Study to Understand the Genetics of the Acute Response to Metformin and Glipizide in Humans (SUGAR-MGH)

Brief description of the dataset

SUGAR-MGH is a pharmacogenetic study in which 1,000 individuals who were naive to type 2 diabetes (T2D) medications received a single-dose glipizide challenge and a short course of metformin. In this study, we applied a genome-wide approach to comprehensively identify novel genetic predictors of acute metformin and glipizide response in individuals at risk of T2D but naive to these medications. We examined the effect of known genetic variants associated with T2D and glycemic traits across all outcomes in SUGAR-MGH to gain further insights into the mechanisms by which they confer an increased risk of T2D or glycemic dysregulation. Overall, we present and make available a resource for studying how genetic variation influences the biochemical response to two common glucose-lowering agents.

Total sample size, and sample size for each phenotype

The total sample in the GWAS analyses comprised 890 individuals. The sample size for each phenotype is detailed in the table below.

Definitions of the phenotypes assayed.

The primary endpoint of metformin response was defined as the fasting glucose at Visit 2 (V2), adjusted for fasting glucose at Visit 1 (V1). For the primary outcomes of glipizide response, we selected the following endpoints: insulin peak adjusted for baseline insulin, glucose trough adjusted for baseline glucose, and time to glucose trough. We identified secondary outcomes of metformin and glipizide response based on measurements taken during the glipizide challenge and the 75-g oral glucose tolerance test (OGTT) following metformin including insulin, incretin, and homeostasis model assessments.

Table of the 46 traits for which GWAS summary statistics are shared.

Trait description	Adjustments	Name of file
Area under the curve of Insulin at V2 adjusted for fasting insulin at V2	Age+Gender+BMI+PCs	SUGARMGH.AUC insulin V2 no exclusion adjAge+Gender+BMI+PCs.sumstat.txt.gz
Fasting Glucose at V2	Age+Gender+BMI+PCs+glucose0	SUGARMGH.Glu_V2_0_no_exclusion_glucose0V1_adjAge+Gender+BMI+PCs+glucose0.sumstat.txt.gz
Glucose at 120 mins at V2	Age+Gender+BMI+PCs	SUGARMGH.Glu V2 120 no exclusion adjAge+Gender+BMI+PCs.sumstat.txt.gz
Glucose at 120 mins at V2	Age+Gender+BMI+PCs+Glu0	SUGARMGH.Glu_V2_120_no_exclusion_glu0V2_adjAge+Gender+BMI+PCs+Glu0.sumstat.txt.gz
Glucose at 30 mins at V2	Age+Gender+BMI+PCs	SUGARMGH.Glu_V2_30_no_exclusion_adjAge+Gender+BMI+PCs.sumstat.txt.gz
Glucose at 30 mins at V2	Age+Gender+BMI+PCs+Glu0	SUGARMGH.Glu_V2_30_no_exclusion_glu0V2_adjAge+Gender+BMI+PCs+Glu0.sumstat.txt.gz
Glucose at 60 mins at V2	Age+Gender+BMI+PCs	SUGARMGH.Glu_V2_60_no_exclusion_adjAge+Gender+BMI+PCs.sumstat.txt.gz
Glucose at 60 mins at V2	Age+Gender+BMI+PCs+Glu0	SUGARMGH.Glu_V2_60_no_exclusion_glu0V2_adjAge+Gender+BMI+PCs+Glu0.sumstat.txt.gz
Fasting Glucose at V1	Age+Gender+BMI+PCs	SUGARMGH.gluc_V1_0_no_exclusion_adjAge+Gender+BMI+PCs.sumstat.txt.gz
Glucose at 120 mins at V1	Age+Gender+BMI+PCs+glucose0	SUGARMGH.gluc_V1_120_no_exclusion_glucose_adjAge+Gender+BMI+PCs+glucose0.sumstat.txt.gz
Glucose at 180 mins at V1	Age+Gender+BMI+PCs	SUGARMGH.gluc_V1_180_no_exclusion_adjAge+Gender+BMI+PCs.sumstat.txt.gz

