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**Supplementary online material**

**Healthcare Utilization, Mortality, and Cardiovascular Events following GLP1-RA initiation In Chronic Kidney Disease**

Shuyao Zhang, Fnu Sidra, Carlos Alvarez, Mustafa Kinaan, Ildiko Lingvay, Ishak Mansi

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- Figure S2 - Overlap weighting of propensity score distribution between the groups (A) before matching, and (B) after propensity score matching.
- Figure S3 – Forest Plot of subgroup analysis
- Figure S4 - Kaplan-Meier curves using per-protocol analysis

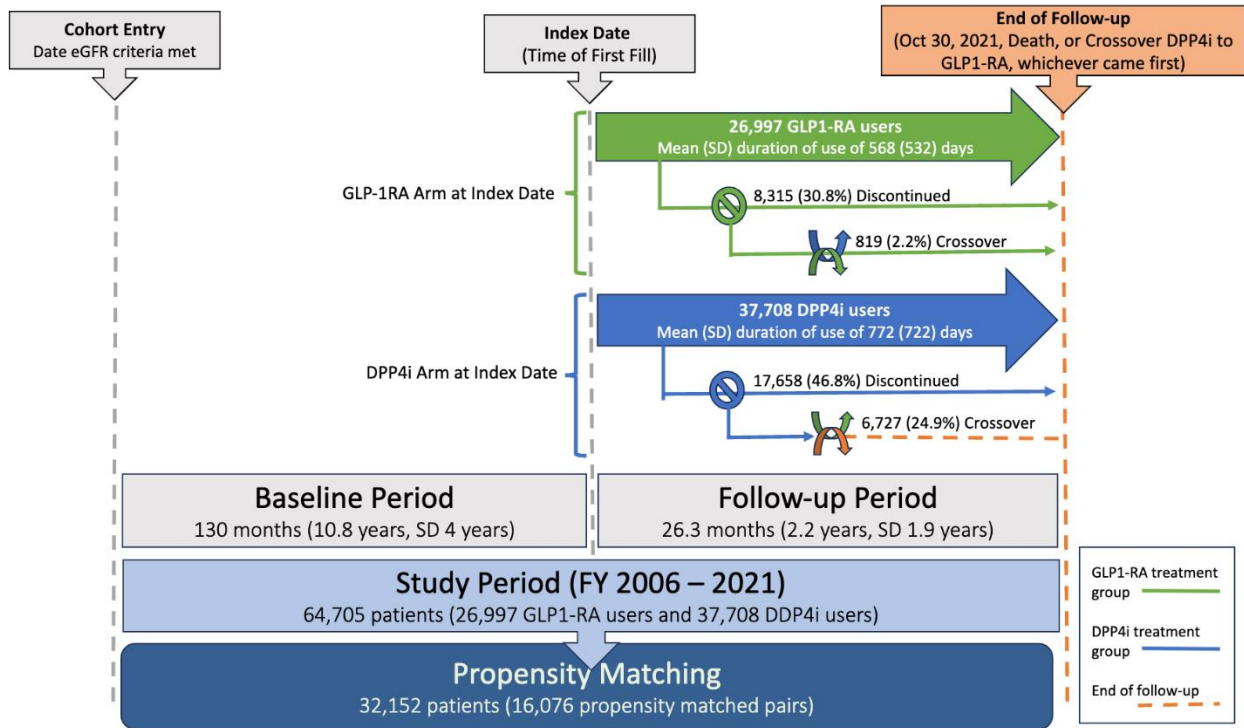
**Supplementary Tables: ..... Page 9**

- Table S1 - Incidence and progression of albuminuria during follow up period
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36 **SUPPLEMENTARY FIGURES**

37 **Supplemental Figure S1: Study intervals (intention-to-treat primary analysis): Schematic of study**  
 38 **intervals and intention-to-treat protocol.** Prior to propensity score matching, the GLP-1RA treatment  
 39 arm consisted of 26,997 patients, of which 8,315 (30.8%) discontinued medication after a mean (SD)  
 40 period of 434 (490) days. Of the patients that discontinued, 819 (2.2%) later started DPP4i. The DPP4i  
 41 treatment arm consisted of 37,708, of which 17,658 (46.8%) discontinued treatment after a mean (SD)  
 42 period of 603 (634) days. Of the patients that discontinued DPP4i, 6,727 (24.9%) were later started on  
 43 GLP-1RA (these patients were censored at date of GLP-1RA initiation).

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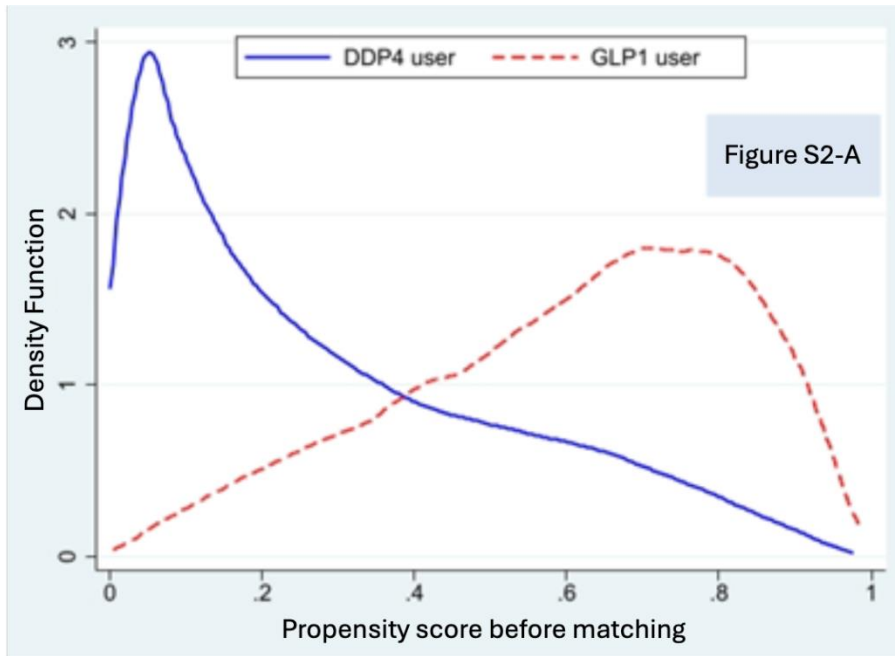
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Figure Legend: GLP1-RA, glucagon like peptide 1 receptor agonists; DPP4i, dipeptidyl peptidase 4.

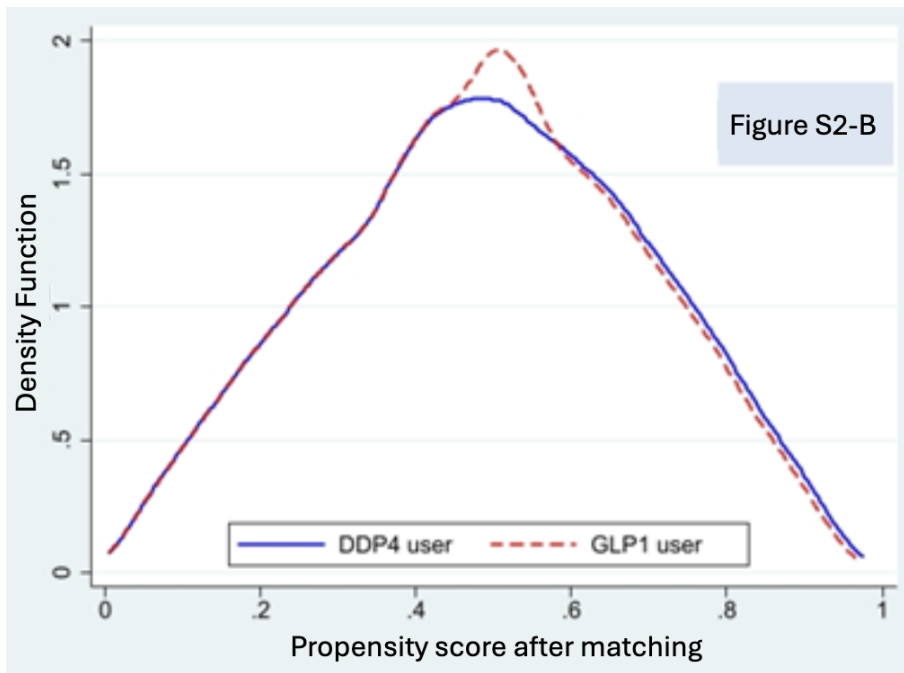
48 Study period = FY 2006-2021. Cohort entry = the date the above eGFR criteria was met. Index date =  
 49 date of first fill of GLP1RA or DPP4i. Baseline period = first available encounter to index date. Follow-up  
 50 period = index date to the end of study (Oct 30, 2021), death, or switch to GLP1-RA in the DPP4i group –  
 51 whichever came first.

