

SUPPLEMENTARY DATA

**Supplementary Table 1. Comparison of baseline characteristics between subjects who were prescribed insulin during the study and those who were not (Intensive Arm)**

<b>Baseline characteristics</b>	<b>Insulin prescribed during study</b>	<b>No insulin prescribed during study</b>	<b>p-value</b>
n	4003	1083	
Age (years)	62.2 ± 6.8	62.4 ± 6.9	0.439
Female	1523 (38.0%)	440 (40.6%)	0.122
Race/ethnicity			<0.001
AA	788 (19.7%)	197 (18.2%)	
Hispanic	253 (6.3%)	102 (9.4%)	
Other	397 (9.9%)	157 (14.5%)	
Non-Hispanic white	2565 (64.1%)	627 (57.9%)	
Diabetes duration			<0.001
≤5 years	909 (22.7%)	553 (51.1%)	
6-10 years	1160 (29.0%)	300 (27.7%)	
11-15 years	876 (21.9%)	135 (12.5%)	
≥16 years	1058 (26.4%)	95 (8.8%)	
History of cardiovascular disease (yes vs. no)	1498 (37.4%)	313 (28.9%)	<0.001
Prior myocardial infarction (yes vs. no)	183 (4.6%)	39 (3.6%)	0.166
Heart failure/congestive heart failure (yes vs. no)	219 (5.5%)	27 (2.5%)	<0.001
Retinal surgery (yes vs. no)	398 (9.9%)	26 (2.4%)	<0.001
Amputation (yes vs. no)	81 (2.0%)	10 (0.9%)	0.015
Education			0.151
Less than high school	619 (15.5%)	178 (16.4%)	
High school graduate	1065 (26.6%)	262 (24.2%)	
Some college	1319 (33.0%)	343 (31.7%)	
College graduate or more	1000 (25.0%)	300 (27.7%)	
Smoking			0.044

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<b>Baseline characteristics</b>	<b>Insulin prescribed during study</b>	<b>No insulin prescribed during study</b>	<b>p-value</b>
Former	1810 (45.2%)	449 (41.5%)	
Current	568 (14.2%)	150 (13.9%)	
Never	1625 (40.6%)	484 (44.7%)	
Alcohol use			0.261
1-6 drinks/week	3068 (76.7%)	814 (75.2%)	
7+ drinks/week	760 (19.0%)	210 (19.4%)	
No drinks/week	173 (4.3%)	59 (5.4%)	
Insulin use (yes vs. no)	1733 (43.3%)	4 (0.4%)	<0.001
ACE inhibitor (yes vs. no)	2172 (54.3%)	525 (48.5%)	<0.001
Angiotensin receptor blockers (yes vs. no)	639 (16.0%)	151 (13.9%)	0.103
Statins (yes vs. no)	2534 (63.3%)	605 (55.9%)	<0.001
Metformin (yes vs. no)	2430 (60.7%)	603 (55.7%)	0.003
Sulfonylureas (yes vs. no)	2037 (50.9%)	552 (51.0%)	0.962
Thiazolidinediones (yes vs. no)	856 (21.4%)	132 (12.2%)	<0.001
BMI (kg/m <sup>2</sup> )	32.3 ± 5.5	31.8 ± 5.5	0.007
Systolic blood pressure (mmHg)	136.2 ± 17.0	136.1 ± 16.9	0.842
Diastolic blood pressure (mmHg)	74.3 ± 10.6	76.4 ± 10.4	<0.001
Visual acuity			0.052
<20/40	931 (24.4%)	221 (21.4%)	
20/20-20/40	2305 (60.5%)	630 (61.1%)	
≥20/20	577 (15.1%)	180 (17.5%)	
Peripheral neuropathy (yes vs. no)	1774 (44.3%)	378 (34.9%)	<0.001
Heart rate	72.9 ± 11.8	72.1 ± 11.6	0.056
Q-T index	101.9 ± 5.2	101.3 ± 4.9	0.002
A1C in % ( mmol/mol)	8.4 ± 1.1 (68 ± 12.0)	7.9 ± 1.0 (63 ± 10.9)	<0.001
Fasting plasma glucose (mg/dl)	177.2 ± 57.4	166.6 ± 48.8	<0.001

