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# ONLINE-ONLY SUPPLEMENTARY MATERIAL

### SUPPLEMENTARY METHODS

### **Propensity score matching**

The following characteristics were used for propensity score (PS) matching.

#### **Baseline characteristics**

- Age
- Sex (male/female)
- Index year quarter
- Payer type
- Health plan
- HbA<sub>1c</sub>
- HbA<sub>1c</sub> category (exact matching)
- BMI category
- Weight (kg) (weight/composite outcomes cohort only)
- Adapted Diabetes Complication Severity Index score
- Quan–Charlson Comorbidity Index score
- Number of antidiabetic medications

#### Baseline antidiabetic medications (Y/N)

- AGI
- Amylin
- Biguanide (metformin)
- DPP-4i
- D2 dopamine receptor agonist
- GLP-1 RA
- Insulin
- Insulin sensitizing agent (TZD)
- Meglitinides
- SGLT-2i
- Sulfonylurea

### Baseline comorbidities (Y/N)

• Anxiety

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- Cardiovascular
  - Congestive heart failure
  - Acute myocardial infarction
  - Old myocardial infarction
  - Stable angina
  - Unstable angina
- Cerebrovascular
- Depression
- Diabetic nephropathy
- Diabetic neuropathy
- Diabetic retinopathy
- Hyperlipidemia
- Hypertension
- Obesity
- Peripheral vascular disease
- Renal (including chronic kidney disease, end-stage renal disease, renal failure, renal osteodystrophy, kidney transplant, and dialysis)
- Stroke/transient ischemic attack

### Statistical analyses

All analyses were performed using SAS EG version 7.13 (SAS Institute, Cary, NC, USA). For estimation of hazard ratios (HRs) using a Cox proportional hazard model, we checked the assumption regarding proportional hazards by visual inspection of the survival curves. The plots did not suggest any violation of the assumption. Furthermore, a log rank test was used as a sensitivity analysis to check for consistency with the Cox model.

An iterative backward selection method using PROC GLMSELECT for ANCOVA, PROC HPGENSELECT for odds ratios (ORs), and PROC PHREG for hazard ratios (HRs) was used to select the significant covariates (p<0.05) for adjustment of each model. The variables that could be included in the models are listed below. For most of the continuous variables, squared transformation was also used.

• Index treatment

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- Weight (kg) value and squared transformation of weight (for all analyses performed on weight/composite outcomes cohort)
- BMI value and squared transformation of BMI (for all analyses performed on weight/composite outcomes cohort)
- HbA<sub>1c</sub> value and squared transformation of HbA<sub>1c</sub>
- Age and squared transformation of age value
- Time to HbA<sub>1c</sub> measurement from index date (and squared transformation) (not for adherence/persistence, drop in baseline OADs, and weight analyses)
- Sex (male/female)
- Adapted Diabetes Complication Severity Index score
- Quan-Charlson Comorbidity Index score
- Baseline antidiabetic medications (Y/N)
  - Biguanide
  - DPP-4i
  - Insulin sensitizing agent (TZD)
  - SGLT-2i
  - Sulfonylurea
  - Other antidiabetic medication
- Baseline comorbidities (Y/N)
  - Anxiety
  - Cardiovascular
    - Congestive heart failure
    - Acute myocardial infarction
    - Old myocardial infarction
    - Stable angina
    - Unstable angina
  - Cerebrovascular
  - Depression
  - Diabetic nephropathy
  - Diabetic neuropathy
  - Diabetic retinopathy
  - Hyperlipidemia
  - Hypertension

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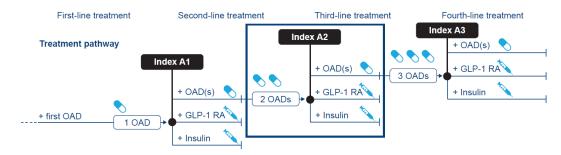
- Obesity
- Peripheral vascular disease
- Renal (including chronic kidney disease, end-stage renal disease, renal failure, renal osteodystrophy, kidney transplant, and dialysis)
- Stroke/TIA

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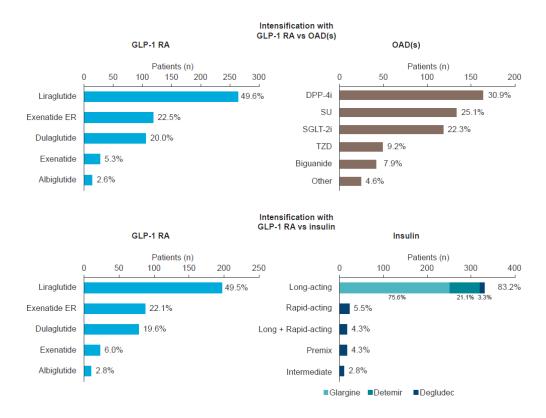
# SUPPLEMENTARY FIGURES

Supplementary Figure 1 Treatment intensification timepoints in the PATHWAY study, and focus of our analysis (Index A2).



