S1. Identification of incident type 1 diabetes

For identification of incident type 1 diabetes cases, we used information from NDR, PR, and PDR. The NDR started in 1996 and collects information on diabetes care from Swedish health centres, including characteristics of the patients, year of onset, risk factors, and diabetes complications (16). The PR collects data on hospital discharges regionally since 1964, and nationally since 1987 with high quality (17). Additionally, the register covers > 80% of all outpatient specialist care in Sweden since 2001. The PDR collects information on all prescribed drugs dispensed at Swedish pharmacies since July 1, 2005 (18).

We identified incident cases of type 1 diabetes during the follow-up period based on information from NDR, as well as PR using ICD-9 code 250 and ICD-10 code E10, and timed them according to the first recording. The first record of type 1 diabetes was used to identify a case; when a case was initially diagnosed using ICD-9, a later record of ICD-10 code E10 was used as a confirmation of type 1 diabetes, but the first record was used as date of diagnosis. Individuals with a recording of type 2 diabetes at any time, in either register, were not included as a case.

In total, 2,534 individuals had a record of type 1 diabetes in NDR or PR during follow-up (ICD-9 code 250 and/or ICD-10 code E10); to additionally exclude any potentially misclassified cases with type 2 diabetes, we defined that type 1 diabetes cases either had an age of diagnosis of < 30 years of age as recorded in NDR or PR, a record of insulin prescription as recorded in PDR (ATC code A10A), or a combination of these (n = 1,122) (Figure S1). Due to the available measurements, the number of type 1 diabetes cases studied varied between biomarkers, e.g. 987 cases had glucose levels assessed at baseline. Of the 591,239 individuals included in the study, 46,962 were censored during the follow-up due to a diagnosis of type 2 diabetes (ICD-10 code E11), likely type 2 diabetes diagnosis based on record in PDR (ATC code A10B only), or unclear diabetes diagnosis (ICD-9 code 250 only, or ICD-10 code E12-E14), including conflicting results in NDR and PR (Figure S1).

S2. Statistical analysis – Details on R packages

All analyses were performed in R Studio using R version 3.6.2 and the package *survival* for Cox proportional hazard and conditional logistic regression models (Therneau, 2020. *A Package for Survival Analysis in R*. R package version 3.2-7), as well as the packages *survey* (Lumley, 2020. *survey: analysis of complex survey samples.* R package version 4.0) and *ggplot2* (Wickham, 2016. *ggplot2: Elegant Graphics for Data Analysis*. R package version 3.3.2) for estimation of weighted means and visualisation of trajectories.

S3. Sensitivity analysis – fasting samples and adjustments for BMI

We furthermore performed restricted analysis using values obtained in fasting samples only; the proportion of fasting vs. non-fasting samples was comparable between type 1 diabetes cases (57.6% vs. 42.5%) and healthy individuals (55.9% vs. 44.1%). To evaluate the potential confounding of lipid biomarkers by BMI, we additionally adjusted the analyses in a sub-population of the study cohort with information on BMI.

Table S1. HRs and 95% CIs of Type 1 Diabetes for continuous biomarkers (sensitivity analyses by age, insulin prescription, and fasting status).

A

Biomarker	Stratified by age: two segments (median age at measurement)			
	≤ 43 yrs		*> 43 yrs*	
	N	HR (95% CI)	N	HR (95% CI)
Biomarkers related to glycaemia				
Glucose (mmol/L)	264 227	1.69 (1.58-1.80)	259 875	1.75 (1.66-1.85)
Fructosamine (mmol/L)	209 813	1.37 (1.24-1.52)	221 738	1.54 (1.39-1.70)
Biomarkers of lipid metabolism				
Triglycerides (mmol/L)	269 859	1.35 (1.24-1.46)	272 975	1.65 (1.52-1.80)
Total cholesterol (mmol/L)	270 676	1.07 (0.99-1.13)	274 151	1.05 (0.95-1.15)
ApoB/A-I ratio	58 778	1.37 (1.19-1.58)	101 666	1.33 (1.18-1.50)
ApoA-I (g/L)	72 321	0.62 (0.52-0.75)	111 842	0.70 (0.60-0.81)
ApoB (g/L)	65 165	1.15 (0.96-1.40)	106 306	1.18 (1.03-1.35)
Biomarkers related to inflammation				
Haptoglobin (g/L)	204 286	1.15 (1.05-1.26)	206 870	1.17 (1.07-1.28)
Uric acid (umol/L)	250 758	1.40 (1.27-1.54)	253 175	1.51 (1.38-1.65)
Albumine (g/L)	241 569	0.94 (0.85-1.03)	256 323	1.00 (0.90-1.11)
C-reactive protein (mg/L)	157 361	1.03 (0.97-1.10)	186 617	1.05 (1.01-1.10)
Leukocytes (10^9 cells/L)	80 595	1.08 (1.02-1.14)	107 462	1.08 (1.04-1.13)
Other				
Urea (mmol/L)	181 326	0.99 (0.87-1.13)	201 822	1.09 (0.99-1.20)
y-glutamyl transferase (ukat/L)	264 223	1.09 (1.06-1.12)	263 606	1.09 (1.07-1.11)
Alkaline phosphatase (ukat/L)	241 504	1.16 (1.12-1.21)	252 876	1.16 (1.12-1.19)
BMI (kg/m2)	69 207	1.19 (0.99-1.44)	63 000	1.37 (1.14-1.65)

