Linking US registry data with geomarker data: longitudinal associations between environmental factors and lung function decline

European Cystic Fibrosis Conference

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Introduction: Motivation

A lot of information is available

➔ Electronic medical records

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Different types of information

- ➔ Baseline characteristics: Sex, F508del, SESlow, Enzymes
- ➔ Biomarkers: FEV_1 % pred
- ➔ Nutritional status: BMI percentile
- ➔ Geomarkers (environmental/community factors): Deprivation index

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Introduction: Research question

How can we appropriately connect registry data with geomarker data

Introduction: Descriptive statistics

Deprivation index (*https://geomarker.io/dep_index/*)

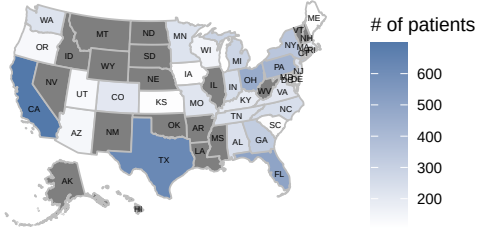
➔ Socioeconomic variables from the American Community Survey (ACS): capture "community deprivation"

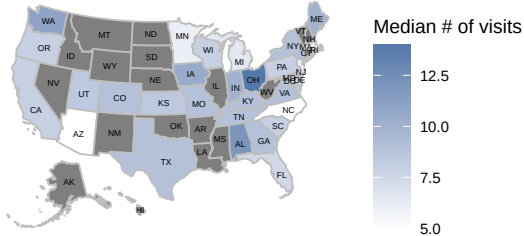
- ◇ Principal components analysis of six different 2015 ACS measures
- ◇ "Deprivation Index": the first component explains over 60% of the total variance
- ◇ Rescaling and normalizing forces the index to range from 0 to 1, with a higher index being more deprived

Cole Brokamp, Andrew F. Beck, Neera K. Goyal, Patrick Ryan, James M. Greenberg, Eric S. Hall. Material Community Deprivation and Hospital Utilization During the First Year of Life: An Urban Population-Based Cohort Study. Annals of Epidemiology. 30. 37-43. 2019

Introduction: Descriptive statistics

Baseline information





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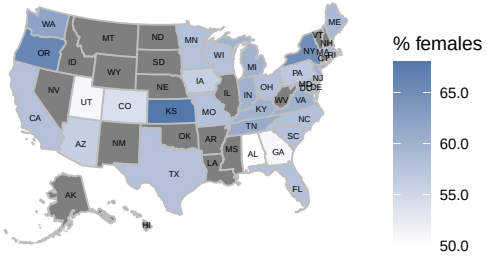

