technische universität dortmund

RUHR UNIVERSITÄT BOCHUM RUB

# Bayesian Bivariate Distributional Copula Regression of Birth Weight and Gestational Age

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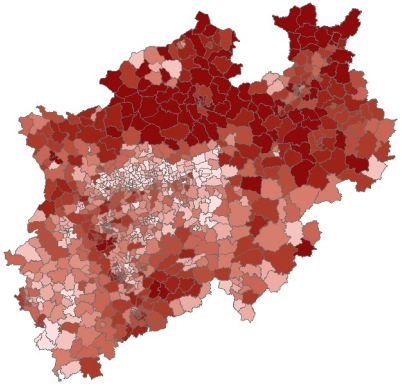
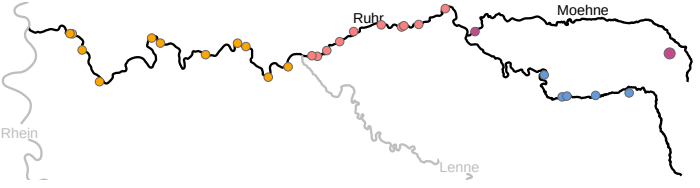
## Project “PerSpat”



mean birth weights in NRW in 2010 by postal code

- environmental epidemiological study on general population
- associations of Perfluorooctanoic Acid (PFOA) with perinatal parameter, esp. birth weight**?**
- data on PFOA in drinking water used for local predictions and individual risk assessment
- state-wide perinatal registry data for North Rhine-Westphalia (NRW), Germany




contaminated river Ruhr

## Today: Birth Data Analysis

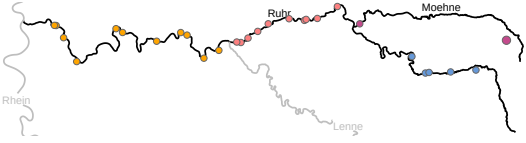
- consider bivariate response (birth weight and gestational age – cf., e.g., Gage, 2003; Ananth and Platt, 2004; Schwartz et al., 2010)
- modelled using copulas in distributional regression (Klein and Kneib, 2016)
- model fit of marginal and copula families
- covariate selection
- comparison to usual univariate regression for birth weight (cf., e.g., Gardosi et al., 1995; Salomon et al., 2007)
- introduction of PFOA exposure risk to analysis

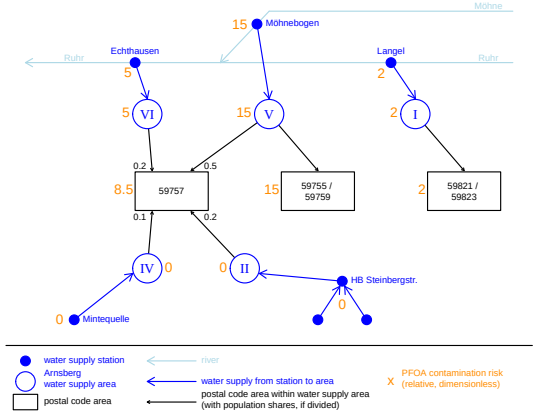
## Data Source and Overview

- collected by hospitals
- combined and processed at state medical association for quality assurance in obstetrical healthcare
- from 2003 until 2014
- about 1.7 million records
- more than 200 biometric, medical and social variables on mother and child, pregnancy, birth and treatment
- restricted to singletons born alive within NRW, and anonymised

## Data Subset

- PFOA contamination in drinking water of Arnsberg, NRW, about 2004
- restriction to data from this town
- 4451 complete records
  (of 6442 with missings, mainly of social variables and smoking)