B

Biomarker	Stratified by age: three segments (quartiles of age at measurement)					
	< 33 yrs		*34-52 yrs*		*≥ 53 yrs*	
	N	HR (95% CI)	N	HR (95% CI)	N	HR (95% CI)
Biomarkers related to glycaemia						
Glucose (mmol/L)	127 257	1.50 (1.34-1.69)	256 415	1.76 (1.66-1.86)	140 430	1.78 (1.67-1.91)
Fructosamine (mmol/L)	101 161	1.38 (1.20-1.60)	211 313	1.39 (1.25-1.54)	119 077	1.66 (1.44-1.91)
Biomarkers of lipid metabolism						
Triglycerides (mmol/L)	129 266	1.14 (1.01-1.29)	264 659	1.55 (1.44-1.68)	148 909	1.74 (1.55-1.96)
Total cholesterol (mmol/L)	129 651	1.07 (0.92-1.24)	265 485	1.07 (0.98-1.18)	149 691	1.03 (0.91-1.17)
ApoB/A-I ratio	22 640	1.23 (0.94-1.62)	78 873	1.41 (1.25-1.58)	58 931	1.29 (1.08-1.54)
ApoA-I (g/L)	29 420	0.70 (0.53-0.94)	90 650	0.63 (0.53-0.74)	64 093	0.72 (0.59-0.88)
ApoB (g/L)	26 001	1.06 (0.77-1.47)	84 387	1.26 (1.09-1.46)	61 083	1.08 (0.88-1.31)
Biomarkers related to inflammation						
Haptoglobin (g/L)	96 162	1.09 (0.94-1.25)	201 002	1.21 (1.10-1.30)	113 992	1.14 (1.02-1.29)
Uric acid (umol/L)	120 812	1.26 (1.10-1.45)	243 246	1.55 (1.42-1.70)	139 875	1.46 (1.30-1.64)
Albumine (g/L)	117 681	0.94 (0.82-1.06)	235 679	0.94 (0.85-1.05)	144 532	1.05 (0.91-1.22)
C-reactive protein (mg/L)	75 278	1.05 (0.99-1.12)	167 649	1.04 (0.99-1.11)	101 051	1.04 (0.96-1.12)
Leukocytes (10^9 cells/L)	42 178	1.17 (0.96-1.43)	76 214	1.08 (1.04-1.13)	69 665	1.08 (1.01-1.15)
Other						
Urea (mmol/L)	86 131	1.00 (0.84-1.20)	180 989	1.01 (0.89-1.14)	116 028	1.11 (1.00-1.24)
y-glutamyl transferase (ukat/L)	129 491	1.09 (0.99-1.20)	252 332	1.09 (1.07-1.11)	146 006	1.09 (1.05-1.13)
Alkaline phosphatase (ukat/L)	117 421	1.12 (1.04-1.21)	234 315	1.17 (1.14-1.21)	142 644	1.15 (1.10-1.20)
BMI (kg/m2)	28 578	1.07 (0.81-1.41)	72 350	1.39 (1.16-1.66)	31 279	1.29 (0.99-1.67)

C

Biomarker	Only cases without any oral glucose lowering therapy HR (95% CI)	Only cases with insulin prescribed within one year of diagnosis HR (95% CI)
Biomarkers related to glycaemia		
Glucose (mmol/L)	1.61 (1.52-1.71)	1.80 (1.44-2.24)
Fructosamine (mmol/L)	1.48 (1.35-1.62)	1.30 (0.89-1.89)
Biomarkers of lipid metabolism		
Triglycerides (mmol/L)	1.24 (1.15-1.34)	1.64 (1.20-2.24)
Total cholesterol (mmol/L)	0.97 (0.88-1.06)	0.80 (0.54-1.19)
ApoB/A-I ratio	1.16 (1.00-1.34)	0.97 (0.48-1.98)
ApoA-I (g/L)	0.74 (0.63-0.86)	0.97 (0.47-2.01)
ApoB (g/L)	0.97 (0.83-1.14)	1.16 (0.60-2.23)
Biomarkers related to inflammation		
Haptoglobin (g/L)	1.12 (1.03-1.22)	1.12 (0.78-1.62)
Uric acid (umol/L)	1.25 (1.13-1.37)	1.62 (1.15-2.29)
Albumine (g/L)	0.96 (0.87-1.05)	0.79 (0.56-1.13)
C-reactive protein (mg/L)	1.00 (0.92-1.10)	0.38 (0.06-2.34)
Leukocytes (10^9 cells/L)	1.07 (1.00-1.13)	1.09 (0.89-1.34)
Other		
Urea (mmol/L)	1.02 (0.92-1.14)	1.08 (0.69-1.68)
y-glutamyl transferase (ukat/L)	1.09 (1.07-1.11)	1.08 (0.97-1.20)
Alkaline phosphatase (ukat/L)	1.16 (1.12-1.20)	1.14 (0.96-1.36)
BMI (kg/m2)	0.97 (0.80-1.16)	1.02 (0.53-1.95)

