SUPPLEMENTARY DATA

Supplementary Table 1. Observed incidence rates of hypoglycemia hospitalization per 1000 person years in adults with type 1 and type 2 diabetes, in all years combined and by each single year*

	All years	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
Type 1 diabetes																	
Overall																	
Number of hospitalizations	1,591	38	60	51	66	65	76	97	119	118	115	132	130	168	112	121	123
Incidence rate	13.12	9.57	12.10	8.40	9.80	8.80	9.87	12.25	14.69	14.19	13.41	15.20	14.78	19.21	13.10	14.34	14.80
Subgroups																	
Age group																	
18-44 years	9.02	5.91	6.33	5.51	6.49	5.63	4.51	10.99	11.09	9.75	11.55	10.31	9.71	13.31	8.23	11.62	7.68
45-64 years	10.94	5.99	11.03	7.28	7.62	7.66	8.96	4.53	11.89	12.46	10.02	9.96	14.86	18.28	10.13	10.99	15.88
65-79 years	21.47	20.13	19.16	15.99	13.00	11.52	19.94	24.30	22.94	22.77	18.10	33.74	25.02	24.76	30.64	21.11	22.00
≥80 years	48.69	25.29	48.33	15.51	39.91	35.48	35.97	36.33	46.79	51.72	49.44	64.94	48.34	88.2	49.39	59.73	86.31
Gender																	
Male	12.05	8.31	10.57	7.14	10.79	8.22	9.61	12.57	12.58	12.67	13.49	13.69	12.24	17.01	12.59	12.03	14.07
Female	14.60	11.27	14.15	10.12	8.45	9.59	10.22	11.80	17.60	16.27	13.31	17.29	18.36	22.30	13.81	17.53	15.81
Diabetes duration																	
0-4 years	10.22	9.79	9.21	5.03	7.05	7.13	10.86	8.64	15.17	11.36	13.20	12.86	6.83	13.77	8.63	10.72	12.45
5-9 years	8.79	7.75	7.52	9.56	13.12	4.67	4.75	9.36	11.13	11.12	4.56	9.31	11.80	11.20	6.59	10.97	6.66
10-14 years	11.83	9.30	18.45	8.78	8.60	12.05	10.04	12.55	12.78	14.78	12.83	16.29	10.09	11.33	8.71	13.53	10.49
≥15 years	15.36	10.26	12.88	9.00	10.17	9.46	10.83	13.94	15.97	15.54	15.95	16.99	18.39	24.17	16.69	16.09	18.54
Type 2 Diabetes <65 years old																	
Overall																	
Number of hospitalizations	553	7	13	9	9	7	22	28	43	35	33	57	64	63	49	53	61
Incidence rate	0.99	0.73	1.03	0.54	0.44	0.28	0.77	0.86	1.19	0.88	0.76	1.24	1.33	1.26	0.97	1.05	1.19
Subgroups																	
Age group																	
18-44 years	0.73	0	0.63	0	0.36	0.29	0.77	0.22	0.98	0.72	0.99	0.63	0.75	1.02	1.00	0.86	0.70
45-64 years	1.03	0.84	1.09	0.62	0.46	0.28	0.77	0.97	1.23	0.90	0.73	1.34	1.42	1.29	0.96	1.08	1.27
Gender																	
Male	0.94	0.87	1.06	0.60	0.58	0.34	0.59	0.83	0.89	0.72	0.86	1.39	1.28	1.27	0.66	1.03	1.18
Female	1.05	0.53	0.99	0.45	0.25	0.2	1.05	0.92	1.64	1.11	0.63	1.02	1.39	1.24	1.42	1.08	1.21
Diabetes duration																	
0-9 years	0.70	0.62	0.57	0.22	0.41	0.24	0.50	0.73	0.79	0.75	0.50	1.00	1.01	0.97	0.73	0.59	0.69
≥10 years	2.24	1.36	3.52	2.16	0.60	0.51	2.22	1.57	3.34	1.56	2.09	2.36	2.74	2.44	1.85	2.57	2.80
Current glucose-lowering drugs																	