Glucose at 180 mins at V1	Age+Gender+BMI+PCs+glucose0	SUGARMGH.gluc_V1_180_no_exclusion_glucose_adjAge+Gender+BMI+PCs+glucose0.sumstat.txt.gz
Glucose at 240 mins at V1	Age+Gender+BMI+PCs	SUGARMGH.gluc_V1_240_no_exclusion_adjAge+Gender+BMI+PCs.sumstat.txt.gz
Glucose at 240 mins at V1	Age+Gender+BMI+PCs+glucose0	SUGARMGH.gluc_V1_240_no_exclusion_glucose_adjAge+Gender+BMI+PCs+glucose0.sumstat.txt.gz
Glucose at 30 mins at V1	Age+Gender+BMI+PCs	SUGARMGH.gluc_V1_30_no_exclusion_adjAge+Gender+BMI+PCs.sumstat.txt.gz
Glucose at 30 mins at V1	Age+Gender+BMI+PCs+glucose0	SUGARMGH.gluc_V1_30_no_exclusion_glucose_adjAge+Gender+BMI+PCs+glucose0.sumstat.txt.gz
Glucose at 60 mins at V1	Age+Gender+BMI+PCs	SUGARMGH.gluc_V1_60_no_exclusion_adjAge+Gender+BMI+PCs.sumstat.txt.gz
Glucose at 60 mins at V1	Age+Gender+BMI+PCs+glucose0	SUGARMGH.gluc_V1_60_no_exclusion_glucose_adjAge+Gender+BMI+PCs+glucose0.sumstat.txt.gz
Glucose at 90 mins at V1	Age+Gender+BMI+PCs	SUGARMGH.gluc_V1_90_no_exclusion_adjAge+Gender+BMI+PCs.sumstat.txt.gz
Glucose at 90 mins at V1	Age+Gender+BMI+PCs+glucose0	SUGARMGH.gluc_V1_90_no_exclusion_glucose_adjAge+Gender+BMI+PCs+glucose0.sumstat.txt.gz
Glucose trough at V1 (all samples)	Age+Gender+BMI+PCs+glucose0	SUGARMGH.Glucose_trough_V1_no_exclusion_glucose0V1_allsamples_adjAge+Gender+BMI+PCs+glucose0.sumstat.txt.gz
Fasting Glucose at V2 minus Fasting Glucose at V1	Age+Gender+BMI+PCs	SUGARMGH.Glucose0V2_glucose0V1_no_exclusion_adjAge+Gender+BMI+PCs.sumstat.txt.gz
Fasting Glucose at V2 minus Fasting Glucose at V1	Age+Gender+BMI+PCs+glucose0	SUGARMGH.Glucose0V2_glucose0V1_no_exclusion_glucose0V1_adjAge+Gender+BMI+PCs+glucose0.sumstat.txt.gz
Fasting Insulin at V2 minus Fasting Insulin at V1	Age+Gender+BMI+PCs	SUGARMGH.Insulin0V2_insulin0V1_no_exclusion_adjAge+Gender+BMI+PCs.sumstat.txt.gz
Fasting Insulin at V2 minus Fasting Insulin at V1	Age+Gender+BMI+PCs+logInsulin0	SUGARMGH.Insulin0V2_insulin0V1_no_exclusion_insulin0V1_adjAge+Gender+BMI+PCs+logInsulin0.sumstat.txt.gz
log of (Fasting glucose at V1 - trough glucose)/time to glucose trough	Age+Gender+BMI+PCs	SUGARMGH.logglucose0_trough_time_V1_no_exclusion_adjAge+Gender+BMI+PCs.sumstat.txt.gz
log of (Fasting glucose at V1 - trough glucose)/time to glucose trough	Age+Gender+BMI+PCs+glucose0	SUGARMGH.logglucose0_trough_time_V1_no_exclusion_glucose0V1_adjAge+Gender+BMI+PCs+glucose0.sumstat.txt.gz
log of (Glucose at 240 mins - trough glucose)/time to glucose trough	Age+Gender+BMI+PCs	SUGARMGH.logglucose240_trough_time_V1_no_exclusion_adjAge+Gender+BMI+PCs.sumstat.txt.gz
log of (Glucose at 240 mins - trough glucose)/time to glucose trough	Age+Gender+BMI+PCs+glucose0	SUGARMGH.logglucose240_trough_time_V1_no_exclusion_glucose0V1_adjAge+Gender+BMI+PCs+glucose0.sumstat.txt.gz
log of Fasting Insulin at V2	Age+Gender+BMI+PCs	SUGARMGH.logIns_V2_0_no_exclusion_adjAge+Gender+BMI+PCs.sumstat.txt.gz
log of Insulin at 120 mins at V2	Age+Gender+BMI+PCs	SUGARMGH.logIns_V2_120_no_exclusion_adjAge+Gender+BMI+PCs.sumstat.txt.gz
log of Insulin at 30 mins at V2	Age+Gender+BMI+PCs	SUGARMGH.logIns_V2_30_no_exclusion_adjAge+Gender+BMI+PCs.sumstat.txt.gz
log of Insulin at 60 mins at V2	Age+Gender+BMI+PCs	SUGARMGH.logIns_V2_60_no_exclusion_adjAge+Gender+BMI+PCs.sumstat.txt.gz
log of Fasting Insulin at V1	Age+Gender+BMI+PCs+glucose0	SUGARMGH.logInsulin_V1_0_no_exclusion_glucose0V1_adjAge+Gender+BMI+PCs+glucose0.sumstat.txt.gz
log of Insulin at 120 mins at V1	Age+Gender+BMI+PCs	SUGARMGH.logInsulin_V1_120_no_exclusion_adjAge+Gender+BMI+PCs.sumstat.txt.gz
log of Insulin at 180 mins at V1	Age+Gender+BMI+PCs	SUGARMGH.logInsulin_V1_180_no_exclusion_adjAge+Gender+BMI+PCs.sumstat.txt.gz
log of Insulin at 240 mins at V1	Age+Gender+BMI+PCs	SUGARMGH.logInsulin_V1_240_no_exclusion_adjAge+Gender+BMI+PCs.sumstat.txt.gz
log of Insuin at 30 mins at V1	Age+Gender+BMI+PCs	SUGARMGH.logInsulin_V1_30_no_exclusion_adjAge+Gender+BMI+PCs.sumstat.txt.gz
log of Insulin at 60 mins at V1	Age+Gender+BMI+PCs	SUGARMGH.logInsulin_V1_60_no_exclusion_adjAge+Gender+BMI+PCs.sumstat.txt.gz