D

Biomarker	Overnight fasted samples only	
	N	HR (95% CI)
Biomarkers related to glycaemia		
Glucose (mmol/L)	289 861	2.38 (2.17-2.61)
Fructosamine (mmol/L)	241 280	1.32 (1.20-1.45)
Biomarkers of lipid metabolism		
Triglycerides (mmol/L)	297 711	1.57 (1.45-1.70)
Total cholesterol (mmol/L)	297 714	1.07 (0.98-1.17)
ApoB/A-I ratio	98 419	1.35 (1.20-1.51)
ApoA-I (g/L)	107 601	0.65 (0.56-0.75)
ApoB (g/L)	102 337	1.16 (1.01-1.33)
Biomarkers related to inflammation		
Haptoglobin (g/L)	242 413	1.20 (1.10-1.30)
Uric acid (umol/L)	277 098	1.39 (1.25-1.53)
Albumine (g/L)	267 492	0.90 (0.82-0.99)
C-reactive protein (mg/L)	178 618	1.05 (1.01-1.09)
Leukocytes (10^9 cells/L)	92 690	1.07 (1.03-1.12)
Other		
Urea (mmol/L)	220 025	1.09 (0.98-1.22)
y-glutamyl transferase (ukat/L)	278 641	1.13 (1.09-1.16)
Alkaline phosphatase (ukat/L)	266 721	1.16 (1.12-1.20)
BMI (kg/m2)	NA	NA

HRs were estimated using adjusted Cox models with attained age as the underlying time scale and date of birth as the time origin. Models were adjusted for sex, age at first blood sampling, fasting status (overnight fasting vs non-fasting), occupation, and country of birth. Restricted analysis based on (A) median and (B) quartiles of age at biomarker measurement. Furthermore, in C) restricted analyses were performed using only using cases without any oral glucose lowering therapy, and using only cases with insulin prescribed within one year of diagnosis (only possible for the 28.3% diagnosed from 2005 onwards when the PDR was started). In D) restricted analyses were performed using only values determined in overnight fasting samples. Abbreviations: CI, confidence interval; HR, hazard ratios; YRS, years.

Table S2. HRs and 95% CIs of Type 1 Diabetes for high vs. low levels of biomarkers.

Biomarker	No. of individuals with high value	Threshold value	HR (95% CI)	
			Model 1	Model 2
Biomarkers related to glycaemia				
Glucose (mmol/L)	29 968 (5.72%)	5.6 (FS) 7.8 (NFS)	4.69 (3.97-5.54)	5.00 (4.18-5.98)
Fructosamine (mmol/L)	45 872 (10.63%)	2.30	2.54 (2.15-3.00)	2.37 (2.00-2.80)
Biomarkers of lipid metabolism				
Triglycerides (mmol/L)	55 034 (10.14%)	2.25	2.49 (2.14-2.91)	2.39 (2.04-2.80)
Total cholesterol (mmol/L)	150 119 (27.55%)	6.19	1.07 (0.93-1.24)	1.08 (0.93-1.25)
ApoB/A-I ratio	81 408 (50.74%)	0.8 (F) 0.9 (M)	1.74 (1.37-2.21)	1.69 (1.33-2.15)
ApoA-I (g/L)	178 132 (96.73%)	1.05	0.33 (0.23-0.47)	0.36 (0.25-0.52)
ApoB (g/L)	38 079 (22.21%)	1.50	1.37 (1.07-1.76)	1.32 (1.02-1.70)
Biomarkers related to inflammation				
Haptoglobin (g/L)	6 025 (1.47%)	2.00	1.68 (1.02-2.77)	1.70 (1.03-2.80)
Uric acid (umol/L)	79 326 (15.74%)	360	1.88 (1.62-2.19)	1.74 (1.48-2.04)
Albumine (g/L)	3 163 (0.64%)	35	1.43 (0.64-3.20)	1.59 (0.71-3.55)
C-reactive protein (mg/L)	50 814 (14.77%)	10	1.40 (1.14-1.72)	1.25 (1.01-1.55)
Leukocytes (10^9 cells/L)	6 001 (3.19%)	11	1.95 (1.21-3.13)	1.98 (1.23-3.19)
Other				
Urea (mmol/L)	29 312 (7.65%)	7.20	1.21 (0.92-1.58)	1.10 (0.84-1.44)
y-glutamyl transferase (ukat/L)	47 824 (9.06%)	0.80	2.46 (2.09-2.91)	2.40 (2.02-2.85)
Alkaline phosphatase (ukat/L)	400 556 (81.02%)	1.92	1.88 (1.54-2.29)	1.74 (1.42-2.12)
BMI (kg/m2)	45 295 (34.26%)	25	1.97 (1.50-2.57)	1.88 (1.43-2.47)

HRs were estimated using adjusted Cox models with attained age as the underlying time scale and date of birth as the time origin. Model 1 was not adjusted; model 2 was adjusted for sex age at first blood sampling fasting status (overnight fasting vs non-fasting) occupation and country of birth. Abbreviations: CI confidence interval; HR hazard ratios; F female; FS fasting blood sample; M male; NFS non-fasting blood sample.

Table S3. HRs and 95% CIs of Type 1 Diabetes for high vs. low levels of biomarkers (stratified analyses by age).