Insulin with/without NIGLD	4.33	3.72	4.87	1.22	1.28	1.04	3.07	2.99	4.88	3.85	3.24	6.00	6.10	5.52	3.61	4.99	6.30
Sulfonylureas with/without other NIGLD	0.64	0.66	0.68	0.66	0.35	0.31	0.49	0.65	1.08	0.51	0.48	0.75	0.63	0.87	0.94	0.55	0.44
Other§	0.21	0	0.20	0.15	0.24	0	0.22	0.31	0.11	0.18	0.17	0.08	0.30	0.25	0.25	0.25	0.27
Type 2 Diabetes ≥65 years old																	
Overall																	
Number of hospitalizations	3,185	15	42	53	88	120	136	158	204	225	251	327	346	329	316	324	251
Incidence rate	4.06	1.12	2.34	2.20	3.00	3.40	3.35	3.45	4.02	4.06	4.19	5.17	5.18	4.78	4.51	4.53	3.52
Subgroups																	
Age group																	
65-79 years	2.62	0.79	1.61	1.77	2.10	2.32	1.99	1.86	2.57	2.66	2.89	3.12	3.66	2.91	2.91	2.97	2.25
≥80 years	7.78	2.16	4.68	3.51	5.65	6.51	7.29	7.98	8.06	7.81	7.59	10.31	8.93	9.24	8.23	8.16	6.45
Gender																	
Male	3.81	0.90	2.57	1.99	2.30	3.30	2.95	2.61	3.54	3.92	4.24	4.73	4.83	4.16	4.55	4.41	3.57
Female	4.34	1.33	2.11	2.41	3.71	3.50	3.77	4.33	4.51	4.21	4.15	5.63	5.56	5.46	4.47	4.67	3.47
Diabetes duration																	
0-4 years	1.41	0.53	0.95	1.19	1.77	1.96	1.51	1.09	1.71	1.65	1.33	1.40	1.99	1.39	1.10	0.88	1.20
5-9 years	2.57	1.35	2.40	2.50	2.92	3.80	3.01	3.68	3.37	2.52	3.02	2.52	3.12	2.43	1.79	1.92	1.57
10-14 years	5.63	2.70	4.11	3.92	5.19	4.69	5.65	5.21	4.97	5.43	6.62	8.82	7.06	6.97	5.25	5.05	4.07
≥15 years	11.47	0.66	4.90	2.58	4.49	5.91	7.69	9.02	11.51	12.57	11.36	15.55	13.99	13.25	14.25	13.76	9.31
Current glucose-lowering drugs																	
Sulfonylureas only	5.10	1.09	2.34	2.50	2.36	4.76	5.50	4.35	4.33	5.74	4.46	7.76	10.68	9.21	6.05	7.71	6.65
Sulfonylureas + other NIGLD	4.63	0.87	1.89	2.67	4.16	3.35	2.94	4.70	5.45	4.20	4.81	5.98	5.61	5.19	5.09	4.49	5.33
Insulin only	19.70	7.20	10.47	7.87	7.63	13.39	16.95	11.08	14.98	20.02	16.44	25.08	23.80	27.95	23.55	29.25	20.01
Insulin + NIGLD	12.09	3.63	9.13	5.88	10.36	8.50	7.04	8.69	10.52	12.35	14.41	14.57	16.02	12.21	15.04	13.71	9.19
Other†	0.40	0.23	0.51	0	0.30	0.30	0.30	0.35	0.51	0.34	0.61	0.59	0.29	0.50	0.40	0.41	0.24

Abbreviation: NIGLD, non-insulin glucose-lowering drug.
*Cell counts <5 were not reported with specific values.
† Included self-management alone (i.e., not currently taking any glucose-lowering drug), non-insulin glucose-lowering drug monotherapy (excluding sulfonylureas) or combinations of any glucose-lowering drugs (excluding insulin and sulfonylureas).

SUPPLEMENTARY DATA

Supplementary Table 2. Trends in hypoglycemia hospitalization in elderly adults with type 2 diabetes after removing specific patients

	Trend 1			Trend 2		
	Period	APC (95% CI)	P	Period	APC (95% CI)	P
After removing users with insulin and non-insulin glucose-lowering drug	1998-2009	7.12 (3.88 to 10.47)	0.0005	2009-2013	-7.61 (-15.23 to 0.70)	0.07
After removing those with duration of diabetes ≥10 years	1998-2009	1.59 (-2.39 to 5.73)	0.40	2009-2013	-13.83 (-25.44 to -0.42)	0.04

Abbreviation: APC, annual percent change; CI, confidence interval.

SUPPLEMENTARY DATA

Supplementary Table 3. Proportion of patients with type 1 diabetes captured by each criterion of our case definition

Criteria	Description	Proportion,%
A*	≥1 type 1 code and use of insulin only	88.14
B	**≥1 type 1 code and use of insulin only on the diagnosis date and non-insulin glucose-lowering drug (NIGLD), if any, was introduced 6 months later**	**0.62**
C	**≥2 insulin prescriptions only and ≥1 unspecified diabetes code**	**11.24**
	Total	100

Abbreviation: NIGLD, non-insulin glucose-lowering drug.
Criteria most likely to misclassify diabetes type were in bold.
* 14.72% of the type 1 patients captured by criterion A had at least one type 2 code.

SUPPLEMENTARY DATA

Supplementary Table 4. Proportion of patients with type 2 diabetes captured by each criterion of our case definition

Criteria	Description	Proportion,%
A	≥2 type 2 codes and 0 type 1 code, regardless of drug use	81.58
B	≥1 type 2 code and 0 type 1 code and non-insulin glucose-lowering drug (NIGLD) only	4.33
C	**≥1 type 2 code and 0 type 1 code and on NIGLD and insulin, but NIGLD prescribed no later than insulin**	**0.33**
D	≥2 classes of NIGLD	12.16
E	≥2 prescriptions of a non-insulin non-metformin glucose-lowering drug only and ≥1 unspecified diabetes code	1.60
	Total	100

Abbreviation: NIGLD, non-insulin glucose-lowering drug.
The criterion most likely to misclassify diabetes type was in bold.