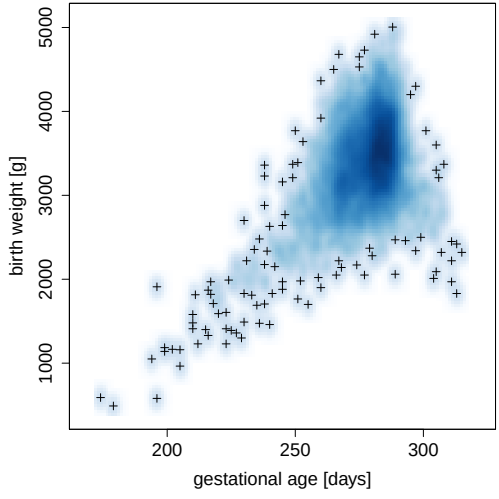



Arnsberg contamination risk by postal code in 2006

## Response Variables

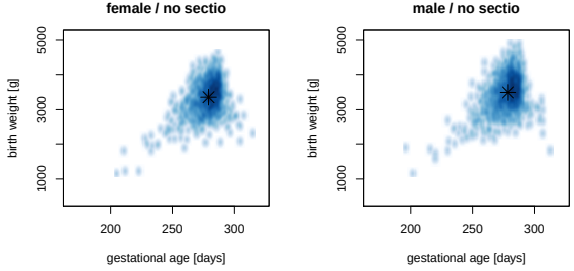
- birth weight ($y_1$) measured in g, of primary interest
- gestational age ($y_2$) in days, usually as most important influence (e.g., Gardosi et al., 1995)



## Covariates of Interest

- the child's sex,
- the number of previous pregnancies of the mother,
- whether the child has been delivered by Cesarean section,
- whether the birth has been induced,
- the mother's age in years,
- the mother's height in **cm**,
- the mother's body mass index measured in $\mathbf{kg/m^2}$ at the beginning of pregnancy,
- the gain of weight of the mother during pregnancy measured in **kg**,
- the number of cigarettes the mother reports to smoke per day,
- whether the mother is single and
- whether the mother is employed.

## Conditional on Covariates




Data Situation

## Distributional Regression

- joint response density $f$ with copula density $c_\rho$:

$$f(y_1, y_2) = c_\rho(F_1(y_1), F_2(y_2)) \cdot f_1(y_1) \cdot f_2(y_2)$$

- marginal parameters (location, scale, shape, ...) according to distribution families
- copula parameter $\rho$
- GLM with linear predictors

$$\eta^{(\theta)} = \beta_0^{(\theta)} + \beta_1^{(\theta)} x_1 + \ldots + \beta_m^{(\theta)} x_m$$

  and response functions $g_\theta(\eta^{(\theta)}) = \theta$, individually for all parameters $\theta$
- several combinations of copula and marginal families implemented in `BayesX` (Belitz et al., 2015)
- MCMC estimation with flat normal priors

## Copula families

Gauss:

$$c_\rho(u,v) = \frac{1}{\sqrt{1-\rho^2}} \exp\left(-\frac{1}{2}\frac{\rho}{1-\rho^2}\left(\rho(\Phi^{-1}(u))^2 - 2\Phi^{-1}(u)\Phi^{-1}(v) + \rho(\Phi^{-1}(v))^2\right)\right),$$

Clayton:

$$c_\rho(u,v) = (1+\rho)(uv)^{-1-\rho}\left(u^{-\rho} + v^{-\rho} - 1\right)^{-2-\frac{1}{\rho}},$$

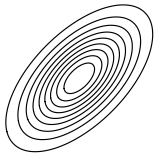
Gumbel:

$$c_\rho(u,v) = \frac{1}{uv}(-\ln u)^{\rho-1}(-\ln v)^{\rho-1}\exp\left(-h^{\frac{1}{\rho}}\right)\left(h^{\frac{2}{\rho}-2} - (1-\rho)h^{\frac{1}{\rho}-2}\right),$$

