

Appendix Table 1. Selected ICD-9-CM and ICD-10-CM Codes

Condition	ICD-9-CM Diagnosis Codes	ICD-10-CM Diagnosis Codes
Type 1 diabetes mellitus	250.x1, 250.x3	E10.%
Type 2 diabetes mellitus	250.x0, 250.x2	E11.%
Secondary diabetes	249.xx	E08.%, E09.%, E13.%
Diabetes mellitus complicating pregnancy, childbirth, or the puerperium (including gestational diabetes)	648.0x, 648.8x	O24.%
Hypertension	401.xx, 402.xx, 403.xx, 404.xx, 405.xx	I10.%, I11.%, I12.%, I13.%, I15.%, H35.03, I67.4%
Dyslipidemia	272.xx	E78.0%, E78.1%, E78.2%, E78.3%, E78.4%, E78.5%, E78.6%,
Obesity	278.00, 278.01, V85.3x, V85.4x	E66.%
Depression	296.2x, 296.3x, 311.xx	F32.%, F33.%

For ICD-9-CM codes, “x” is used as a wildcard character, while for ICD-10-CM codes, “%” is used as a wildcard since “x” is a valid character in the ICD-10-CM system.

Appendix Table 2. Pre-Matching Patient Demographic and Clinical Characteristics at Baseline

	Dulaglutide Initiators (n=1,103)	Basal Insulin Initiators (n=3,193)	Std. Diff. [†]
Female, n (%)	561 (50.9)	1,412 (44.2)*	0.133
Age (years), mean (SD)	53.7 (8.91)	55.3 (9.66)*	-0.167
Health plan type, n (%)			
PPO	598 (54.2)	1,540 (48.2)*	0.120
HMO	292 (26.5)	1,095 (34.3)*	-0.171
CDHP	213 (19.3)	558 (17.5)	0.047
Medicare Advantage, n (%)	10 (0.9)	51 (1.6)	-0.062
ACA exchange, n (%)	103 (9.3)	490 (15.3)*	-0.183
Geographic region ⁶ , n (%)			
South	642 (58.2)	1,623 (50.8)*	0.149
West	241 (21.8)	815 (25.5)*	-0.087
Northeast	138 (12.5)	532 (16.7)*	-0.118
Midwest	82 (7.4)	223 (7.0)	0.017
Prescribing HCP specialty, n (%)			
Primary care physician (PCP)	523 (47.4)	1,775 (55.6)*	-0.164
Endocrinologist	315 (28.6)	503 (15.8)*	0.312
Other	247 (22.4)	815 (25.5)*	-0.073
Quan-Charlson Comorbidity Index, mean (SD)	0.6 (0.94)	0.8 (1.26)*	-0.196
aDCSI score, mean (SD)	0.6 (1.04)	0.9 (1.35)*	-0.234
Comorbid conditions, n (%)			
Dyslipidemia	841 (76.2)	2,273 (71.2)*	0.115
Hypertension	805 (73.0)	2,371 (74.3)	-0.029
Obesity	348 (31.6)	686 (21.5)*	0.230
Cardiovascular	133 (12.1)	488 (15.3)*	-0.094
Nephropathy	101 (9.2)	432 (13.5)*	-0.138
Neuropathy	55 (5.0)	315 (9.9)*	-0.187
Retinopathy	31 (2.8)	198 (6.2)*	-0.164
Endocrinologist visits, n (%)	343 (31.1)	534 (16.7)*	0.342