SUPPLEMENTARY DATA

Supplementary Table 5. Trends of hypoglycemia hospitalization in adults with type 1 and type 2 diabetes

Population	Period	Annual percent change (95% CI)	
		New case definition*	Original case definition†
Patients with type 1 diabetes	1998-2013	3.24 (1.15, 5.38)	3.74 (1.70, 5.83)
Young and middle aged patients with type 2 diabetes	1998-2013	4.06 (0.38, 7.88)	4.12 (0.61, 7.75)
Elderly patients with type 2 diabetes	1998-2009	8.96 (6.16, 11.84)	8.59 (5.76, 11.50)
	2009-2013	-8.10 (-14.29, -1.47)	-8.05 (-14.48, -1.13)

*New case definition removed the bold-highlighted criteria in the Supplementary Table 3 and 4.
†Original case definition kept all criteria.

SUPPLEMENTARY DATA

Supplementary Table 6. Trends of hypoglycemia hospitalization using exactly the same published case definitions for type 2 diabetes from the CPRD literature

Authors	Published type 2 diabetes definition	Population (years of age)	period	Annual percent change (95% CI)	*P*
Bannister et al.(1)	*1) c*linical codes exclusively indicative of type 2 diabetes; *2*) at least one clinical code indicative of type 2 diabetes (regardless of others indicative of type 1 or nonspecific diabetes) and at least one prescription for an oral hypoglycemic agent (OHA); *3*) prescription of two or more classes of OHA; and *4*) diagnoses of both type 1 and type 2 diabetes and an age of diagnosis older than 35 years.	18-64	1998-2013	3.05 (-0.04, 6.24)	0.05
		≥65	1998-2009	8.88 (6.56, 11.26)	<0.0001
			2009-2013	-7.74 (-13.00, -2.16)	0.01
Currie et al.(2)	1) more than one diagnosis recorded exclusively for T2DM; 2) prescription of two or more differing classes of oral antidiabetic drug; or 3) a diagnostic code indicative of T2DM (regardless of a conflicting diagnosis of type 1 or nonspecific diabetes) plus a prescription for an oral antidiabetic drug.	18-64	1998-2013	3.00 (-0.22, 6.32)	0.07
		≥65	1998-2009	9.07 (6.74, 11.46)	<0.0001
			2009-2013	-8.09 (-13.34, -2.53)	0.009
Hirji et al.(3)	2 OXMIS/Read codes of type 2 diabetes or 1 OXMIS/Read code plus one oral anti-diabetic drug (OAD) or 2 continuous OAD treatments	18-64	1998-2013	2.61 (-0.43, 5.73)	0.09
		≥65	1998-2009	9.65 (7.10, 12.25)	<0.0001
			2009-2013	-8.35 (-14.00, -2.32)	0.01

SUPPLEMENTARY DATA

References

1. Bannister CA, Poole CD, Jenkins-Jones S, et al. External validation of the UKPDS risk engine in incident type 2 diabetes: A need for new type 2 diabetes-specific risk equations. Diabetes Care 2014;37:537-545

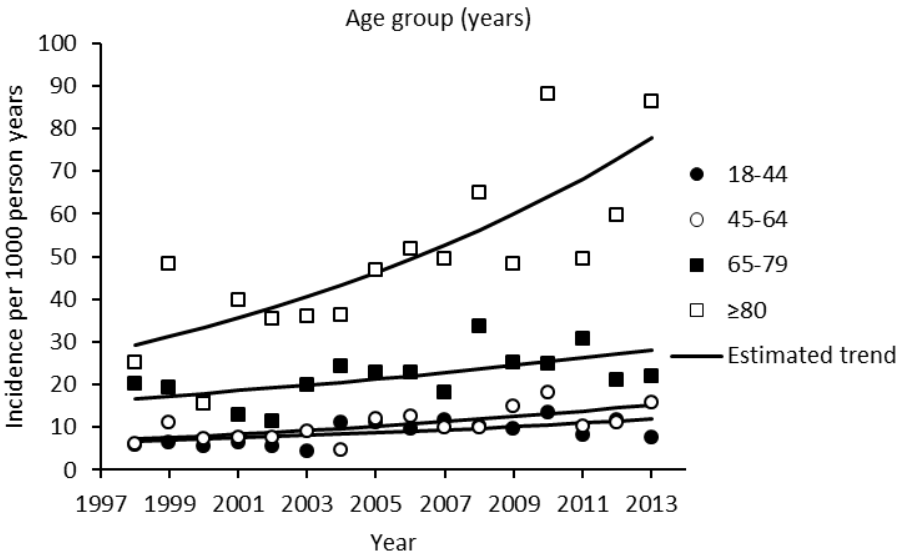
2. Currie CJ, Poole CD, Evans M, Peters JR, Morgan CL. Mortality and other important diabetes-related outcomes with insulin vs other antihyperglycemic therapies in type 2 diabetes. J Clin Endocrinol Metab 2013;98:668-677

3. Hirji I, Andersson SW, Guo Z, Hammar N, Gomez-Caminero A. Incidence of genital infection among patients with type 2 diabetes in the UK General Practice Research Database. J Diabetes Complications 2012;26:501-505