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55 **Supplemental Figure S2:** Kernel graphs of propensity score before (Figure S2-A) and after (Figure S2-B)  
56 matching.



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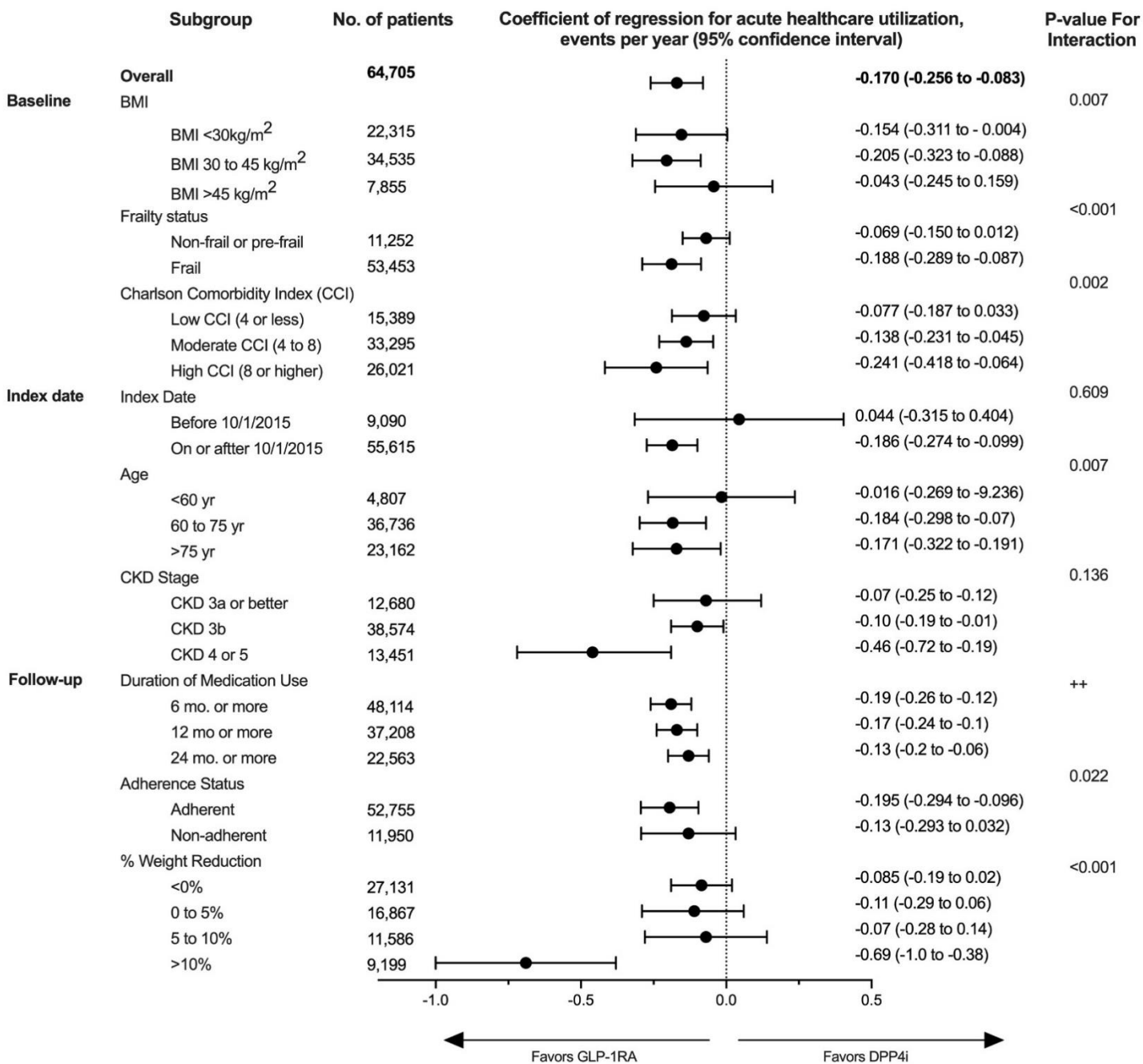
58

59 Figure Legend: GLP1, glucagon like peptide 1; DPP4i, dipeptidyl peptidase 4 inhibitors; HR

60 **Supplemental Figure S3:** Forest plot diagram illustration coefficient of regression or adjusted odds ratio by subgroup for  
 61 the following outcomes: acute healthcare utilization (panel A), CV events (panel B), CKD progression (panel C), and All-  
 62 cause death (panel D).

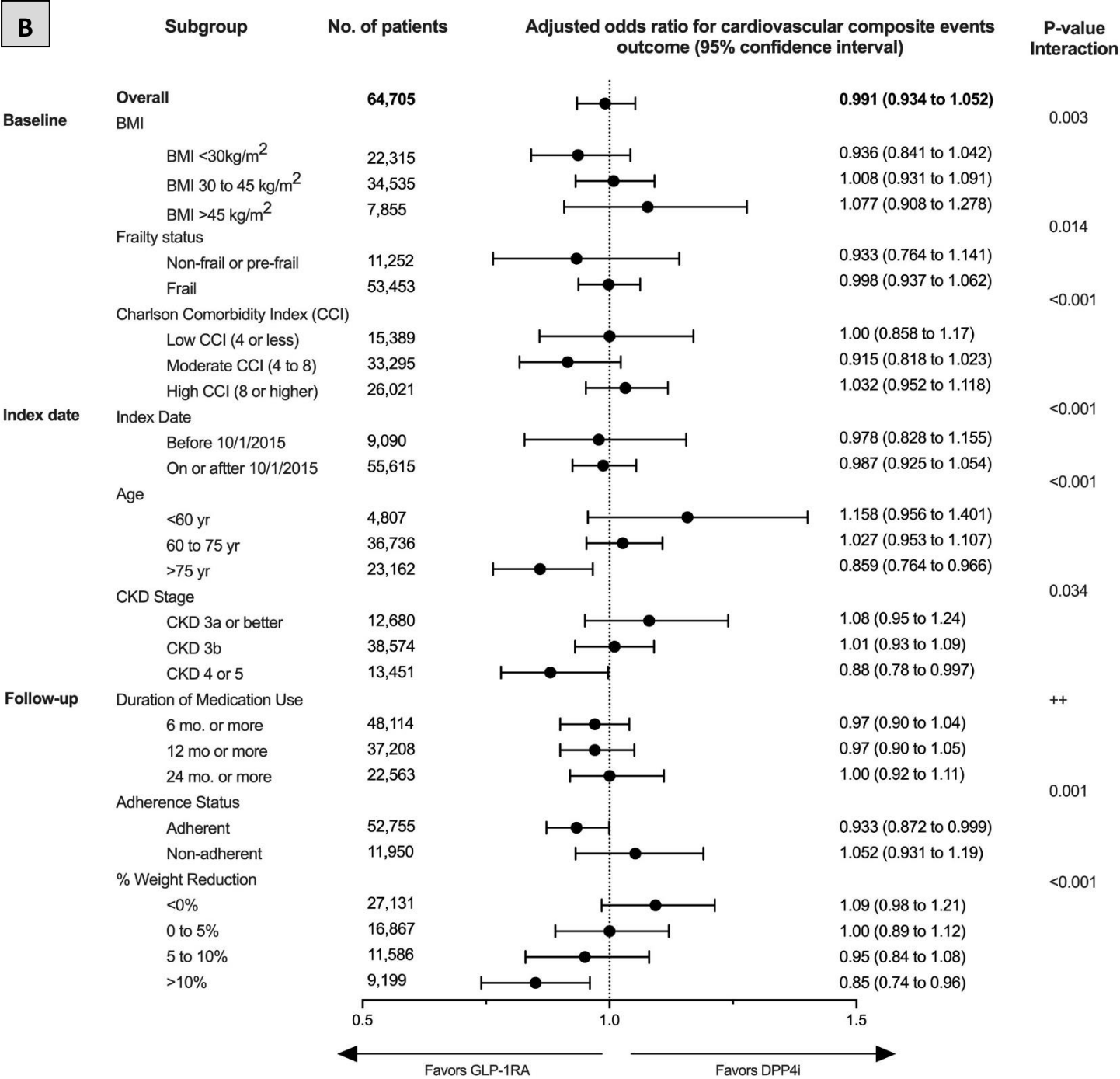
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**A**