A

Biomarker	Stratified by age: two segments (median age at measurement)			
	≤ 43 yrs		*> 43 yrs*	
	N	HR (95% CI)	N	HR (95% CI)
Biomarkers related to glycaemia				
Glucose (mmol/L)	264 227	6.63 (5.15-8.54)	259 875	4.15 (3.31-5.20)
Fructosamine (mmol/L)	209 813	2.16 (1.67-2.79)	221 738	2.54 (2.04-3.17)
Biomarkers of lipid metabolism				
Triglycerides (mmol/L)	269 859	2.23 (1.76-2.82)	272 975	2.52 (2.06-3.09)
Total cholesterol (mmol/L)	270 676	1.20 (0.95-1.51)	274 151	1.02 (0.85-1.22)
ApoB/A-I ratio	58 778	1.82 (1.29-2.56)	101 666	1.61 (1.19-2.16)
ApoA-I (g/L)	72 321	0.39 (0.25-0.60)	111 842	0.33 (0.22-0.50)
ApoB (g/L)	65 165	1.46 (0.92-2.31)	106 306	1.27 (0.95-1.70)
Biomarkers related to inflammation				
Haptoglobin (g/L)	204 286	1.87 (0.88-3.97)	206 870	1.59 (0.82-3.08)
Uric acid (umol/L)	250 758	1.69 (1.35-2.11)	253 175	1.79 (1.44-2.21)
Albumine (g/L)	241 569	2.54 (0.95-6.80)	256 323	0.91 (0.23-3.65)
C-reactive protein (mg/L)	157 361	1.07 (0.78-1.47)	186 617	1.42 (1.08-1.88)
Leukocytes (10^9 cells/L)	80 595	2.07 (1.06-4.06)	107 462	1.90 (0.97-3.72)
Other				
Urea (mmol/L)	181 326	0.78 (0.45-1.36)	201 822	1.25 (0.92-1.71)
y-glutamyl transferase (ukat/L)	264 223	2.83 (1.83-3.08)	263 606	2.42 (1.95-3.00)
Alkaline phosphatase (ukat/L)	241 504	1.72 (1.37-2.17)	252 876	1.76 (1.36-2.27)
BMI (kg/m2)	69 207	1.86 (1.27-2.73)	63 000	1.89 (1.32-2.71)

B

Biomarker	Stratified by age: three segments (quartiles of age at measurement)					
	< 33 yrs		*34-52 yrs*		*≥ 53 yrs*	
	N	HR (95% CI)	N	HR (95% CI)	N	HR (95% CI)
Biomarkers related to glycaemia						
Glucose (mmol/L)	127 257	5.12 (3.12-8.39)	256 415	5.55 (4.43-6.96)	140 430	4.18 (3.12-5.61)
Fructosamine (mmol/L)	101 161	2.06 (1.39-3.06)	211 313	2.39 (1.90-3.01)	119 077	2.54 (1.89-3.42)
Biomarkers of lipid metabolism						
Triglycerides (mmol/L)	129 266	1.71 (1.13-2.60)	264 659	2.33 (1.89-2.88)	148 909	2.92 (2.25-3.80)
Total cholesterol (mmol/L)	129 651	1.29 (0.84-1.98)	265 485	1.18 (0.98-1.42)	149 691	0.89 (0.70-1.13)
ApoB/A-I ratio	22 640	1.37 (0.78-2.41)	78 873	1.78 (1.31-2.41)	58 931	1.75 (1.17-2.60)
ApoA-I (g/L)	29 420	0.42 (0.23-0.78)	90 650	0.34 (0.23-0.52)	64 093	0.33 (0.20-0.56)
ApoB (g/L)	26 001	1.96 (0.84-4.53)	84 387	1.28 (0.91-1.80)	61 083	1.28 (0.87-1.88)
Biomarkers related to inflammation						
Haptoglobin (g/L)	96 162	1.82 (0.57-5.85)	201 002	1.65 (0.78-3.48)	113 992	1.70 (0.76-3.85)
Uric acid (umol/L)	120 812	1.49 (1.07-2.07)	243 246	1.88 (1.52-2.32)	139 875	1.71 (1.29-2.27)
Albumine (g/L)	117 681	2.43 (0.60-9.77)	235 679	2.14 (0.69-6.66)	144 532	0.64 (0.09-4.59)
C-reactive protein (mg/L)	75 278	0.98 (0.61-1.55)	167 649	1.36 (1.01-1.82)	101 051	1.31 (0.89-1.92)
Leukocytes (10^9 cells/L)	42 178	2.94 (1.18-7.32)	76 214	1.56 (0.77-3.18)	69 665	2.20 (0.90-5.39)
Other						
Urea (mmol/L)	86 131	1.07 (0.50-2.27)	180 989	0.92 (0.59-1.45)	116 028	1.27 (0.87-1.86)
y-glutamyl transferase (ukat/L)	129 491	2.09 (1.28-3.41)	252 332	2.76 (2.23-3.41)	146 006	1.90 (1.37-2.62)
Alkaline phosphatase (ukat/L)	117 421	1.70 (1.25-2.33)	234 315	1.76 (1.40-2.19)	142 644	1.72 (1.22-2.43)
BMI (kg/m2)	28 578	1.32 (0.72-2.43)	72 350	2.00 (1.40-2.84)	31 279	2.18 (1.35-3.50)

HRs were estimated using adjusted Cox models with attained age as the underlying time scale and date of birth as the time origin. Models were adjusted for sex age at first blood sampling fasting status (overnight fasting vs non-fasting) occupation and country of birth. Restricted analysis based on (A) median and (B) quartiles of age at biomarker measurement. In B) restricted analyses were performed with individuals < 18 and ≥ 18 years of age at measurement. Abbreviations: CI confidence interval; HR hazard ratios; YRS years.

