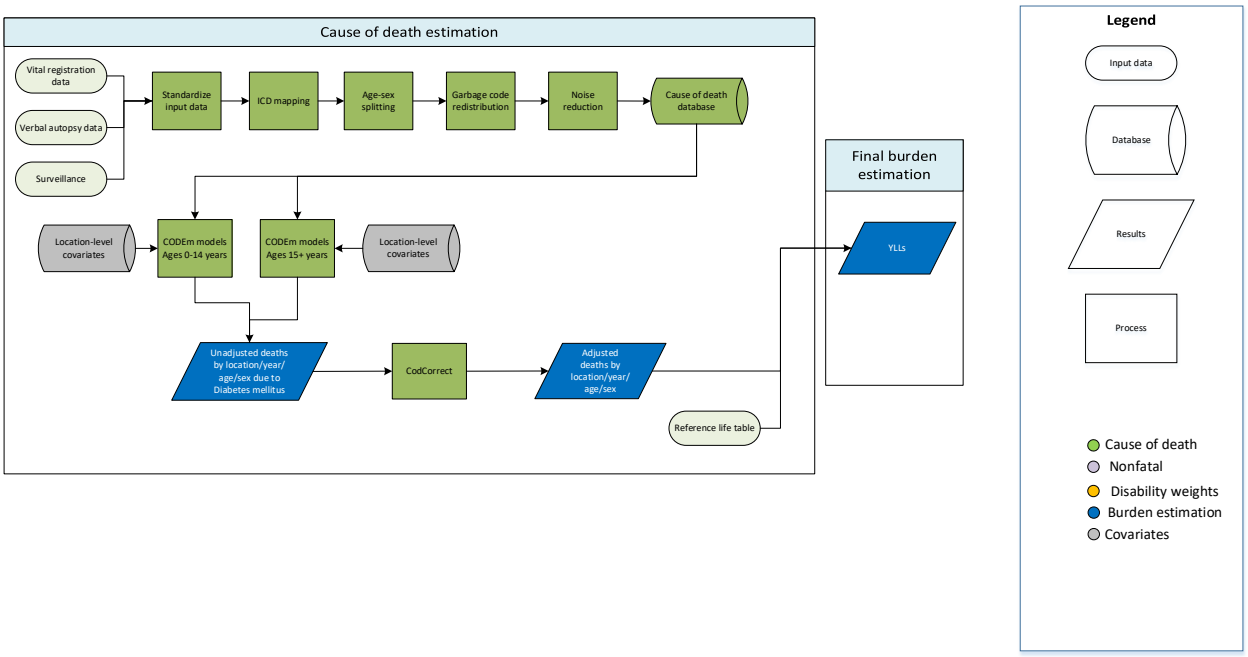
Diabetes mellitus

Diabetes mellitus mortality was estimated for overall diabetes mellitus, diabetes mellitus type 1, and diabetes mellitus type 2 in GBD 2020.

Overall diabetes mellitus

Flowchart



Input data and methodological summary for diabetes mellitus

Input data

Overall diabetes mellitus mortality was estimated using deaths directly attributed to diabetes mellitus. We used verbal autopsy and vital registration data as inputs into the model.

Verbal autopsy data: We outliered datapoints from sources where there were zero deaths estimated in an age group as this was not realistic for deaths due to diabetes and we determined that these data sources were unreliable.

Vital registration data: We outliered all data from the India Medical Certification of Cause of Death report since the source of the data were unreliable according to expert opinion. We also outliered ICD-9-BTL datapoints that were inconsistent with the rest of the data series and created unlikely time trends.

Modelling strategy

The Cause of Death Ensemble model (CODEm)[1] was used for deaths due to diabetes mellitus estimation. Additional information on CODEm methods can be found in appendix 1, section 3 of the reference article.

In the overall diabetes mellitus model, we used two models to estimate overall diabetes deaths with different age restrictions. This is because deaths in younger age groups are almost exclusively due to type 1 diabetes, while deaths in older ages are primarily due to type 2 diabetes. This allowed us to select predictive covariates that are specific to the pathophysiology of diabetes type 1 and type 2. We set the younger age model from 0 to 14 years and the older age model from 15 to 95+ years. We determined the age threshold based on evidence of the onset of diabetes type 2 occurring at younger ages.