GLP-1 RA, glucagon-like peptide-1 receptor agonist; OAD, oral antidiabetic drug.

# Supplementary Figure 2 Treatments received at intensification in the post-matching $HbA_{1c}$ cohorts.



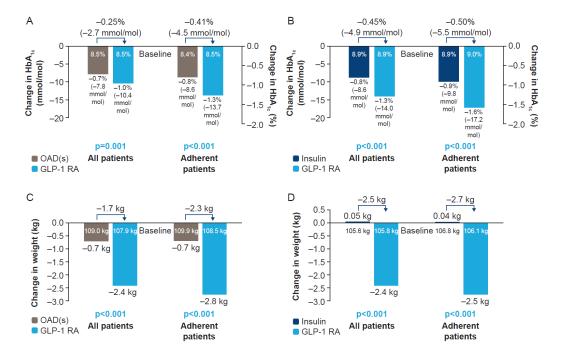
No patients intensifying treatment with semaglutide met the criteria for inclusion in the analyses.

Distributions of intensification treatments were similar in the weight/composite outcomes cohorts (data not shown).

DPP-4i, dipeptidyl peptidase-4 inhibitor; ER, extended release; GLP-1 RA, glucagon-like peptide-1 agonist; HbA1<sub>c</sub>, glycated hemoglobin; OAD, oral antidiabetic drug; SGLT-2i, sodium-glucose co-transporter-2 inhibitor; SU, sulfonylurea; TZD, thiazolidinedione.

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# Supplementary Figure 3 Absolute mean $HbA_{1c}(A,B)$ and weight (C,D) reductions from baseline for GLP-1 RAs versus OAD(s) and versus insulin.



GLP-1 RA, glucagon-like peptide-1 receptor agonist; HbA<sub>1c</sub>, glycated hemoglobin; OAD, oral antidiabetic drug.

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# SUPPLEMENTARY TABLES

Supplementary Table 1 Study attrition.

| Criteria                              |                 |          |            |         | Num   | ber of eligible |  |
|---------------------------------------|-----------------|----------|------------|---------|-------|-----------------|--|
|                                       |                 |          |            |         |       | patients in     |  |
|                                       |                 |          |            |         | datab | oase            |  |
| Aged $\geq$ 18 years with type 2      | diabetes, ini   | tiating  | ≥ 1 antidi | abetic  | 183,8 | 82              |  |
| medication                            | ŕ               | J        |            |         |       |                 |  |
| Continuous enrolment ≥ 18             | 0 davs before   | and af   | ter index. |         | 102,7 | 71              |  |
| excluding patients with $\geq 1$      | <u>•</u>        |          |            |         | , ,   |                 |  |
| pregnancy, gestational diab           | v               |          | • •        |         |       |                 |  |
| Receiving exactly 2 OADs a            | 23,46           | 7        |            |         |       |                 |  |
| HbA <sub>1c</sub> cohort              | - Buseline      |          |            |         | 23,40 |                 |  |
| HbA <sub>1c</sub> measurements at bas | salina and fall | loweur   |            |         | 4792  |                 |  |
| Patients with a treatment             | OAD(s)          | w-up     | GLP-1 I    | D A     |       | ulin            |  |
|                                       | . ,             |          |            | KA      |       |                 |  |
| claim                                 | 3263            | - I      | 578        | T =     | 107   |                 |  |
| Pre-matching (patients                | OAD(s)          | GL       | P-1 RA     | Insulin |       | GLP-1 RA        |  |
| assigned to index treatment           | 3252            | 531      |            | 1074    |       | 576             |  |
| based on first claim)                 | 3232            | 331      |            | 1071    |       | 370             |  |
| Post-matching                         | OAD(s)          | GL       | P-1 RA     | Insulin |       | GLP-1 RA        |  |
|                                       | 530             | 530      |            | 398     |       | 398             |  |
| Adherent patients only                | OAD(s)          | GL       | P-1 RA     | Insulin |       | GLP-1 RA        |  |
|                                       | 313             | 278      |            | 142     |       | 215             |  |
| Weight and composite outcome          | omes cohort     |          |            |         |       | ı               |  |
| HbA <sub>1c</sub> and weight measure  | nents at base   | line and | d follow-u | ıp      | 392   | 7               |  |
| Patients with a treatment             | OAD(s)          |          | GLP-1 l    | RA      | Ins   | ulin            |  |
| claim                                 | 2678            |          | 468        |         | 884   |                 |  |
| Pre-matching (patients                | OAD(s)          | GL       | P-1 RA     | Insulin |       | GLP-1 RA        |  |
| assigned to index treatment           | 2.550           |          |            |         |       |                 |  |
| based on first claim)                 | 2669            | 429      |            | 882     |       | 466             |  |
| Post-matching                         | OAD(s)          | GL       | P-1 RA     | Insulin |       | GLP-1 RA        |  |
|                                       | 429             | 429      |            | 298     |       | 298             |  |
| Adherent patients only                | OAD(s)          | GL       | P-1 RA     | Insulin |       | GLP-1 RA        |  |

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|------------------|-----|--------------|-----|----------------|
|                  |     |              |     |                |
|                  | 270 | 223          | 105 | 160            |

GLP-1 RA, glucagon-like peptide-1 receptor agonist; HbA<sub>1c</sub>, glycated hemoglobin; OAD, oral antidiabetic drug.

