Introduction: We used a machine-learning algorithm (gradient boosting) to test the association of genetic risk for 11 glycemic traits with osteoporosis and fractures in the UK Biobank population.

Methods: The study was performed with 409,633 caucasian participants in the UKBIobank. We identified 4626 SNPs associated with 11 glycemic traits from the NGHRI catalogue for GWAS studies. Weighted genetic risk scores (wGRS) were calculated using the effect estimates from the GWAS studies. We used a gradient-boosting machine-learning (GBM) model to identify the relative influence (RI) of baseline variables and wGRS of the glycemic traits on osteoporosis and all-cause fractures in the UK Biobank population. We split the data into training (2/3) and testing set (1/3) and calculated the discriminatory power of the models using the area under the curve (AUC) with the testing model.

Results: The study consisted of 409,633 individuals (53% females) with a median age of 58 (51-63) years and a median BMI of 26.7 (24.1-29.8) kg/m^2. The study population had 41954 (10.2%) all-cause fractures and 4995 (1.2%) participants with osteoporosis. In the GBM model, top wGRS associated with all-cause fractures were wGRS for Type 1 diabetes (RI=4.49) and fasting glucose (4.17). In contrast, the top wGRS associated with osteoporosis were wGRS for acute insulin response to glucose (RI=6.74) and Type 1 diabetes (RI=5.62). Both models showed low to moderate discriminatory power with the area under the AUC of 0.57(CI: 0.56-0.57) for fractures and 0.75(CI: 0.74-0.76) for osteoporosis.

Conclusion: We showed a differential effect of wGRS for various glycemic traits on the risk of fractures and osteoporosis in the UK Biobank population. However, the machine-learning model with wGRS for glycemic traits demonstrated limited capacity to predict fractures and osteoporosis in the general population.

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Estimating the relative influence (RI) of genetic risk of 11 glycemic traits on osteoporosis and fractures in 409633 participants in the UK Biobank using Machine learning

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