Covariate selection

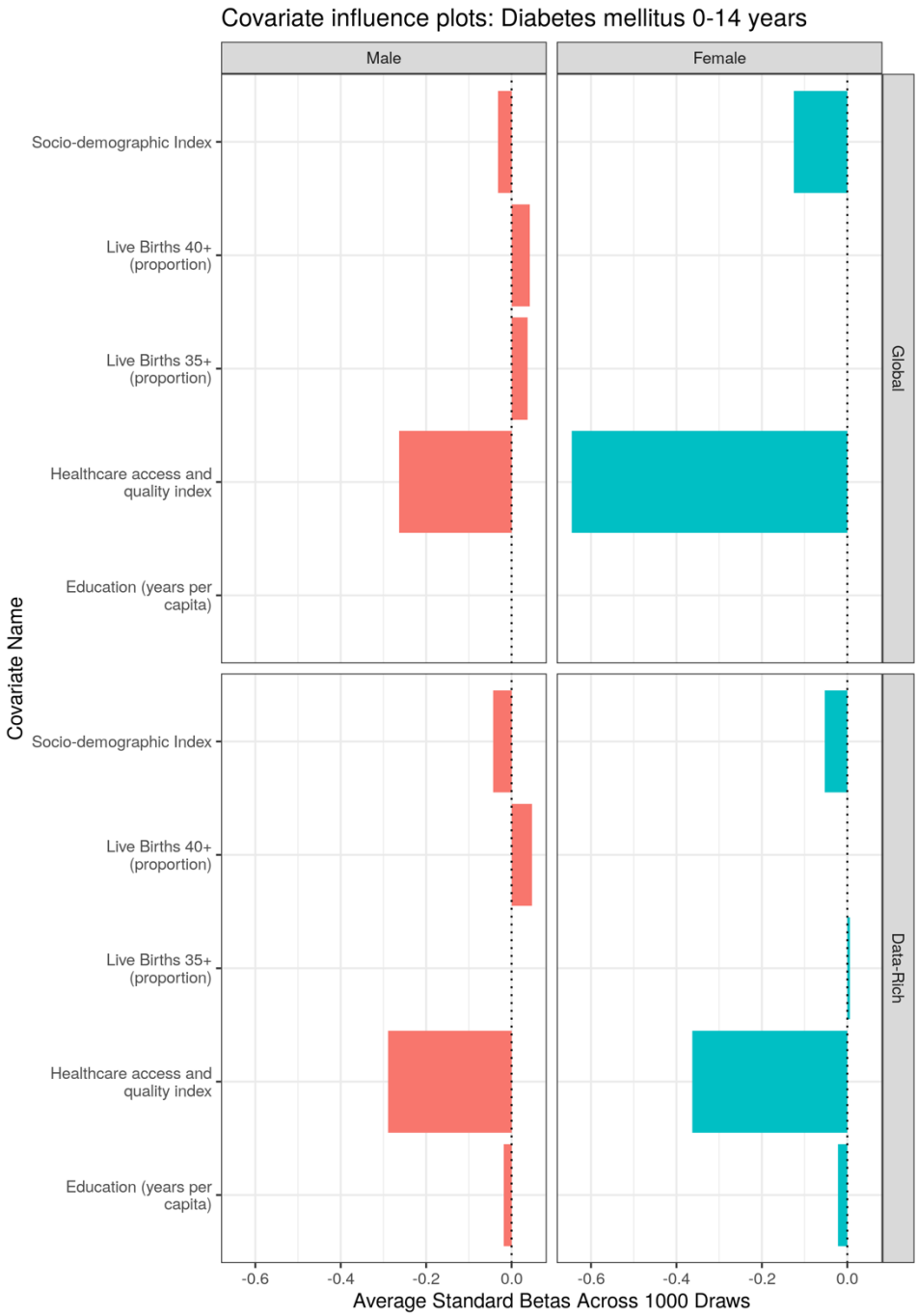
The following table lists the covariates included in the model. This requires that the covariate selected for the model must have the directional relationship with diabetes mellitus deaths. For GBD 2020, no significant updates were made for diabetes mellitus covariate selection. Covariate directions were selected based on the strength of the evidence.