Table S4. HRs and 95% CIs of Type 1 Diabetes for high vs. low levels of biomarkers (stratified analyses by sex and age of onset and fasting status).

A

Biomarker	Stratified by sex			
	Men		*Women*	
	N	HR (95% CI)	N	HR (95% CI)
Biomarkers related to glycaemia				
Glucose (mmol/L)	276 274	4.47 (3.58-5.58)	247 828	6.48 (4.80-8.75)
Fructosamine (mmol/L)	226 584	2.29 (1.87-2.81)	204 967	2.55 (1.89-3.46)
Biomarkers of lipid metabolism				
Triglycerides (mmol/L)	286 762	2.08 (1.73-2.50)	256 072	3.43 (2.56-4.60)
Total cholesterol (mmol/L)	287 889	0.99 (0.83-1.19)	256 938	1.17 (0.91-1.50)
ApoB/A-I ratio	89 616	1.60 (1.17-2.17)	70 828	1.75 (1.18-2.58)
ApoA-I (g/L)	103 016	0.36 (0.24-0.54)	81 147	0.37 (0.14-1.02)
ApoB (g/L)	95 262	1.12 (0.82-1.55)	76 209	1.65 (1.08-2.51)
Biomarkers related to inflammation				
Haptoglobin (g/L)	217 344	1.70 (0.93-3.10)	193 812	1.71 (4.80-8.75)
Uric acid (umol/L)	264 102	1.71 (1.44-2.03)	239 831	1.85 (1.19-2.89)
Albumine (g/L)	256 437	0.69 (0.10-4.95)	241 455	2.20 (0.91-5.33)
C-reactive protein (mg/L)	176 509	1.20 (0.91-1.59)	167 469	1.32 (0.94-1.85)
Leukocytes (10^9 cells/L)	80 434	2.07 (1.09-3.93)	107 623	1.90 (0.93-3.88)
Other				
Urea (mmol/L)	198 705	1.01 (0.73-1.39)	184 443	1.42 (0.86-2.36)
y-glutamyl transferase (ukat/L)	276 793	2.29 (1.88-2.79)	251 036	2.70 (1.92-3.80)
Alkaline phosphatase (ukat/L)	257 418	1.62 (1.20-2.18)	236 962	1.81 (1.37-2.38)
BMI (kg/m2)	58 584	2.04 (1.42-2.93)	73 623	1.55 (1.00-2.40)

B

Biomarker	Stratification limited by age of onset				Overnight fasted samples only	
	Age of onset ≤ 30 yrs		*Age of onset ≤ 40 yrs*			
	N (T1D cases)	HR (95% CI)	N (T1D cases)	HR (95% CI)	N	HR (95% CI)
Biomarkers related to glycaemia						
Glucose (mmol/L)	83	6.11 (2.38-15.70)	222	3.86 (2.11-7.05)	289 861	5.04 (4.15-6.10)
Fructosamine (mmol/L)	71	2.63 (1.29-45.36)	30	2.62 (1.75-3.93)	241 280	2.00 (1.59-2.50)
Biomarkers of lipid metabolism						
Triglycerides (mmol/L)	86	2.18 (1.04-4.57)	228	1.66 (1.05-2.62)	297 711	2.52 (2.02-3.16)
Total cholesterol (mmol/L)	86	1.15 (0.42-3.15)	228	0.90 (0.52-1.56)	297 714	1.02 (0.85-1.24)
ApoB/A-I ratio	13	1.35 (0.41-4.43)	47	1.06 (0.56-1.98)	98 419	1.69 (1.25-2.28)
ApoA-I (g/L)	16	0.22 (0.06-0.79)	54	0.28 (0.13-0.57)	107 601	0.37 (0.23-0.59)
ApoB (g/L)	18	1.71 (0.22-13.30)	54	1.11 (0.39-3.15)	102 337	1.13 (0.83-1.55)
Biomarkers related to inflammation						
Haptoglobin (g/L)	65	1.49 (0.19-11.90)	173	2.98 (1.07-8.32)	242 413	1.65 (0.82-3.32)
Uric acid (umol/L)	82	1.42 (0.70-2.87)	213	1.40 (0.94-2.07)	277 098	1.53 (1.23-1.90)
Albumine (g/L)	81	7.01 (1.71-28.70)	203	2.84 (0.70-11.50)	267 492	2.63 (1.09-6.34)
C-reactive protein (mg/L)	51	0.85 (0.35-2.04)	131	0.95 (0.56-1.61)	178 618	1.19 (0.90-1.57)
Leukocytes (10^9 cells/L)	22	3.01 (0.69-13.10)	55	2.67 (0.96-7.43)	92 690	0.92 (0.34-2.49)
Other						
Urea (mmol/L)	53	2.98 (1.05-8.46)	144	1.18 (0.52-2.69)	220 025	1.32 (0.94-1.86)
y-glutamyl transferase (ukat/L)	86	1.53 (0.48-4.89)	226	1.58 (0.88-2.85)	278 641	2.43 (1.92-3.07)
Alkaline phosphatase (ukat/L)	78	1.73 (0.81-3.71)	208	1.58 (1.03-2.43)	266 721	1.67 (1.30-2.16)
BMI (kg/m2)	15	0.81 (0.18-3.64)	48	1.72 (0.91-3.27)	NA	NA

Restricted analysis by (A) sex and (B) age of onset and values determined in fasting samples. HRs were estimated using adjusted Cox models with attained age as the underlying time scale and date of birth as the time origin. Models were adjusted for sex age at first blood sampling fasting status (overnight fasting vs non-fasting) [unless stratified for these specific variables] occupation and country of birth. Abbreviations: CI confidence interval; HR hazard ratios; NA not applicable; YRS years.

