Inference of Genetic Effects via Approximate Message Passing

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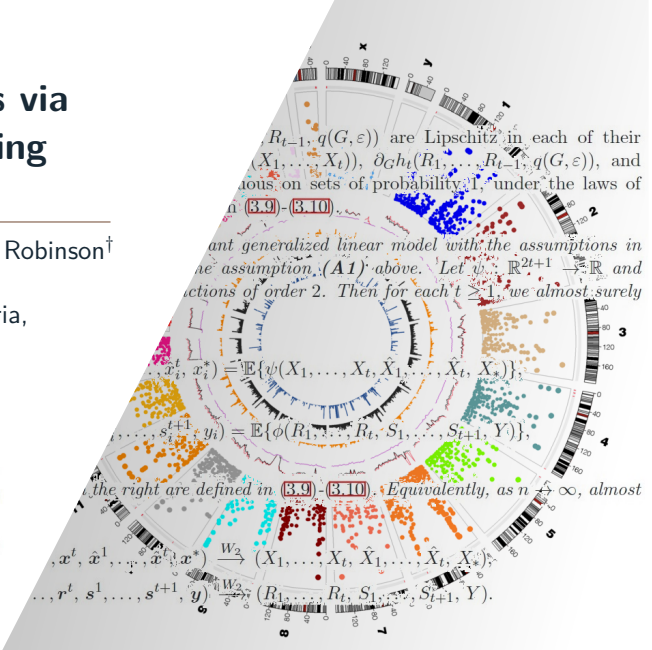
ICASSP 2024 KOREA



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3. Comparison to the state-of-the-art methods (regenie, GMRM)

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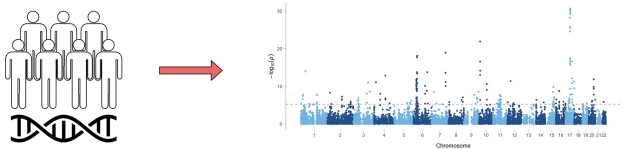
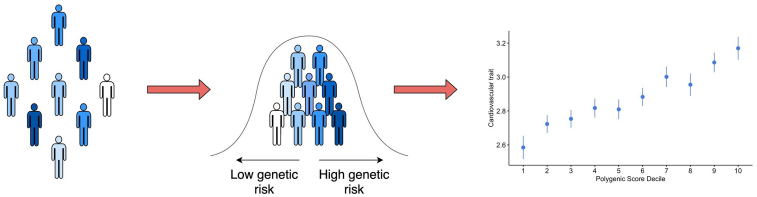
Step 1: Genome-wide association studies in adult populations from the UK Biobank



Step 2: Whole genome polygenic risk scores



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- almost no limit to the amount of measured genetic variants (hundreds of millions; more genetic variants $\implies$ better generalization), but limited sample size

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$$\mathbf{X}_{ij} = \begin{cases} 2, & aa \\ 1, & Aa \\ 0, & AA \end{cases} \qquad \Longrightarrow \qquad \{0,1,2\}^{N\times P} \ni \mathbf{X} = \underbrace{\left.\begin{bmatrix} 1 & 2 & \dots & 0 \\ 0 & 0 & \dots & 1 \\ \vdots & \vdots & \ddots & \vdots \\ 0 & 2 & \dots & 2 \end{bmatrix}\right\} \sim 10^5}_{\sim 10^6}$$

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$$y_i = \langle \mathbf{X}(i,:), \beta \rangle + \epsilon_i \text{ for } i \in [N] = \{1, \dots, N\}$$