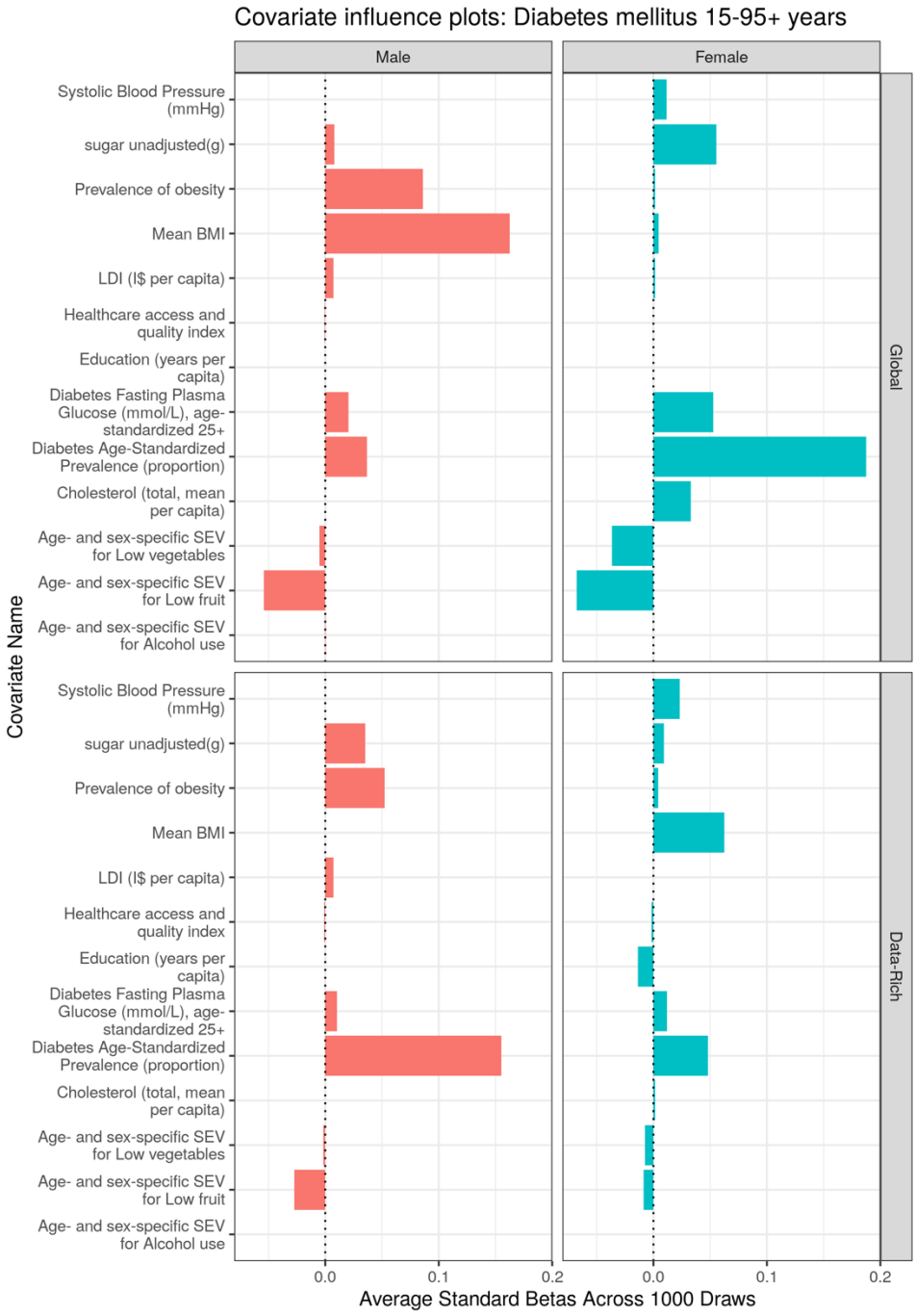
Table 1. Covariates used in diabetes mellitus mortality modelling

