

Supplementary material

Assessment of channelling bias among initiators of glucose lowering drugs - A UK cohort study

Authors

On behalf of GetReal Work Package 2

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In the supplementary material the following can be found

- **Figure S1** Flow chart.
- **Figure S2** Histograms of propensity score over time. GLP-1 versus basal insulin and DPP-4i versus sulfonylurea. Intention-to-treat and per-protocol cohorts.
- **Figure S3** Characteristics over time in GLP-1 versus basal insulin. Individual covariates.
- **Figure S4** Characteristics over time in DPP-4i versus sulfonylurea. Individual covariates.
- **Table S1** Standardized difference before and after matching in GLP-1 versus basal insulin
- **Table S2** Standardized difference before and after matching DPP-4i versus sulfonylurea

Figure S1 Flow chart.

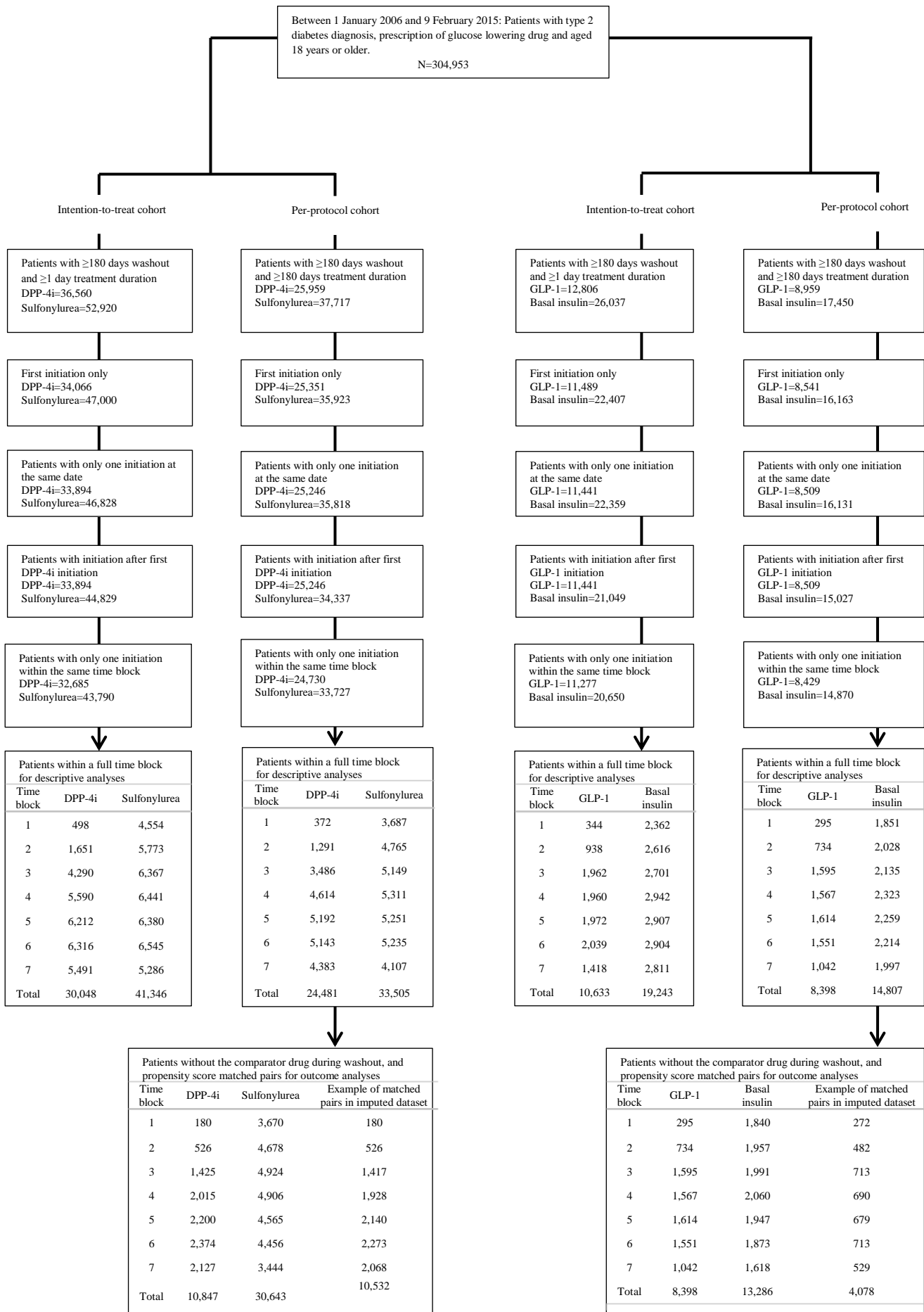
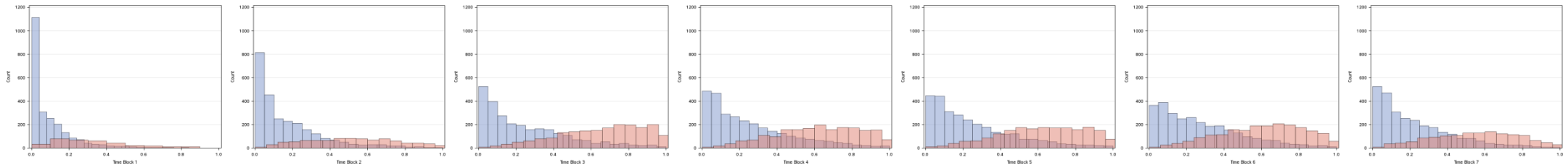
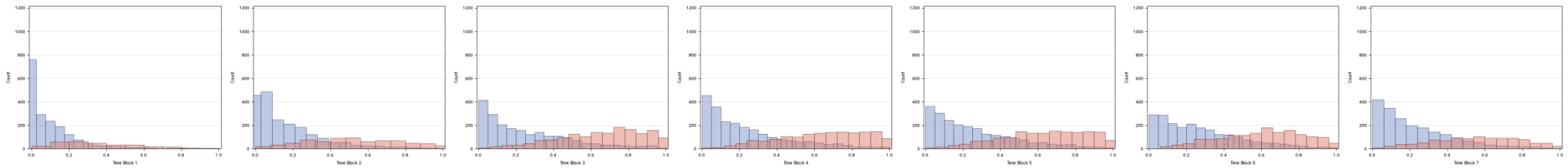