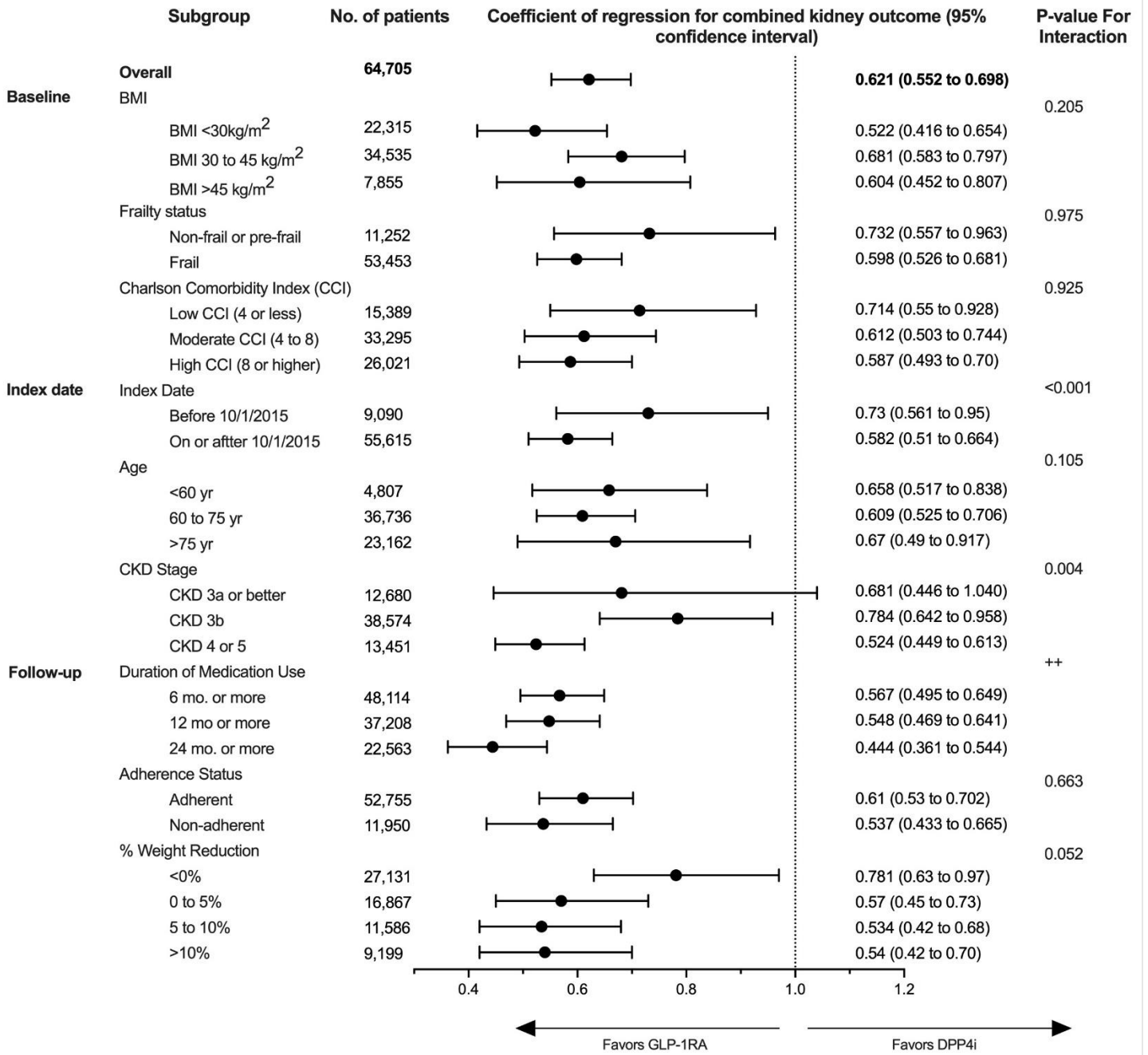


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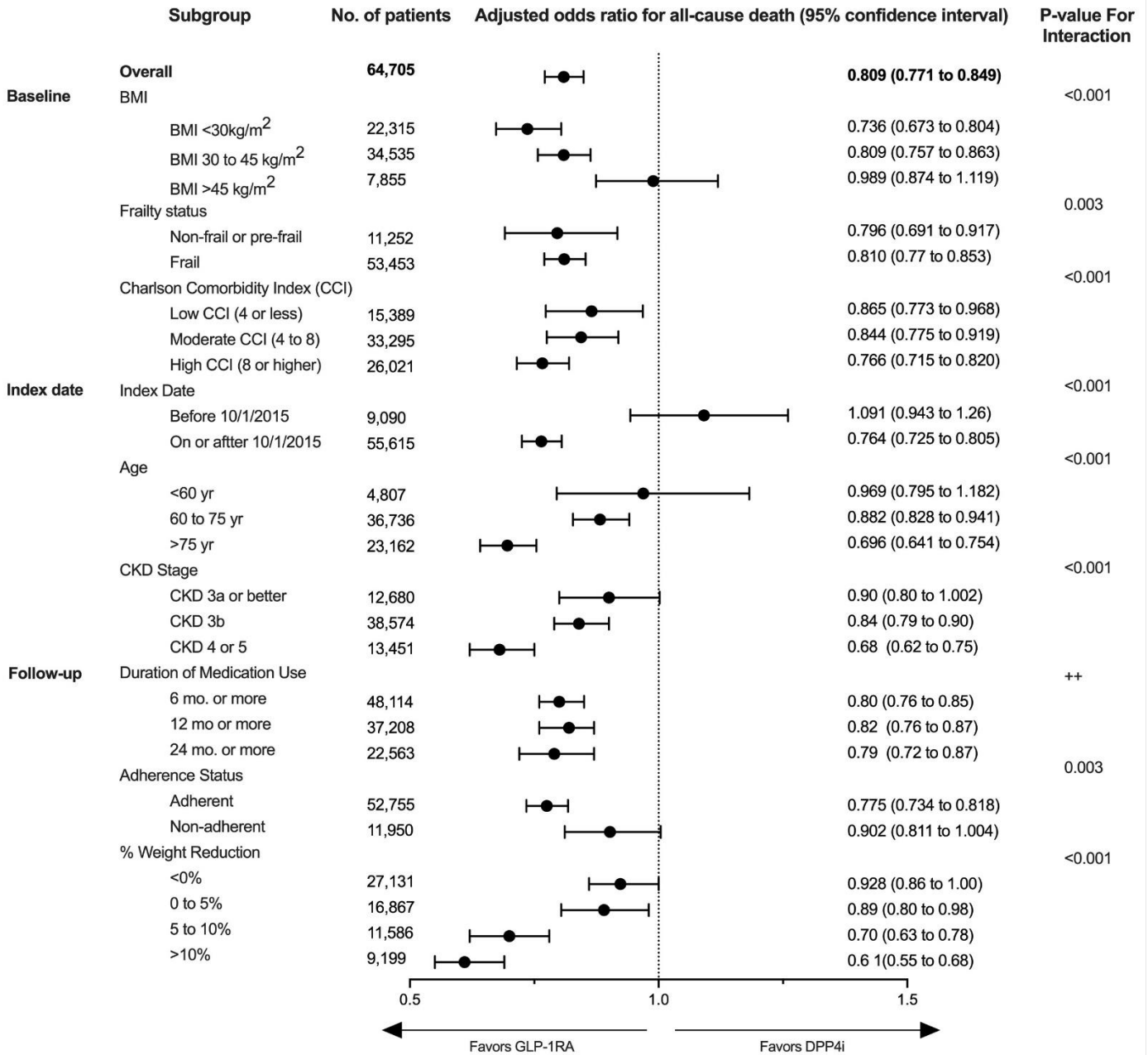


C



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D



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76 **Figure Legend:** Analyses are adjusted for propensity score. Applying Bonferroni correction for multiple comparisons,  
77  $p < 0.0012$  indicates statistically significant interaction.