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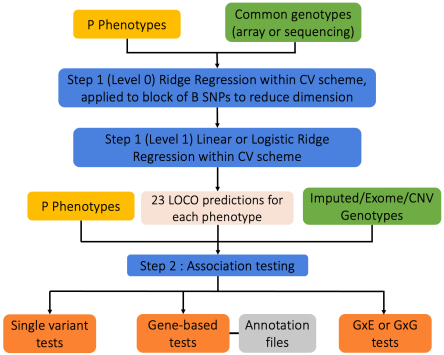
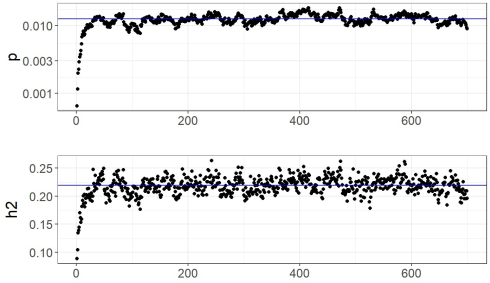
$$\beta_j \sim (1-\lambda) \cdot \delta_0(\cdot) + \lambda \cdot \sum_{i=1}^{L} \pi_i \cdot \mathcal{N}(\cdot, 0, \sigma_i^2), \quad \epsilon_i \sim \mathcal{N}(0, {\gamma_\epsilon}^{-1})$$

Prior Work



[regenie, PLINK]



[LDpred2, SBayesR, SBayesRC, GMRM]

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- achieves Bayes-optimal performance for some models [DM14, DJM13, BKM+19]

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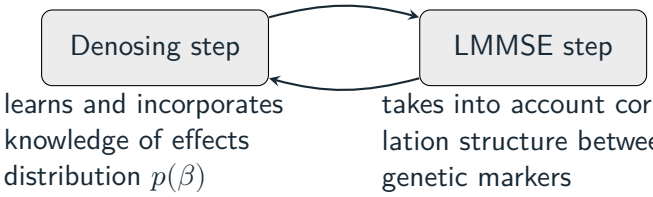

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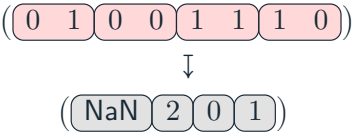
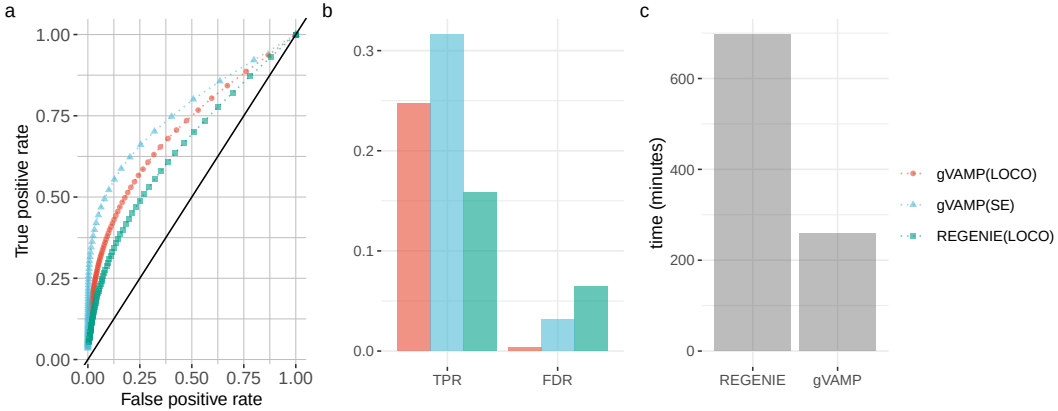
8. data processing by using a lookup table + SIMD:

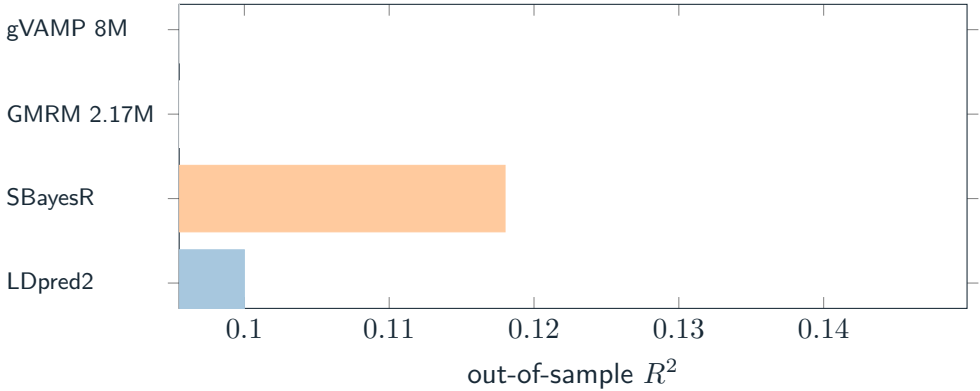


3. Association testing

$$y^{(i)} := y - \mathbf{X}_{\setminus \mathsf{chr}(i)} \hat{\beta}_{\setminus \mathsf{chr}(i)} \sim \mathbf{X}(:, i)$$