Number of visits, mean (SD)	0.5 (0.92)	0.3 (0.76)*	0.288
Oral antidiabetic medications, n (%)			
Metformin	872 (79.1)	2,214 (69.3)*	0.223
Sulfonylureas	390 (35.4)	1,464 (45.9)*	-0.215
DPP-4 inhibitors	405 (36.7)	1,114 (34.9)	0.038
SGLT2 inhibitors	304 (27.6)	403 (12.6)*	0.380
Thiazolidinediones	96 (8.7)	254 (8.0)	0.027
Meglitinides	11 (1.0)	67 (2.1)*	-0.089
Alpha-glucosidase inhibitors	<10 (-)	16 (0.5)	-0.037
OAD classes per patient, mean (SD)	1.9 (1.09)	1.7 (1.12)*	0.139
OAD fills, mean (SD)	4.8 (3.54)	4.1 (3.51)*	0.208
HbA1c (%), mean (SD)	8.37 (1.68)	9.86 (2.12)*	-0.777
HbA1c (%), categorical n (%)			
<7%	219 (19.9)	201 (6.3)*	0.411
7% to <8%	305 (27.7)	439 (13.7)*	0.348
8% to <9%	250 (22.7)	577 (18.1)*	0.114
9% to <10%	140 (12.7)	552 (17.3)*	-0.129
10% to <11%	97 (8.8)	483 (15.1)*	-0.196
≥11%	92 (8.3)	941 (29.5)*	-0.560

ACA=Affordable Care Act; aDCSI=adapted Diabetes Complication Severity Index; CDHP=consumer-driven health plan; DPP-4=dipeptidyl peptidase-4; GLP-1RA=glucagon-like peptide receptor agonist; HCP=healthcare provider; HMO=health maintenance organization; OAD=oral antidiabetic drug; PPO=preferred provider organization; SD=standard deviation; SGLT2=sodium-glucose co-transporter-2

†Standardized differences: Absolute standardized differences of less than 0.10 were considered to denote balance in baseline characteristics between the cohorts.

*P<0.05 based on Chi² or t-test.

Appendix Table 3. 1-Year Post-Index Antidiabetic Medication Use Among Matched Cohorts

	Matched Dulaglutide Initiators (n=903)	Matched Basal Insulin Initiators (n=903)	p-Value [†]
OADs			
Patients with ≥ 1 fill, n (%)	827 (91.6)	843 (93.4)	.154
Metformin	717 (79.4)	725 (80.3)	.639
Sulfonylureas	341 (37.8)	323 (35.8)	.380
DPP-4 inhibitors	221 (24.5)	355 (39.3)	<.001
SGLT2 inhibitors	308 (34.1)	210 (23.3)	<.001
Thiazolidinediones	100 (11.1)	73 (8.1)	.031
Meglitinides	10 (1.1)	21 (2.3)	.046
Alpha-glucosidase inhibitors	<10 (-)	<10 (-)	.479
OAD classes per patient, mean (SD)	1.9 (1.08)	1.9 (1.01)	.788
0 classes, n (%)	76 (8.4)	60 (6.6)	.154
1 classes, n (%)	274 (30.3)	264 (29.2)	.607
2 classes, n (%)	311 (34.4)	352 (39.0)	.045
3+ classes, n (%)	242 (26.8)	227 (25.1)	.421
Fills, mean (SD)	9.0 (6.59)	8.7 (6.65)	.328
Basal insulin [‡]			
Patients with ≥ 1 fill, n (%)	97 (10.7)	903 (100.0)	<.001
Fills, mean (SD)	0.4 (1.26)	5.0 (3.26)	<.001
Non-basal insulin			
Patients with ≥ 1 fill, n (%)	24 (2.7)	156 (17.3)	<.001
Rapid-acting	19 (2.1)	142 (15.7)	<.001

Short-acting	<10 (-)	<10 (-)	.011
Intermediate-acting	<10 (-)	<10 (-)	.179
U500	0 (0)	<10 (-)	.317
Premix	<10 (-)	15 (1.7)	.011
Fills, mean (SD)	0.1 (0.63)	0.6 (1.75)	<.001
GLP-1 RAs			
Patients with ≥ 1 fill, n (%)	903 (100.0)	88 (9.7)	<.001
Dulaglutide	903 (100.0)	35 (3.9)	<.001
Liraglutide	31 (3.4)	33 (3.7)	.799
Exenatide QW pen	19 (2.1)	11 (1.2)	.141
Exenatide QW vial/syringe	3 (0.3)	<10 (-)	1.000
Exenatide BID	<10 (-)	<10 (-)	.317
Semaglutide	<10 (-)	0 (0)	.317
Albiglutide	<10 (-)	10 (1.1)	.315
Fills, mean (SD)	8.2 (4.08)	0.4 (1.61)	<.001

BID=twice daily; DPP-4=dipeptidyl peptidase-4; GLP-1 RA=glucagon-like peptide receptor agonist; OAD=oral antidiabetic drug; SD=standard deviation; SGLT2, sodium-glucose co-transporter-2; QW=once weekly

[†]p-Values for comparing categorical variables between matched dulaglutide and matched basal insulin initiators were obtained using χ^2 tests; p-values for continuous variables were obtained using t-tests

[‡]Includes insulin glargine, insulin detemir, and insulin degludec in any concentration.