Figure S2 Histograms of propensity score over time. Intention-to-treat and per-protocol cohorts of all identified initiators of GLP-1 and insulin, and DPP-4i and sulfonylurea, respectively. Blue: GLP-1 and DPP-4i initiators, respectively. Red: insulin and sulfonylurea initiators, respectively.

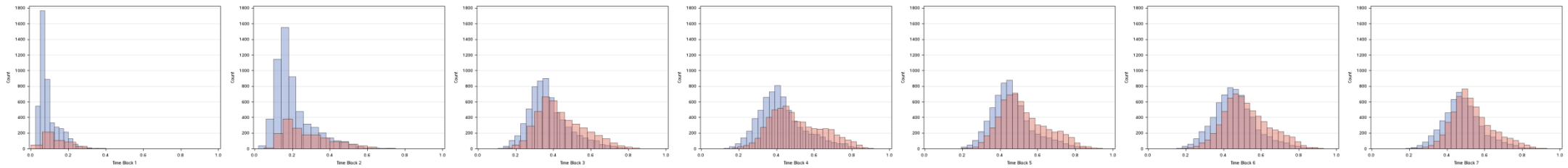
GLP-1 vs. basal insulin, intention-to-treat cohort



GLP-1 vs. basal insulin, per-protocol cohort



DPP-4i vs. sulfonylurea, intention-to-treat cohort



DPP-4i vs. sulfonylurea, per-protocol cohort

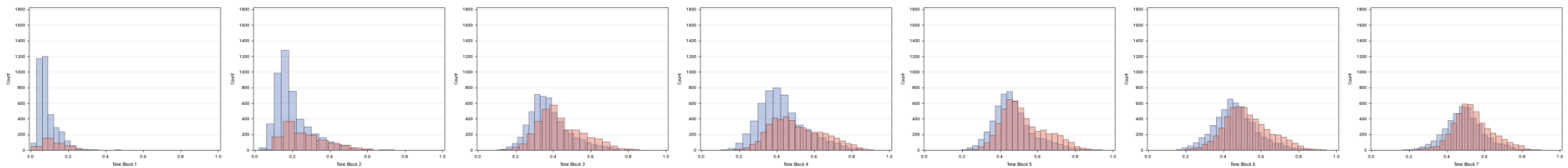


Figure S3 Characteristics over time in GLP-1 versus basal insulin. Mean and 95%CI. Green dash line and triangle: GLP-1 initiators from intention-to-treat cohort. Blue solid line and triangle: GLP-1 initiators from per-protocol cohort. Purple dash line and square: insulin initiators from intention-to-treat cohort. Red solid line and square: insulin initiators from per-protocol cohort.

