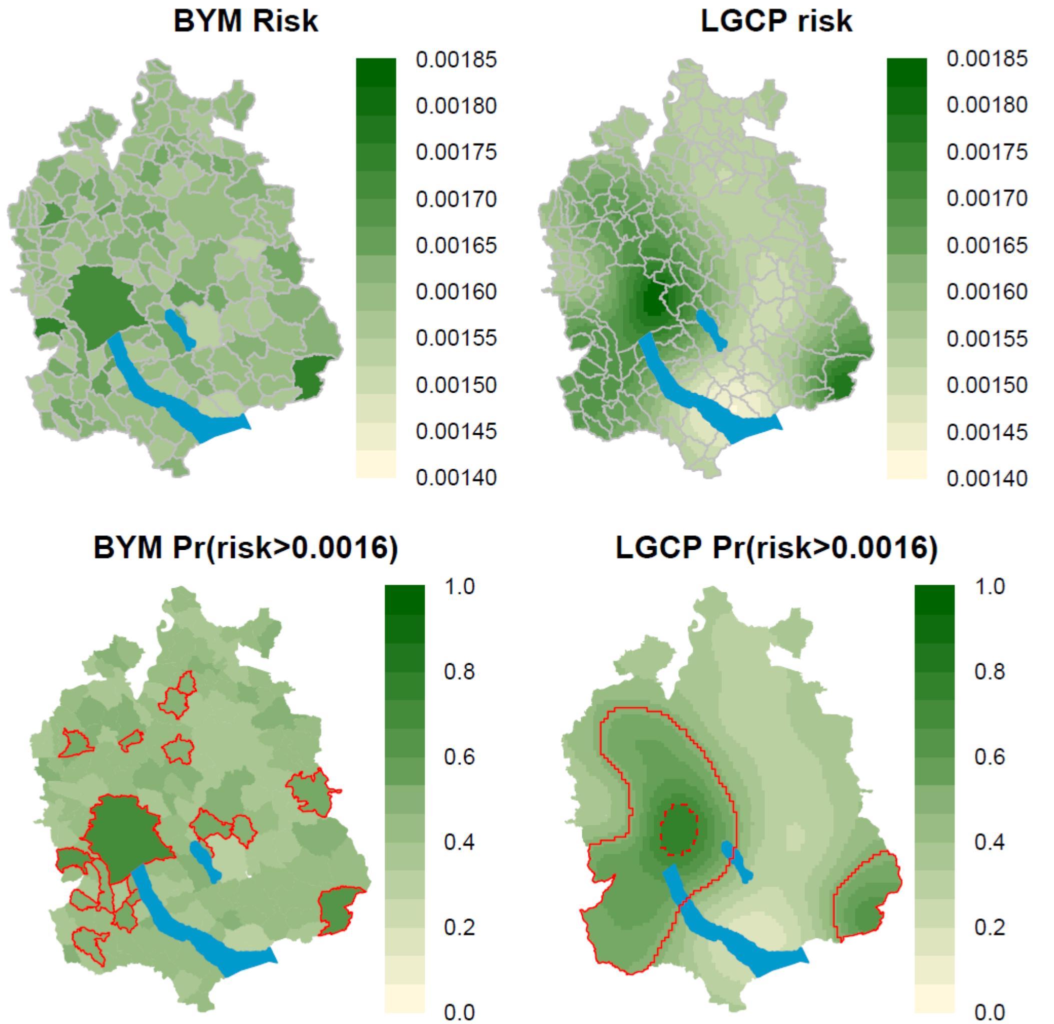
	Step function		Smooth function	
Model	BYM	LGCP	BYM	LGCP
Radius = 1km				
RR=2	**4.47 (3.17, 6.81)**	6.62 (4.24, 9.88)	**4.48 (3.1, 6.88)**	6.51 (4.27, 9.9)
RR=5	**10.4 (8.77, 12.5)**	14.8 (13.1, 17.1)	**10.8 (8.82, 12.5)**	14.8 (13, 16.8)
Radius = 5km				
RR=2	**11.6 (10.6, 13.1)**	12.2 (10.8, 14.7)	**10.4 (9.32, 12)**	11 (9.33, 14.3)
RR=5	22.8 (21.4, 24.5)	**21.5 (19.6, 24.6)**	19.2 (18, 20.6)	**16.8 (14.8, 19.9)**
Radius = 10km				
RR=2	14.9 (14.3, 15.8)	**12.1 (11, 14.4)**	12.3 (11.5, 13.4)	**10.1 (8.57, 12.7)**
RR=5	28.4 (27.3, 29.8)	**22.3 (20.8, 24.6)**	21.8 (21, 22.8)	**13.9 (12.7, 17)**

Results: ROC-curves, Step-function, 5n



Example: Childhood leukaemia in Zurich

- $\Pr\left(Y(s) > \frac{n}{N}\right) > 0.50$ (red solid line)
- $\Pr\left(Y(s) > \frac{n}{N}\right) > 0.80$ (red dotted line)
- 95% CI 1.11 (0.89, 1.38)



Discussion

UNIVERSITÄT BERN

- Overall LGCPs preform better compared to BYM models in almost all scenarios considered
- Our results are consistent with the literature
- We identified an area of higher leukaemia risk in the canton of Zurich
- Possible explanations: Failure to correct for population density or environmental risk factors such as air pollution

Our study suggests that LGCPs are preferable over the widely used BYM models.

Thank you for your attention!

Funded by:

- Swiss cancer research (4012–08-2016)
- Swiss national science foundation (PZ00P3_147987)

Garyfallos.konstantinoudis@ispm.unibe.ch

Konstantinoudis G, Schuhmacher D, Rue H, Spycher B. Continuous versus discrete models for disease mapping. *ArXiv preprint arXiv:180804765v1* 2018.

KREBSFORSCHUNG SCHWEIZ
RECHERCHE SUISSE CONTRE LE CANCER
RICERCA SVIZZERA CONTRO IL CANCRO

FNSNF
FONDS NATIONAL SUISSE
SCHWEIZERISCHER NATIONALFONDS
FONDO NAZIONALE SVIZZERO
SWISS NATIONAL SCIENCE FOUNDATION