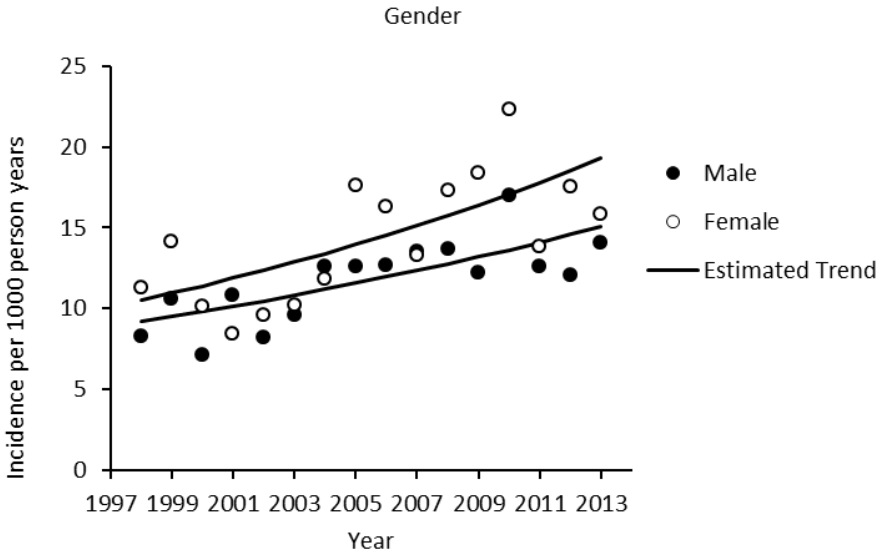
SUPPLEMENTARY DATA

Supplementary Figure 1. Incidence and trends in hypoglycemia hospitalization in adults with type 1 diabetes by age (1A), gender (1B), and length of recorded diabetes history (1C)

1A

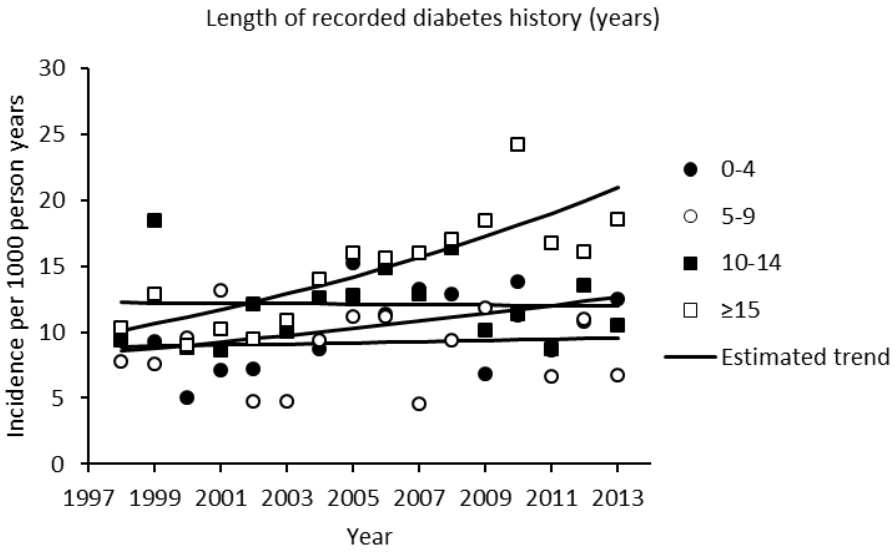


1B



1C

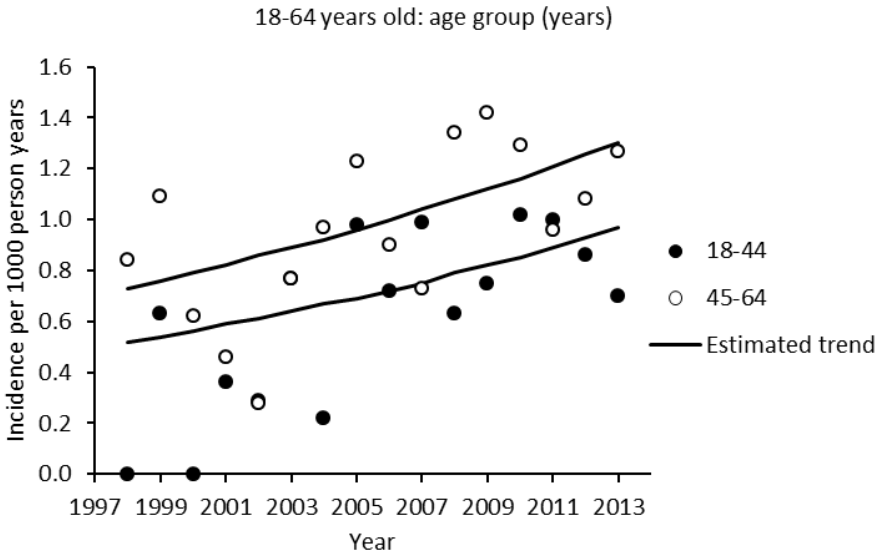
SUPPLEMENTARY DATA



SUPPLEMENTARY DATA

Supplementary Figure 2. Incidence and trends in hypoglycemia hospitalization in adults with type 2 diabetes by age (2A, 2B), gender (2C, 2D), length of recorded diabetes history (2E, 2F), and current use of glucose-lowering medications (2G, 2H)

