

Bayesian Modelling of Metabolic Syndrome Risk in AVIS Blood Donors

A longitudinal analysis of routine laboratory data

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- ▶ 100,203 laboratory measurements.
- ▶ 4,300 donors - longitudinal data.
- ▶ 42 variables per visit.

Research question:

Is it feasible to implement a **Metabolic Syndrome screening**, based on AVIS laboratory measurements?
Is this able to identify the predictive biomarkers for high-risk patients and support clinicians in treatment strategies?

Definition of metabolic syndrome

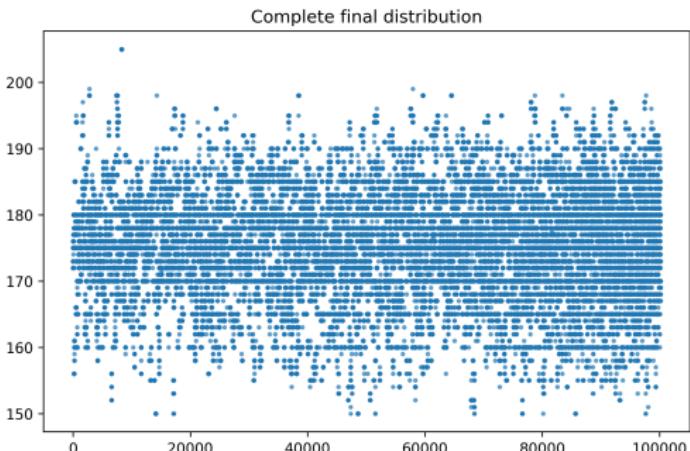
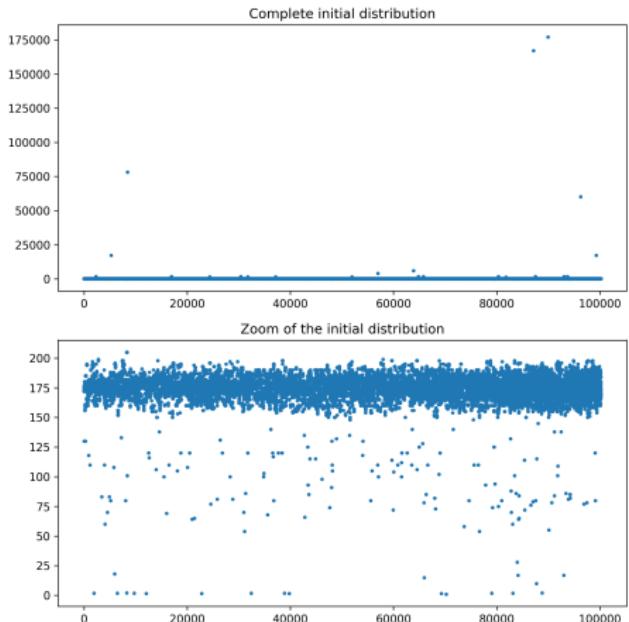
- ▶ Metabolic Syndrome (MetS) is a **cluster of conditions** that increase the risk of type 2 diabetes, myocardial infarction, stroke, and other cardiovascular diseases.
- ▶ Diagnosis requires at least **three** of the five diagnostic components out of range.

Component	Men	Women
Waist circumference (cm)	> 102	> 88
Blood pressure (mmHg)	≥ 130 / ≥ 85	SAME
Fasting Glucose (mg/dL)	≥ 100	SAME
Triglycerides (mg/dL)	≥ 150	SAME
HDL cholesterol (mg/dL)	< 40	< 50