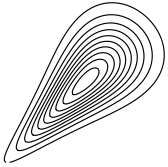
where

$$h = (-\ln u)^\rho + (-\ln v)^\rho$$

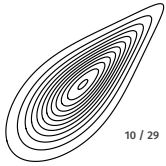
Gauss with $\rho = 0.6$



Clayton with $\rho = 1.5$



Gumbel with $\rho = 2$

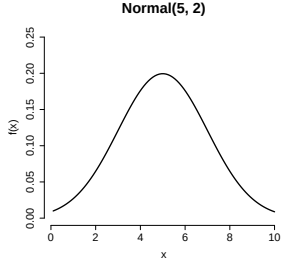


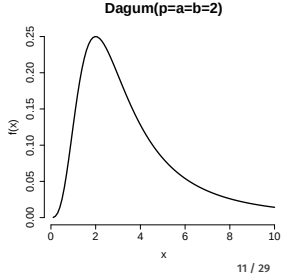
## Marginal Families

- Normal distribution $N(\mu, \sigma^2)$
- Dagum distribution:

$$f_{p,a,b}(y) = \frac{ap}{y} \cdot \frac{\left(\frac{y}{b}\right)^{ap}}{\left(\left(\frac{y}{b}\right)^{a} + 1\right)^{p+1}}$$

- independently chosen for both response variables



## Univariate Polynomial Model

- standard approach (cf., e.g., Gardosi et al., 1995; Salomon et al., 2007)
- application for comparison to bivariate model regarding performance of birth weight prediction

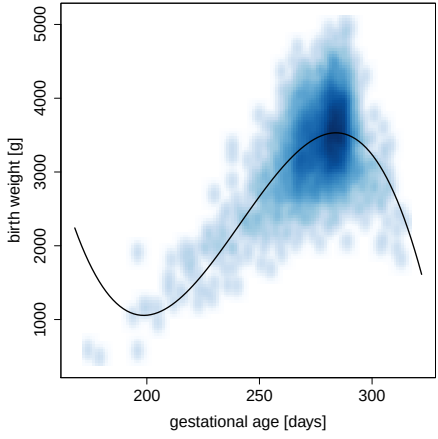
- standard polynomial regression

$$y_1 = \beta_0 + p_\lambda(y_2) + \beta_1 x_1 + \ldots + \beta_m x_m + \epsilon$$

- 'full' polynomial

$$p_\lambda(y_2) = \lambda_1 y_2 + \lambda_2 y_2^2 + \lambda_3 y_2^3$$

has fitted best in preliminary study




(without further covariates)

## Work Flow

1. data preparation
   - import, cleansing, NA-omitting
   - response standardisation
2. choice of marginal families
   - Normal and Dagum models for each univariate response
   - select covariates with sign. influence ($0 \notin CI_{95\%}(\beta)$)
   - compare families by quantile plots and log-scores
3. choice of copula family
   - Gauss, (rotated) Clayton and (rotated) Gumbel copula, combined with optimal marginals
   - select covariates with influence on copula (dependence) parameter
   - compare families by DIC and WAIC
4. evaluation of final model
   - estimated regression coefficients
   - compare to standard polynomial regression approach
   - add PFOA exposure risk, and time

## Data Preparation

- response data transformations for numerical reasons:
- data-independent pre-standardisation for Normal distribution:

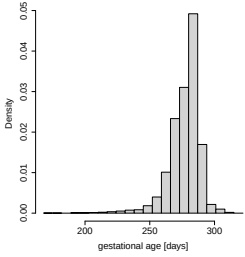
$$\tilde{y}_1 = \frac{y_1 - 3500}{500}, \qquad \tilde{y}_2 = \frac{y_2 - 280}{14}$$

- pre-normalisation for Dagum distribution:

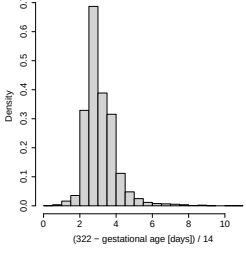
$$\tilde{y}_1 = \frac{y_1}{500}$$

with additional shift for gestational age:

$$\tilde{y}_2 = \frac{322 - y_2}{14}$$

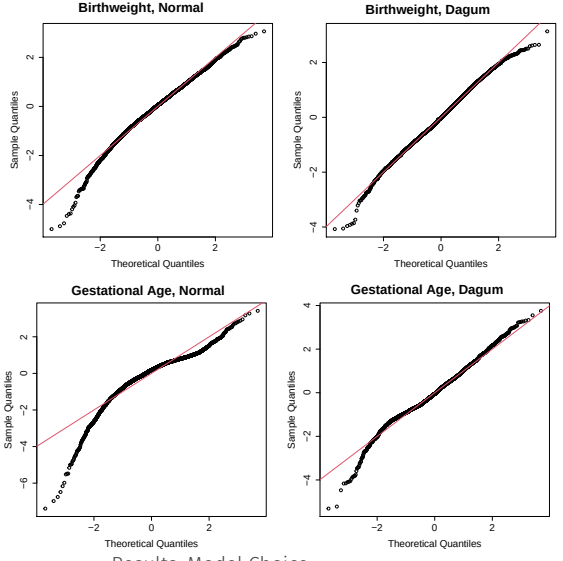



shifted to



## Marginals

quantile plots of residuals ($\Phi^{-1}(F(y;\hat{\beta}))$ with posterior means of the $\beta$'s):



## Marginals

### log-scores

- sample $y$ from a sample of the respective $\beta$'s posteriors and
- compare to observations by log-scores obtained with `scoringRules::logs_sample`
- calculate mean scores:

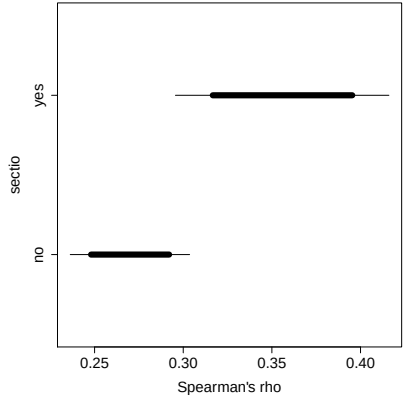
| | birth weight | gest. age |
|---|---|---|
| Normal | 7.58 | 3.97 |
| Dagum | 7.56 | 3.73 |

### family selection

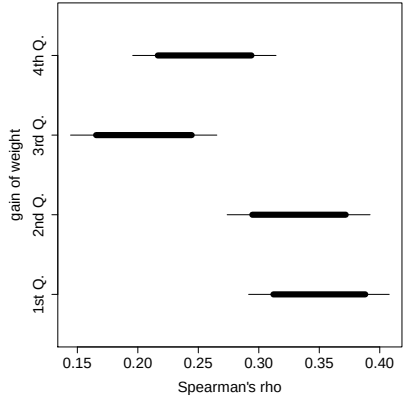
- **Dagum model for gestational age** (better score, convincing quantile plot)
- in doubt, we use **Normal model for birth weight** due to
  - interpretability (influences on mean birth weight of primary interest)
  - comparability to other approaches
  - ease of computation

## Exploration: Conditional Correlation

rank correlation of birth weight and gestational age (80% and 95% confidence intervals) from data subsets according to covariate values:




by sectio




by quartiles of maternal gain of weight

## Copula families

### information criteria

| | DIC | WAIC |
|---|---|---|
| Gauss | Inf | Inf |
| Gumbel | Inf | Inf |
| – 90° | Inf | Inf |
| **Clayton** | **20 981** | **21 245** |
| – 90° | 21 293 | 21 302 |

### selection

- possible **90°** rotation of Gumbel and Clayton copula, to cover all possible directions of tail dependence
- technical MCMC problems when using to many covariates in $\eta^{(\rho)}$
- therefore pre-selection based on Gauss copula result and conditional correlation estimation

- (non-rotated) Clayton copula fits best
- in accordance with lower tail visible in data**?**
- but with low estimates of $\rho$, not far from independence
- copula parameter not influenced by most of the covariates

## Significant Covariate Influences in Final Model

### on birth weight's mean

- − sex (female)
- + previous pregnancies
- − sectio
- + induction
- + maternal height
- + maternal BMI
- + maternal gain of weight
- − maternal smoking