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#### Supplementary Table 2 Pre-matching baseline characteristics for the HbA<sub>1c</sub> cohort.

|   | OAD(s)      | GLP-1 RA     | Insulin     |
|---|-------------|--------------|-------------|
|   | n=3263      | n=578        | n=1078      |
| Age, years  | 60.8 (11.6) | 56.3 (9.7)   | 62.6 (12.5) |
| Sex (men/women), %  | 56.6/43.4   | 49.5/50.5    | 54.4/45.6   |
| BMI, kg/m <sup>2</sup>  | 33.7 (6.9)  | 36.4 (7.1)   | 33.0 (7.1)  |
| Weight, kg  | 98.7 (22.9) | 106.7 (24.2) | 96.6 (23.5) |
| HbA <sub>1c</sub> , %   | 8.3 (1.5)   | 8.5 (1.6)    | 9.5 (2.0)   |
| HbA <sub>1c</sub> , (mmol/mol)                                  | 67 (16.5)   | 69 (16.9)    | 80 (22.2)   |
| Adapted Diabetes Complications Severity Index                   | 0.73 (1.18) | 0.51 (0.98)  | 1.21 (1.61) |
| score[13]   |             |              |             |
| Quan-Charlson Comorbidity Index score [14,15]                   | 0.70 (1.16) | 0.60 (0.96)  | 1.25 (1.79) |
| Baseline antidiabetic medication, %                             |             |              |             |
| AGI   | 0.5         | 0.2          | 0.7         |
| Biguanide (metformin)   | 86.1        | 87.0         | 82.8        |
| DPP-4i  | 40.8        | 37.5         | 33.8        |
| D2 dopamine receptor agonist                                    | 0.0         | 0.2          | 0.0         |
| Insulin-sensitizing agent (TZD)                                 | 9.9         | 8.5          | 6.9         |
| Meglitinide   | 1.2         | 0.7          | 1.4         |
| SGLT-2i   | 5.6         | 13.5         | 2.8         |
| SU  | 56.0        | 52.4         | 71.6        |
| Comorbidities (selected), (%)                                   | 1           | 1            |             |
| Hyperlipidemia  | 65.7        | 65.6         | 69.1        |
| Hypertension  | 68.6        | 64.4         | 72.6        |
| Obesity   | 14.4        | 25.3         | 20.0        |
| Diabetic neuropathy   | 11.4        | 10.7         | 15.4        |
| Depression  | 7.8         | 11.9         | 10.3        |
| Cardiovascular  | 7.0         | 3.5          | 14.9        |
| Renal   | 5.8         | 4.8          | 14.0        |
| Diabetic retinopathy  | 5.4         | 4.5          | 5.6         |
| Anxiety   | 5.3         | 5.4          | 6.3         |
| Diabetic nephropathy  | 5.1         | 4.7          | 10.1        |
| Peripheral vascular disease                                     | 4.4         | 2.4          | 9.9         |
| Cerebrovascular   | 4.3         | 2.2          | 8.9         |
| Stroke/TIA  | 4.0         | 2.1          | 7.6         |
| Type of payer (%)   | <u> </u>    | 0.1.1        | 66.3        |
| Commercial  | 67.4        | 84.4         | 60.3        |
| Medicare  | 32.6        | 15.6         | 39.7        |
| Health plan (%)   | 25.6        | 40.2         | 20.0        |
| Preferred provider organization                                 | 35.6        | 49.3         | 30.9        |
| Comprehensive   | 21.0        | 12.3         | 21.0        |
| Health maintenance organization                                 | 22.6        | 13.5         | 27.2        |
| Consumer-driven health plan                                     | 7.1         | 8.5          | 5.9         |
| Other/unknown  Data are mean (SD) except where otherwise stated | 13.7        | 16.4         | 15.0        |

Data are mean (SD) except where otherwise stated.

The Adapted Diabetes Complications Severity Index is based on a scale ranging from 0 to 2 for each complication as follows: 0 = no abnormality, 1 = some abnormality, 2 = severe abnormality. Each patient receives one score from each of the 7 complication categories. The higher score is used when a patient has more than 1 condition in a given category. After summing scores from all 7 categories, a patient may have a total score between 0 to a maximum of 13.