Appendix Table 4. Glycemic Outcomes at 1-year Post-Index Among Patients Initiating Dulaglutide vs Patients Initiating Basal Insulin

Outcomes at 1-Year Post-Index	Dulaglutide Initiators (n=903)	Basal Insulin Initiators (n=903)	p-Value
Total population			
Baseline HbA1c, mean (SD)	8.65 (1.66)	8.64 (1.63)	-
Change in HbA1c from baseline, adjusted mean (SE)	-1.12 (0.05)	-0.51 (0.05)	<.001 [†]
HbA1c <7%, n (%)	384 (42.5)	226 (25.0)	<.001 [‡]
HbA1c <8%, n (%)	650 (72.0)	490 (54.3)	<.001 [‡]
Reduction of ≥1% in HbA1c, n (%)	436 (48.3)	307 (34.0)	<.001 [‡]
Reduction of ≥1% in HbA1c or achieved HbA1c <7%, n (%)	592 (65.6)	409 (45.3)	<.001 [‡]
Patients with baseline HbA1c >9%, n	316	316	
Baseline HbA1c, mean (SD)	10.47 (1.282)	10.44 (1.195)	-
Change in HbA1c from baseline, adjusted mean (SE)	-2.11 (0.100)	-1.52 (0.100)	<.001 [†]
HbA1c <7%, n (%)	68 (21.5)	39 (12.3)	.002 [‡]
HbA1c <8%, n (%)	160 (50.6)	108 (34.2)	<.001
Patients with baseline age ≥65 years, n	68	68	
Baseline HbA1c, mean (SD)	7.94 (1.028)	8.51 (1.626)	-
Change in HbA1c from baseline, adjusted mean (SE)	-1.10 (0.123)	-0.54 (0.123)	.002 [†]
HbA1c <7%, n (%)	34 (50.0)	15 (22.1)	.001 [‡]
HbA1c <8%, n (%)	58 (85.3)	45 (66.2)	.009

SD=standard deviation; SE=standard error

[†]p-Values obtained using ANCOVA with baseline HbA1c level (continuous variable) as covariate[‡]p-Values obtained using χ^2 test

Appendix Table 5. Glycemic Outcomes at 1-year Post-Index Among Patients Initiating Dulaglutide vs Patients Initiating Basal Insulin, in mmol/mol units

Outcomes at 1-Year Post-Index	Dulaglutide Initiators	Basal Insulin Initiators	p-Value
	(n=903)	(n=903)	
Total population			
Baseline HbA1c, mean (SD), <i>pre-matching</i>	67.98 (18.4)	84.27 (23.2)	-
Baseline HbA1c, mean (SD)	71.04 (18.1)	70.94 (17.8)	0.88
Change in HbA1c from baseline, adjusted mean (SE)	-12.20 (0.5)	-5.60 (0.5)	<.001 [†]
HbA1c <53 mmol/mol, n (%)	384 (42.5)	226 (25.0)	<.001 [‡]
HbA1c <64 mmol/mol, n (%)	650 (72.0)	490 (54.3)	<.001 [‡]
Reduction of ≥11 mmol/mol, n (%)	436 (48.3)	307 (34.0)	<.001 [‡]
Reduction of ≥11 mmol/mol or achieved HbA1c <53 mmol/mol, n (%)	592 (65.6)	409 (45.3)	<.001 [‡]
Patients with baseline HbA1c >75 mmol/mol, n	316	316	
Baseline HbA1c, mean (SD)	90.94 (14.0)	90.61 (13.1)	-
Change in HbA1c from baseline, adjusted mean (SE)	-23.10 (1.1)	-16.60 (1.1)	<.001 [†]
HbA1c <53 mmol/mol, n (%)	68 (21.5)	39 (12.3)	.002 [‡]
HbA1c <64 mmol/mol, n (%)	160 (50.6)	108 (34.2)	<.001
Patients with baseline age ≥65 years, n	68	68	
Baseline HbA1c, mean (SD)	63.28 (11.2)	69.51 (17.8)	-
Change in HbA1c from baseline, adjusted mean (SE)	-12.00 (1.3)	-5.90 (1.3)	.002 [†]
HbA1c <53 mmol/mol, n (%)	34 (50.0)	15 (22.1)	.001 [‡]
HbA1c <64 mmol/mol, n (%)	58 (85.3)	45 (66.2)	0.009