78 ++p-value for interaction not calculated due to overlap among subgroups

79 BMI, body mass index; CKD, chronic kidney disease; yr, year; mo. Months

80 % weight reduction expressed as [weight at follow-up – weight at index date] / [weight at index date].

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84 **Supplemental Figure S4:** Kaplan-Meier curves for time to first composite cardiovascular event using per-protocol  
85 analysis and total mortality.

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88 Figure

89 Legend:

90 Kaplan

91 GLP1-RA,

92 glucagon

93 peptide 1

94 receptor

95 agonists;

96 dipeptidyl

97 peptidase

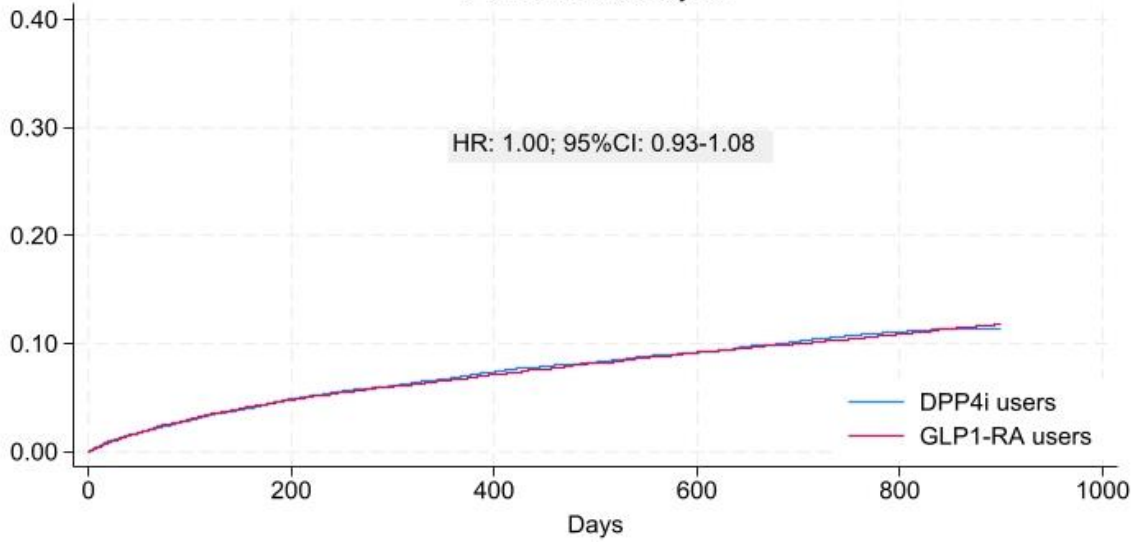
98 inhibitors;

99 hazard

100 CI,

### K-M curve of Cardiovascular outcome

Per-Protocol Analysis



K-M,  
Meier;

like

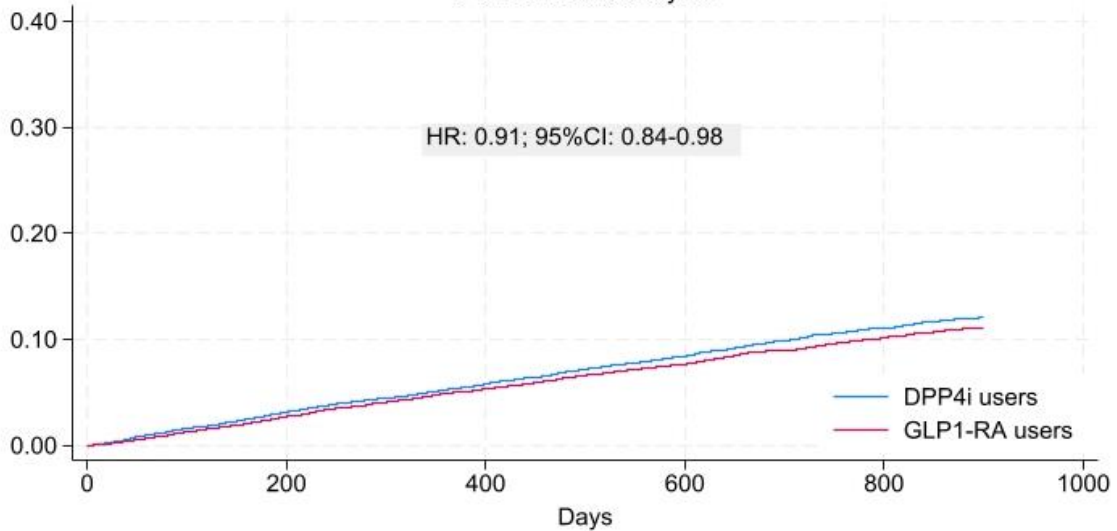
DPP4i,

4

HR,  
ratio;

### K-M curve of total mortality

Per-Protocol Analysis



101 confidence interval.



102 **SUPPLEMENTARY TABLES**

103 **Supplemental Table S1:**

104 A) Table S1-A: Incidence of albuminuria during baseline period.

105 B) Table S1-B: Incidence and progression of albuminuria during follow up period.

| <b>Table S1-A. Incidence of albuminuria during baseline period</b> |                  |                  |                                |
|--|------------------|------------------|--------------------------------|
|  | <b>GLP1-RA</b>   | <b>DPP4i</b>     | <b>Standardized Difference</b> |
|  | <b>n= 16,076</b> | <b>n= 16,076</b> |                                |
| Mean albumin in urine in mg  |                  |                  | -0.185                         |
| Missing  | 1,462 (9.09%)    | 1,601 (9.96%)    |                                |
| <30  | 8,802 (54.75%)   | 9,120 (56.73%)   |                                |
| >= 3 to <300   | 4,680 (29.11%)   | 4,792 (29.81%)   |                                |
| >=300 to <3000   | 793 (4.93%)      | 869 (5.41%)      |                                |
| > 3000   | 21 (0.13%)       | 12 (0.07%)       |                                |

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| <b>Table S1-B. Incidence and progression of albuminuria during follow up period</b> |                  |                  |                            |                |
|---|------------------|------------------|----------------------------|----------------|
|   | <b>GLP1-RA</b>   | <b>DPP4i</b>     | <b>Odds ratio (95%CI)*</b> | <b>p-value</b> |
|   | <b>n= 16,076</b> | <b>n= 16,076</b> |                            |                |
| Mean albumin level in urine in mg   |                  |                  |                            |                |
| Missing   | 6,398 (39.80%)   | 6,900 (42.92%)   | -                          |                |
| <30   | 5,480 (34.09%)   | 5,029 (31.28%)   | -                          |                |
| >= 30 to <300   | 3,415 (21.24%)   | 3,293 (20.48%)   | -                          |                |
| >=300 to <3000  | 759 (4.72%)      | 839 (5.220%)     | -                          |                |
| > 3000  | 24 (0.15%)       | 15 (0.09%)       |                            | <0.001         |
| Progression of albuminuria during follow up period                                  | 1,662 (10.34%)   | 1,737 (10.80%)   | 0.95 (0.89 - 1.02)         | 0.17           |

|   |             |             |                  |      |
|---|-------------|-------------|------------------|------|
| Regression of albuminuria during follow up period | 809 (5.03%) | 742 (4.62%) | 1.10 (0.99-1.12) | 0.08 |
|---|-------------|-------------|------------------|------|

Progression of albuminuria was defined as stepwise categorical increase in albuminuria (<30; >= 30 to <300; >=300 to <3000; or > 3000) compared to mean albuminuria at baseline.

Regression of albuminuria was defined as stepwise categorical decrease in albuminuria (<30; >= 3 to <300; >=300 to <3000; or > 3000) compared to mean albuminuria at baseline.

