**Appendix Table 1: Weighted baseline characteristic comparisons**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  |  | **Continuers** | **Interrupters** | **P-value** | **Discontinuers** | **P-value** |
|  |  | **(N = 3,786)** | **(N = 11,880)** | **(N = 3,444)** |
|  |  | **[A]** | **[B]** | **[A vs. B]** | **[C]** | **[A vs. C]** |
| **Demographics** |   |   |  |   |  |  |  |
| Age on index date, mean (SD) | 59.7 (10.9) | 59.4 (12.4) | 0.160 |  | 59.6 (12.8) | 0.859 |  |
| Gender (male), % | 60.1 | 59.9 | 0.800 |  | 59.4 | 0.579 |  |
| **Mode of delivery of index basal insulin, %** |   |  |  |   |  |  |  |
| Pen | 59.5 | 59.3 | 0.877 |  | 60.1 | 0.596 |  |
| Vial | 35.0 | 35.0 | 0.184 |  | 34.2 | 0.496 |  |
| Cartridge | 5.6 | 5.7 | 0.376 |  | 5.7 | 0.781 |  |
| **Index basal insulin, %** |   |  |  |   |  |  |  |
| Insulin glargine | 72.8 | 74.1 | 0.095 |  | 72.6 | 0.848 |  |
| Insulin detemir | 22.3 | 21.2 | 0.184 |  | 22.8 | 0.564 |  |
| NPH | 5.0 | 4.6 | 0.376 |  | 4.6 | 0.467 |  |
| **Select comorbidities, %** |   |  |  |   |  |  |  |
| Retinopathy | 5.7 | 5.5 | 0.555 |  | 5.5 | 0.744 |  |
| Diabetic foot (including lower limb amputations) | 4.1 | 4.2 | 0.710 |  | 4.5 | 0.416 |  |
| Nephropathy | 3.5 | 3.6 | 0.834 |  | 3.5 | 0.943 |  |
| Hypertension | 50.3 | 50.0 | 0.749 |  | 50.4 | 0.944 |  |
| Dyslipidemia | 39.2 | 38.7 | 0.575 |  | 38.9 | 0.777 |  |
| Cardiovascular disease | 16.7 | 16.1 | 0.416 |  | 16.1 | 0.506 |  |
| Congestive heart failure | 8.1 | 7.8 | 0.575 |  | 7.9 | 0.798 |  |
| Peripheral vascular disease | 5.8 | 5.8 | 0.957 |  | 5.8 | 0.978 |  |
| Stroke | 5.6 | 5.3 | 0.499 |  | 5.0 | 0.299 |  |
| Depression | 6.3 | 6.0 | 0.404 |  | 5.8 | 0.331 |  |
| Obesity | 3.8 | 3.7 | 0.688 |  | 3.7 | 0.784 |  |
| Other neurological disorders | 4.1 | 4.0 | 0.783 |  | 4.3 | 0.763 |  |
| Hypoglycemic event | 3.4 | 3.6 | 0.522 |  | 3.7 | 0.472 |  |
| Dementia | 0.6 | 0.6 | 0.980 |  | 0.6 | 0.979 |  |
| **CCI,mean (SD)** | 1.8 (1.6) | 1.7 (1.5) | 0.636 |  | 1.8 (1.5) | 0.665 |  |
| **Medical resource use (% with ≥1 visit)** |  |   |  |   |   |  |  |
| ED | 26.8 | 26.7 | 0.963 |  | 25.6 | 0.266 |  |
| Inpatient | 51.4 | 52.2 | 0.396 |  | 54.1 | 0.025 | \* |
| Outpatient | 91.2 | 92.7 | 0.002 | \* | 92.7 | 0.016 | \* |
| Other | 45.6 | 45.5 | 0.887 |  | 45.1 | 0.638 |  |
| **Primary care visits, mean (SD)****At least one endocrinologist visits, %** | 3.1 (3.3)12.6 | 3.1 (3.3)13.5 | 0.7910.146 |  | 3.1 (3.2)15.1 | 0.6120.002 | \* |
|  | *(contd.)* |  |  |  |  |
|  |  | **Continuers** | **Interrupters** | **P-value** | **Discontinuers** | **P-value** |
|  |  | **(N = 3,786)** | **(N = 11,880)** | **(N = 3,444)** |
|  |  | **[A]** | **[B]** | **[A vs. B]** | **[C]** | **[A vs. C]** |
| **Non-insulin antihyperglycemic prescription use** |  |  |  |  |  |  |  |
| Number of unique classes, mean (SD) | 1.9 (1.3) | 1.9 (1.3) | 0.557 |  | 1.9 (1.3) | 0.710 |  |
| At least one prescription fill, % | 80.1 | 81.7 | 0.031 | \* | 80.7 | 0.518 |  |
| Any oral antihyperglycemic drug  | 79.5 | 80.9 | 0.057 |  | 80.0 | 0.591 |  |
| Any injectable | 11.0 | 11.0 | 0.909 |  | 11.2 | 0.782 |  |