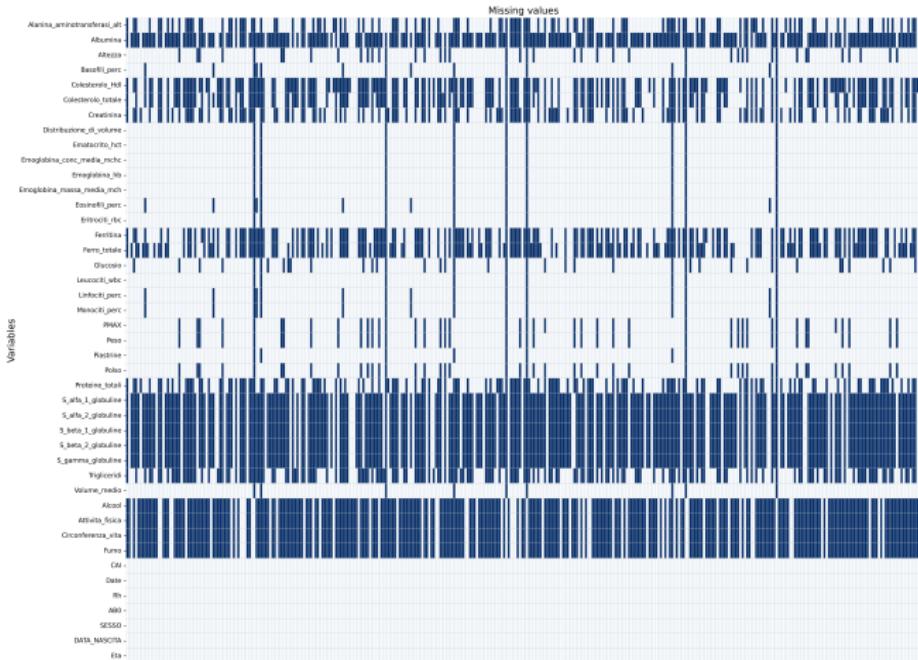
Component	Men	Women
BMI (kg/m^2)	≥ 30	≥ 30
Blood pressure (mmHg)	≥ 130 / ≥ 85	SAME
Fasting Glucose (mg/dL)	≥ 100	SAME
Triglycerides (mg/dL)	≥ 150	SAME
HDL cholesterol (mg/dL)	< 40	< 50

Initial Exploration

Covariate 'Height' [cm]

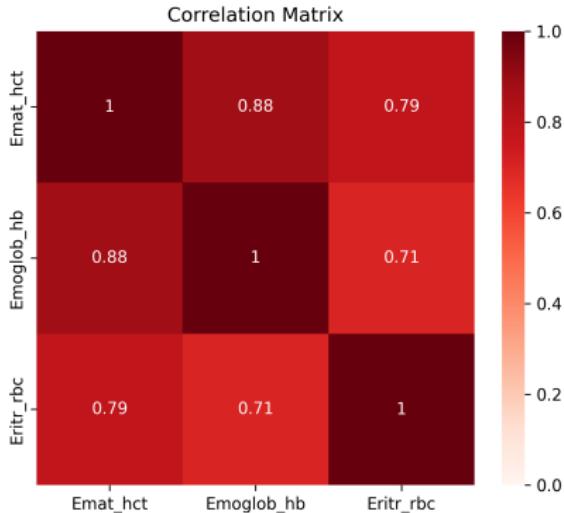
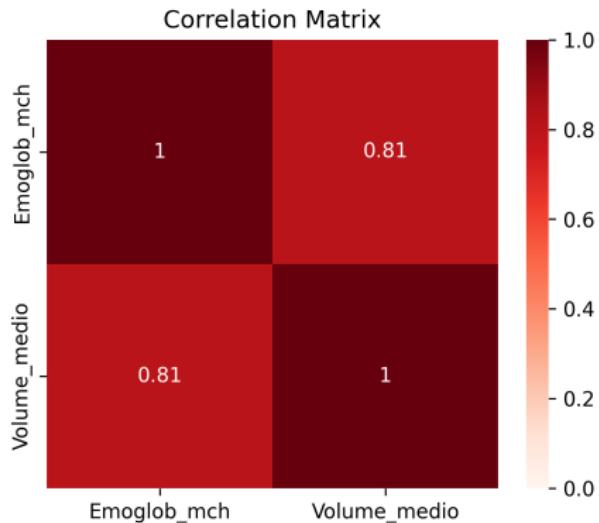


The Missing Data Problem



Solution: **MICE** - Multiple Imputation by Chained Equations (*Van Buuren, et al. 2011*)

Transformations & Variable Selection



- ▶ A reduced dataset of about $n \approx 1000$ observations was obtained by retaining all donors with more than 25 visits.