\*adjusting for propensity score

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110 **Supplemental Table S2:** Primary and Secondary Outcomes in overall cohort excluding subjects with  
 111 eGFR <15 mL per min per 1.73 m<sup>2</sup>.

| <b>Table S2. Primary and Secondary Outcomes in overall cohort excluding subjects with eGFR &lt;15 mL per min per 1.73 m<sup>2</sup></b> |                  |                  |   |                |
|---|------------------|------------------|---|----------------|
|   | <b>GLP1-RA</b>   | <b>DPP4i</b>     | <b>coefficient of regression or odds ratio (95%CI)*</b> | <b>p-value</b> |
|   | <b>n= 26,247</b> | <b>n= 36,205</b> |   |                |
| Rate of acute healthcare utilization, EPY   | 1.49 (4.41)      | 1.53 (4.40)      | -0.178 (-0.26 to -0.09) <sup>a</sup>                    | <0.001         |
| Cardiovascular composite event outcome  | 2813 (10.72%)    | 4,312 (11.91)    | 0.997 (0.94 - 1.06) <sup>b</sup>                        | 0.913          |
| Composite outcome of CKD progression  | 578 (2.2%)       | 1291 (3.57%)     | 0.61 (0.54 - 0.69) <sup>b</sup>                         | <0.001         |
| Death at follow-up  | 3,936 (15%)      | 10,927 (30.18%)  | 0.824 (0.78 - 0.87) <sup>b</sup>                        | <0.001         |

112 \*Multivariate linear regression analysis was performed for annual rate of healthcare utilization. Logistic regression  
 113 analysis performed for all other outcomes, adjusting for propensity score. Each outcome was assessed in a  
 114 separate model where the outcome was the dependent variable and use of GLP1-RA or DPP4i as predictor  
 115 variable.

116 Data are mean (SD) or numbers (%) unless stated otherwise. <sup>a</sup>Coefficient of regression; <sup>b</sup>Odds ratio; EPY, event per  
 117 patient per year; GLP1-RA, glucagon like peptide 1 receptor agonists; DPP4i, dipeptidyl peptidase 4 inhibitors.

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121 **Supplemental Table S3:**

122 Primary and secondary outcomes of the PS-matched cohort, adjusting for A1c and use of other  
 123 hypoglycemic agents at time of follow-up. Average A1c at time of follow-up was 7.915 (1.247) and 7.742  
 124 (1.267) within the GLP-1RA and DPP4i groups respectively; standardized difference= -0.137. Classes of  
 125 anti-hyperglycemic agents included glitazones, glinides, insulins, metformin, SGLT2i, and sulfonylureas.

| <b>Primary and Secondary Outcomes in PS-matched cohort (adjusting for A1c and use of other hypoglycemic agents during follow-up)</b> |                  |                  |   |                |
|--|------------------|------------------|---|----------------|
|  | <b>GLP1-RA</b>   | <b>DPP4i</b>     | <b>coefficient of regression or odds ratio (95%CI)*</b> | <b>p-value</b> |
|  | <b>n= 16,076</b> | <b>n= 16,076</b> |   |                |
| Rate of acute healthcare utilization, EPY  | 1.524 (4.828)    | 1.672 (4.56)     | -0.162 (-0.261 to -0.063) <sup>a</sup>                  | 0.001          |
| Cardiovascular composite event outcome   | 1757 (10.93%)    | 1782 (11.08%)    | 0.974 (0.906 to 1.047) <sup>b</sup>                     | 0.47           |
| Composite outcome of CKD progression   | 359 (2.23%)      | 557 (3.46%)      | 0.618 (0.537 to 0.71) <sup>b</sup>                      | <0.001         |
| Death at follow-up   | 2847 (17.71%)    | 3287 (20.45%)    | 0.867 (0.825 to 0.922) <sup>b</sup>                     | <0.001         |

126 \*Multivariate linear regression analysis was performed for annual rate of healthcare utilization. Logistic regression  
 127 analysis performed for all other outcomes, adjusting for propensity score. Each outcome was assessed in a  
 128 separate model where the outcome was the dependent variable and use of GLP1-RA or DPP4i as predictor  
 129 variable.

130 Data are mean (SD) or numbers (%) unless stated otherwise. <sup>a</sup>Coefficient of regression; <sup>b</sup>Odds ratio; EPY, event per  
 131 patient per year; GLP1-RA, glucagon like peptide 1 receptor agonists; DPP4i, dipeptidyl peptidase 4 inhibitors.

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140 **Supplemental Table S4:** Safety outcomes in the propensity-score matched cohort.

| <b>Supplemental Table S4. Safety Outcomes in PS-matched cohort</b> |                  |                  |                           |                |
|--|------------------|------------------|---------------------------|----------------|
|  | <b>GLP1-RA</b>   | <b>DPP4i</b>     | <b>Odds ratio (95%CI)</b> | <b>p-value</b> |
|  | <b>n= 16,076</b> | <b>n= 16,076</b> |                           |                |
| Hypoglycemic events  | 3743 (23.3%)     | 3644 (22.7%)     | 1.13 (1.05-1.21)          | 0.001          |
| Gastrointestinal symptoms  | 1657 (10.3%)     | 1487 (9.3%)      | 1.04 (0.98-1.09)          | 0.19           |

141 Data are numbers (%) unless stated otherwise. Each outcome was assessed in a separate model where the  
142 outcome was the dependent variable and use of GLP1-RA or DPP4i as predictor variable.

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145 **Supplemental Table S5:** Outcomes in propensity-score matched cohort using per-protocol analysis.

| <b>Supplemental Table S5: Outcomes in PS-matched cohort using per-protocol analysis</b> |                  |                  |                           |                |
|---|------------------|------------------|---------------------------|----------------|
|   | <b>GLP1-RA</b>   | <b>DPP4i</b>     | <b>Parameter Estimate</b> | <b>p-value</b> |
|   | <b>n= 16,057</b> | <b>n= 16,057</b> | <b>(95%CI)*</b>           |                |
| Rate of acute healthcare utilization,<br>EPY: mean (SD)                                 | 1.53 (5.04)      | 1.70 (4.63)      | B: -0.17 (-0.28 to -0.06) | 0.002          |
| Cardiovascular composite event<br>outcome   | 1,342 (8.36%)    | 1,320 (8.36%)    | OR: 1.02 (0.94 – 1.10)    | 0.66           |
| Composite outcome of CKD<br>progression   | 214 (1.33%)      | 347 (2.16%)      | OR: 0.61 (0.52-0.73)      | <0.001         |
| Death at follow-up  | 1,302 (8.11%)    | 1,354 (8.43%)    | OR: 0.96 (0.89-1.04)      | 0.29           |

146 \*Multivariate linear regression analysis was performed for annual rate of healthcare utilization. Logistic regression  
147 analysis performed for all other outcomes, adjusting for propensity score. Each outcome was assessed in a  
148 separate model where the outcome was the dependent variable and use of GLP1-RA or DPP4i as predictor  
149 variable.

150 Data are mean (SD) or numbers (%) unless stated otherwise. B, Coefficient of regression; OR, Odds ratio; EPY,  
151 event per patient per year; GLP1-RA, glucagon like peptide 1 receptor agonists; DPP4i, dipeptidyl peptidase 4  
152 inhibitors.