For GLP-1 initiators first a decrease and then an increase in HbA1c at index was observed, while a steady increase in HbA1c at index for insulin initiators were seen, however, still within a change in HbA1c of 0.5%. For both GLP-1 and insulin initiators an increase in use of DPP-4i during washout and a decrease in use of other oral glucose-lowering during washout were seen. For insulin initiators only an increase in use of sulfonylurea, GLP-1 and metformin during washout were seen. No clinically meaningful changes were observed for initiators of neither GLP-1 nor insulin in the other covariates.

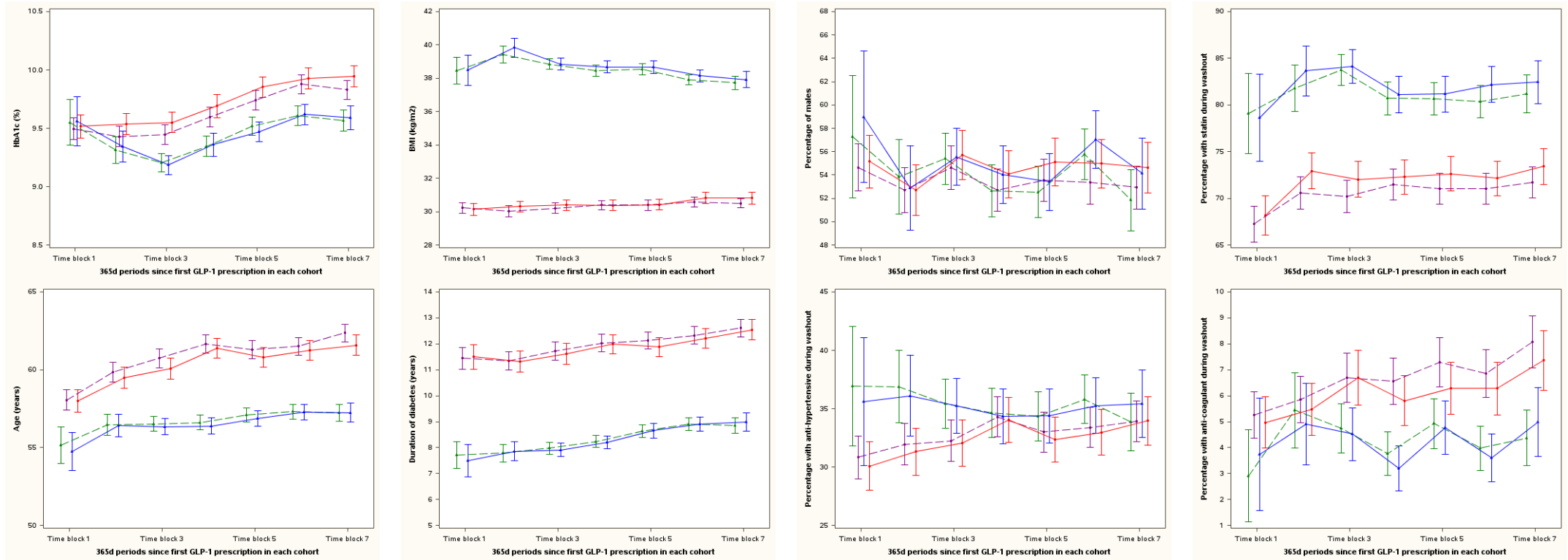


Figure S3 continued

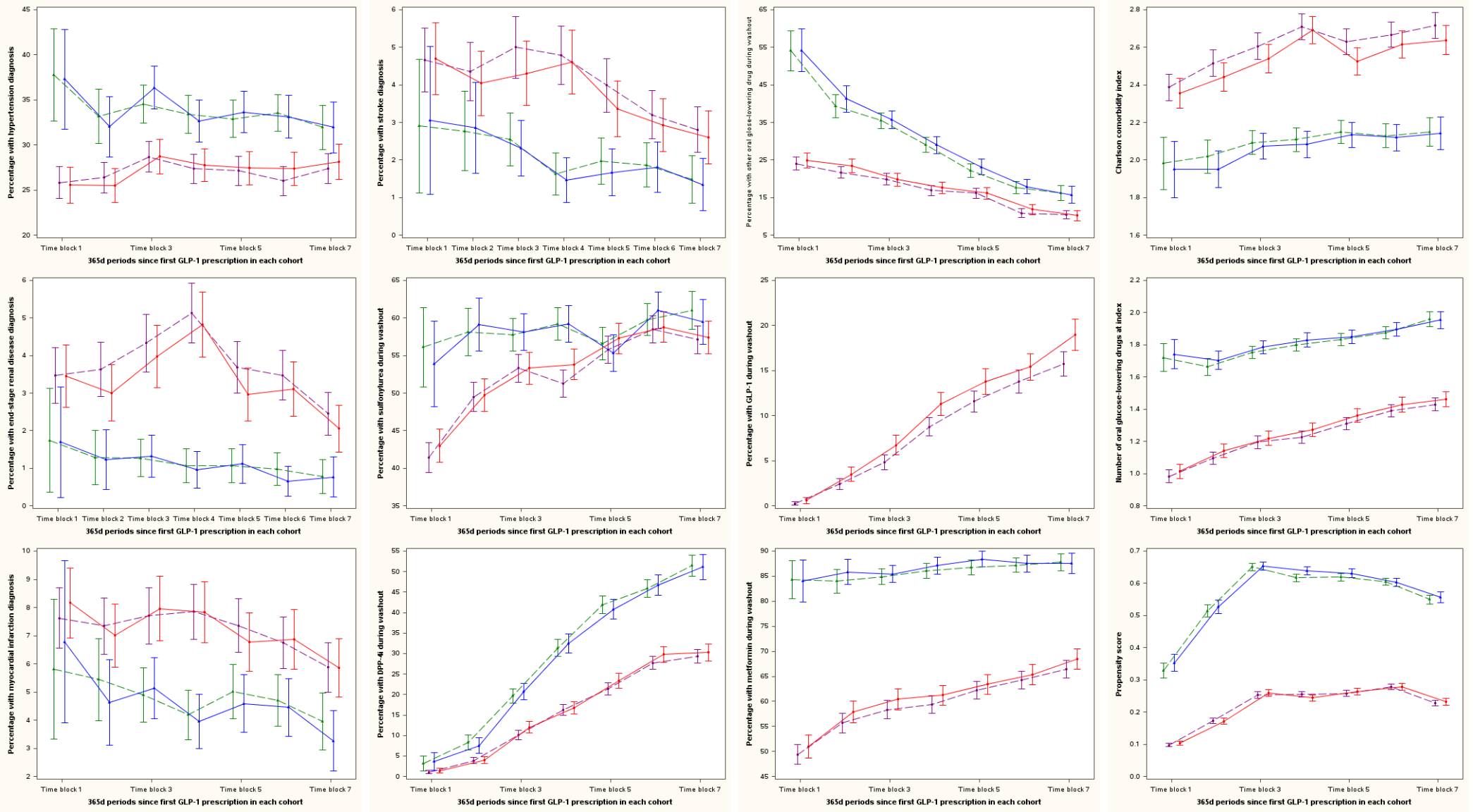


Figure S4 Characteristics over time in DPP-4i versus sulfonylurea. Mean and 95%CI. Orange dash line and circle: DPP-4i initiators from intention-to-treat cohort. Cyan solid line and circle: DPP-4i initiators from per-protocol cohort. Pink dash line and diamond: Sulfonylurea initiators from intention-to-treat cohort. Dark blue solid line and diamond: Sulfonylurea initiators from per-protocol cohort.

An increase in duration of diabetes and use of metformin during washout, and a decrease in other oral glucose-lowering drugs during washout were seen among DPP-4i and sulfonylurea initiators. For sulfonylurea initiators only, a minor increase in HbA1c at index, and an increase in use of DPP-4i and GLP-1 during washout were seen. No clinically meaningful changes were observed for initiators of neither DPP4i nor sulfonylurea in the other covariates.