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<b>Baseline characteristics</b>	<b>Insulin prescribed during study</b>	<b>No insulin prescribed during study</b>	<b>p-value</b>
LDL (mg/dl)	104.3 ± 33.8	107.2 ± 34.5	0.015
HDL (mg/dl)	41.9 ± 11.8	41.5 ± 11.5	0.326
Triglycerides (mg/dl)	190.4 ± 145.7	193.3 ± 156.5	0.579
Serum creatinine (mg/dl)	0.9 ± 0.2	0.9 ± 0.2	<0.001
Urinary albumin-to-creatinine ratio (mg/mg)			<0.001
<30	2647 (66.1%)	828 (76.5%)	
30-≤300	1072 (26.8%)	210 (19.4%)	
>300	284 (7.1%)	45 (4.2%)	
Integrated health plan (yes vs. no)	1633 (40.8%)	397 (36.7%)	0.018
Endocrinologist or diabetologist (either vs. other physician)	2299 (57.4%)	528 (48.8%)	<0.001
Certified diabetes educator on staff at randomization	1625 (40.6%)	347 (32.0%)	<0.001
Site size			0.388
<100	618 (15.4%)	181 (16.7%)	
100-150	1175 (29.4%)	328 (30.3%)	
>150	2210 (55.2%)	574 (53.0%)	

Values are “means ± SD” for continuous variables or “n (%)” for categorical variables.

The sample size for Q-T index is 983 for those who were never prescribed insulin and 3587 for those who were prescribed insulin. The sample size for A1C is 1081 for those who were never prescribed insulin and 3997 for those who were prescribed insulin.

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**Supplementary Table 2. Comparison of baseline characteristics between subjects who were prescribed insulin during the study and those who were not (Standard Arm)**

<b>Baseline characteristics</b>	<b>Insulin prescribed during study</b>	<b>No insulin prescribed during study</b>	<b>p-value</b>
n	3135	1942	
Age (years)	62.0 ± 6.8	62.6 ± 6.8	0.004
Female	1199 (38.2%)	744 (38.3%)	0.963
Race/ethnicity			<0.001
AA	603 (19.2%)	339 (17.5%)	
Hispanic	221 (7.0%)	151 (7.8%)	
Other	291 (9.3%)	265 (13.6%)	
Non-Hispanic white	2020 (64.4%)	1187 (61.1%)	
Diabetes duration			<0.001
≤5 years	572 (18.2%)	862 (44.4%)	
6-10 years	863 (27.5%)	591 (30.4%)	
11-15 years	754 (24.1%)	269 (13.9%)	
≥16 years	946 (30.2%)	220 (11.3%)	
History of cardiovascular disease (yes vs. no)	1200 (38.3%)	565 (29.1%)	<0.001
Prior myocardial infarction (yes vs. no)	159 (5.1%)	90 (4.6%)	0.483
Heart failure/congestive heart failure (yes vs. no)	197 (6.3%)	48 (2.5%)	<0.001
Retinal surgery (yes vs. no)	387 (12.3%)	79 (4.1%)	<0.001
Amputation (yes vs. no)	74 (2.4%)	19 (1.0%)	<0.001
Education			0.342
Less than high school	419 (13.4%)	285 (14.7%)	
High school graduate	845 (27.0%)	510 (26.3%)	
Some college	1055 (33.7%)	620 (31.9%)	
College graduate or more	816 (26.0%)	527 (27.1%)	
Smoking			0.207
Former	1404 (44.8%)	829 (42.7%)	

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<b>Baseline characteristics</b>	<b>Insulin prescribed during study</b>	<b>No insulin prescribed during study</b>	<b>p-value</b>
Current	433 (13.8%)	260 (13.4%)	
Never	1298 (41.4%)	853 (43.9%)	
Alcohol use			0.002
1-6 drinks/week	2421 (77.3%)	1422 (73.2%)	
7+ drinks/week	582 (18.6%)	411 (21.2%)	
No drinks/week	129 (4.1%)	109 (5.6%)	
Insulin use (yes vs. no)	1816 (57.9%)	6 (0.3%)	<0.001
ACE inhibitor (yes vs. no)	1765 (56.3%)	935 (48.1%)	<0.001
Angiotensin receptor blockers (yes vs. no)	549 (17.5%)	279 (14.4%)	0.003
Statins (yes vs. no)	2054 (65.5%)	1118 (57.6%)	<0.001
Metformin (yes vs. no)	1847 (58.9%)	1200 (61.8%)	0.042
Sulfonylureas (yes vs. no)	1415 (45.1%)	1088 (56.0%)	<0.001
Thiazolidinediones (yes vs. no)	650 (20.7%)	329 (16.9%)	0.001
BMI (kg/m <sup>2</sup> )	32.8 ± 5.5	31.3 ± 5.3	<0.001
Systolic blood pressure (mmHg)	136.8 ± 17.5	136.0 ± 16.7	0.109
Diastolic blood pressure (mmHg)	74.4 ± 10.7	75.8 ± 10.4	<0.001
Visual acuity			<0.001
<20/40	765 (25.5%)	393 (21.0%)	
20/20-20/40	1819 (60.6%)	1152 (61.6%)	
≥20/20	419 (14.0%)	326 (17.4%)	
Peripheral neuropathy (yes vs. no)	1464 (46.7%)	712 (36.7%)	<0.001
Heart rate	73.1 ± 11.8	71.7 ± 11.6	<0.001
Q-T index	101.7 ± 5.3	101.6 ± 5.0	0.395
A1C in % (mmol/mol)	8.5 ± 1.1 (69 ± 12.0)	8.1 ± 1.0 (65 ± 10.9)	<0.001
Fasting plasma glucose (mg/dl)	178.6 ± 60.7	170.9 ± 47.9	<0.001
LDL (mg/dl)	103.3 ± 33.4	107.5 ± 34.1	<0.001