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157 **Supplemental Table S6:** within each group (GLP1-RA vs DPP4i).

| <b>Table S6. Proportion of medications prescribed</b> |                    |                   |                    |
|---|--------------------|-------------------|--------------------|
| <b>GLP1-RA</b>  |                    | <b>DPP4i</b>      |                    |
| <b>Medication</b>                                     | <b>Proportions</b> | <b>Medication</b> | <b>Proportions</b> |
| Albiglutide   | 0.03065            | Alogliptin        | 0.34227            |
| Dulaglutide   | 0.25651            | Linagliptin       | 0.08744            |
| Exenatide   | 0.06610            | Saxagliptin       | 0.39293            |
| Liraglutide   | 0.34486            | Sitagliptin       | 0.17736            |
| Lixisenatide  | 0.00015            |                   |                    |
| Semaglutide   | 0.30172            |                   |                    |

158 GLP1-RA, glucagon like peptide 1 receptor agonists; DPP4i, dipeptidyl peptidase 4 inhibitors.

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163 **Supplemental Table S7:** Summary of the protocol with emulation of a randomized control trial

| Protocol Component                  | Hypothetical RCT  | Emulation of RCT   |
|-------------------------------------|---|--|
| Key Eligibility criteria            | Adults aged 35 years who are regular VHA users with moderate to advanced CKD with two or more consecutive eGFR values <45 mL/min/1.73m <sup>2</sup> obtained over a span of three consecutive months. | Adults aged 35 years who are regular VHA users with moderate to advanced CKD with two or more consecutive eGFR values <45 mL/min/1.73m <sup>2</sup> obtained over a span of three consecutive months.                                      |
| Treatment strategies                | Placebo-controlled trial comparing placebo and GLP-1RA.   | Active comparator using DPP4i instead of placebo to help select treatment groups similar in treatment indications, and use of new-user design to assess patients' pretreatment characteristics and capture events during follow-up period. |
| Assignment procedures/Randomization | Randomization - participants are randomly assigned to placebo or treatment.   | Propensity-score matching on 120 baseline characteristics to emulate randomization. Patients are aware of the strategy to which they have been "assigned".   |
| Follow-up period                    | Starts at randomization and ends at study end (October 30, 2021), death, or initiation of a GLP1-RA in the placebo group, whichever occurs first.   | Starts at index date (date of GLP-1RA or DPP4i initiation) and ends at study end (October 30, 2021), death, or initiation of a GLP1-RA in the DPP4i group, whichever occurs first.   |
| Primary Outcome                     | Annual rate of acute healthcare utilization.  | Annual rate of acute healthcare utilization.   |
| Secondary Outcomes                  | All cause-mortality, incidence of cardiovascular composite event outcome, and ad-hoc composite kidney outcome.  | All cause-mortality, incidence of cardiovascular composite event outcome and ad-hoc composite kidney outcome.  |
| Analysis plan                       | Intention-to treat.   | Patients are analyzed regardless of medication discontinuation.  |
|                                     | Per-protocol analysis.  | Follow up period ended, or events censored after discontinuation of the medication in their respective group   |

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**Supplemental Table S8: Definitions of administrative codes (ICD-9 and ICD-10) used in the study outcomes.**

| <b>Table S8. Definitions of administrative codes (ICD-9 and ICD-10) used in the study outcomes</b>   |  |  |
|--|--|--|
|  | <b>ICD-9</b>   | <b>ICD-10</b>  |
| <b>Acute myocardial infarction: These codes has a positive predictive value (PPV) of 0.91.<sup>1</sup></b>   | 41000', '41001', '41002', '41010', '41011', '41012', '41020', '41021', '41022', '41030', '41031', '41032', '41040', '41041', '41042', '41050', '41051', '41052', '41060', '41061', '41062', '41070', '41071', '41072', '41080', '41081', '41082', '41090', '41091', '41092', '412' | I2101', 'I2102', 'I2109', 'I2111', 'I2119', 'I2121', 'I2129', 'I213', 'I214', 'I220', 'I221', 'I222', 'I228', 'I229', 'I252'   |
| <b>Acute cerebrovascular disease: these codes have PPV 73 for &lt;60 yr-old and PPV 82 for &gt;60 yr old, NPV 1; specificity 100%.<sup>2</sup></b> | 430 431 436 434<br>434.0 434.00<br>434.01 434.1<br>434.10 434.11<br>434.9 434.90<br>434.91   | I60, I61, I63, I64 I60 I60.0 I60.1 I60.2 I60.3<br>I60.4 I60.5 I60.6 I60.7 I60.8 I60.9 I61 I61.0<br>I61.1 I61.2 I61.3 I61.4 I61.5 I61.6 I61.8<br>I61.9 I63 I63.0 I63.1 I63.2 I63.3 I63.4 I63.5<br>I63.6 I63.8 I63.9 I64   |
| <b>Cardiac arrest/ventricular fibrillation</b>   | AHRQ-CCS category 107  | I462' 'I468' 'I469' 'I4901' 'I4902' 'I97120' 'I97121' 'I97711' 'O0336' 'O0386' 'O0486' 'O0486' 'O0736' 'O0881' 'O29111' 'O29112' 'O29113' 'O29119' 'Z8674'   |
| <b>Percutaneous coronary intervention procedure codes<sup>1</sup></b>  | 0066', '1755', '3601', '3602', '3605', '3606', '3607', '3609'  | 0270046', '027004Z', '02700D6', '02700DZ', '02700T6', '02700TZ', '02700Z6', '02700ZZ', '0270346', '027034Z', '02703D6', '02703DZ', '02703T6', '02703TZ', '02703Z6', '02703ZZ', '0270446', '027044Z', '02704D6', '02704DZ', '02704T6', '02704TZ', '02704Z6', '02704ZZ', '0271046', '027104Z', '02710D6', '02710DZ', '02710T6', '02710TZ', '02710Z6', '02710ZZ', '0271346', '027134Z', '02713D6', '02713DZ', '02713T6', '02713TZ', '02713Z6', '02713ZZ', '0271446', '027144Z', '02714D6', '02714DZ', '02714T6', '02714TZ', '02714Z6', '02714ZZ', '0272046', '027204Z', '02720D6', '02720DZ', '02720T6', '02720TZ', '02720Z6', '02720ZZ', '0272346', '027234Z', '02723D6', '02723DZ', |



|   |  |
|---|--|
|   | '02723T6', '02723TZ', '02723Z6', '02723ZZ',<br>'0272446', '027244Z', '02724D6', '02724DZ',<br>'02724T6', '02724TZ', '02724Z6', '02724ZZ',<br>'0273046', '027304Z', '02730D6', '02730DZ',<br>'02730T6', '02730TZ', '02730Z6', '02730ZZ',<br>'0273346', '027334Z', '02733D6', '02733DZ',<br>'02733T6', '02733TZ', '02733Z6', '02733ZZ',<br>'0273446', '027344Z', '02734D6', '02734DZ',<br>'02734T6', '02734TZ', '02734Z6', '02734ZZ',<br>'02C03ZZ', '02C04ZZ', '02C13ZZ', '02C14ZZ',<br>'02C23ZZ', '02C24ZZ', '02C33ZZ', '02C34ZZ',<br>'X2C0361', 'X2C1361'  |
| <b>Coronary artery bypass graft procedure codes<sup>1</sup></b> | 33510', '33511', '33512',<br>'33513', '33514', '33516',<br>'33517', '33518', '33519',<br>'33521', '33522', '33523',<br>'33533', '33534', '33535',<br>'33536'   |
|   | 0210093', '0210098', '0210099', '021009C',<br>'021009F', '021009W', '02100A3', '02100A8',<br>'02100A9', '02100AC', '02100AF', '02100AW',<br>'02100J3', '02100J8', '02100J9', '02100JC',<br>'02100JF', '02100JW', '02100K3', '02100K8',<br>'02100K9', '02100KC', '02100KF', '02100KW',<br>'02100Z3', '02100Z8', '02100Z9', '02100ZC',<br>'02100ZF', '0210344', '02103D4', '0210444',<br>'0210493', '0210498', '0210499', '021049C',<br>'021049F', '021049W', '02104A3', '02104A8',<br>'02104A9', '02104AC', '02104AF', '02104AW',<br>'02104D4', '02104J3', '02104J8', '02104J9',<br>'02104JC', '02104JF', '02104JW', '02104K3',<br>'02104K8', '02104K9', '02104KC', '02104KF',<br>'02104KW', '02104Z3', '02104Z8', '02104Z9',<br>'02104ZC', '02104ZF', '0211093', '0211098',<br>'0211099', '021109C', '021109F', '021109W',<br>'02110A3', '02110A8', '02110A9', '02110AC',<br>'02110AF', '02110AW', '02110J3', '02110J8',<br>'02110J9', '02110JC', '02110JF', '02110JW',<br>'02110K3', '02110K8', '02110K9', '02110KC',<br>'02110KF', '02110KW', '02110Z3', '02110Z8',<br>'02110Z9', '02110ZC', '02110ZF', '0211344',<br>'02113D4', '0211444', '0211493', '0211498',<br>'0211499', '021149C', '021149F', '021149W',<br>'02114A3', '02114A8', '02114A9', '02114AC',<br>'02114AF', '02114AW', '02114D4', '02114J3',<br>'02114J8', '02114J9', '02114JC', '02114JF',<br>'02114JW', '02114K3', '02114K8', '02114K9',<br>'02114KC', '02114KF', '02114KW', '02114Z3',<br>'02114Z8', '02114Z9', '02114ZC', '02114ZF', |