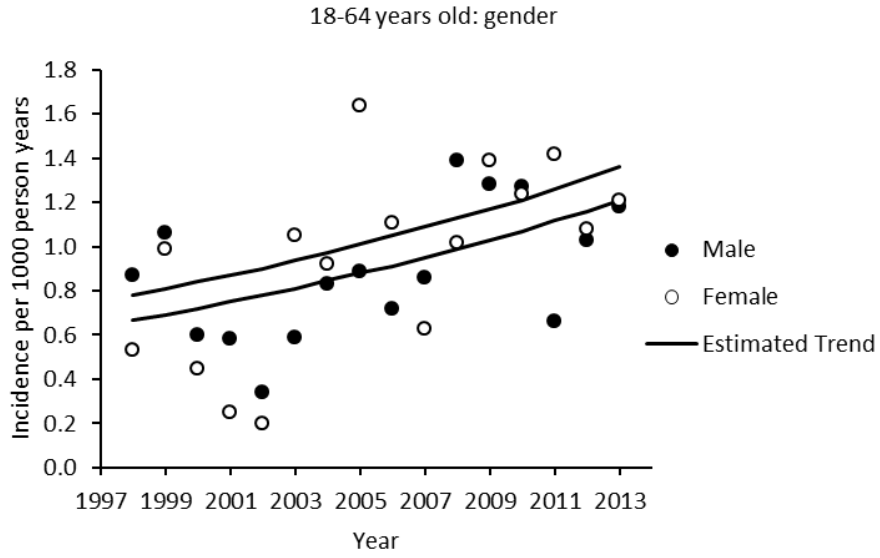
2A



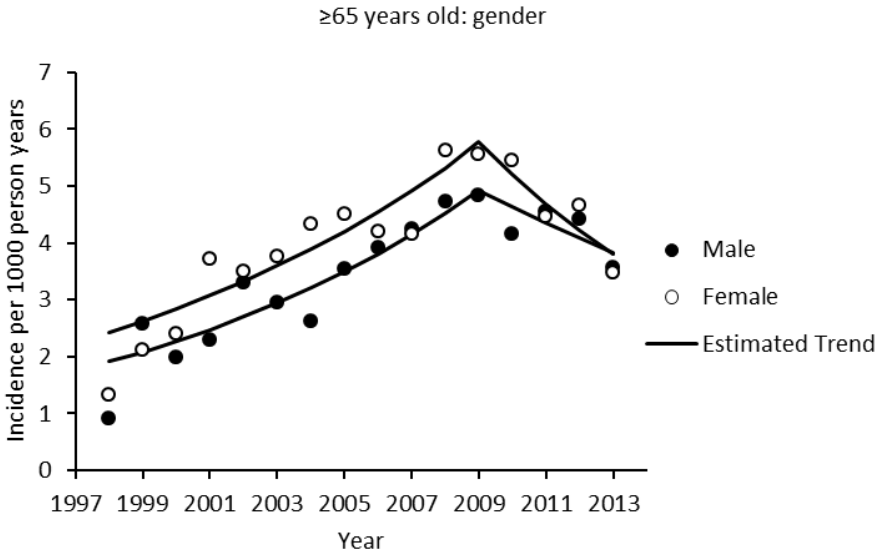
2B

2C

SUPPLEMENTARY DATA



2D



2E