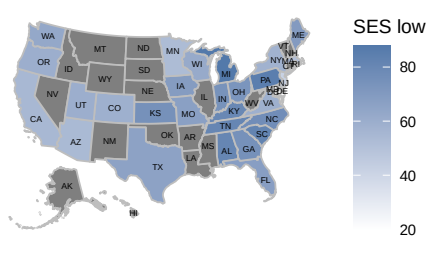

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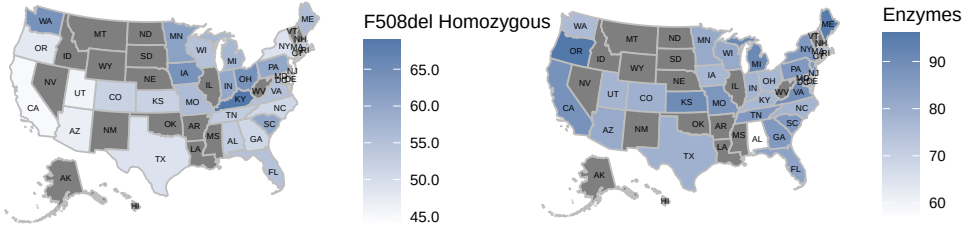
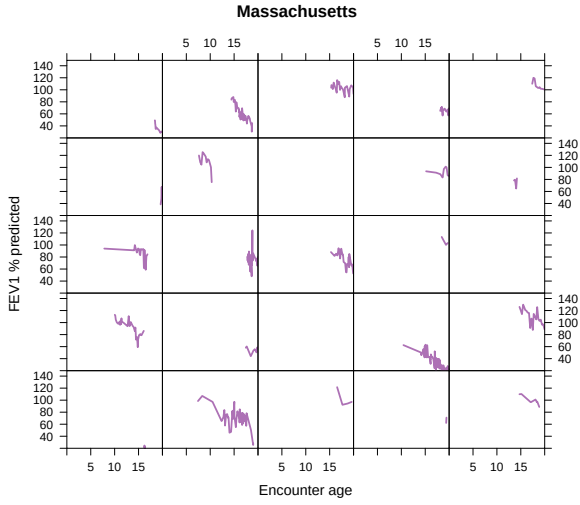


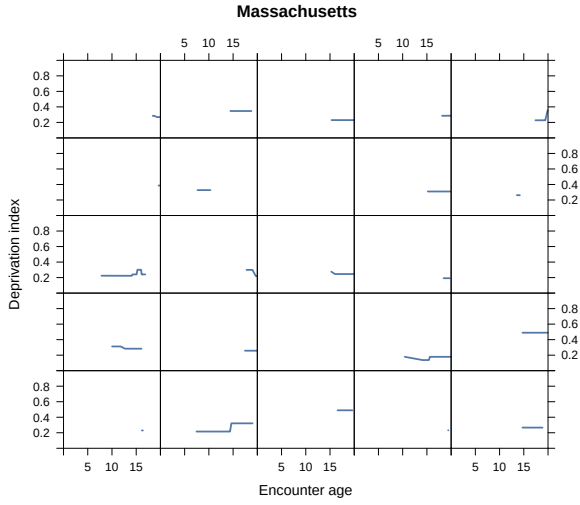
Introduction: Descriptive statistics

Biomarker



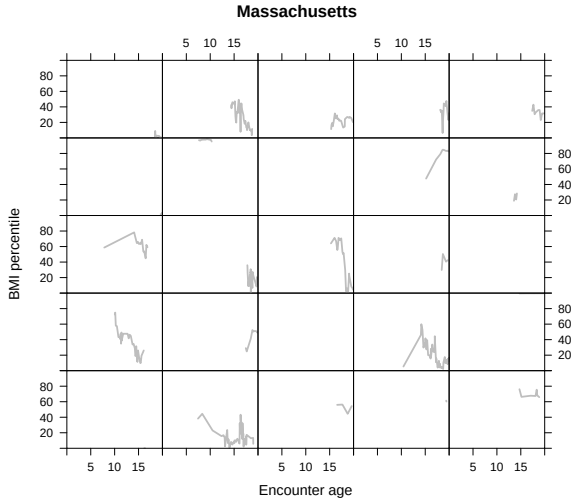
Introduction: Descriptive statistics

Geomarker



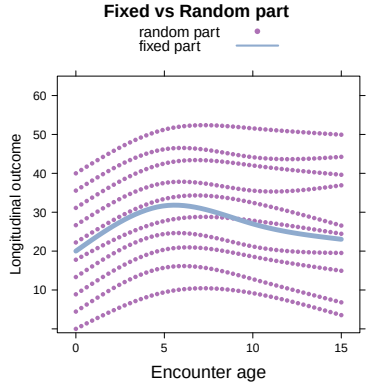
Introduction: Descriptive statistics

Nutritional status



Methods: Univariate Mixed Model

$$y_i(t) = \underbrace{x_i^\top(t)\beta_1}_{\text{fixed effects part}} + \underbrace{z_i(t)^\top b_i}_{\text{random effects part}} + \epsilon_i$$