### on birth weight's scale

- − sex
- + sectio
- + maternal BMI
- + maternal smoking

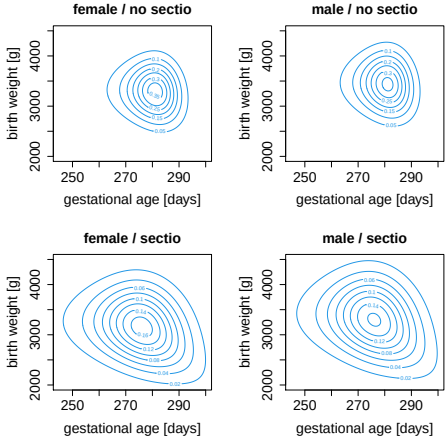
### on Dagum parameters for gestational age

- ○ previous pregnancies
- ○ sectio
- ○ induction
- ○ maternal gain of weight
- ○ maternal smoking
- ○ mother is employed

### on copula parameter (dependence)

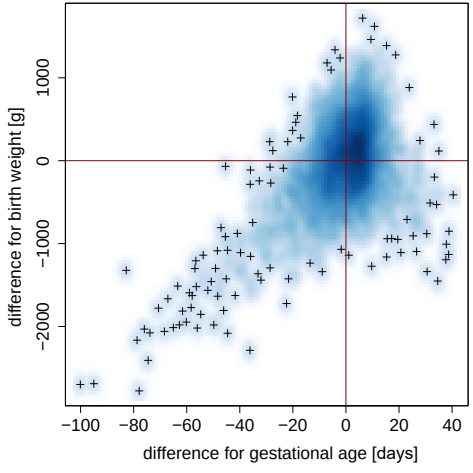
- + sectio

## Predictions



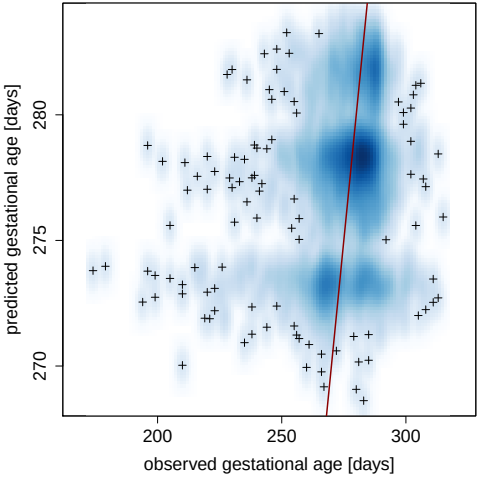

density of $f(y_1, y_2)$ from copula model with posterior mean parameters for certain covariate values (others: maternal height: 170 **cm**, maternal BMI: 20 $\mathbf{kg/m^2}$, maternal gain of weight: 10 **kg**, all others set to 'no'/0)

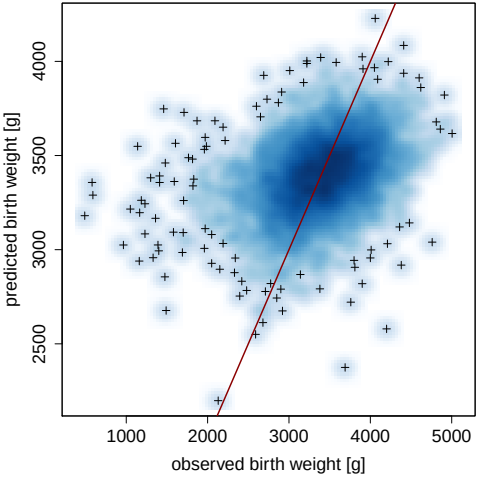
## ‘Residuals’ of Copula Model (Two-dimensional)