HbA1c in % (NGSP standard) were converted into mmol/mol (IFCC standard) using the reference equation ([HbA1c in mmol] = (10.93*[HbA1c in %]) - 23.50) for HbA1c values ≥5%, and the online converter available at <http://www.ngsp.org/convert2.asp> for values between 0.01 and 5%.

[†]p-Values obtained using ANCOVA with baseline HbA1c level (continuous variable) as covariate

[‡]p-Values obtained using χ^2 test

Appendix Table 6. Results From Mixed-Effects Model With Repeated Measurements (MMRM) For HbA1c

	Dulaglutide Initiators (n=903)	Basal Insulin Initiators (n=903)	p-Value
HbA1c, mean (SE)			
Baseline	8.65 (0.05)	8.64 (0.05)	<.001
3 Months post-index	7.43 (0.06)	8.10 (0.06)	<.001
6 Months post-index	7.53 (0.06)	8.07 (0.06)	<.001
9 Months post-index	7.57 (0.06)	8.07 (0.06)	<.001
12 Months post-index	7.53 (0.06)	8.19 (0.06)	<.001

Total number of observations = 6,368. Results are from a mixed-effects model with repeated measurements (MMRM) approach. Baseline reflects HbA1c results obtained between (index date - 183 days) and (index date + 14 days); the value closest to index date was chosen if there were multiple values. 3/6/9/12 months reflects HbA1c results obtained between windows of ± 45 days around index date +92/183/274/365 days, with the value closest to and prior to the anchor date chosen if there were multiple values.