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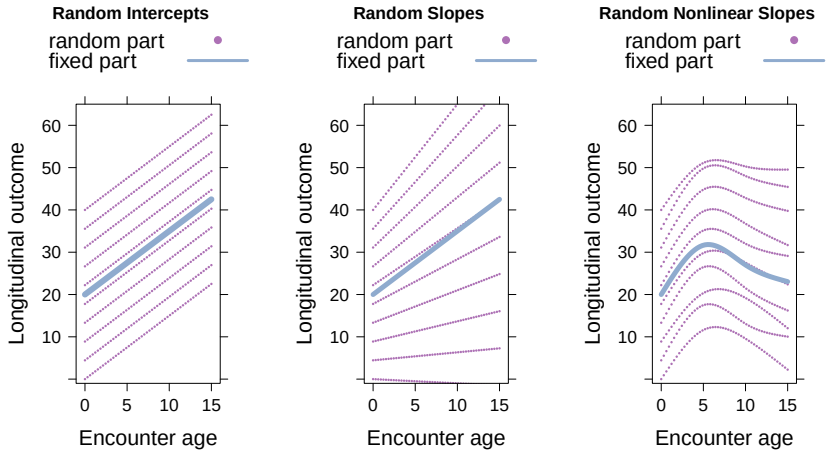

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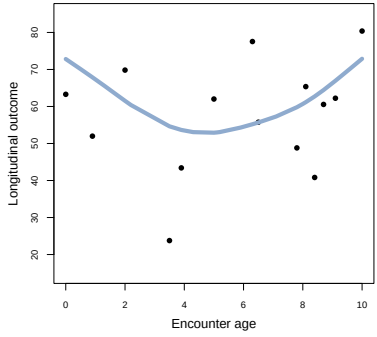
$$= \boldsymbol{m_i(t)} + \epsilon_i$$



Methods: Multivariate Mixed Models

$$\texttt{DepIndex} = \texttt{encounterage}$$

$$\texttt{FEV1\%pred} = \texttt{encounterage} + \texttt{sex} + \texttt{SESlow} +$$
$$\texttt{F508del} + \underbrace{\texttt{BMIpercentile}} + \texttt{Enzymes}$$

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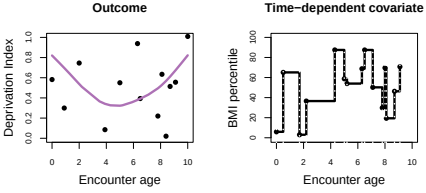

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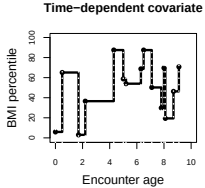
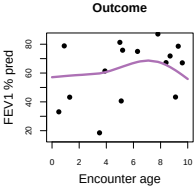




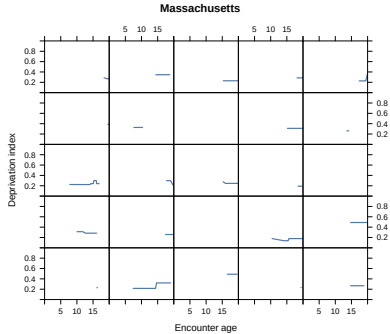
Methods: Multivariate Mixed Models

$$\texttt{DepIndex:} y_{2i}(t) = m_{2i}(t) + \epsilon_{2i}(t) = x_{2i}^{\top}(t)\beta_1 + z_{2i}(t)^{\top} b_{2i} + \epsilon_{2i}(t)$$

$$\texttt{FEV1\%pred:} y_{1i}(t) = x_{1i}^{\top}(t)\beta_1 + z_{1i}(t)^{\top} b_{1i} + \boldsymbol{\alpha}_{S2}\, m_{2i}(t) + \epsilon_{1i}(t)$$