The Quan-Charlson Comorbidity Index score is computed by adding the weights that are assigned to the specific diagnoses. Each diagnosis is only counted once. The minimum possible score is 0 and the maximum possible score is 24.

Cardiovascular comorbidities were congestive heart failure; acute or old myocardial infarction; and stable or unstable angina.

Renal comorbidities included chronic kidney disease, end-stage renal disease, renal failure, renal osteodystrophy, kidney transplant, and dialysis.

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AGI, alpha-glucosidase inhibitor; DPP-4i, dipeptidyl peptidase-4 inhibitor; GLP-1 RA, glucagon-like peptide-1 receptor agonist;  $HbA_{1c}$ , glycated hemoglobin; OAD, oral antidiabetic drug; SGLT-2i, sodium-glucose cotransporter-2 inhibitor; SU, sulfonylurea; TIA, transient ischemic attack; TZD, thiazolidinedione.

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# Supplementary Table 3 Pre-matching baseline characteristics for the weight/composite outcomes cohort.

|   | OAD(s)      | GLP-1 RA     | Insulin     |
|---|-------------|--------------|-------------|
|   | n=3197      | n=548        | n=1102      |
| Age, years                                    | 60.5 (11.7) | 56.0 (10.0)  | 62.4 (12.6) |
| Sex (men/women), %                            | 55.8/44.2   | 49.8/50.2    | 55.0/45.0   |
| BMI, kg/m <sup>2</sup>                        | 33.9 (7.0)  | 36.5 (6.9)   | 33.2 (7.0)  |
| Weight, kg                                    | 99.2 (23.1) | 107.5 (24.0) | 96.9 (23.2) |
| HbA <sub>1c</sub> , %                         | 8.3 (1.5)   | 8.5 (1.6)    | 9.4 (2.0)   |
| HbA <sub>1c</sub> , (mmol/mol)                | 68 (16.8)   | 69 (17.2)    | 79 (22.2)   |
| Adapted Diabetes Complications Severity Index | 0.75 (1.21) | 0.55 (1.02)  | 1.28 (1.64) |
| score[13]                                     | , ,         | , ,          |             |
| Quan-Charlson Comorbidity Index score[14,15]  | 0.72 (1.20) | 0.66 (1.01)  | 1.43 (1.92) |
| Baseline antidiabetic medication, %           |             |              |             |
| AGI   | 0.5         | 0.2          | 0.5         |
| Biguanide (metformin)                         | 86.1        | 85.9         | 81.4        |
| DPP-4i  | 40.7        | 36.5         | 34.8        |
| D2 dopamine receptor agonist                  | 0.0         | 0.0          | 0.0         |
| Insulin-sensitizing agent (TZD)               | 10.2        | 8.9          | 6.4         |
| Meglitinide                                   | 1.3         | 1.1          | 1.5         |
| SGLT-2i                                       | 6.2         | 13.9         | 2.9         |
| SU  | 55.0        | 53.5         | 72.4        |
| Comorbidities (selected), %                   |             |              |             |
| Hypertension                                  | 67.9        | 63.0         | 72.6        |
| Hyperlipidemia                                | 64.4        | 65.1         | 68.4        |
| Obesity                                       | 14.9        | 25.2         | 20.5        |
| Diabetic neuropathy                           | 11.2        | 10.6         | 16.4        |
| Depression                                    | 8.1         | 12.8         | 11.3        |
| Cardiovascular                                | 7.7         | 4.6          | 17.4        |
| Renal   | 5.8         | 5.7          | 15.4        |
| Diabetic retinopathy                          | 5.5         | 3.6          | 5.0         |
| Anxiety                                       | 5.4         | 5.8          | 7.4         |
| Diabetic nephropathy                          | 5.1         | 5.3          | 10.3        |
| Peripheral vascular disease                   | 4.7         | 2.4          | 10.4        |
| Cerebrovascular                               | 4.4         | 2.4          | 8.6         |
| Stroke/TIA                                    | 4.0         | 2.2          | 7.5         |
| Type of payer (%)                             | (7.7        | 0.4.2        | (0.1        |
| Commercial                                    | 67.7        | 84.3         | 60.1        |
| Medicare                                      | 32.3        | 15.7         | 39.9        |
| Health plan (%)                               | 27.5        | 50.2         | 20.7        |
| Preferred provider organization               | 37.5        | 50.2         | 32.7        |
| Comprehensive                                 | 19.8        | 13.5         | 21.6        |
| Health maintenance organization               | 22.2        | 12.8         | 26.4        |
| Consumer-driven health plan                   | 7.4         | 8.6          | 6.1         |
| Other/unknown                                 | 13.1        | 15.0         | 13.2        |

Data are mean (SD) except where otherwise stated.