Prediction accuracy for BMI (Body Mass Index)



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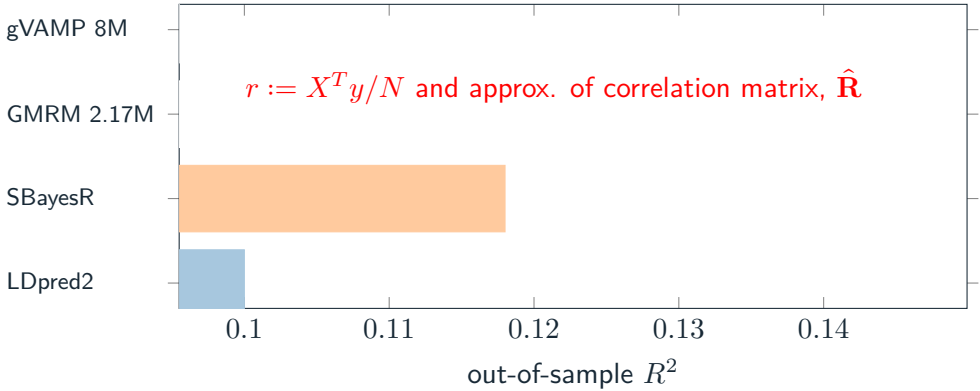

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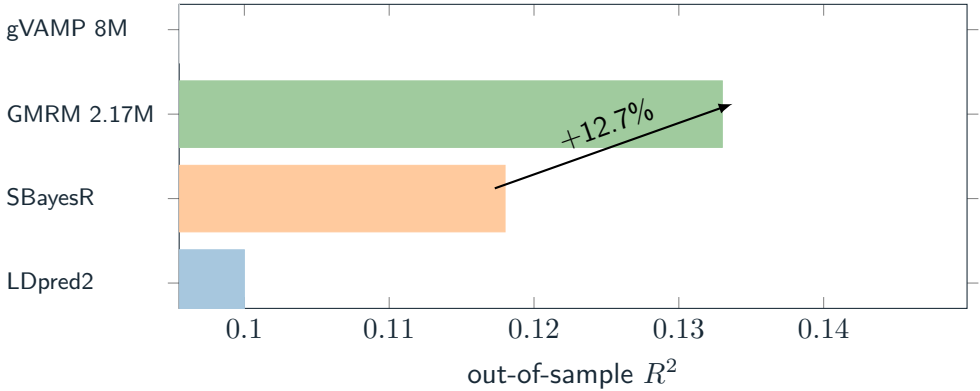