The Bayesian Model: Structure

Hierarchical multivariate Bayesian model:

$$\mathbf{y}_{ij} \mid \boldsymbol{\mu}_{ij}, \Sigma \stackrel{\text{ind}}{\sim} \mathcal{N}_K(\boldsymbol{\mu}_{ij}, \Sigma), \quad i = 1, \dots, I, j = 1, \dots, n_i$$

$$\boldsymbol{\mu}_{ij} = \mathbf{x}_{ij} \boldsymbol{\beta} + \boldsymbol{b}_i$$

$$\Sigma \sim \text{Inv-Wishart}(a_\Sigma, b_\Sigma \mathbf{I}_K)$$

K : number of target variables (5)

$a_\Sigma = 10, b_\Sigma = 1$

I : number of donors (34)

n_i : number of visits per donor

The Bayesian Model: Priors

Random effect:

$$\begin{aligned}\mathbf{b}_i &\stackrel{\text{iid}}{\sim} \mathcal{N}_K(\boldsymbol{\mu}_{\mathbf{b}}, \boldsymbol{\Sigma}_{\mathbf{b}}) \quad i = 1, \dots, I \\ \boldsymbol{\mu}_{\mathbf{b}} &\sim \mathcal{N}_K(\mathbf{0}, \mathbf{I}_K) \quad \boldsymbol{\Sigma}_{\mathbf{b}} \sim \text{Inv-Wishart}(a_{\Sigma_b}, b_{\Sigma_b} \mathbf{I}_K)\end{aligned}$$

Fixed effects - Regularized Horseshoe (*Tew, et al. 2022*):

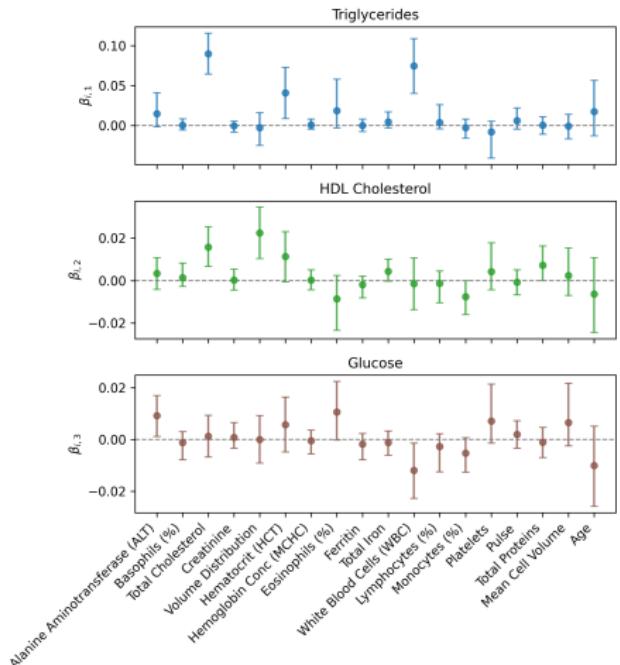
$$\begin{aligned}\tilde{\beta}_{pk} &\stackrel{\text{iid}}{\sim} \mathcal{N}(0, 1), \quad p = 1, \dots, P + 1, \quad k = 1, \dots, K \\ \beta_{pk} &= \tilde{\beta}_{pk} \tau \lambda_p \frac{c}{\sqrt{c^2 + \tau^2 \lambda_p^2}} \\ \lambda_p &\stackrel{\text{iid}}{\sim} \text{HC}(0, 1), \quad \tau \sim \text{HC}(0, \tau_0), \quad c^2 \sim \text{Inv-Gamma}(a_c, b_c)\end{aligned}$$

$$a_{\Sigma_b} = 10, \quad b_{\Sigma_b} = 0.5, \quad \tau_0 = 0.002, \quad a_c = 2, \quad b_c = 8$$