Model	Level	Covariate	Direction
0–14 years	1	Healthcare Access and Quality Index	-
	3	Education years per capita	-
	2	Age-standardised fertility rate	+
	2	Latitude	+
	2	Age-standardised underweight (weight-for-age) summary exposure variable	-
	2	Percentage of births occurring in women >35 years old	+
	2	Percentage of births occurring in women >40 years old	+
	3	Socio-demographic Index	-
	2	Age-standardised stunting (height-for-age) summary exposure variable	-
	2	Mean birthweight	-
15+ years	1	Age-standardised mean fasting plasma glucose (mmol/L)	+
	1	Age-standardised prevalence of diabetes	+
	3	Education years per capita	-
	3	Lag-distributed income per capita	+
	1	Mean BMI	+
	2	Mean cholesterol	+
	2	Mean systolic blood pressure	+
	1	Prevalence of obesity	+
	2	Age- and sex-specific summary exposure variable for low fruit	-
	2	Energy-adjusted grams of sugar	+
	2	Age- and sex-specific summary exposure variable for low vegetables	-
	3	Healthcare Access and Quality Index	-
	2	Age- and sex-specific summary exposure variable for alcohol use	+

Covariate influences

The following plots show the influence of each covariate on the four CODEm models (male global, male data-rich, female global, and female data-rich). A positive standardised beta (to the right) means that the covariate was associated with increased death. A negative standardised beta (to the left) means the covariate was associated with decreased death.

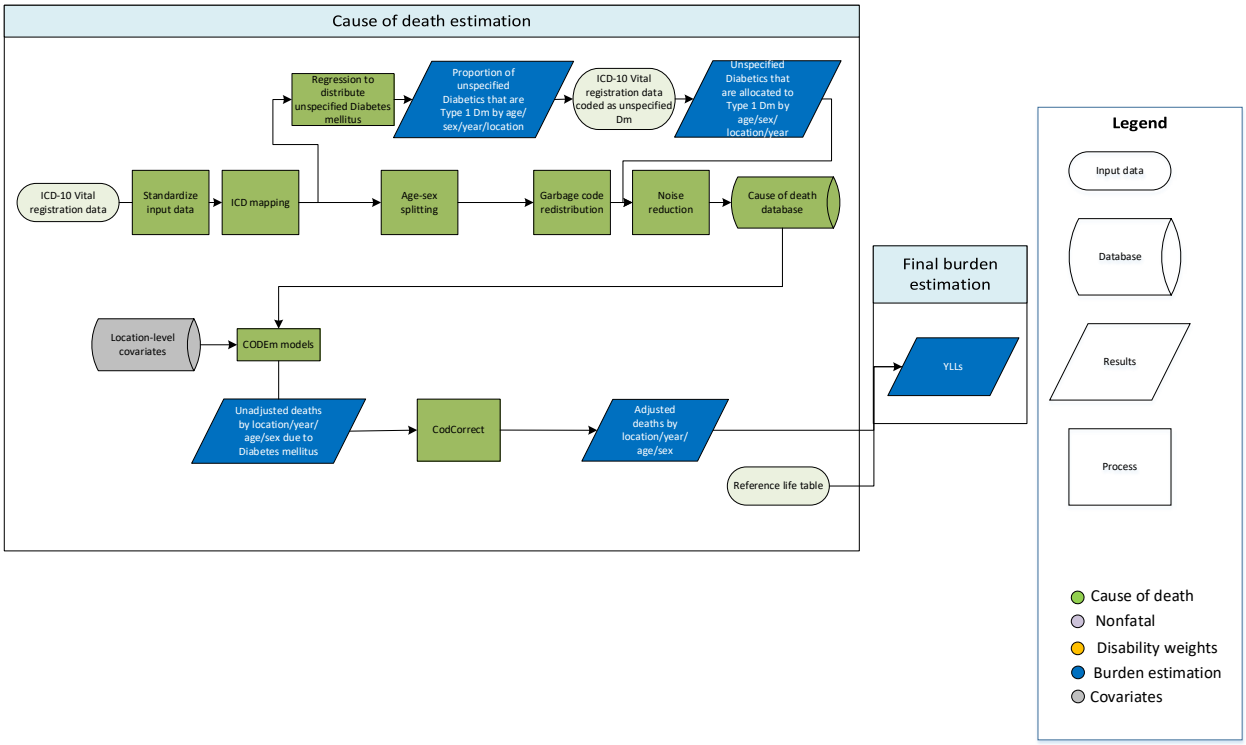



Covariate influence plots: Diabetes mellitus 15-95+ years
Male
Female
Global
Data-Rich
Covariate Name
Systolic Blood Pressure (mmHg)
sugar unadjusted(g)
Prevalence of obesity
Mean BMI
LDI (I$ per capita)
Healthcare access and quality index
Education (years per capita)
Diabetes Fasting Plasma Glucose (mmol/L), age-standardized 25+
Diabetes Age-Standardized Prevalence (proportion)
Cholesterol (total, mean per capita)
Age- and sex-specific SEV for Low vegetables
Age- and sex-specific SEV for Low fruit
Age- and sex-specific SEV for Alcohol use
0.0
0.1
0.2
Average Standard Betas Across 1000 Draws