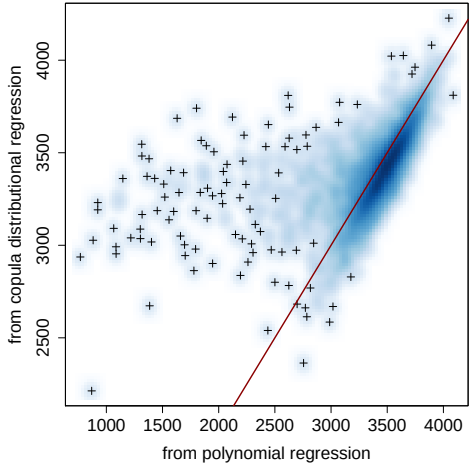

observed – predicted values

## ‘Residuals’ of Copula Model (Dimension-wise)



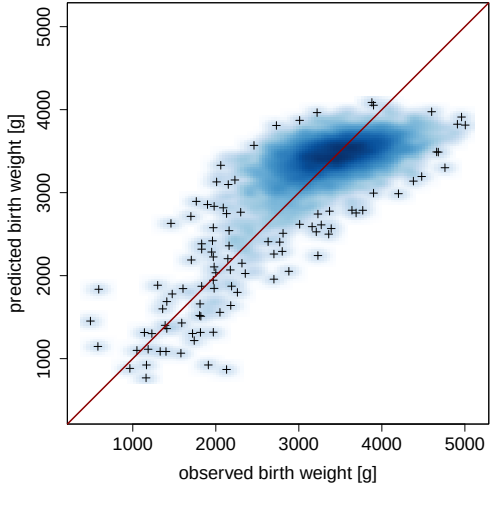
## Comparison to Univariate Polynomial Regression




predicted birth weight

Results: Evaluation

## Univariate Polynomial Regression

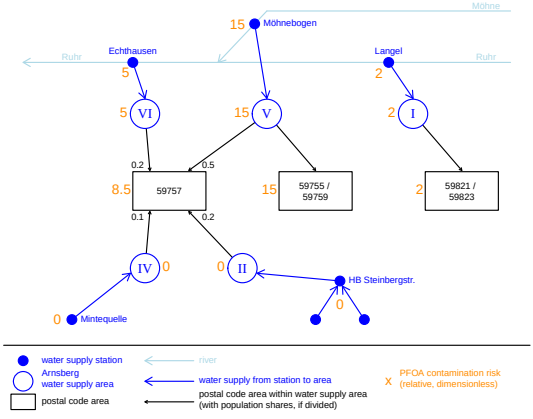


## Regression Results for Mean Birth Weight

Posterior mean (and sd.) of regression coefficients for parameter $\mu$ of (standardised) birth weight:

| Covariate | Polynomial | | $\mu$ from copula model | |
|---|---|---|---|---|
| sex (female) | -0.2908 | (± 0.0237) | -0.2896 | (± 0.0273) |
| previous pregnancies | 0.0583 | (± 0.0085) | 0.0484 | (± 0.0065) |
| sectio | not signif. | | -0.2907 | (± 0.0535) |
| induction | not signif. | | 0.0870 | (± 0.0280) |
| maternal height | 0.0279 | (± 0.0018) | 0.0290 | (± 0.0015) |
| maternal BMI | 0.0302 | (± 0.0023) | 0.0368 | (± 0.0029) |
| maternal gain of weight | 0.0144 | (± 0.0022) | 0.0249 | (± 0.0024) |
| maternal smoking | -0.0308 | (± 0.0029) | -0.0416 | (± 0.0031) |
| mother is single | -0.1271 | (± 0.0480) | not signif. | |
| gestational age | -2.6145 | (± 0.1717) | | |
| squared gestational age | 0.0112 | (± 0.0007) | | |
| cubic gestational age | -0.0000 | (± 0.0000) | | |

# Introduction of PFOA exposure risk




Arnsberg contamination risk by postal code in 2006

- estimated PFOA concentrations in drinking water (Rathjens et al., 2020)
- by postal code and time
- add to polynomial regression and to birth weight mean regression in copula model
- also time as linear covariate

⇒

- no significant effect of PFOA risk in either model
- significant effect of time in copula model (birth weight becoming less)

## Discussion

- birth weight sufficiently modelled with normal distribution
- gestational age better with Dagum distribution
- distributional regression useful to allow for influences on scale and dependence
- with regard to birth weight, the result of the more general copula model is close to the more specified univariate polynomial model
- rather weak dependence between response variables in copula model
- much variance remains unexplained
- lower tail in data not reflected in copula predictions (main data part in center predominating)

## Perspectives

- cross-validated prediction results
- temporal modelling:
- more complex GAM, e.g., with splines
- individual PFOA data from Arnsberg cohort study
- spatial modelling (with larger region)

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