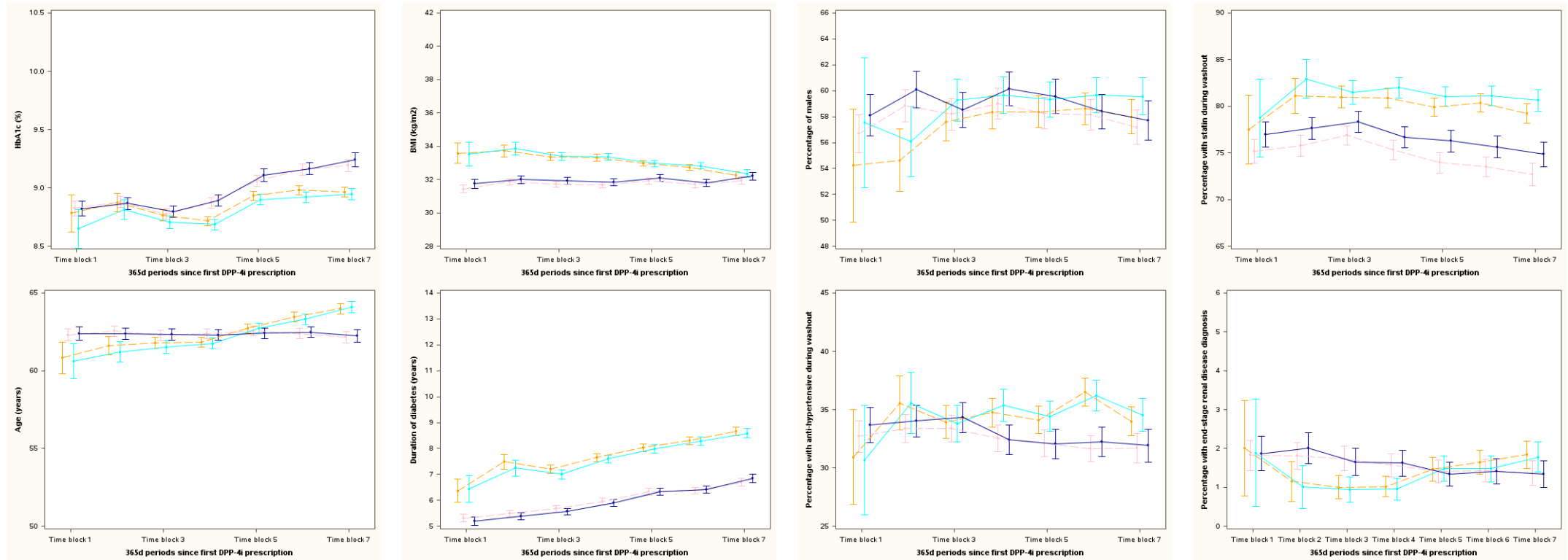


Figure S4 continued

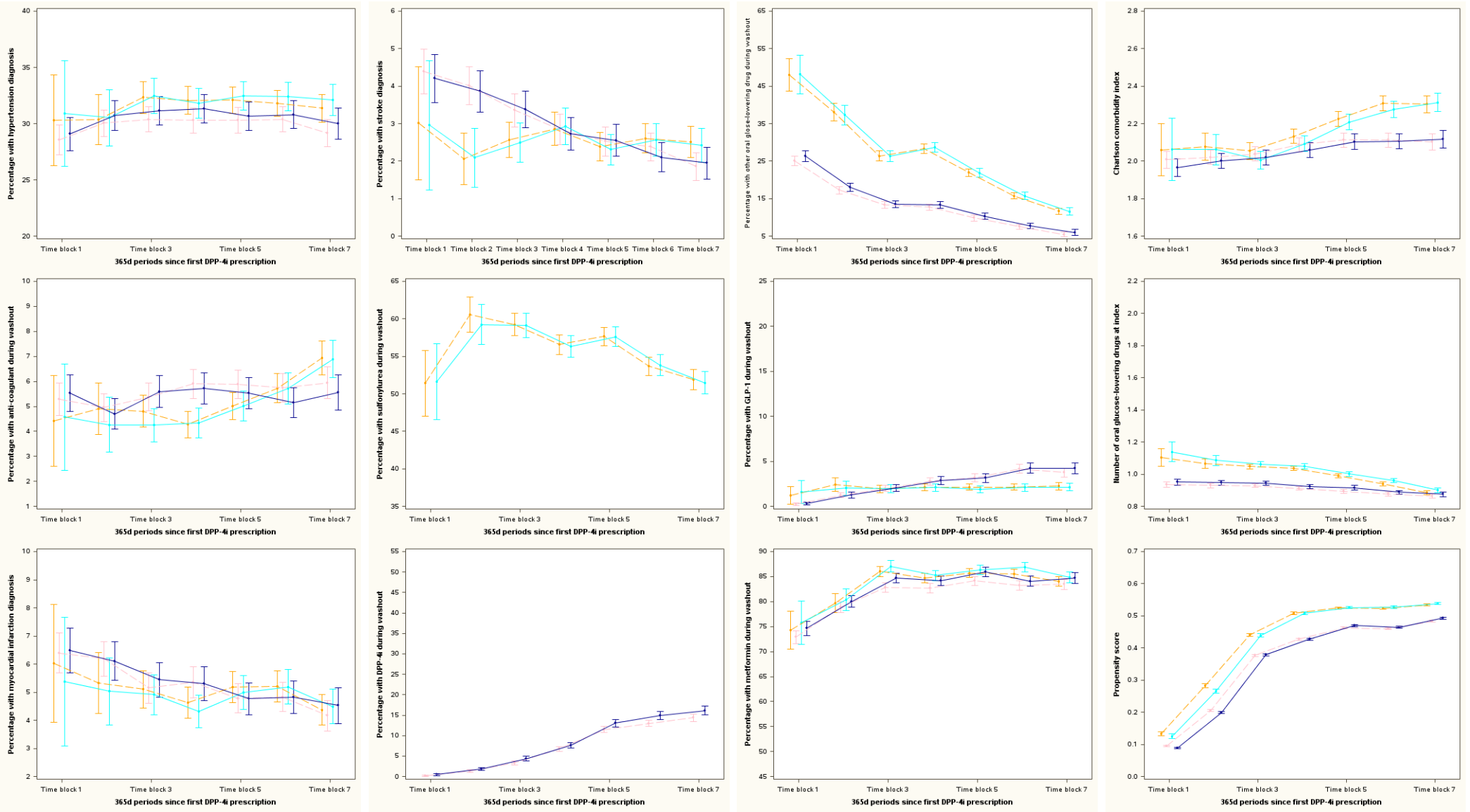


Table S1 Standardized difference before and after matching in GLP-1 versus basal insulin initiators

Time block	BMI	Diabetes duration	age	HbA1c	Charlson comorbidity index	Number of other oral glycoside-lowering drugs	males	Any use during washout							Any diagnosis of			
								Anti-hypertension	statin	Anti-coagulants	Other oral glucose-lowering drugs	metformin	sulfonylurea	DPP-4i	Hypertension	End-stage renal disease	Myocardial infarction	stroke
BEFORE MATCHING																		
1	1.159	-0.493	-0.240	0.024	-0.261	0.806	0.077	0.117	0.239	-0.061	0.630	0.755	0.219	0.147	0.255	-0.111	-0.052	-0.086
2	1.323	-0.461	-0.236	-0.107	-0.316	0.629	0.003	0.102	0.262	-0.026	0.389	0.654	0.189	0.153	0.145	-0.124	-0.101	-0.065
3	1.238	-0.495	-0.274	-0.210	-0.289	0.605	-0.003	0.068	0.296	-0.095	0.362	0.587	0.097	0.238	0.164	-0.167	-0.114	-0.111
4	1.221	-0.523	-0.378	-0.184	-0.375	0.586	0.000	0.006	0.210	-0.127	0.271	0.618	0.109	0.370	0.107	-0.232	-0.165	-0.184
5	1.193	-0.437	-0.302	-0.211	-0.247	0.506	-0.034	0.043	0.203	-0.066	0.175	0.612	-0.039	0.379	0.135	-0.131	-0.095	-0.108