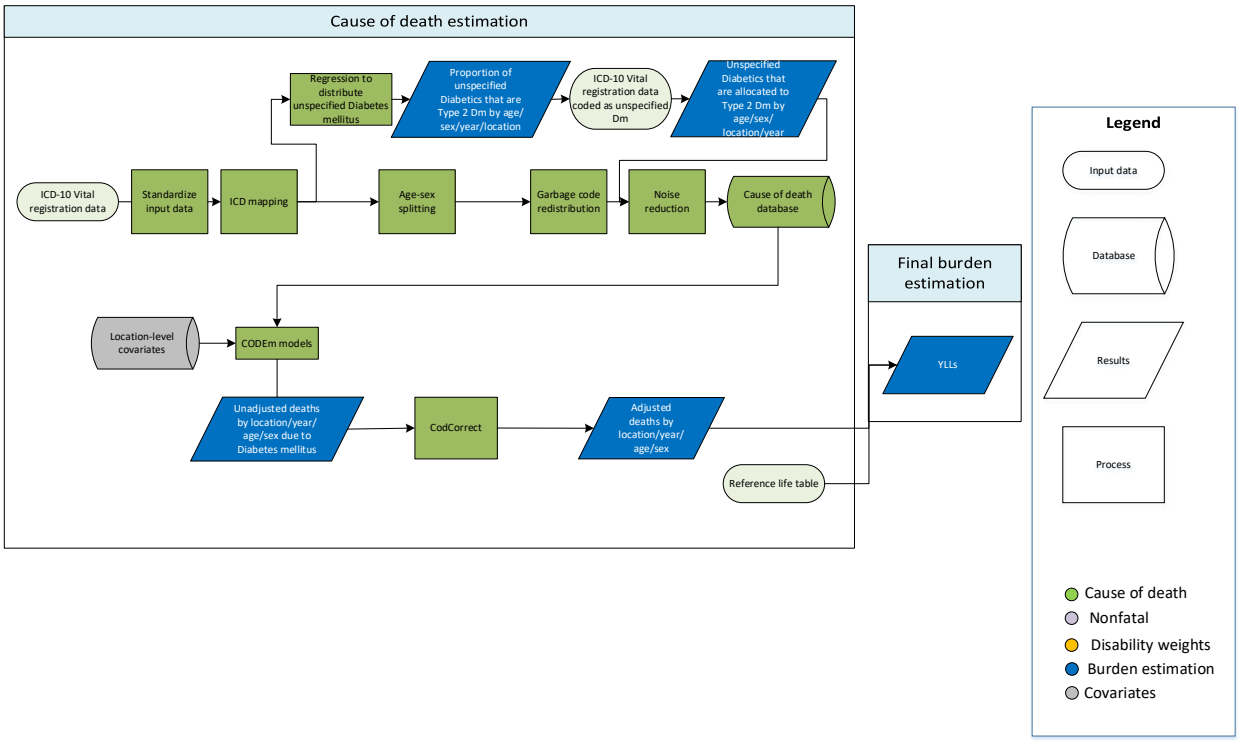
Diabetes mellitus type 1 and type 2

Flowchart

Diabetes mellitus type 1



Diabetes mellitus type 2



Input data and methodological summary for type 1 and type 2 diabetes mellitus

Input data

Type-specific diabetes mellitus mortality was estimated using deaths from vital registration sources in ICD-10 codes only. Diabetes type-specific information was not available in ICD-9 codes or deaths determined by verbal autopsy.

Modelling strategy

CODEm was used for deaths due to diabetes mellitus type-specific estimation.

Deaths in younger age groups are almost exclusively due to type 1 diabetes, while deaths in older ages are primarily due to type 2 diabetes. To account for this age pattern, we set the age range of the diabetes type 1 model to 0–95+ years and the age range of the diabetes type 2 model to 15–95+ years. We used the same covariates in the diabetes type 1 model and diabetes type 2 model as the 0–14 year and 15–95+ year in the overall diabetes models, respectively.

