

**Vitamin D Status, Vitamin D Receptor Polymorphisms, and Risk of Microvascular Complications among Individuals with Type 2 Diabetes: A Prospective Study**

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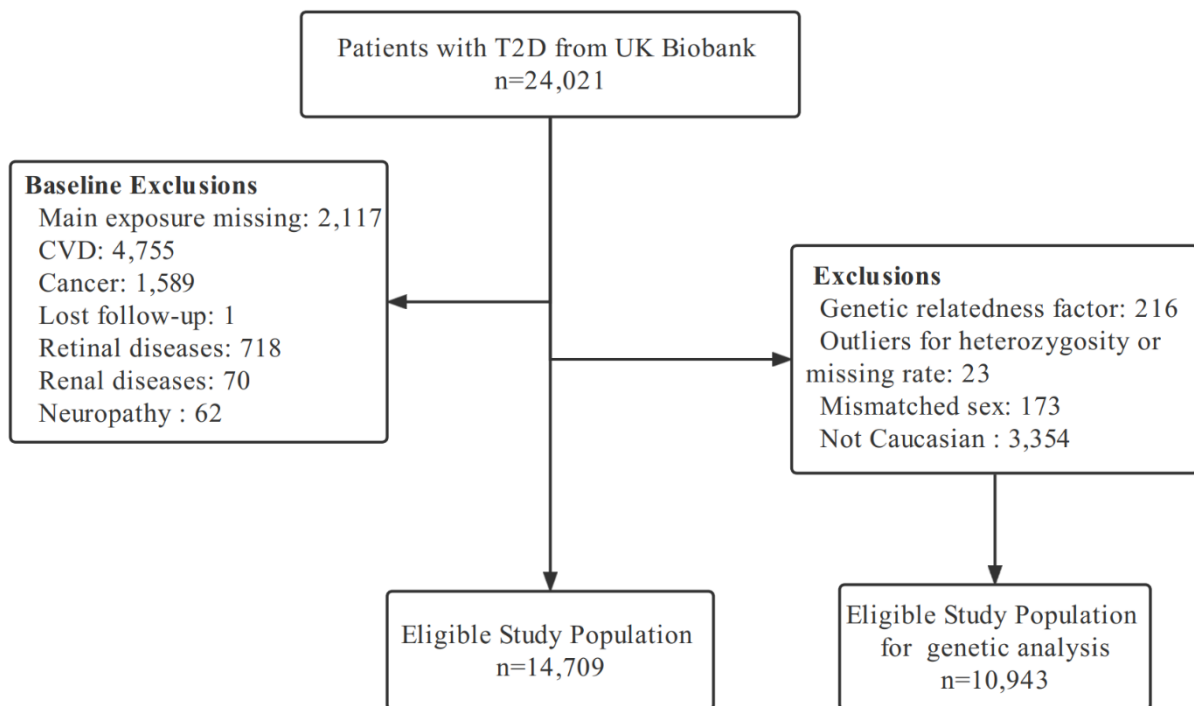
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**Supplementary Figure 1.** Flowchart of the study participants

**Supplementary Table 1.** Least-square means of cardiometabolic markers according to levels of serum 25(OH)D among patients with T2D in the UK Biobank

| Characteristics                                   | Serum 25(OH)D concentrations (nmol/L) |              |              |              | <i>P</i> <sub>trend</sub> |
|---------------------------------------------------|---------------------------------------|--------------|--------------|--------------|---------------------------|
|                                                   | < 25.0                                | 25.0-49.9    | 50.0-74.9    | ≥ 75.0       |                           |
| Glucose (n=13,458, mmol/L)                        | 7.82 ± 0.12                           | 7.35 ± 0.10  | 7.04 ± 0.11  | 6.75 ± 0.15  | <0.001                    |
| HbA <sub>1c</sub> (n=13,891, mmol/mol)            | 55.31 ± 0.45                          | 53.58 ± 0.40 | 52.38 ± 0.43 | 50.69 ± 0.58 | <0.001                    |
| High density cholesterol (n=13,469, mmol/L)       | 1.29 ± 0.01                           | 1.28 ± 0.01  | 1.29 ± 0.01  | 1.30 ± 0.01  | 0.409                     |
| Low density cholesterol direct (n=14,663, mmol/L) | 2.88 ± 0.02                           | 2.80 ± 0.02  | 2.70 ± 0.02  | 2.54 ± 0.03  | <0.001                    |
| Triglyceride (n=14,681, mmol/L)                   | 2.28 ± 0.04                           | 1.99 ± 0.04  | 1.67 ± 0.04  | 1.35 ± 0.05  | <0.001                    |
| Total cholesterol (n=14,701, mmol/L)              | 4.83 ± 0.03                           | 4.68 ± 0.03  | 4.53 ± 0.03  | 4.30 ± 0.04  | <0.001                    |