The Adapted Diabetes Complications Severity Index is based on a scale ranging from 0 to 2 for each complication as follows: 0 = no abnormality, 1 = some abnormality, 2 = severe abnormality. Each patient receives one score from each of the 7 complication categories. The higher score is used when a patient has more than 1 condition in a given category. After summing scores from all 7 categories, a patient may have a total score between 0 to a maximum of 13.

The Quan-Charlson Comorbidity Index score is computed by adding the weights that are assigned to the specific diagnoses. Each diagnosis is only counted once. The minimum possible score is 0 and the maximum possible score is 24.

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Cardiovascular comorbidities were congestive heart failure; acute or old myocardial infarction; and stable or unstable angina.

Renal comorbidities included chronic kidney disease, end-stage renal disease, renal failure, renal osteodystrophy, kidney transplant, and dialysis.

AGI, alpha-glucosidase inhibitor; DPP-4i, dipeptidyl peptidase-4 inhibitor; GLP-1 RA, glucagon-like peptide-1 receptor agonist; HbA<sub>1c</sub>, glycated hemoglobin; OAD, oral antidiabetic drug; SGLT-2i, sodium-glucose cotransporter-2 inhibitor; SU, sulfonylurea; TIA, transient ischemic attack; TZD, thiazolidinedione.

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# Supplementary Table 4 Post-matching baseline characteristics for the weight/composite outcomes cohort.

|          |   | OAD(s)      | GLP-1 RA    |           | Insulin     | GLP-1 RA      |            |
|----------|---|-------------|-------------|-----------|-------------|---------------|------------|
|          |   | n=429       | n=429       | SMD       | n=298       | n=298         | SMD        |
| Age      | e, years                                  | 55.7 (7.2)  | 55.6 (9.6)  | -0.01     | 56.8 (11.1) | 57.0 (10.0)   | 0.02       |
| Sex      | (men/women), %                            | 50.1/49.9   | 50.3/49.7   | 0.00/0.00 | 51.0/49.0   | 51.7/48.3     | 0.01/-0.01 |
| BM       | II, kg/m <sup>2</sup>                     | 37.1 (5.5)  | 36.6 (7.0)  | -0.06     | 36.1 (7.0)  | 35.9 (6.3)    | -0.02      |
| We       | ight, kg                                  | 109.0       | 107.9       | -0.04     | 105.6       | 105.8         | 0.01       |
|          |   | (18.0)      | (24.4)      |           | (22.5)      | (22.6)        |            |
| Hb       | A <sub>1c</sub> , %                       | 8.5 (1.1)   | 8.5 (1.6)   | -0.01     | 9.0 (1.6)   | 9.0 (1.6)     | 0.00       |
|          | A <sub>1c</sub> , mmol/mol*               | 70 (12.0)   | 69 (16.9)   | _         | 75 (16.9)   | 75 (17.2)     | _          |
|          | apted Diabetes                            | 0.53 (0.97) | 0.52 (1.00) | -0.01     | 0.64 (1.09) | 0.62 (1.12)   | -0.02      |
|          | mplications Severity Index                |             |             |           |             |               |            |
|          | re[13]                                    | 0.60 (1.01) | 0.65 (4.04) | 0.01      | 0 =0 (4 0=) | 0 = ( ( 0 = ) | 0.07       |
|          | an-Charlson Comorbidity                   | 0.69 (1.21) | 0.65 (1.01) | -0.04     | 0.70 (1.27) | 0.76 (1.07)   | 0.05       |
|          | ex score[14,15]                           | (~)         |             |           |             |               |            |
| Bas      | seline antidiabetic medication,           |             | 0.2         | 0.00      | 0.0         | 0.2           | 0.00       |
|          | AGI Biguanide (metformin)                 | 0.2<br>88.1 | 0.2<br>88.6 | 0.00      | 0.0<br>85.2 | 0.3<br>85.2   | 0.08       |
|          | DPP-4i                                    | 38.7        | 36.4        | -0.05     | 37.6        | 38.9          | 0.00       |
|          | D2 dopamine receptor                      | 0.0         | 0.0         | -0.03     | 0.0         | 0.0           | 0.03       |
|          | agonist                                   | 0.0         | 0.0         | _         | 0.0         | 0.0           | _          |
|          | Insulin-sensitizing agent                 | 8.9         | 9.1         | 0.01      | 7.0         | 7.7           | 0.03       |
|          | (TZD)                                     |             |             |           |             |               |            |
|          | Meglitinide                               | 0.7         | 0.7         | 0.00      | 1.7         | 1.0           | -0.06      |
|          | SGLT-2i                                   | 10.7        | 12.4        | 0.05      | 6.0         | 4.4           | -0.08      |
|          | SU  | 52.7        | 52.7        | 0.00      | 62.4        | 62.4          | 0.00       |
| Bas      | seline OAD combination,                   |             |             |           |             |               |            |
| (%)      | •   |             |             |           |             |               |            |
|          | Metformin + SU                            | 42.2        | 44.8        | _         | 49.7        | 50.3          | _          |
|          | Metformin + DPP-4i                        | 32.4        | 26.8        |           | 26.2        | 26.5          | _          |
|          | Metformin + SGLT-2i                       | 7.0         | 10.3        | _         | 4.7         | 3.0           | _          |
|          | Metformin + TZD                           | 5.6         | 6.5         |           | 4.0         | 4.7           |            |
|          | DPP-4i + SU                               | 5.1         | 6.3         | _         | 10.1        | 9.7           | _          |
| <u>C</u> | Others                                    | 7.7         | 5.3         |           | 5.3         | 5.8           | _          |
| Col      | morbidities (selected), %  Hyperlipidemia | 62.2        | 63.9        | 0.03      | 65.1        | 65.1          | 0.00       |
|          | Hypertension                              | 59.9        | 60.8        | 0.03      | 63.4        | 64.1          | 0.00       |
|          | Obesity                                   | 24.9        | 25.9        | 0.02      | 24.2        | 22.5          | -0.04      |
|          | Depression                                | 11.9        | 12.6        | 0.02      | 11.4        | 12.1          | 0.02       |
|          | Diabetic neuropathy                       | 10.0        | 11.4        | 0.05      | 11.1        | 11.4          | 0.01       |
|          | Diabetic nephropathy                      | 6.8         | 4.9         | -0.08     | 6.0         | 6.4           | 0.01       |
|          | Anxiety                                   | 5.8         | 5.6         | -0.01     | 5.7         | 4.7           | -0.05      |
|          | Renal                                     | 5.4         | 5.1         | -0.01     | 6.7         | 7.0           | 0.01       |
|          | Cardiovascular                            | 3.7         | 4.0         | 0.01      | 3.7         | 5.0           | 0.07       |
|          | Cerebrovascular                           | 2.8         | 2.6         | -0.01     | 3.0         | 3.4           | 0.02       |
|          | Stroke/TIA                                | 2.6         | 2.3         | -0.02     | 3.0         | 3.0           | 0.00       |
|          | Diabetic retinopathy                      | 2.1         | 3.7         | 0.10      | 5.0         | 5.0           | 0.00       |
|          | Peripheral vascular disease               | 1.6         | 2.8         | 0.08      | 4.4         | 3.7           | -0.03      |
| Ty       | pe of payer (%)                           | 1 .         | T           |           | 1           | T             |            |
| <u> </u> | Commercial                                | 86.0        | 86.2        | 0.01      | 81.9        | 79.9          | -0.05      |
|          | Medicare                                  | 14.0        | 13.8        | -0.01     | 18.1        | 20.1          | 0.05       |
| Hea      | alth plan (%)                             | 40.4        | 51.0        | 0.02      | 42.6        | 46.0          | 0.05       |
|          | Preferred provider                        | 49.4        | 51.0        | 0.03      | 43.6        | 46.0          | 0.05       |
|          | organization                              | 110         | 10.1        | 0.01      | 1.4.1       | 14.0          | 0.02       |
|          | Comprehensive                             | 11.9        | 12.1        | 0.01      | 14.1        | 14.8          | 0.02       |