***Notes:*** CCI = Charlson comorbidity index, ED = emergency department, SD = standard deviation; \*Statistically significant at p<0.05; P-values estimated relative to continuers cohort using weighted chi-squared tests for categorical variables and weighted t-tests for continuous variables. Weights were estimated as the inverse of propensity scores. Propensity scores were estimated among the full sample of continuers, interrupters, and discontinuers using a multinomial logistic regression that accounted for observed differences in demographics, index basal insulin (type and mode of delivery), year of index date, select baseline comorbidities, select non-insulin antihyperglycemic and other prescription drug use in baseline, and resource use in baseline; Any injectable includes amylin analogues and GLP-1 receptor agonists.

**Appendix Table 2: Adjusted healthcare resource use and costs in the second year after treatment initiation**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  |  | **Continuers** | **Interrupters** | **P-value** | **Discontinuers** | **P-value** |
|  |  | **(N = 3,786)** | **(N = 11,880)** | **(N = 3,444)** |
|  |  | **[A]** | **[B]** | **[A vs. B]** | **[C]** | **[A vs. C]** |
| **Medical resource use, % with ≥1 visit** |  |  |   |  |  |  |
| All-cause |  |  |  |   |  |  |  |
| Emergency department  | 32.3 | 35.9 | <0.001 | \* | 35.4 | 0.006 | \* |
| Inpatient | 62.6 | 63.0 | 0.668 |  | 62.0 | 0.593 |  |
| Outpatient | 98.4 | 97.5 | <0.001 | \* | 95.1 | <0.001 | \* |
| Other | 61.1 | 58.4 | 0.004 | \* | 55.7 | <0.001 | \* |
| T2DM-related |  |  |  |   |  |  |  |
| Emergency department | 8.9 | 10.0 | 0.043 | \* | 9.5 | 0.335 |  |
| Inpatient | 32.3 | 33.5 | 0.203 |  | 31.2 | 0.278 |  |
| Hypoglycemia-related |  |  |  |   |  |  |  |
| Emergency department  | 1.4 | 1.8 | 0.088 |  | 1.6 | 0.567 |  |
| Inpatient | 1.8 | 2.4 | 0.025 | \* | 2.1 | 0.313 |  |
| **Medical resource use, mean (SD) days/visits** |  |  |   |  |  |  |
| All-cause |  |  |  |   |  |  |  |
| Emergency department visits | 0.7 (1.7) | 0.9 (2.1) | <0.001 | \* | 0.9 (2.1) | <0.013 | \* |
| Inpatient days | 7.8 (22.0) | 8.6 (23.9) | <0.049 | \* | 7.9 (21.2) | 0.801 |  |
| Outpatient visits | 16.9 (15.0) | 16.0 (15.7) | <0.001 | \* | 15.1 (15.6) | <0.001 | \* |
| Other visits | 4.0 (8.9) | 3.9 (9.8) | 0.286 |   | 3.4 (8.1) | 0.002 | \* |
| T2DM-related |  |  |  |   |  |  |  |
| Emergency department visits | 0.1 (0.5) | 0.1 (0.6) | 0.233 |  | 0.1 (0.5) | 0.773 |  |
| Inpatient days | 2.8 (13.2) | 3.0 (14.0) | 0.380 |  | 2.6 (11.7) | 0.483 |  |
| Hypoglycemia-related |  |  |  |   |  |  |  |
| Emergency department visits | 0.0 (0.2) | 0.0 (0.3) | 0.558 |  | 0.0 (0.2) | 0.606 |  |
| Inpatient days | 0.2 (2.9) | 0.3 (3.2) | 0.377 |  | 0.3 (4.6) | 0.204 |  |
| **Prescription drug use** |  |  |  |   |  |  |  |
| Pre-mixed and non-basal insulin use |  |  |  |   |  |  |  |
| At least one prescription fill, % | 37.2 | 30.6 | <0.001 | \* | 16.3 | <0.001 | \* |
| Pre-mixed | 7.0 | 4.0 | <0.001 | \* | 2.7 | <0.001 | \* |
| Non-basal | 31.7 | 26.8 | <0.001 | \* | 14.4 | <0.001 | \* |
| Non-insulin antihyperglycemic prescription drug use |  |  |  |   |  |  |  |
| Number of unique classes, mean (SD) | 1.4 (1.1) | 1.5 (1.1) | <0.001 | \* | 1.6 (1.3) | <0.001 | \* |
| ≥1 prescription fill, % | 75.3 | 77.3 | 0.012 | \* | 73.8 | 0.149 |  |
| Any oral antihyperglycemic drug | 73.6 | 76.1 | 0.001 | \* | 72.4 | 0.279 |  |
| Any injectable | 11.3 | 10.0 | 0.024 | \* | 10.6 | 0.347 |  |