Table S5. ORs and 95% CIs of Type 1 Diabetes biomarker levels (nested case-control setup).
A

Biomarker	No. of individuals		OR (95% CI)	
	T1D cases	Controls	Continous biomarkers	Dichotomised biomarkers
Biomarkers related to glycaemia				
Glucose (mmol/L)	987	24 675	1.89 (1.68-2.13)	2.70 (2.05-3.55)
Fructosamine (mmol/L)	812	20 300	5.89 (3.55-9.79)	2.09 (1.64-2.67)
Biomarkers of lipid metabolism				
Triglycerides (mmol/L)	1 040	26 000	1.33 (1.27-1.40)	2.45 (2.08-2.89)
Total cholesterol (mmol/L)	1 040	26 000	0.97 (0.90-1.05)	0.91 (0.75-1.10)
ApoB/A-I ratio	305	7 625	2.11 (1.36-3.26)	1.46 (1.08-1.99)
ApoA-I (g/L)	348	8 700	0.38 (0.20-0.73)	0.40 (0.23-0.69)
ApoB (g/L)	332	8 300	1.36 (0.89-2.06)	1.19 (0.85-1.67)
Biomarkers related to inflammation				
Haptoglobin (g/L)	822	20 500	1.24 (0.95-1.61)	0.94 (0.49-1.82)
Uric acid (umol/L)	963	24 075	1.00 (1.00-1.00)	1.32 (1.07-1.63)
Albumine (g/L)	930	23 250	0.98 (0.95-1.01)	0.83 (0.24-2.88)
C-reactive protein (mg/L)	582	14 550	1.00 (1.00-1.00)	1.28 (1.03-1.60)
Leukocytes (10^9 cells/L)	323	8 075	1.13 (1.07-1.18)	2.12 (1.29-3.48)
Other				
Urea (mmol/L)	744	18 600	1.08 (1.00-1.16)	0.94 (0.64-1.37)
y-glutamyl transferase (ukat/L)	1 001	25 025	1.08 (1.00-1.16)	1.39 (1.09-1.76)
Alkaline phosphatase (ukat/L)	951	23 775	1.15 (1.09-1.22)	1.60 (1.23-2.07)
BMI (kg/m2)	228	5 700	4.93 (1.92-12.66)	1.91 (1.44-2.53)

B

Biomarker	No. of Individuals		OR (95% CI)			
			Continous biomarkers		Dichotomised biomarkers	
	T1D cases	Controls	Model 1	Model 2	Model 1	Model 2
Triglycerides (mmol/L)	227	5 675	1.26 (1.13-1.41)	1.26 (1.13-1.41)	1.82 (1.23-2.70)	1.80 (1.22-2.67)
ApoB/A-I ratio	72	1 800	1.11 (0.91-1.37)	1.11 (0.91-1.37)	1.30 (0.79-2.16)	1.28 (0.77-2.13)
ApoA-I (g/L)	88	2 200	0.69 (0.53-0.90)	0.70 (0.54-0.91)	0.48 (0.20-1.15)	0.48 (0.20-1.15)

A) ORs were estimated using conditional logistic regression with stratification on the matched sets. Models were adjusted for sex age at first blood sampling fasting status (overnight fasting vs non-fasting) occupation and country of birth. Abbreviations: CI confidence interval; OR odds ratios. B) Repeated analyses with additional adjustment of models for BMI for lipid biomarkers. Model 1 was adjusted for sex age at first blood sampling fasting status occupation and country of birth; model 2 was additionally adjusted for BMI.

Figure S1. **Overview of definition of Type 1 diabetes cases and censored individuals.**