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| Health maintenance     | 12.6 | 12.1 | -0.01 | 14.1 | 14.8 | 0.02  |
|------------------------|------|------|-------|------|------|-------|
| organization           |      |      |       |      |      |       |
| Consumer-driven health | 9.8  | 9.1  | -0.02 | 9.1  | 8.1  | -0.04 |
| plan                   |      |      |       |      |      |       |
| Other/unknown          | 16.4 | 15.6 | _     | 19.1 | 16.4 | _     |

<sup>\*</sup>Matching performed for HbA<sub>1c</sub> expressed as percentages only.

Data are mean (SD) except where otherwise stated.

The Adapted Diabetes Complications Severity Index is based on a scale ranging from 0 to 2 for each complication as follows: 0 = no abnormality, 1 = some abnormality, 2 = severe abnormality. Each patient receives one score from each of the 7 complication categories. The higher score is used when a patient has more than 1 condition in a given category. After summing scores from all 7 categories, a patient may have a total score between 0 to a maximum of 13.

The Quan-Charlson Comorbidity Index score is computed by adding the weights that are assigned to the specific diagnoses. Each diagnosis is only counted once. The minimum possible score is 0 and the maximum possible score is 24.

Cardiovascular comorbidities were congestive heart failure; acute or old myocardial infarction; and stable or unstable angina.

Renal comorbidities included chronic kidney disease, end-stage renal disease, renal failure, renal osteodystrophy, kidney transplant, and dialysis.