where

- $b_i^{\top} = (b_{1i}^{\top}, b_{2i}^{\top}) \sim N(0, D)$



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$$\texttt{FEV1\%pred:} y_{1i}(t) = x_{1i}^{\top}(t)\beta_1 + z_{1i}(t)^{\top} b_{1i} + \alpha_{S2} \int_0^t m_{2i}(s)ds + \epsilon_{1i}(t)$$

where

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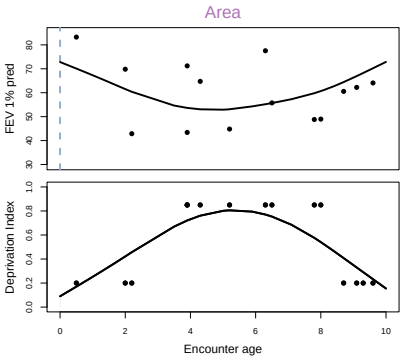
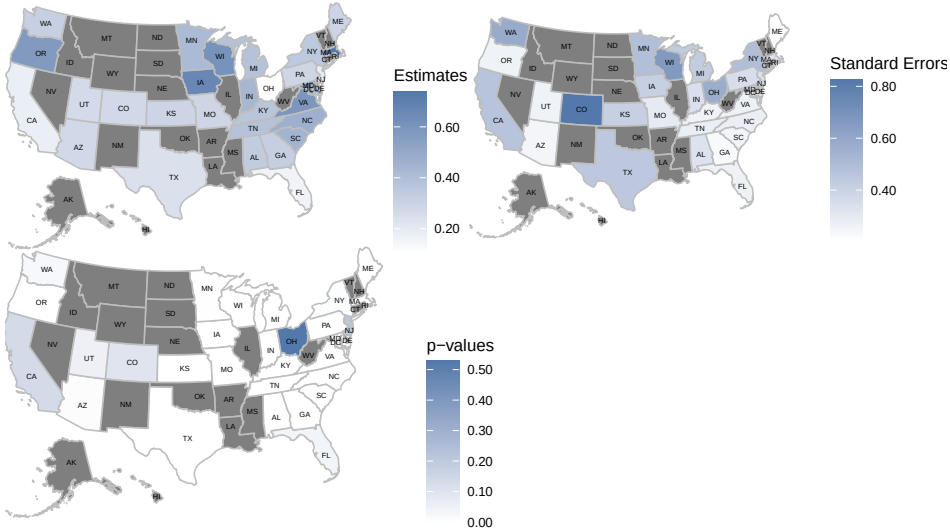


Results: Multivariate Mixed Models

Estimate: for 0.1 unit increase in the area under the curve of the deprivation index



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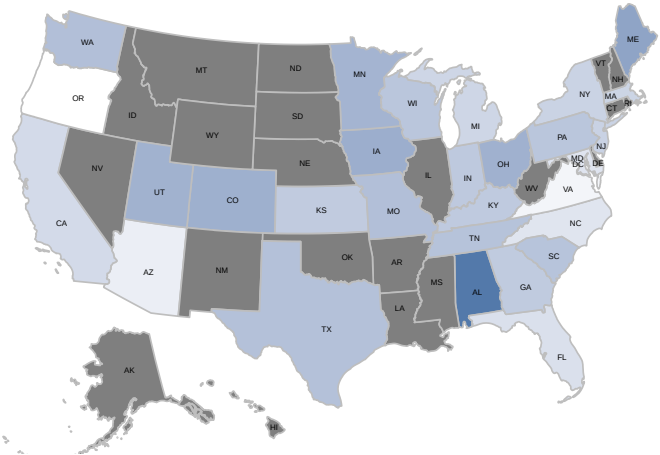
Introduction: Descriptive statistics