There were two unique data manipulation steps that occurred to prepare the data as part of the modelling process.

1. We assumed that all deaths <15 years were due to type 1 regardless of the ICD-10 code assigned to the death. We imposed 100% attribution of diabetes mellitus deaths in <15 years to type 1 diabetes mellitus.
2. ICD-10 diabetes data were reported as type 1, type 2, or unspecified. We assumed that all deaths in persons >50 years were unspecified regardless of the ICD-10 code assigned to the death because we found an unreasonably high proportion of deaths due to diabetes were assigned to type 1 diabetes. We developed a regression to estimate the fraction of unspecified diabetes mellitus that was type 1 and type 2. We only used data from 703 country-years to inform the regression. This is because these country-years had more than 50% of the deaths typed to type 1 or type 2 AND at least 70% of type-specific deaths in people >25 years were coded to type 2. Since there was a separate regression to estimate the proportion of type 1 diabetes mellitus and type 2 diabetes mellitus, we scaled the predicted proportions to 1. These scaled proportions were then applied to number of deaths coded to unspecified diabetes in each location, year, sex where ICD-10 data were reported.

<u>Regression equations</u>:

Type 1:

$$logit\left(\frac{number\ type\ 1\ DM}{number\ total\ DM}\right) \sim logit\left(\frac{number\ unspecified\ DM}{number\ total\ DM}\right) + \beta_1 age\ group + \beta_2 age\text{-}st\ prev\ obesity * age\ group + age\text{-}st\ prev\ obesity$$

Type 2:

$$logit\left(\frac{number\ type\ 2\ DM}{number\ total\ DM}\right) \sim logit\left(\frac{number\ unspecified\ DM}{number\ total\ DM}\right) + \beta_1 age\ group + \beta_2 age\text{-}st\ prev\ obesity * age\ group + age\text{-}st\ prev\ obesity$$

Covariate selection

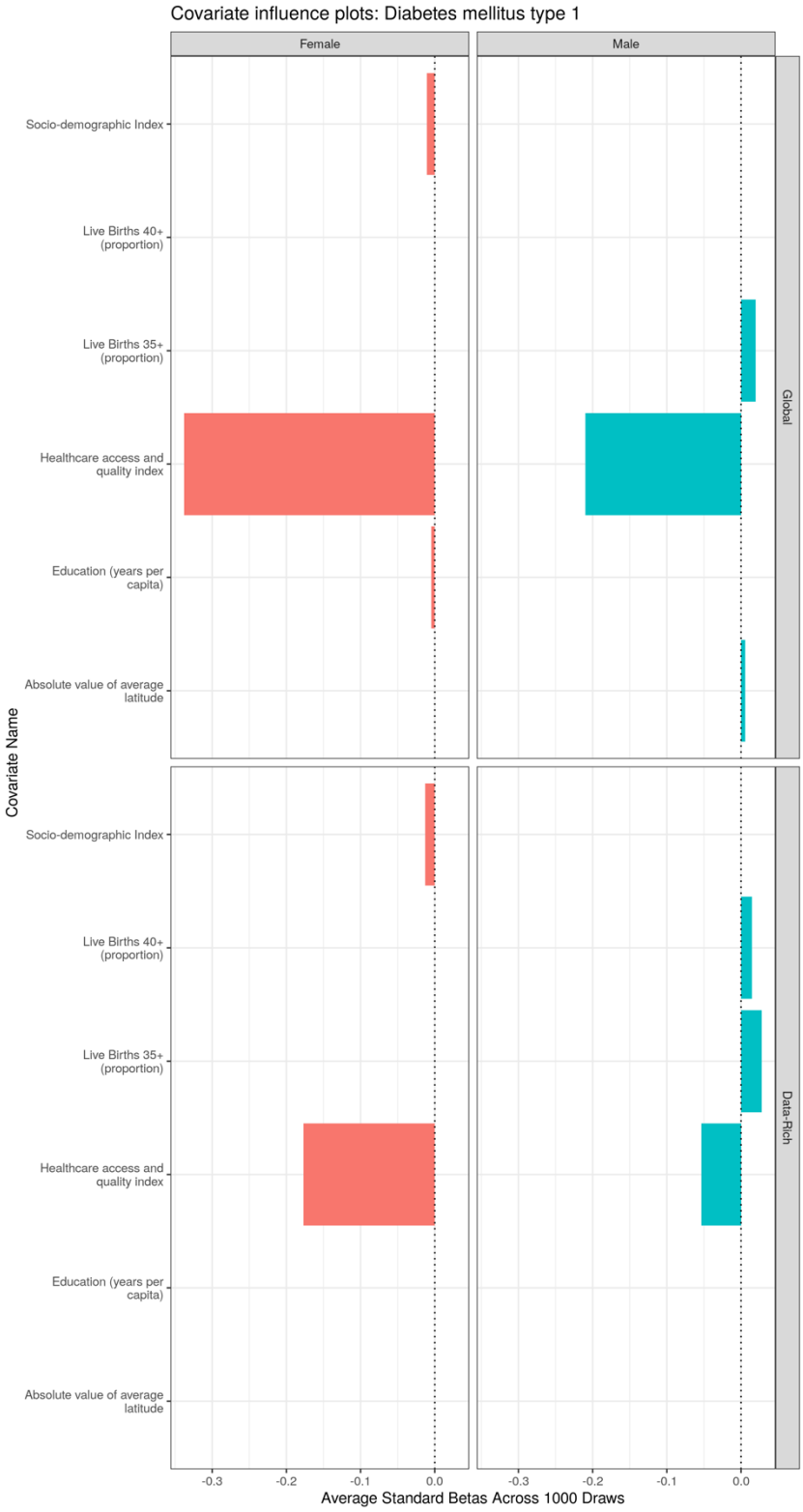
The following are the covariates included in the model. We selected the same covariates for the type 1 diabetes model as the 0–14-year diabetes parent model and the type 2 diabetes model as the 15–95+ year diabetes parent model. For GBD 2020, no significant updates were made for the type-specific diabetes covariate selection. Covariate directions were selected based on the strength of the evidence.