*(contd.)*

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  |  | **Continuers** | **Interrupters** | **P-value** | **Discontinuers** | **P-value** |
|  |  | **(N = 3,786)** | **(N = 11,880)** | **(N = 3,444)** |
|  |  | **[A]** | **[B]** | **[A vs. B]** | **[C]** | **[A vs. C]** |
| **Healthcare costs, mean (SD)** |  |  |  |   |  |  |  |
| All-cause |  |  |  |   |  |  |  |
| Total | $20,265 ($51,115) | $18,777 ($44,816) | 0.197 |  | $15,678 ($32,732) | <0.001 | \* |
| Medical costs | $12,494 ($49,742) | $13,553 ($43,263) | 0.344 |  | $11,327 ($29,990) | 0.330 |  |
| Pharmacy costs | $7,772 ($8,569) | $5,224 ($7,874) | <0.001 | \* | $4,351 ($10,043) | <0.001 | \* |
| T2DM-related |  |  |  |   |  |  |  |
| Total | $8,027 ($13,565) | $6,210 ($17,139) | 0.007 | \* | $4,858 ($16,672) | <0.001 | \* |
| Medical costs | $4,157 ($31,512) | $3,858 ($17,039) | 0.654 |  | $3,304 ($16,538) | 0.243 |  |
| Pharmacy costs | $3,870 ($3,052) | $2,352 ($2,181) | <0.001 | \* | $1,554 ($2,033) | <0.001 | \* |

***Notes:*** SD= standard deviation; \*Statistically significant at p<0.05; P-values estimated relative to continuers cohort using weighted chi-squared tests for categorical variables and weighted t-tests for continuous variables. Weights were estimated as the inverse of propensity scores. Propensity scores were estimated among the full sample of continuers, interrupters, and discontinuers using a multinomial logistic regression that accounted for observed differences in demographics, index basal insulin (type and mode of delivery), year of index date, select baseline comorbidities, select non-insulin antihyperglycemic and other prescription drug use in baseline, and resource use in baseline; Hypoglycemia-related claims include those associated with one or more of the following ICD-9 CM codes: 250.8x, 251.0x-251.2x; T2DM-related medical claims include those associated with one or more of the following ICD-9 CM codes: 250.x0 and 250.x2; Any injectable includes amylin analogues and GLP-1 receptor agonists; Healthcare costs were only estimated for people with complete cost data (i.e., people aged <65 years) throughout the 30-month observation period. T2DM-related costs include medical costs associated with T2DM-related medical claims and pharmacy costs for antihyperglycemic medications.

**Appendix Table 3: Prescription drug use during the first gap in therapy among interrupters and discontinuers**

|  |  |  |  |
| --- | --- | --- | --- |
|  |  | **Interrupters** | **Discontinuers** |
| **At least one prescription, %** |  81.6 | 81.6 |
| Non-basal insulin | 9.0 | 9.7 |
| Any oral antihyperglycemic agent | 77.239.1 | 76.938.2 |
| Sulfonylurea |
| Metformin (biguanide) | 44.7 | 48.4 |
| Thiazolidinedione | 18.7 | 17.1 |
| DPP-4 inhibitor | 12.0 | 13.0 |
| Fixed-dose combination | 12.2 | 13.9 |
| Any non-insulin injectable | 6.9 | 8.9 |

***Notes:*** Only those classes of medications that were used by at least 5% of interrupters and discontinuers are reported. Any non-insulin injectable includes GLP-1 receptor agonists and amylin analogues. Prescriptions filled prior to the start of the first gap but with days of supply that overlap with the first gap were included.

**Appendix Table 4: Basal insulin persistence in the first year after treatment initiation – sensitivity analyses**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | **Continuers** | **Interrupters** | **Discontinuers** |
| **Duration of maximum allowable gap, %** |   |   |  |
| 30 days (Core analyses) | 19.8 | 62.2 | 18.0 |
| 60 days | 39.7 | 39.5 | 20.8 |
| 90 days | 54.7 | 23.7 | 21.6 |
| 120 days | 65.4 | 14.0 | 20.6 |
| <90th percentile of days between two prescriptions, stratified by quantity dispensed | 44.1 | 34.5 | 21.4 |