6	1.057	-0.443	-0.309	-0.174	-0.316	0.483	0.042	0.048	0.242	-0.123	0.170	0.540	0.046	0.352	0.126	-0.183	-0.105	-0.074
7	1.047	-0.472	-0.341	-0.197	-0.307	0.509	-0.010	0.031	0.219	-0.099	0.165	0.472	0.043	0.436	0.083	-0.109	-0.125	-0.091
AFTER MATCHING																		
1	0.003	0.041	-0.008	-0.022	-0.012	-0.028	0.015	0.023	-0.011	-0.028	0.020	-0.042	-0.025	-0.021	0.024	0.025	-0.017	-0.019
2	0.009	0.013	-0.011	-0.002	-0.026	0.008	-0.004	-0.003	-0.030	-0.020	-0.004	-0.002	0.007	0.014	-0.015	-0.022	0.011	-0.023
3	0.030	0.019	0.006	0.001	-0.016	-0.034	-0.014	0.011	-0.013	-0.008	-0.006	-0.019	-0.024	-0.014	0.005	0.021	0.019	-0.020
4	0.034	0.028	0.004	-0.004	0.008	-0.047	-0.011	-0.010	-0.002	0.016	-0.004	-0.023	-0.039	-0.017	-0.002	0.013	-0.007	-0.001
5	0.021	0.032	-0.023	0.010	-0.010	-0.026	-0.006	0.003	-0.026	0.010	-0.005	-0.019	-0.017	-0.013	0.014	-0.026	-0.006	0.005
6	0.043	0.036	0.003	0.008	0.011	-0.044	-0.015	0.009	-0.024	-0.002	-0.005	-0.031	-0.015	-0.020	-0.005	0.014	-0.005	-0.008
7	0.038	0.051	0.014	-0.019	0.025	-0.046	0.004	-0.022	-0.013	0.015	0.003	-0.016	-0.046	-0.020	-0.016	0.013	0.022	-0.012