AGI, alpha-glucosidase inhibitor; DPP-4i, dipeptidyl peptidase-4 inhibitor; GLP-1 RA, glucagon-like peptide-1 receptor agonist; HbA<sub>1c</sub>, glycated hemoglobin; OAD, oral antidiabetic drug; SGLT-2i, sodium-glucose cotransporter-2 inhibitor; SMD, standardized mean difference; SU, sulfonylurea; TIA, transient ischemic attack; TZD, thiazolidinedione.

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# Supplementary Table 5 Baseline medications discontinued during follow-up by patients in the $HbA_{1c}$ cohorts.

| GLP-1 RA vs OAD(s)           |              |                 |                                   |                          |  |
|------------------------------|--------------|-----------------|-----------------------------------|--------------------------|--|
|                              | Patients wl  | ho received     | Patients with                     | no claims during follow- |  |
|                              | treatment of | during baseline | up period, n (                    | % of patients            |  |
|                              | period, n    |                 | discontinuing                     | baseline treatment)      |  |
| Treatment                    | OAD(s)       | GLP-1 RA        | OAD(s)                            | GLP-1 RA                 |  |
| AGI                          | 2            | 1               | 1 ( <b>50.0</b> )                 | 0 (0.0)                  |  |
| Biguanide (metformin)        | 463          | 471             | 55 (11.9)                         | 68 (14.4)                |  |
| DPP-4i                       | 204          | 196             | 53 ( <b>26.0</b> )                | 104 (53.1)               |  |
| D2 dopamine receptor agonist | 0            | 1               | NA                                | 0 (0.0)                  |  |
| TZD                          | 42           | 47              | 9 (21.4)                          | 17 (36.2)                |  |
| Meglitinide                  | 2            | 3               | 1 ( <b>50.0</b> )                 | 2 (66.7)                 |  |
| SGLT-2i                      | 68           | 65              | 14 (20.6)                         | 21 ( <b>32.3</b> )       |  |
| SU                           | 279          | 276             | 52 (18.6)                         | 68 (24.6)                |  |
| GLP-1 RA vs insulin          |              |                 | 1                                 |                          |  |
|                              | Patients wl  | ho received     | Patients with                     | no claims during follow- |  |
|                              | treatment of | during baseline | up period, n (                    | % of patients            |  |
|                              | period, n    |                 | discontinuing baseline treatment) |                          |  |
| Treatment                    | Insulin      | GLP-1 RA        | Insulin                           | GLP-1 RA                 |  |
| AGI                          | 3            | 1               | 1 (33.3)                          | 0 (0.0)                  |  |
| Biguanide (metformin)        | 340          | 346             | 49 (14.4)                         | 46 (13.3)                |  |
| DPP-4i                       | 149          | 150             | 48 (32.2)                         | 83 (55.3)                |  |
| D2 dopamine receptor agonist | 0            | 1               | NA                                | 0 (0.0)                  |  |
| TZD                          | 34           | 25              | 15 (44.1)                         | 5 (20.0)                 |  |
| Meglitinide                  | 4            | 3               | 2 (50.0)                          | 1 (33.3)                 |  |
| SGLT-2i                      | 26           | 28              | 11 (42.3)                         | 11 (39.3)                |  |
| SU                           | 240          | 242             | 68 (28.3)                         | 46 (19.0)                |  |

AGI, alpha-glucosidase inhibitors; DPP-4i, dipeptidyl peptidase-4 inhibitor; OAD, oral antidiabetic drug; SGLT-2i, sodium-glucose co-transporter-2 inhibitor; SU, sulfonylurea; TZD, thiazolidinedione.

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# Supplementary Table 6 Absolute $HbA_{1c}$ and weight changes from baseline – full data.