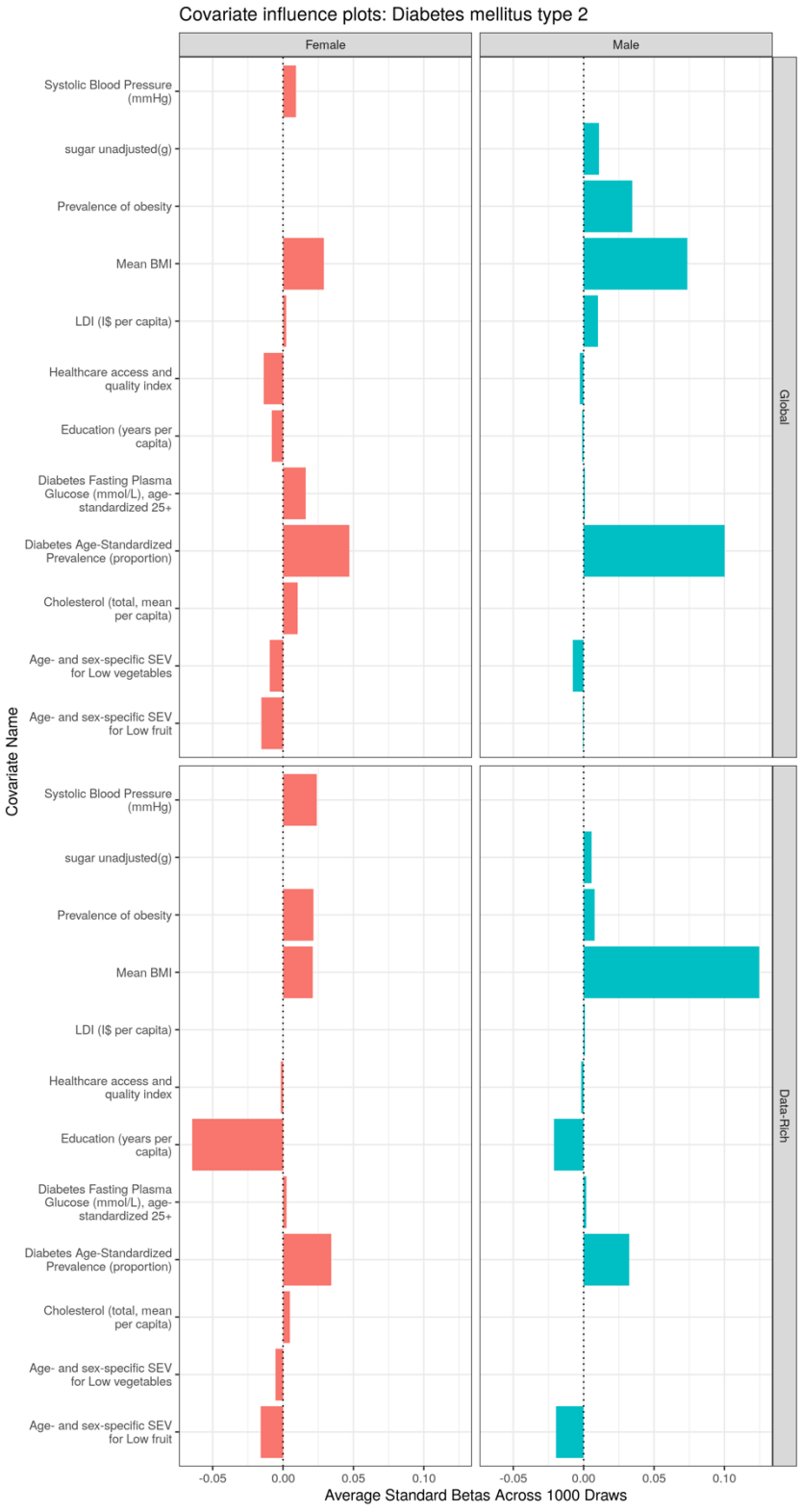
Table 2. Covariates used in diabetes mellitus type 1 and type 2 mortality modelling