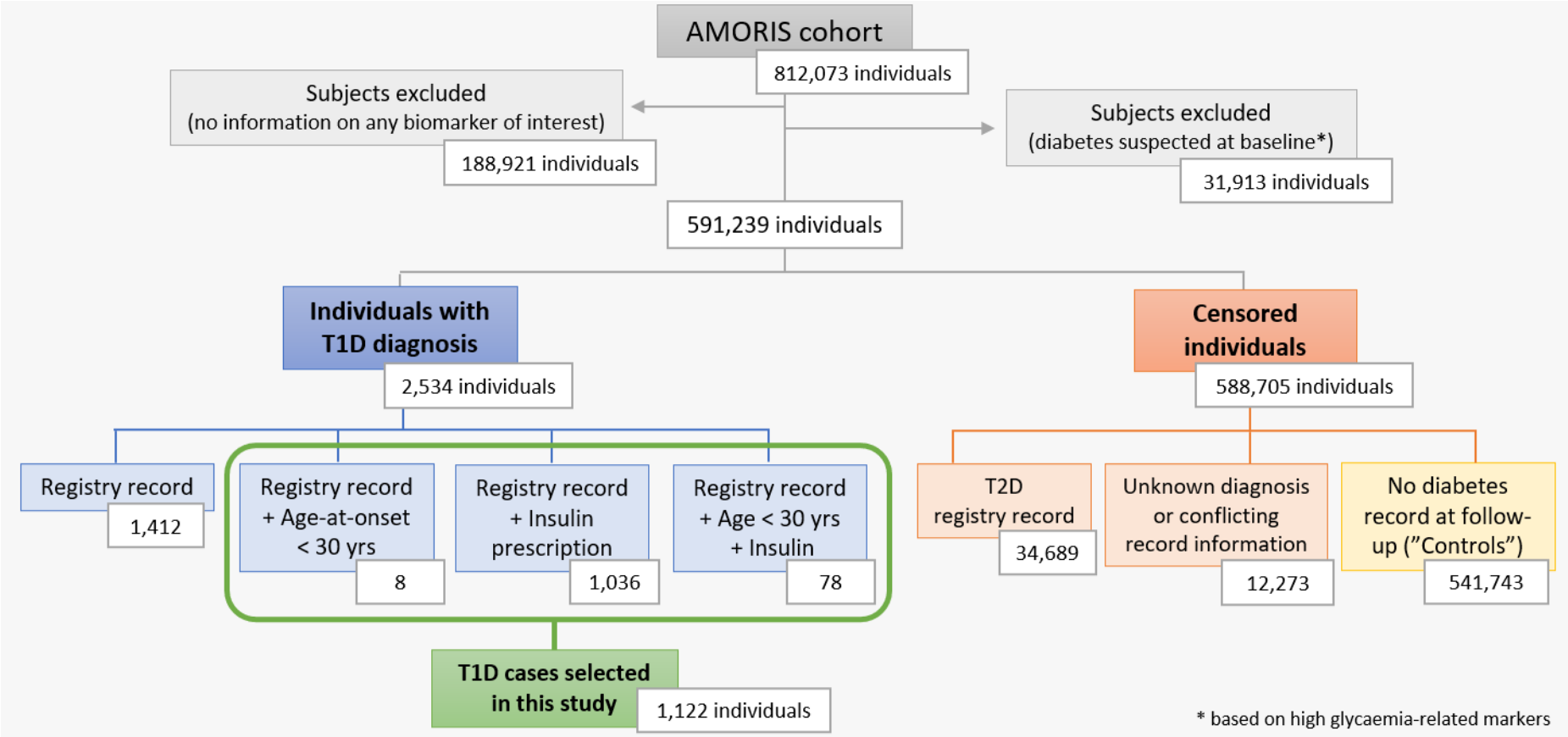
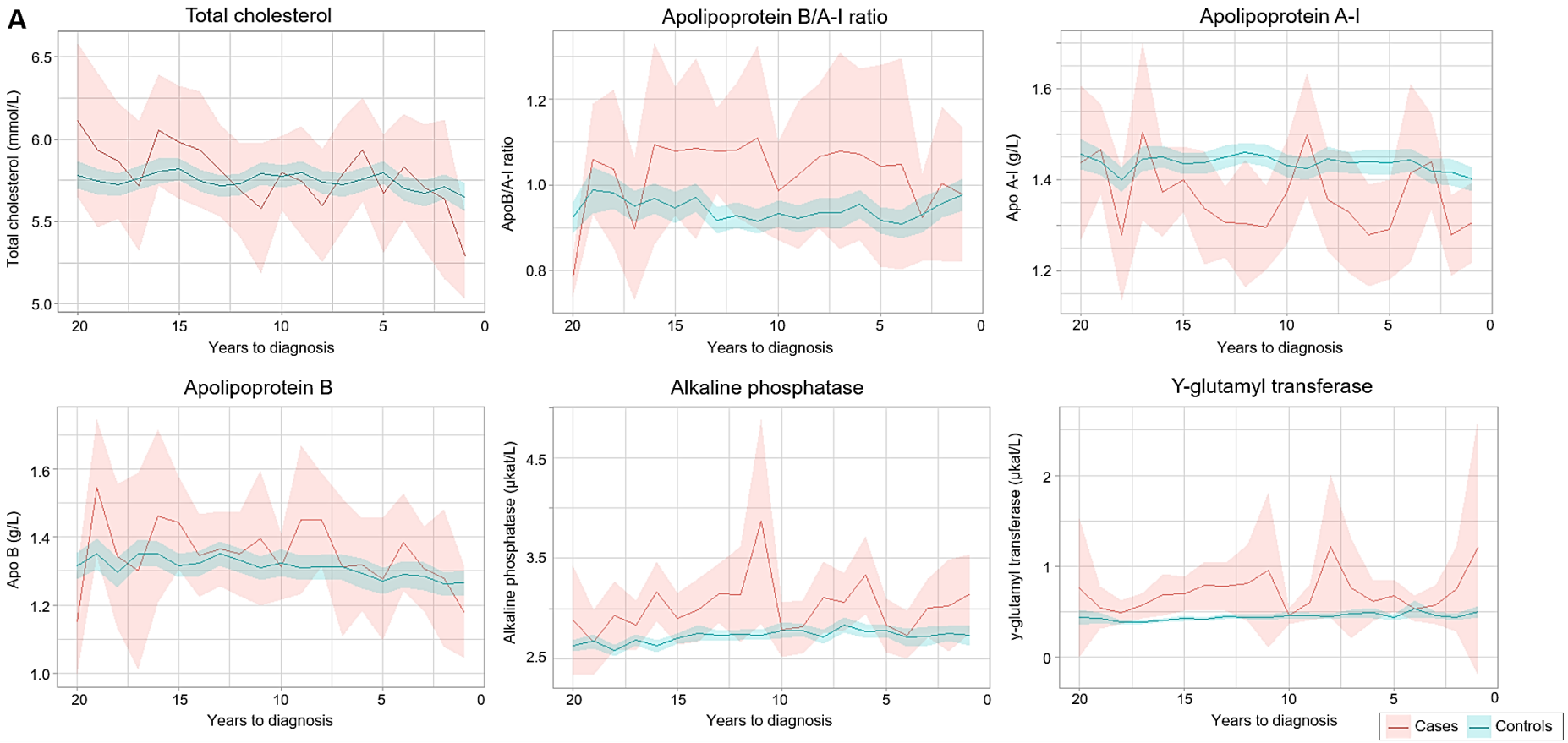
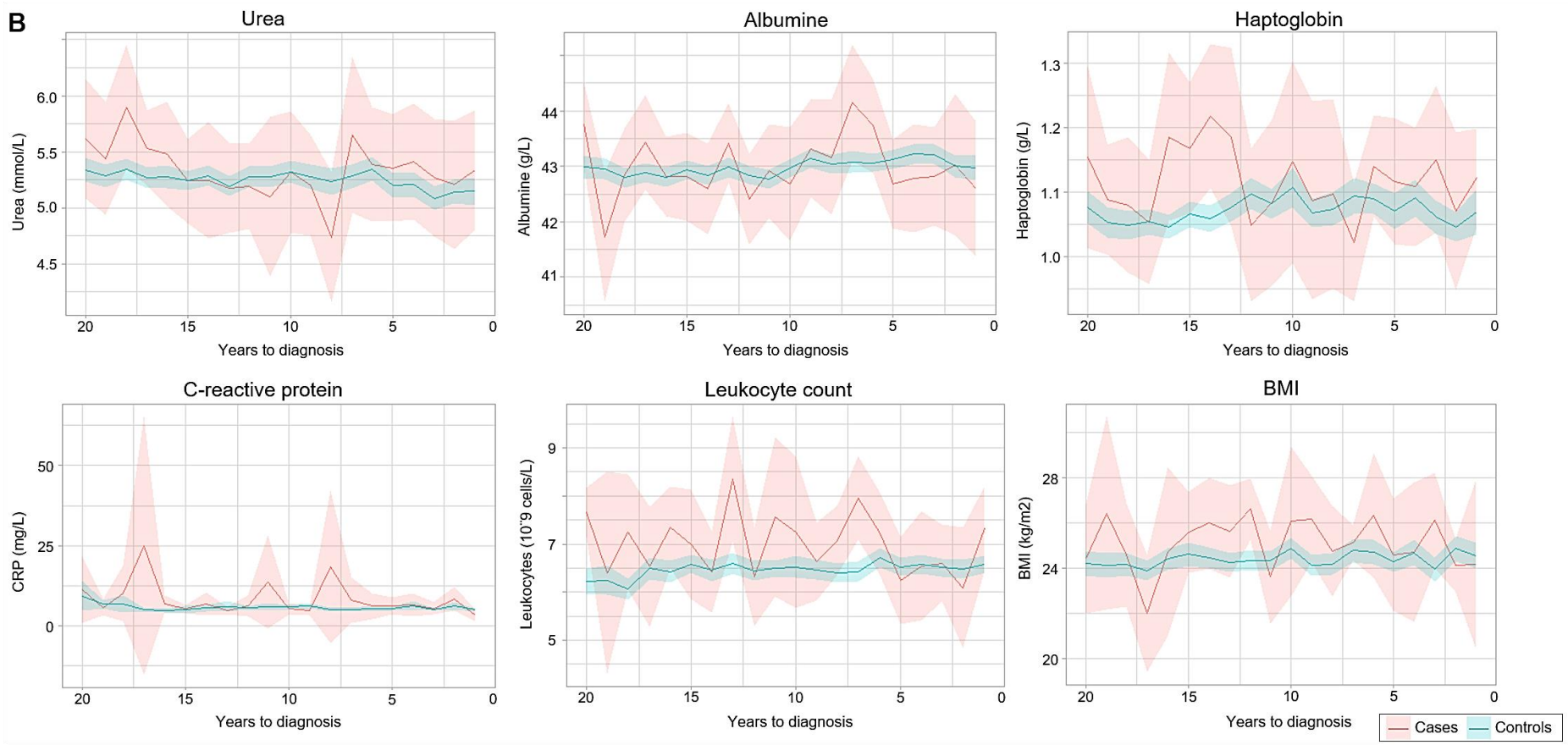


Figure S2. Trajectories of biomarker values during the 20 years before the diagnosis of Type 1 diabetes. Weighted mean biomarkers values and 95% confidence bands are plotted by time to index date for T1D cases (red) and controls (blue) respectively.




B
Urea
Urea (mmol/L)
6.0
5.5
5.0
4.5
Albumine
Albumine (g/L)
44
43
42
41
Haptoglobin
Haptoglobin (g/L)
1.3
1.2
1.1
1.0
C-reactive protein
CRP (mg/L)
50
25
0
Leukocyte count
Leukocytes (10^9 cells/L)
9
7
5
BMI
BMI (kg/m2)
28
24
20
20
15
10
5
0
Years to diagnosis
Cases
Controls