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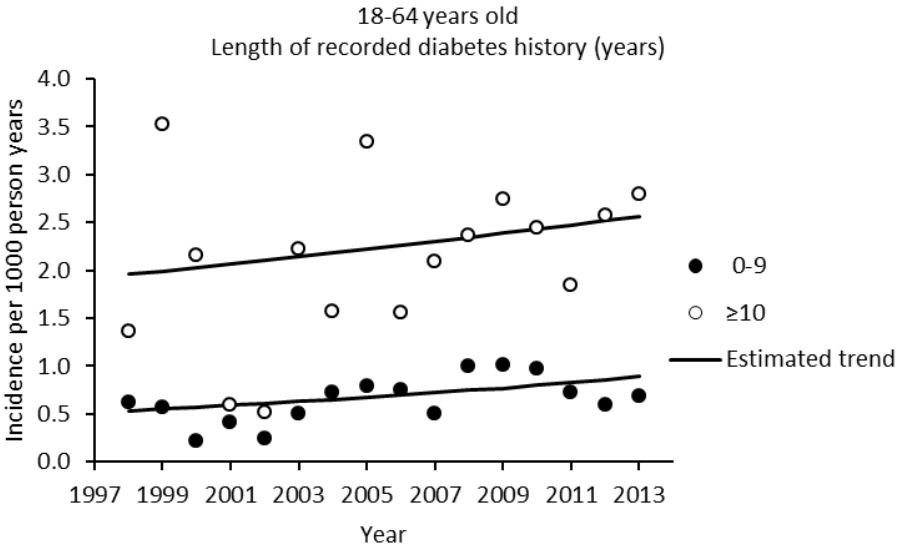
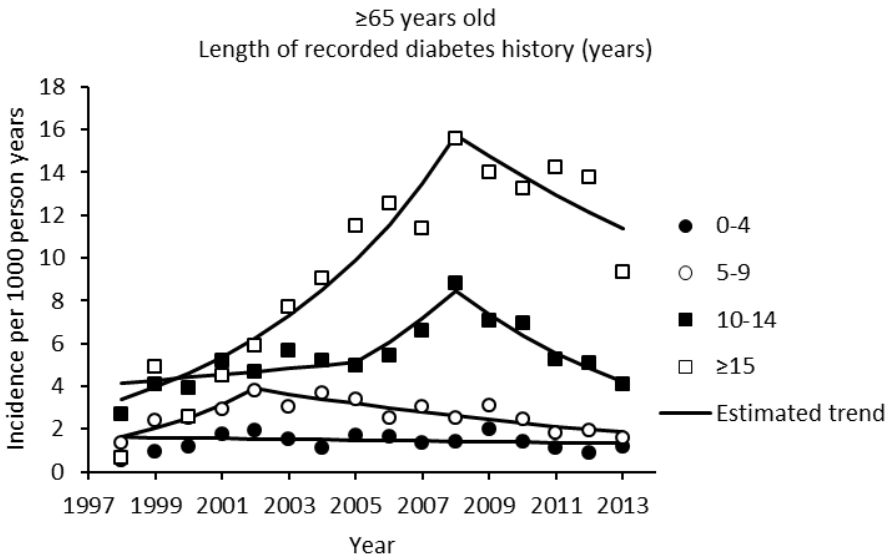
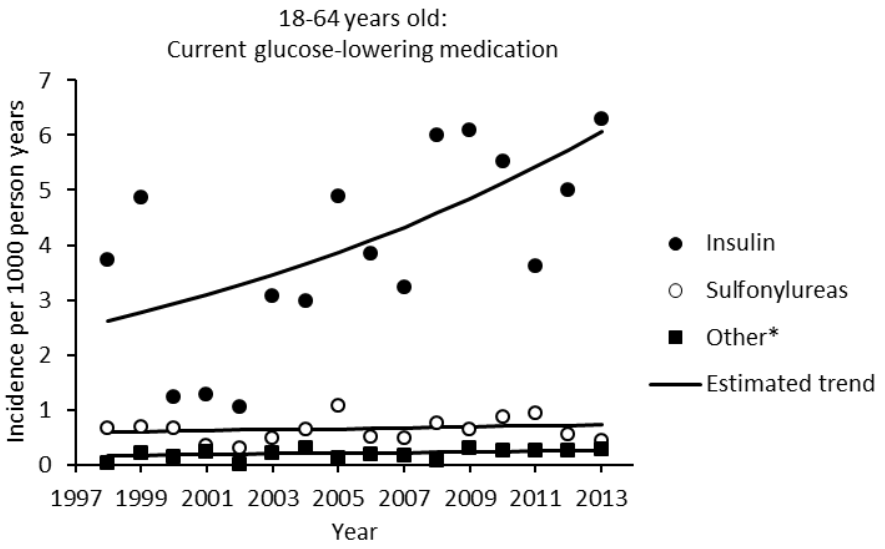