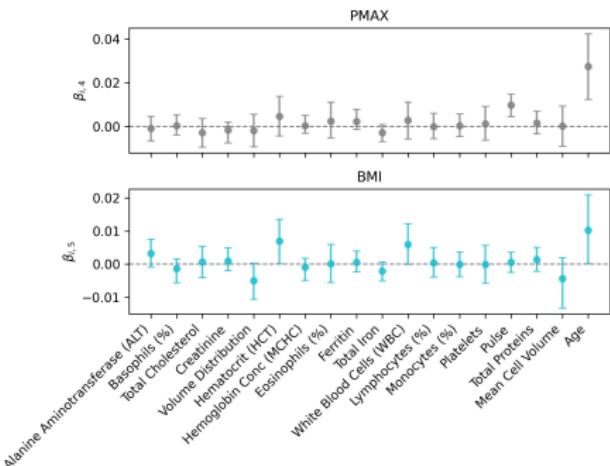
P : number of covariates (23)

K : number of target variables (5)

Results

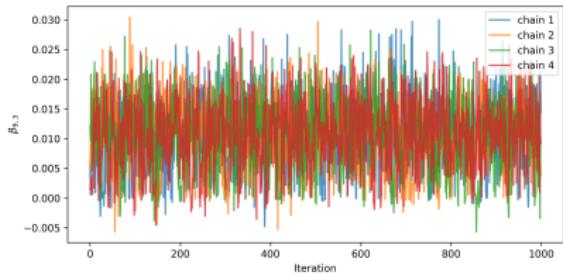
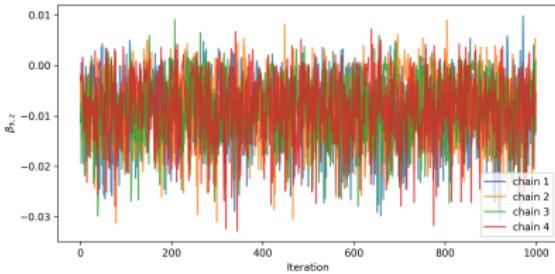
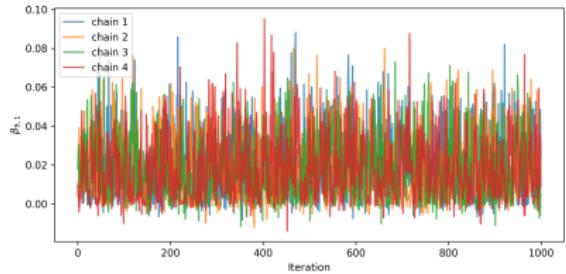


95% Credible Intervals
of fixed effect



Results

Trace plots of fixed effects of *Eosinophils* on *Triglycerides*, *HDL Cholesterol* and *Glucose*



Next Steps

- ▶ Investigate a **new prior for Σ** , e.g. LKJ (*Wang, et al. 2018*).
- ▶ Experiment with **different priors for the random effects**, including Dirichlet process priors.
- ▶ Use the **complete dataset** on the relevant covariates identified.
- ▶ Fine-tune the **model hyperparameters**.
- ▶ Better exploit the **longitudinal structure** of the data.

References

- ▶ Samson, S. L., Garber, A. J. (2014). *Metabolic syndrome. Endocrinology and Metabolism Clinics*, 43(1), 1-23.
- ▶ Van Buuren, S., Groothuis-Oudshoorn, K. (2011). *mice: Multivariate imputation by chained equations in R. Journal of statistical software*, 45, 1-67.
- ▶ Tew, S. Y., Schmidt, D. F., Makalic, E. (2022, September). *Sparse horseshoe estimation via expectation-maximisation. In Joint European Conference on Machine Learning and Knowledge Discovery in Databases (pp. 123-139)*. Cham: Springer Nature Switzerland.
- ▶ Wang, Z., Wu, Y., Chu, H. (2018). *On equivalence of the LKJ distribution and the restricted Wishart distribution*.