Baseline information



Methods: Multivariate Mixed Models

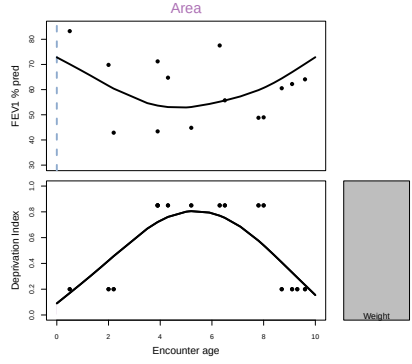
DepIndex: $y_{2i}(t) = m_{2i}(t) + \epsilon_{2i}(t) = x_{2i}^{\top}(t)\beta_1 + z_{2i}(t)^{\top} b_{2i} + \epsilon_{2i}(t)$

FEV1%pred: $y_{1i}(t) = x_{1i}^{\top}(t)\beta_1 + z_{1i}(t)^{\top} b_{1i} + \boldsymbol{\alpha}_{S2} \frac{1}{t} \int_0^t m_{2i}(s)ds + \epsilon_{1i}(t)$

Weight

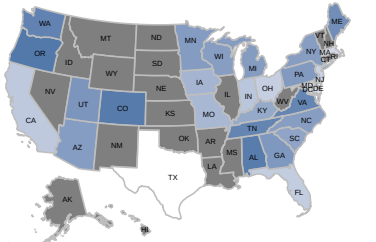
where

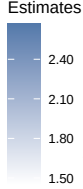
- $b_i^{\top} = (b_{1i}^{\top}, b_{2i}^{\top}) \sim N(0, D)$

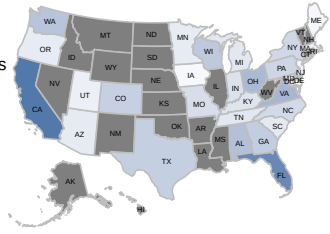


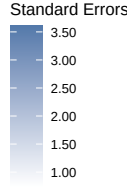
Results: Multivariate Mixed Models

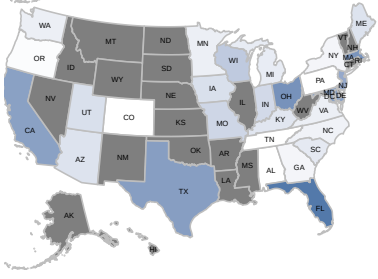
Estimate: for 0.1 unit increase in the normalized area under the curve of deprivation index

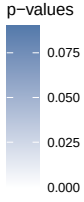












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$$\texttt{FEV1\%pred} = \texttt{encounterage}$$

$$\texttt{DepIndex} = \texttt{encounterage} + \texttt{FEV1\%pred}$$

Methods: Multivariate Mixed Models

$$\texttt{FEV1\%pred:}\; y_{1i}(t) = m_{1i}(t) + \epsilon_{1i} = x_{1i}^{\top}(t)\beta_1 + z_{1i}(t)^{\top} b_{1i} + \epsilon_{1i}(t)$$

$$\texttt{DepIndex:}\; y_{2i}(t) = m_{2i}(t) + \epsilon_{2i} = x_{2i}^{\top}(t)\beta_1 + z_{2i}(t)^{\top} b_{2i} + \boldsymbol{\alpha}_{S1} \frac{d}{dt} m_{1i}(t) + \epsilon_{2i}(t)$$

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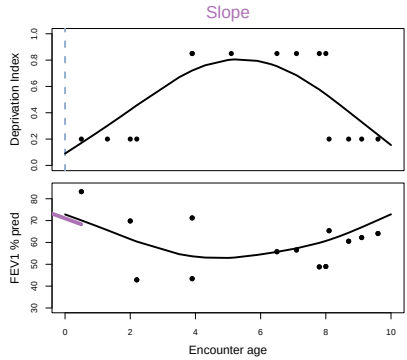

Discussion

- ➔ A lot of data is available
- ➔ Better treatment and monitoring strategies if all information is used
- ➔ Challenge in combining different types of information
- ➔ Investigate other geomarker data

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Thank you for your attention!

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