'0212093', '0212098', '0212099', '021209C',  
 '021209F', '021209W', '02120A3', '02120A8',  
 '02120A9', '02120AC', '02120AF', '02120AW',  
 '02120J3', '02120J8', '02120J9', '02120JC',  
 '02120JF', '02120JW', '02120K3', '02120K8',  
 '02120K9', '02120KC', '02120KF', '02120KW',  
 '02120Z3', '02120Z8', '02120Z9', '02120ZC',  
 '02120ZF', '0212344', '02123D4', '0212444',  
 '0212493', '0212498', '0212499', '021249C',  
 '021249F', '021249W', '02124A3', '02124A8',  
 '02124A9', '02124AC', '02124AF', '02124AW',  
 '02124D4', '02124J3', '02124J8', '02124J9',  
 '02124JC', '02124JF', '02124JW', '02124K3',  
 '02124K8', '02124K9', '02124KC', '02124KF',  
 '02124KW', '02124Z3', '02124Z8', '02124Z9',  
 '02124ZC', '02124ZF', '0213093', '0213098',  
 '0213099', '021309C', '021309F', '021309W',  
 '02130A3', '02130A8', '02130A9', '02130AC',  
 '02130AF', '02130AW', '02130J3', '02130J8',  
 '02130J9', '02130JC', '02130JF', '02130JW',  
 '02130K3', '02130K8', '02130K9', '02130KC',  
 '02130KF', '02130KW', '02130Z3', '02130Z8',  
 '02130Z9', '02130ZC', '02130ZF', '0213344',  
 '02133D4', '0213444', '0213493', '0213498',  
 '0213499', '021349C', '021349F', '021349W',  
 '02134A3', '02134A8', '02134A9', '02134AC',  
 '02134AF', '02134AW', '02134D4', '02134J3',  
 '02134J8', '02134J9', '02134JC', '02134JF',  
 '02134JW', '02134K3', '02134K8', '02134K9',  
 '02134KC', '02134KF', '02134KW', '02134Z3',  
 '02134Z8', '02134Z9', '02134ZC', '02134ZF'

**Percutaneous coronary intervention procedure codes<sup>1</sup> CPT codes** 92920', '92921', '92924', '92925', '92928', '92929', '92933', '92934', '92937', '92938', '92941', '92943', '92944', '92980', '92981', '92982', '92984', '92995', '92996', 'C9600', 'C9601', 'C9602', 'C9603', 'C9604', 'C9605', 'C9606', 'C9607', 'C9608', 'G0290', 'G0291'

**Coronary artery bypass graft procedure codes<sup>1</sup>** 33510', '33511', '33512', '33513', '33514', '33516', '33517', '33518', '33519', '33521', '33522', '33523', '33533', '33534', '33535', '33536'

**Stop codes identifying emergency visits** 130, 101, 1, 297, 131

**AHRQ-CCS = the Agency for Health Research and Quality Clinical Classifications Software<sup>3</sup>**

168 **Supplemental Table S9: Administrative codes (ICD-9 and ICD-10) used in definitions of baseline**  
 169 **characteristics.**

| <b>Table S9. Administrative codes (ICD-9 and ICD-10) used in definitions of baseline characteristics.</b> |   |  |
|---|---|--|
| <b>Baseline characteristic</b>  | <b>ICD-9 Definition</b>   | <b>ICD-10-definition</b>   |
| Gender  | Self-identified   |  |
| Race and ethnicity  | Self-identified   |  |
| Family history of cardiovascular diseases   | ICD-9-CM codes: V171, V1749, V174, V1741, and V173.   | Z8249 Z8241 Z8674  |
| Smoking   | ICD-9-CM codes: 3051 and V1582  | AHRQ-CCS category MBD024   |
| Alcohol-related disorders   | AHRQ-CCS category 660   | AHRQ-CCS category MBD017   |
| Substance-related disorders   | AHRQ-CCS category 661   | AHRQ-CCS category SYM009   |
| Diabetes with ketoacidosis or uncontrolled diabetes   | AHRQ-CCS category 3.3.1 and Selected codes from AHRQ-CCS category 3.3.7 (24920 24921 24930 24931 25020 25021 25022 25023 25030 25032 25033) | E0800 E0801 E0810 E0811 E0865 E0900 E0901 E0910 E0911 E0965 E1010 E1011 E1065 E1100 E1101 E1110 E1111 E1165 E1300 E1301 E1310 E1311 E1365  |
| Diabetes with ophthalmic manifestations   | 24950 24951 25050 25051 25052 25053   | E08311 E08319 E08321 E083211 E083212 E083213 E083219 E08329 E083291 E083292 E083293 E083299 E08331 E083311 E083312 E083313 E083319 E08339 E083391 E083392 E083393 E083399 E08341 E083411 E083412 E083413 E083419 E08349 E083491 E083492 E083493 E083499 E08351 E083511 E083512 E083513 E083519 E083521 E083522 E083523 E083529 E083531 E083532 E083533 E083539 E083541 E083542 E083543 E083549 E083551 E083552 E083553 E083559 E08359 E083591 E083592 E083593 E083599 E0836 E0837X1 E0837X2 E0837X3 E0837X9 E0839 E09311 E09319 E09321 E093211 E093212 E093213 E093219 E09329 E093291 E093292 E093293 E093299 E09331 E093311 E093312 E093313 E093319 E09339 E093391 E093392 E093393 E093399 E09341 E093411 E093412 E093413 |

E093419 E09349 E093491 E093492  
E093493 E093499 E09351 E093511  
E093512 E093513 E093519 E093521  
E093522 E093523 E093529 E093531  
E093532 E093533 E093539 E093541  
E093542 E093543 E093549 E093551  
E093552 E093553 E093559 E09359  
E093591 E093592 E093593 E093599  
E0936 E0937X1 E0937X2 E0937X3  
E0937X9 E0939 E10311 E10319 E10321  
E103211 E103212 E103213 E103219  
E10329 E103291 E103292 E103293  
E103299 E10331 E103311 E103312  
E103313 E103319 E10339 E103391  
E103392 E103393 E103399 E10341  
E103411 E103412 E103413 E103419  
E10349 E103491 E103492 E103493  
E103499 E10351 E103511 E103512  
E103513 E103519 E103521 E103522  
E103523 E103529 E103531 E103532  
E103533 E103539 E103541 E103542  
E103543 E103549 E103551 E103552  
E103553 E103559 E10359 E103591  
E103592 E103593 E103599 E1036  
E1037X1 E1037X2 E1037X3 E1037X9  
E1039 E11311 E11319 E11321 E113211  
E113212 E113213 E113219 E11329  
E113291 E113292 E113293 E113299  
E11331 E113311 E113312 E113313  
E113319 E11339 E113391 E113392  
E113393 E113399 E11341 E113411  
E113412 E113413 E113419 E11349  
E113491 E113492 E113493 E113499  
E11351 E113511 E113512 E113513  
E113519 E113521 E113522 E113523  
E113529 E113531 E113532 E113533  
E113539 E113541 E113542 E113543  
E113549 E113551 E113552 E113553  
E113559 E11359 E113591 E113592  
E113593 E113599 E1136 E1137X1  
E1137X2 E1137X3 E1137X9 E1139 E13311  
E13319 E13321 E133211 E133212  
E133213 E133219 E13329 E133291  
E133292 E133293 E133299 E13331