2F

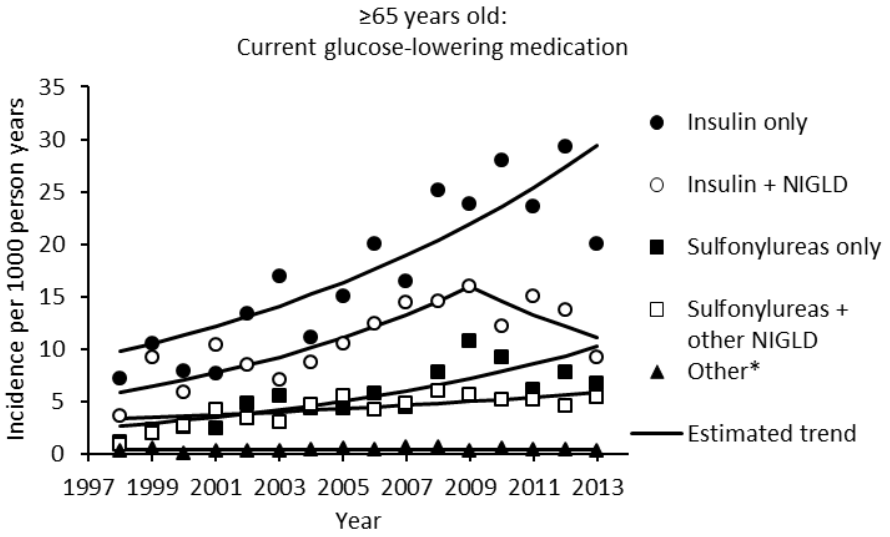


2G

SUPPLEMENTARY DATA



2H

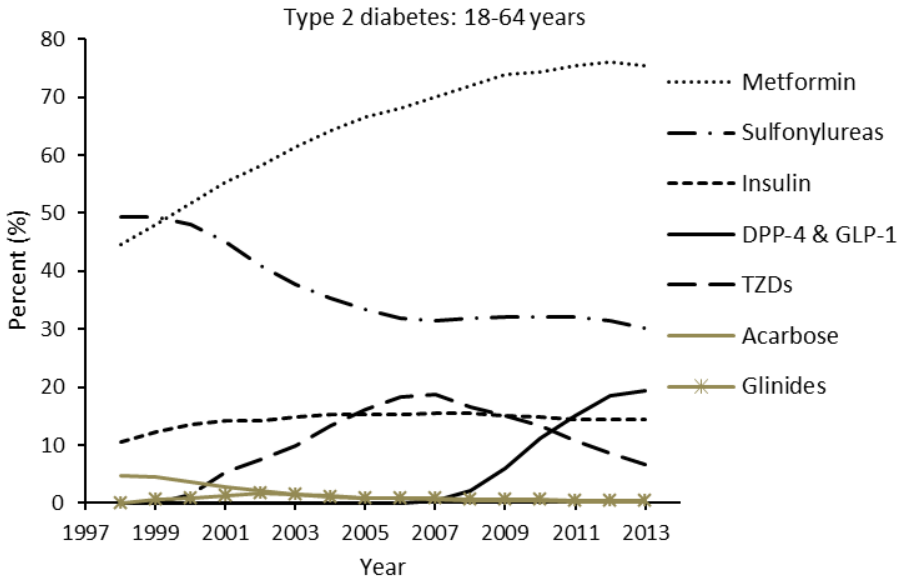


Legend: NIGLD, non-insulin glucose-lowering drug. * "Other" in Fig. 2G and 2H included self-management alone (i.e., currently not taking any glucose-lowering drug), non-insulin glucose-lowering drug monotherapy (excluding sulfonylureas) or combinations of any glucose-lowering drugs (excluding insulin and sulfonylureas).

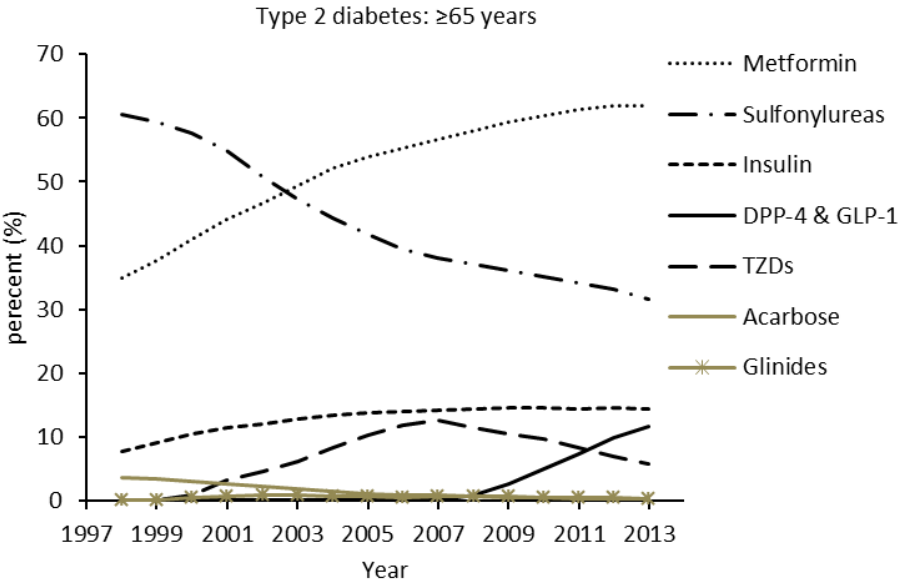
SUPPLEMENTARY DATA

Supplementary Figure 3. Trends in current use of glucose-lowering medications in young and middle aged adults (3A) and elderly adults (3B) with type 2 diabetes

3A



3B



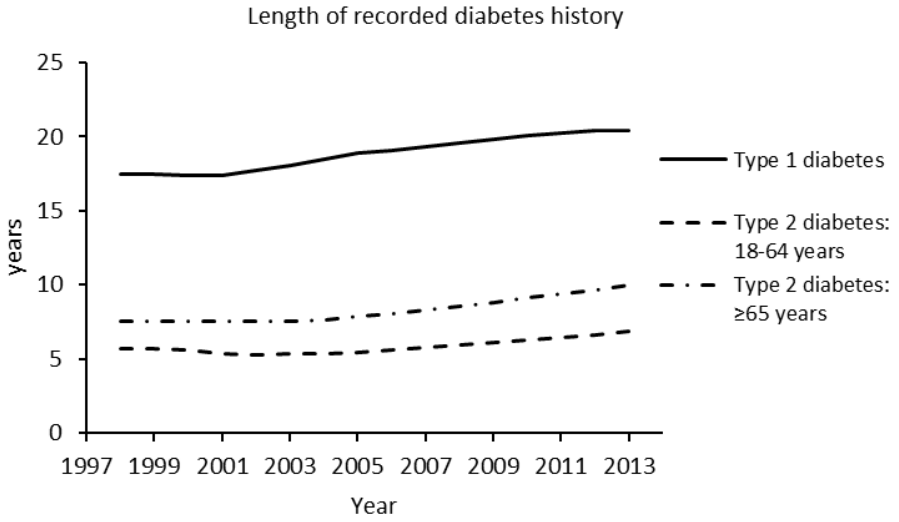
Legend: DPP-4, dipeptidyl peptidase-4 inhibitors; GLP-1, glucagon-like peptide-1 receptor agonists; TZDs, thiazolidinediones. Use of sodium-glucose co-transporter-2 inhibitors was not plotted because it had not been used until 2013.