|   | OAD(s)               | GLP-1 RA       | Insulin        | GLP-1 RA             |  |  |
|---|----------------------|----------------|----------------|----------------------|--|--|
|   | O/1D(3)              | GET TREE       | mgami          | GET THE              |  |  |
| Change in HbA <sub>1c</sub> , %         |                      |                |                | 1                    |  |  |
| All patients, n                         | 530                  | 530            | 398            | 398                  |  |  |
| Baseline HbA <sub>1c</sub> , mean (SD)  | 8.47 (1.52)          | 8.46 (1.53)    | 8.91 (1.51)    | 8.94 (1.55)          |  |  |
| Change in HbA <sub>1c</sub> , mean (SD) | -0.71 (1.01)         | -0.95 (1.54)   | -0.79 (1.74)   | -1.28 (1.61)         |  |  |
| Difference between groups (95% CI)      | -0.25 (-0.           | 39, -0.10)     | -0.45 (-0      | .64, -0.26)          |  |  |
| P value                                 | 0.0                  | 014            | <0.            | 001                  |  |  |
| Adherent patients, n                    | 313                  | 278            | 142            | 215                  |  |  |
| Baseline HbA <sub>1c</sub> , mean (SD)  | 8.42 (1.52)          | 8.48 (1.59)    | 8.88 (1.35)    | 8.97 (1.61)          |  |  |
| Change in HbA <sub>1c</sub> , mean (SD) | -0.79 (1.06)         | -1.25 (1.51)   | -0.90 (1.74)   | -1.57 (1.53)         |  |  |
| Difference between groups (95% CI)      | -0.41 (-0.           | 60, -0.23)     | -0.50 (-0      | .77, -0.23)          |  |  |
| P value                                 | <0.                  | 001            | <0.            | 001                  |  |  |
| Change in HbA <sub>1c</sub> , mmol/     |                      |                |                |                      |  |  |
| All patients, n                         | 530                  | 530            | 398            | 398                  |  |  |
| Baseline HbA <sub>1c</sub> , mean (SD)  | 69 (16.6)            | 69 (16.7)      | 74 (16.5)      | 74 (16.9)            |  |  |
| Change in HbA <sub>1c</sub> , mean (SD) | -7.8 (11.0)          | -10.4 (16.8)   | -8.6 (19.0)    | -14.0 (17.6)         |  |  |
| Difference between groups (95% CI)      | -2.7 (-4             | 3, -1.1)       | -4.9 (-7       | 7.0, -2.8)           |  |  |
| P value                                 | 0.0                  | 014            | <0.            | 001                  |  |  |
| Adherent patients, n                    | 313                  | 278            | 142            | 215                  |  |  |
| Baseline HbA <sub>1c</sub> , mean (SD)  | 69 (16.6)            | 69 (17.4)      | 74 (14.8)      | 75 (17.6)            |  |  |
| Change in HbA <sub>1c</sub> , mean (SD) | -8.6 (11.6)          | -13.7 (16.5)   | -9.8 (19.0)    | -17.2 (16.7)         |  |  |
| Difference between groups (95% CI)      | -4.5 (-6             | 5.6, -2.5)     | -5.5 (-8       | 3.4, -2.5)           |  |  |
| P value                                 | <0.                  | 001            | <0.            | 001                  |  |  |
| Change in weight, kg                    |                      | <u> </u>       | <b>"</b>       |                      |  |  |
| All patients, n                         | 429                  | 429            | 298            | 298                  |  |  |
| Baseline weight, mean (SD)              | 108.96 (24.70)       | 107.89 (24.62) | 105.58 (22.49) | 105.76 (22.59)       |  |  |
| Change in weight, mean (SD)             | -0.69 (4.66)         | -2.40 (4.92)   | +0.05 (5.21)   | -2.42 (4.96)         |  |  |
| Difference between groups (95% CI)      | -1.72 (-2.35, -1.08) |                | -2.46 (-3      | .25, -1.67)          |  |  |
| P value                                 | <0.                  | 001            | <0.            | 001                  |  |  |
| Adherent patients, n                    | 270                  | 223            | 105            | 160                  |  |  |
| Baseline weight, mean (SD)              | 109.94 (24.63)       | 108.47 (24.98) | 106.80 (21.73) | 106.14 (23.92)       |  |  |
| Change in weight, mean (SD)             | -0.70 (4.76)         | -2.76 (5.31)   | +0.04 (4.65)   | -2.53 (5.05)         |  |  |
| Difference between groups (95% CI)      | -2.34 (-3.           | 19, -1.48)     | -2.66 (-3      | -2.66 (-3.80, -1.52) |  |  |

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| P value                            | <0.0                 | <0.001       |                      | 001          |  |  |
|------------------------------------|----------------------|--------------|----------------------|--------------|--|--|
| Change in weight, %                |                      |              |                      |              |  |  |
| All patients, n                    | 429                  | 429          | 298                  | 298          |  |  |
| Change in weight, mean (SD)        | -0.56 (4.17)         | -2.17 (4.38) | +0.29 (4.55)         | -2.25 (4.38) |  |  |
| Difference between groups (95% CI) | -1.62 (-2.19, -1.06) |              | -2.52 (-3.22, -1.82) |              |  |  |
| P value                            | <0.0                 | 001          | < 0.001              |              |  |  |
| Adherent patients, n               | 270                  | 223          | 105                  | 160          |  |  |
|                                    | 270                  | 223          | 103                  | 100          |  |  |
| Change in weight, mean (SD)        | -0.53 (4.22)         | -2.44 (4.73) | +0.26 (4.04)         | -2.34 (4.49) |  |  |
| Change in weight, mean             | _, -                 | -2.44 (4.73) | +0.26 (4.04)         |              |  |  |

CI, confidence interval; GLP-1 RA, glucagon-like peptide-1 receptor agonist; HbA<sub>1c</sub>, glycated hemoglobin; OAD, oral antidiabetic drug; SD, standard deviation.