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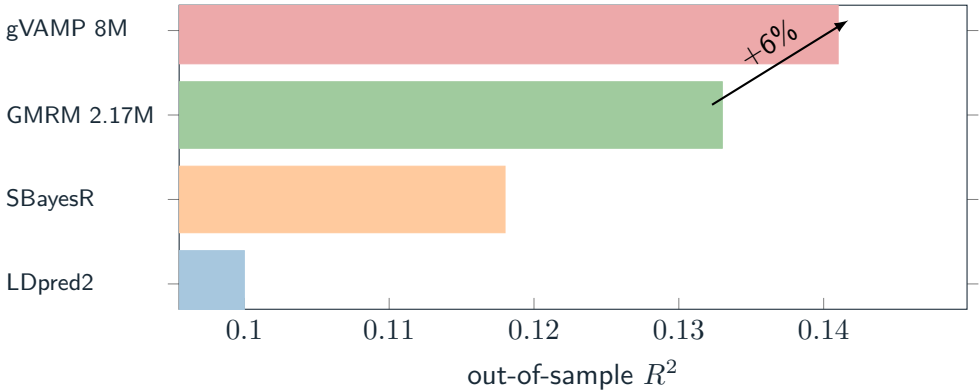
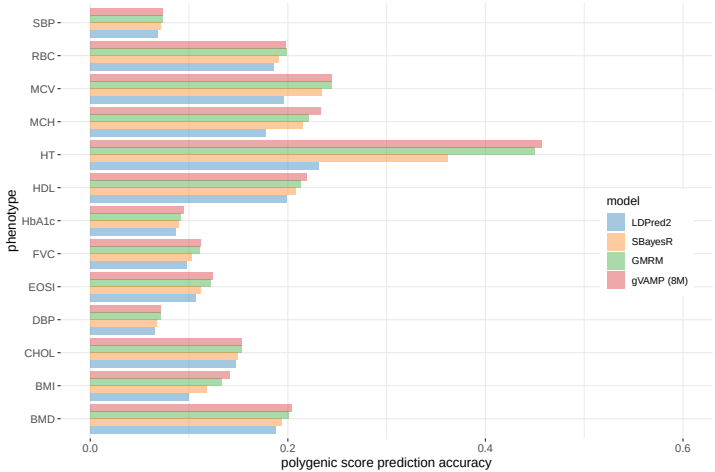


Prediction accuracy

SBP: Systolic blood pressure
RBC: Red blood cell count
MCV: Mean corpuscular volume
MCH: Mean corpuscular haemoglobin
HT: Standing height
HDL: High density lipoprotein
HbA1c: Glycated haemoglobin
FVC: Forced vital capacity
EOSI: Eosinophill count
DBP: Diastolic blood pressure
CHOL: Cholesterol
BMI: Body mass index
BMD: Heel bone mineral density



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   - access only to $r := X^T y/N$ and an approximation of a correlation matrix, called $\hat{\mathbf{R}}$
   - merging information from different databases/cohorts

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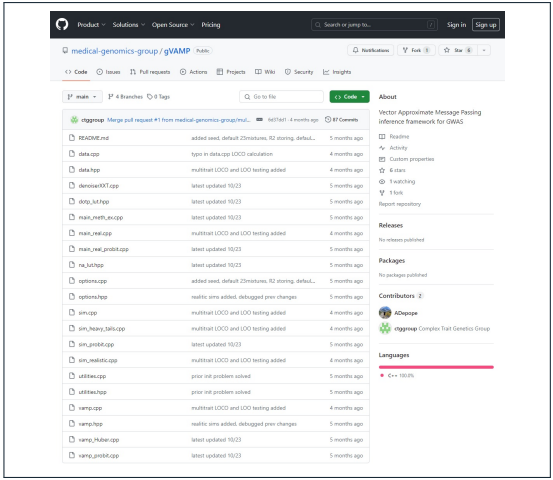
4. **low-complexity alternatives to VAMP?**

gVAMP git repo: https://github.com/medical-genomics-group/gVAMP



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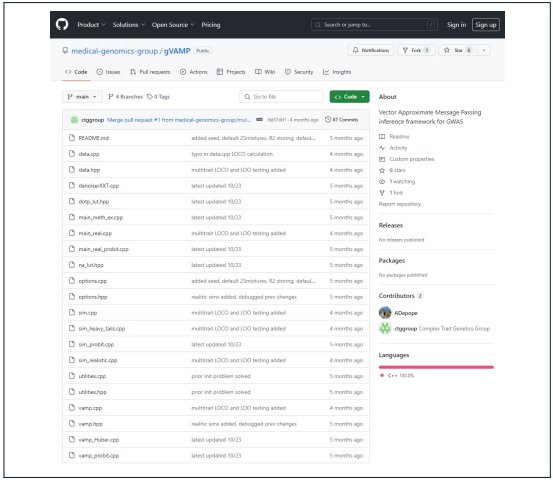

The End

Thanks for your attention!