Model	Level	Covariate	Direction
Type 1	1	Healthcare Access and Quality Index	-
	3	Education years per capita	-
	2	Age-standardised fertility rate	+
	2	Latitude	+
	2	Age-standardised underweight (weight-for-age) summary exposure variable	-
	2	Percentage of births occurring in women >35 years old	+
	2	Percentage of births occurring in women >40 years old	+
	3	Socio-demographic Index	-
	2	Age-standardised stunting (height-for-age) summary exposure variable	-
	2	Mean birthweight	-
Type 2	1	Age-standardised mean fasting plasma glucose (mmol/L)	+
	1	Age-standardised prevalence of diabetes	+
	3	Education years per capita	-
	3	Lag-distributed income per capita	+
	1	Mean BMI	+
	2	Mean cholesterol	+
	2	Mean systolic blood pressure	+
	1	Prevalence of obesity	+
	2	Age- and sex-specific summary exposure variable for low fruit	-
	2	Energy-adjusted grams of sugar	+
	2	Age- and sex-specific summary exposure variable for low vegetables	-
	3	Healthcare Access and Quality Index	-
	2	Age- and sex-specific summary exposure variable for alcohol use	+

Covariate influences

The following plots show the influence of each covariate on the four CODEm models (male global, male data-rich, female global, and female data-rich). A positive standardised beta (to the right) means that the covariate was associated with increased death. A negative standardised beta (to the left) means the covariate was associated with decreased death.


Covariate influence plots: Diabetes mellitus type 1
Female
Male
Global
Data-Rich
Covariate Name
Socio-demographic Index
Live Births 40+ (proportion)
Live Births 35+ (proportion)
Healthcare access and quality index
Education (years per capita)
Absolute value of average latitude
-0.3
-0.2
-0.1
0.0
Average Standard Betas Across 1000 Draws


Covariate influence plots: Diabetes mellitus type 2
Female
Male
Global
Data-Rich
Covariate Name
Systolic Blood Pressure (mmHg)
sugar unadjusted(g)
Prevalence of obesity
Mean BMI
LDI (I$ per capita)
Healthcare access and quality index
Education (years per capita)
Diabetes Fasting Plasma Glucose (mmol/L), age-standardized 25+
Diabetes Age-Standardized Prevalence (proportion)
Cholesterol (total, mean per capita)
Age- and sex-specific SEV for Low vegetables
Age- and sex-specific SEV for Low fruit
-0.05
0.00
0.05
0.10
Average Standard Betas Across 1000 Draws

References

[1]Vos T, Lim SS, Abbafati C, et al. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *The Lancet* 2020; 396: 1204–22. doi: https://doi.org/10.1016/S0140-6736(20)30925-9