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<b>Baseline characteristics</b>	<b>Insulin prescribed during study</b>	<b>No insulin prescribed during study</b>	<b>p-value</b>
HDL (mg/dl)	42.0 ± 11.7	41.8 ± 11.1	0.614
Triglycerides (mg/dl)	189.8 ± 160.2	189.4 ± 127.6	0.924
Serum creatinine (mg/dl)	0.9 ± 0.2	0.9 ± 0.2	<0.001
Urinary albumin-to-creatinine ratio (mg/mg)			<0.001
<30	2021 (64.5%)	1441 (74.2%)	
30-≤300	851 (27.1%)	423 (21.8%)	
>300	263 (8.4%)	78 (4.0%)	
Integrated health plan (yes vs. no)	1325 (42.3%)	695 (35.8%)	<0.001
Endocrinologist or diabetologist (either vs. other physician)	1860 (59.3%)	977 (50.3%)	<0.001
Certified diabetes educator on staff at randomization	1248 (39.8%)	707 (36.4%)	0.016
Site size			0.974
<100	474 (15.1%)	295 (15.2%)	
100-150	938 (29.9%)	586 (30.2%)	
>150	1723 (55.0%)	1061 (54.6%)	

Values are “means ± SD” for continuous variables or “n (%)” for categorical variables.

The sample size for Q-T index is 1759 for those who were never prescribed insulin and 2820 for those who were prescribed insulin. The sample size for A1C is 1936 for those who were never prescribed insulin and 3129 for those who were prescribed insulin.

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**Supplementary Table 3. Evaluation of Model 1 in Table 2: The HR for CV mortality of updated, average daily total insulin dose (per 1 unit/ kg)**

<b>Variable</b>	<b>HR (p-value) for Updated, Average Daily Total Insulin on CV Mortality Adjusted Only For Listed Variable</b>	<b>HR (p-value) for Updated, Average Daily Total Insulin on CV Mortality Adjusted For All Variables Except Listed Variable</b>	<b>HR (p-value) for Updated, Average Daily Total Insulin on CV Mortality – stepwise*</b>
Unadjusted	1.83 (<0.001)		1.83 (<0.001)
Baseline A1c	1.72 (<0.001)	1.27 (0.082)	1.72 (<0.001)
Heart failure	1.56 (<0.001)	1.31 (0.050)	1.46 (0.002)
Peripheral neuropathy	1.71 (<0.001)	1.24 (0.131)	1.38 (0.011)
History of cardiovascular disease	1.61 (<0.001)	1.29 (0.072)	1.27 (0.063)
Albumin-to-creatinine ratio	1.63 (<0.001)	1.27 (0.084)	1.19 (0.175)
Q-T index	1.69 (<0.001)	1.30 (0.047)	1.14 (0.342)
Amputation	1.77 (<0.001)	1.22 (0.151)	1.13 (0.383)
Angiotensin receptor blockers	1.87 (<0.001)	1.18 (0.234)	1.17 (0.274)
Serum creatinine	1.76 (<0.001)	1.24 (0.128)	1.14 (0.344)
Certified diabetes educator on staff at randomization	1.85 (<0.001)	1.20 (0.204)	1.15 (0.318)
Integrated health plan	1.79 (<0.001)	1.23 (0.147)	1.14 (0.360)
Age	1.98 (<0.001)	1.12 (0.437)	1.24 (0.126)
HDL	1.76 (<0.001)	1.23 (0.151)	1.23 (0.144)
Education	1.80 (<0.001)	1.23 (0.144) <sup>`</sup>	1.21 (0.173) <sup>†</sup>

\* stepwise: sequential adjustment; adjust for the variable listed in the row and all the previous variables listed in rows above this variable. Sequence was determined by adding those variables with the smallest p-value, among variables not previously entered in the model.

† Note that the final model containing education is identical to Model 1.