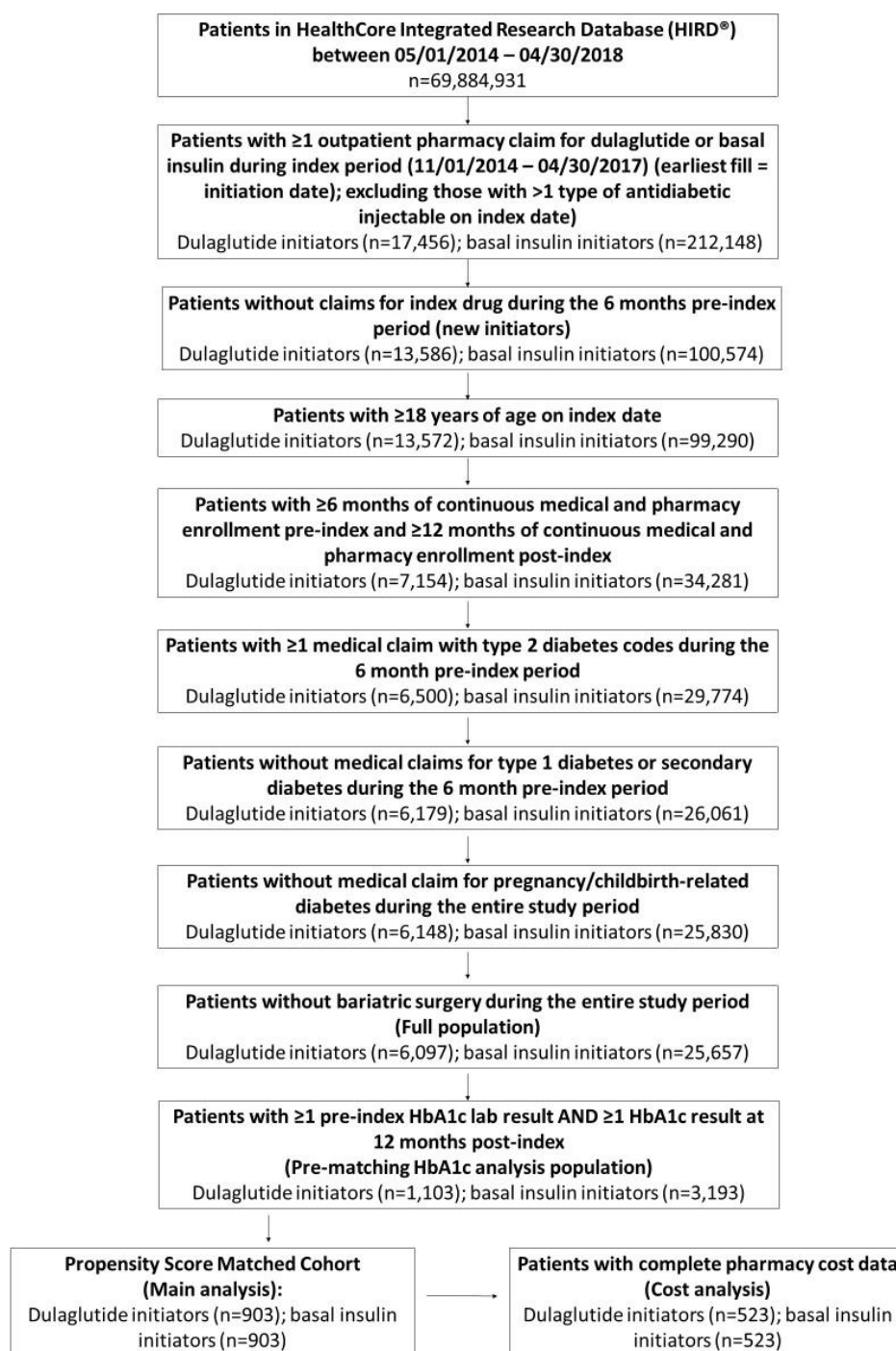
Appendix Table 7. Baseline Patient Characteristics Among Complete Cost Data Population

	Dulaglutide Initiators (n=523)	Basal Insulin Initiators (n=523)	Std. Diff. [†]
Female, n (%)	257 (49.1)	253 (48.4)	0.015
Age (years), mean (SD)	54.1 (8.62)	53.7 (8.83)	0.047
Quan-Charlson Comorbidity Index, mean (SD)	0.6 (0.98)	0.6 (1.02)	0.015
aDCSI score, mean (SD)	0.6 (0.97)	0.6 (1.03)	-0.029
OAD classes per patient, mean (SD)	1.9 (1.10)	2.0 (1.11)	-0.054
OAD fills, mean (SD)	5.2 (3.82)	5.1 (3.85)	0.027
Patients with ≥1 fill of any OAD, n (%)	471 (90.1)	475 (90.8)	-0.026
<i>All-cause total costs</i>			
Medical	\$7,090 (\$16,946)	\$9,276 (\$23,670)	-0.106
Pharmacy	\$5,884 (\$6,987)	\$5,662 (\$8,838)	0.028
Medical + pharmacy	\$12,974 (\$19,033)	\$14,938 (\$25,554)	-0.087
<i>Diabetes-related total costs</i>			
Medical	\$3,758 (\$13,317)	\$4,720 (\$14,929)	-0.068
Pharmacy	\$2,777 (\$3,162)	\$2,700 (\$3,210)	0.024
Medical + pharmacy	\$6,535 (\$13,677)	\$7,420 (\$15,214)	-0.061

aDCSI=adapted Diabetes Complications Severity Index; OAD=oral antidiabetic drug; SD=standard deviation

[†]Standardized differences: Absolute standardized differences of less than 0.10 were considered to denote balance in baseline characteristics between the cohorts. The 6-month baseline costs reported in this table are annualized, in order to allow comparison with the 12-months follow-up costs reported in Table 2.

Appendix Figure 1: Patient Identification



Appendix Figure 2. Changes in HbA1c Distribution Among Patients Initiating Dulaglutide vs Patients Initiating Basal Insulin