SUPPLEMENTARY DATA

Supplementary Figure 4. Trends in age (4A), length of recorded diabetes history (4B), BMI (4C), and Charlson comorbidity score (4D)

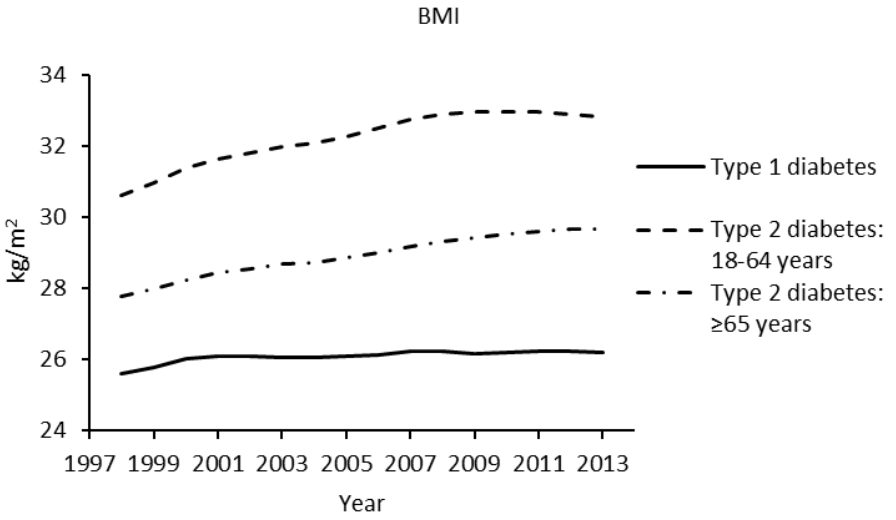
4A

4B

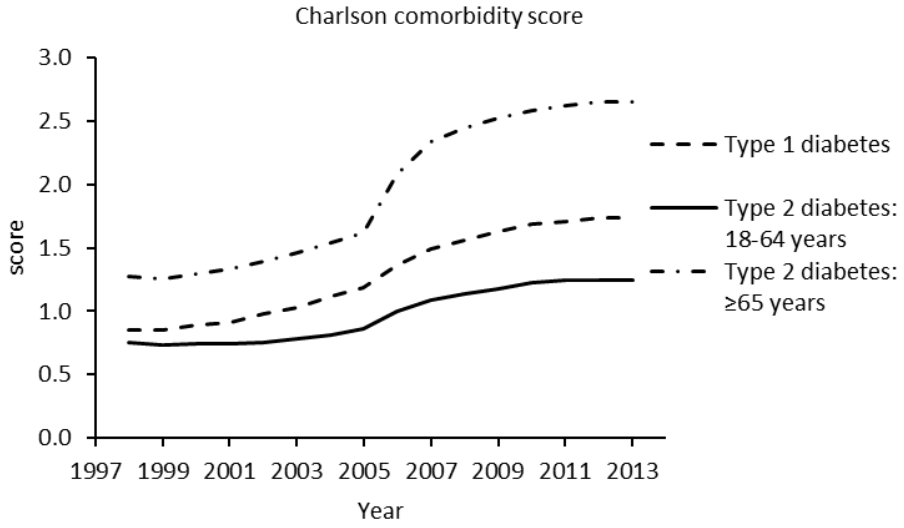


4C

SUPPLEMENTARY DATA



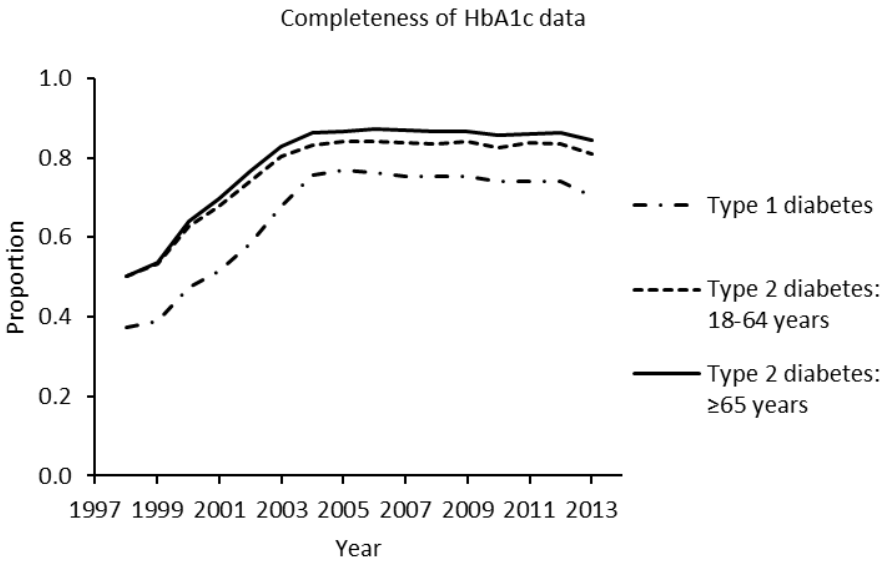
4D



SUPPLEMENTARY DATA

Supplementary Figure 5. Trends in completeness of HbA1c (5A) and BMI data (5B)

5A



5B