Table S2 Standardized difference before and after matching DPP-4i versus sulfonylurea initiators.

Time block	BMI	Diabetes duration	Age	HbA1c	Charlson comorbidity index	Number of other oral glucose-lowering drugs	Males	Any use during washout					Any diagnosis of			
								Anti-hypertension	statin	Anti-coagulants	Other oral glucose-lowering drugs	metformin	Hypertension	End-stage renal disease	Myocardial infarction	stroke
BEFORE MATCHING																
1	0.267	0.250	-0.147	-0.107	0.062	0.321	-0.012	-0.065	0.044	-0.044	0.464	0.026	0.040	0.001	-0.047	-0.067
2	0.269	0.350	-0.094	-0.034	0.042	0.248	-0.081	0.032	0.134	-0.021	0.440	0.008	-0.004	-0.083	-0.047	-0.104
3	0.226	0.290	-0.064	-0.057	-0.011	0.231	0.015	-0.010	0.078	-0.062	0.324	0.068	0.028	-0.062	-0.024	-0.052
4	0.241	0.330	-0.044	-0.128	0.022	0.250	-0.010	0.062	0.131	-0.064	0.384	0.029	0.010	-0.059	-0.047	0.012
5	0.131	0.309	0.028	-0.125	0.069	0.171	-0.005	0.050	0.117	-0.023	0.319	0.011	0.039	0.013	0.011	-0.016
6	0.163	0.345	0.066	-0.147	0.109	0.152	0.026	0.084	0.133	0.025	0.248	0.080	0.034	0.005	0.017	0.031
7	0.016	0.307	0.147	-0.180	0.122	0.055	0.038	0.056	0.140	0.055	0.198	0.003	0.046	0.036	-0.002	0.032
AFTER MATCHING																
1	-0.042	-0.038	0.009	-0.033	-0.002	0.025	0.013	-0.010	0.043	-0.030	0.026	-0.015	0.009	-0.005	0.022	-0.050
2	0.024	-0.012	-0.016	0.002	-0.016	-0.015	-0.025	-0.004	-0.011	0.025	-0.001	-0.028	-0.016	0.034	0.010	0.004
3	0.001	-0.002	0.021	-0.010	0.032	0.008	-0.016	0.002	-0.018	0.009	0.026	-0.023	0.001	-0.029	0.004	0.007
4	-0.005	0.008	0.018	0.003	0.021	0.002	0.000	0.002	-0.009	0.008	0.021	-0.027	-0.004	0.010	0.001	0.009
5	0.004	0.001	0.009	0.003	0.007	0.006	0.001	0.000	-0.015	0.009	0.025	-0.018	-0.004	0.006	0.002	-0.002
6	0.003	0.006	-0.005	0.006	0.007	0.004	-0.003	0.002	-0.002	0.001	0.016	-0.006	0.000	-0.006	0.000	-0.004
7	0.010	0.012	-0.007	0.008	0.010	0.011	0.008	0.004	-0.003	0.001	0.043	-0.028	0.003	0.007	-0.015	0.002