|   |  |  |
|---|--|--|
|   |  | E133311 E133312 E133313 E133319<br>E13339 E133391 E133392 E133393<br>E133399 E13341 E133411 E133412<br>E133413 E133419 E13349 E133491<br>E133492 E133493 E133499 E13351<br>E133511 E133512 E133513 E133519<br>E133521 E133522 E133523 E133529<br>E133531 E133532 E133533 E133539<br>E133541 E133542 E133543 E133549<br>E133551 E133552 E133553 E133559<br>E13359 E133591 E133592 E133593<br>E133599 E1336 E1337X1 E1337X2<br>E1337X3 E1337X9 E1339 |
| Diabetes with renal manifestations        | 24940 24941 25040 25041<br>25042 25043         | E0821 E0822 E0829 E0921 E0922 E0929<br>E1021 E1022 E1029 E1121 E1122 E1129<br>E1321 E1322 E1329  |
| Diabetes with neurological manifestations | 24960 24961 25060 25061<br>25062 25063         | E0840 E0841 E0842 E0843 E0844 E0849<br>E08610 E0940 E0941 E0942 E0943 E0944<br>E0949 E09610 E1040 E1041 E1042 E1043<br>E1044 E1049 E10610 E1140 E1141 E1142<br>E1143 E1144 E1149 E11610 E1340 E1341<br>E1342 E1343 E1344 E1349 E13610  |
| Diabetes with circulatory manifestations  | AHRQ-CCS category 3.3.5                        | E0851 E0852 E0859 E0951 E0952 E0959<br>E1051 E1052 E1059 E1151 E1152 E1159<br>E1351 E1352 E1359  |
| Diabetes with unspecified manifestations  | AHRQ-CCS category 3.3.6                        | E08618 E08620 E08621 E08622 E08628<br>E08630 E08638 E0869 E088 E09618<br>E09620 E09621 E09622 E09628 E09630<br>E09638 E0969 E098 E10618 E10620<br>E10621 E10622 E10628 E10630 E10638<br>E1069 E108 E11618 E11620 E11621<br>E11622 E11628 E11630 E11638 E1169<br>E118 E13618 E13620 E13621 E13622<br>E13628 E13630 E13638 E1369 E138  |
| Diabetes with hypoglycemia                | 2510 2511 2512 2703 7750<br>7756 9623          | E08641 E08649 E09641 E09649 E10641<br>E10649 E11641 E11649 E13641 E13649<br>E15 E160 E161 E162 T383X1A T383X1D<br>T383X1S T383X2A T383X2D T383X2S<br>T383X3A T383X3D T383X3S T383X4A<br>T383X4D T383X4S T383X5A T383X5D<br>T383X5S   |
| Hemiplegia/quadreplegia<br>Dementia       | CCI using Deyo method<br>CCI using Deyo method | CCI using Beyrer validated codes<br>CCI using Beyrer validated codes   |

|  |                             |                                  |
|--|-----------------------------|----------------------------------|
| Liver disease-mild   | CCI using Deyo method       | CCI using Beyrer validated codes |
| Liver disease-severe   | CCI using Deyo method       | CCI using Beyrer validated codes |
| Malignancy other than skin cancer  | CCI using Deyo method       | CCI using Beyrer validated codes |
| Metastatic neoplasm  | CCI using Deyo method       | CCI using Beyrer validated codes |
| Acquired Immunodeficiency Syndrome   | CCI using Deyo method       | CCI using Beyrer validated codes |
| Hypertension   | AHRQ-CCS category 98        | AHRQ-CCS category CIR007         |
| Hypertension with complications and secondary hypertension   | AHRQ-CCS category 99        | AHRQ-CCS category CIR008         |
| Diabetes   | AHRQ-CCS category 49        | AHRQ-CCS category END002         |
| Diabetes with complication   | AHRQ-CCS category 50        | AHRQ-CCS category END003         |
| Rheumatoid arthritis and related disease; Systemic lupus erythematosus and connective tissue disorders | AHRQ-CCS category 202 & 210 | AHRQ-CCS category MUS003         |
| schizophrenia and other psychotic disorders  | AHRQ-CCS category 659       | AHRQ-CCS category MBD001         |
| suicide and intentional self-inflicted injury  | AHRQ-CCS category 662       | AHRQ-CCS category MBD027         |
| Anemia   | VAFI codes                  | VAFI codes                       |
| Atrial fibrillation  | VAFI codes                  | VAFI codes                       |
| Thyroid disease  | VAFI codes                  | VAFI codes                       |
| Gait abnormality   | VAFI codes                  | VAFI codes                       |
| Arthritis  | VAFI codes                  | VAFI codes                       |
| Falls  | VAFI codes                  | VAFI codes                       |
| Incontinence   | VAFI codes                  | VAFI codes                       |
| Muscle wasting   | VAFI codes                  | VAFI codes                       |
| Osteoporosis   | VAFI codes                  | VAFI codes                       |
| Parkinsonism   | VAFI codes                  | VAFI codes                       |
| Peripheral neuropathy  | VAFI codes                  | VAFI codes                       |
| Impaired vision  | VAFI codes                  | VAFI codes                       |
| Weight loss  | VAFI codes                  | VAFI codes                       |
| Anxiety  | VAFI codes                  | VAFI codes                       |
| Depression   | VAFI codes                  | VAFI codes                       |
| Chronic pain   | VAFI codes                  | VAFI codes                       |
| Failure to thrive  | VAFI codes                  | VAFI codes                       |
| Fatigue  | VAFI codes                  | VAFI codes                       |
| Congestive heart failure   | VAFI codes                  | VAFI codes                       |
| Coronary artery disease  | VAFI codes                  | VAFI codes                       |

| Obesity | VAFI codes | VAFI codes |
|---------|------------|------------|
|---------|------------|------------|

- 170 AHRQ-CCS = the Agency for Health Research and Quality Clinical Classifications Software<sup>3</sup>
- 171 \*CCI using Deyo et al method in calculating the Charlson comorbidity index. <sup>4</sup>
- 172 CCI using validated set of ICD-10 codes by Beyrer et al<sup>5</sup>
- 173 VAFI codes denote VA-Frailty index using Orkaby et al method, which was validated in VA population. <sup>6</sup>

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175 **Supplemental Table S10:** LOINC codes used to identify laboratory tests

| <b>LOINC codes used to identify laboratory tests</b> |                                   |
|--|-----------------------------------|
| Laboratory test name                                 | LOINC codes                       |
| Hemoglobin A1C (Glycohemoglobin)                     | 17855-8, 17856-6, 4548-4, 4549-2  |
| LDL-Cholesterol (both calculated and direct)         | 13457-7, 18262-6, 2089-1, 49132-4 |
| HDL-Cholesterol                                      | 2085-9                            |
| Total Cholesterol                                    | 2093-3                            |
| Serum Creatinine                                     | 2160-0                            |

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178 **Table S11:** Handling of missing values at baseline

| <b>Handling of missing lab values at baseline</b> |              |                |                         |                      |
|---|--------------|----------------|-------------------------|----------------------|
|   | <b>Total</b> | <b>Missing</b> | <b>Replaced by mean</b> | <b>Still missing</b> |
| DDP4 basic cohort                                 |              |                |                         |                      |
| A1C   | 37,999       | 151            | 129                     | 22                   |
| Glucose   | 37,999       | 65             | 61                      | 4                    |
| Creatinine  | 37,999       | 60             | 60                      | 0                    |
| LDL_Cholest                                       | 37,999       | 250            | 188                     | 62                   |
| HDL_Cholest                                       | 37,999       | 241            | 185                     | 56                   |
| T_Cholesterol                                     | 37,999       | 269            | 208                     | 61                   |
| GLP1 basic cohort                                 |              |                |                         |                      |
| A1C   | 27,146       | 35             | 22                      | 13                   |
| Glucose   | 27,146       | 12             | 12                      | 0                    |
| Creatinine  | 27,146       | 5              | 5                       | 0                    |
| LDL_Cholest                                       | 27,146       | 111            | 75                      | 36                   |
| HDL_Cholest                                       | 27,146       | 96             | 64                      | 32                   |
| T_Cholesterol                                     | 27,146       | 93             | 61                      | 32                   |
| <b>Handling missing vitals at baseline</b>        |              |                |                         |                      |
|   | <b>Total</b> | <b>Missing</b> | <b>Replaced by mean</b> | <b>Still missing</b> |
| DDP4 basic cohort                                 |              |                |                         |                      |
| Weight  | 37,999       | 87             | 69                      | 18                   |
| Systolic/ Diastolic BP                            | 37,999       | 76             | 61                      | 15                   |
| GLP1 basic cohort                                 |              |                |                         |                      |
| Weight  | 27,146       | 39             | 32                      | 7                    |
| Systolic/ Diastolic BP                            | 27,146       | 30             | 23                      | 7                    |

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