log of Insulin at 90 mins at V1	Age+Gender+BMI+PCs	SUGARMGH.logInsulin_V1_90_no_exclusion_adjAge+Gender+BMI+PCs.sumstat.txt.gz
log of Peak Insulin at V1	Age+Gender+BMI+PCs+logInsulin0	SUGARMGH.logpeak insulin V1 no exclusion Insulin0V1 adj Age+Gender+BMI+PCs+logInsulin0.sumstat.txt.gz
Time to reach peak Insulin at V1	Age+Gender+BMI+PCs	SUGARMGH.Timetopeak_insulin_V1_no_exclusion_allsamples_adjAge+Gender+BMI+PCs.sumstat.txt.gz
Time to reach peak Insulin at V1	Age+Gender+BMI+PCs+logInsulin0	SUGARMGH.Timetopeak_insulin_V1_no_exclusion_Insulin0V1_allsamples_adjAge+Gender+BMI+PCs+logInsulin0.sumstat.txt.gz
Time to reach glucose trough at V1	Age+Gender+BMI+PCs+glucose0	SUGARMGH.Timetotrough_glucose_V1_no_exclusion_glucose0V1_allsamples_adjAge+Gender+BMI+PCs+glucose0.sumstat.txt.gz
HOMA-B at V2 minus HOMA-B at V1	Age+Gender+BMI+PCs	SUGARMGH.V2HOMAB_V1HOMAB_no_exclusion_adjAge+Gender+BMI+PCs.sumstat.txt.gz
HOMA-IR at V2 minus HOMA-IR at V1	Age+Gender+BMI+PCs	SUGARMGH.V2HOMAIR_V1HOMAIR_no_exclusion_adjAge+Gender+BMI+PCs.sumstat.txt.gz

V1: visit 1; V2: visit 2

Ancestry of the participants
The sample includes individuals of diverse ancestries. Approximately 53% of participants were female, the mean age was 47 years, and 37% of participants self-reported as non-white.

Reference to a publication describing the study, if available
The manuscript has been accepted for publication in the Diabetologia journal (pending link).

Image file for logo of consortia involved, if you would like us to display them in the dataset documentation.
File provided.

if you would like us to provide the summary statistic files for download, please also supply a README file to accompany them.
README provided.