The least-square mean ( $\pm$  SE) were estimated using the general linear model with the adjustment of age (continuous), sex (female, male), ethnic (White people, non-White people [including Black people, Asian people, and multiethnic participants]), the Townsend Deprivation Index (continuous), education (College/University degree, A levels/AS levels or equivalent or O levels/GCSEs or equivalent or other professional qualifications, none of the above), employed (yes, no), smoking status (never, past, current), drinking status (never, 1-2 times/week, 3-4 times/week,  $\geq 5$  times/week), healthy diet (yes, no), use of multivitamin/mineral supplements (yes, no), total physical activity level (MET-minutes/week, continuous), time spend outdoors in summer (continuous, hours/day), season of blood drawn (March to May, June to August, September to November, December to February), estimated glomerular filtration rate (eGFR,  $\leq 90$ ,  $>90$  mL/min/1.73 m<sup>2</sup>), BMI (continuous), history of hypertension (yes, no), diabetic medication (no insulin or pills, only diabetes pills, or insulin and/or others), and diabetes duration ( $\leq 3$ , 3-10 years,  $>10$  years).

**Supplementary Table 2.** Serum 25(OH)D concentrations according to different VDR genotypes among patients with T2D in the UK Biobank

|                                 | Serum 25(OH)D, nmol/L | <i>P</i> value |
|---------------------------------|-----------------------|----------------|
| <b>rs7975232 (<i>ApalI</i>)</b> |                       | 0.601          |
| CC (N=2,486)                    | 43.4 (30.5, 58.5)     |                |
| AC (N=5,397)                    | 43.7 (30.2, 59.1)     |                |
| AA (N=3,060)                    | 42.9 (29.2, 58.6)     |                |
| <b>rs1544410 (<i>BsmI</i>)</b>  |                       | 0.289          |
| CC (N=3,831)                    | 43.9 (30.5, 59.2)     |                |
| CT (N=5,267)                    | 43.4 (29.9, 58.9)     |                |
| TT (N=1,845)                    | 42.6 (29.3, 57.8)     |                |
| <b>rs2228570 (<i>FokI</i>)</b>  |                       | 0.462          |
| AA (N=1,667)                    | 43.8 (30.1, 59.1)     |                |
| AG (N=5,171)                    | 43.3 (30.1, 58.3)     |                |
| GG (N=4,105)                    | 43.5 (30.1, 59.4)     |                |
| <b>rs731236 (<i>TaqI</i>)</b>   |                       | 0.238          |
| AA (N=3,882)                    | 43.9 (30.7, 59.3)     |                |
| AG (N=5,252)                    | 43.4 (29.8, 58.8)     |                |
| GG (N=1,809)                    | 42.6 (29.3, 57.7)     |                |

Data are presented as median (interquartile range).

**Supplementary Table 3.** Multivariable-adjusted HRs (95% CIs) for associations between VDR polymorphisms and diabetic microvascular complications among patients with T2D in the UK Biobank

|                                 | <b>Composite<br/>microvascular<br/>complications</b> | <b>Diabetic<br/>retinopathy</b> | <b>Diabetic<br/>nephropathy</b> | <b>Diabetic<br/>neuropathy</b> |
|---------------------------------|------------------------------------------------------|---------------------------------|---------------------------------|--------------------------------|
|                                 | HR (95% CI)                                          | HR (95% CI)                     | HR (95% CI)                     | HR (95% CI)                    |
| <b>rs7975232 (<i>ApalI</i>)</b> |                                                      |                                 |                                 |                                |
| CC (n=2,486)                    | 1 (ref.)                                             | 1 (ref.)                        | 1 (ref.)                        | 1 (ref.)                       |
| AC (n=5,397)                    | 1.03 (0.88, 1.21)                                    | 1.10 (0.85, 1.44)               | 0.95 (0.77, 1.17)               | 1.16 (0.82, 1.64)              |
| AA (n=3,060)                    | 1.12 (0.95, 1.33)                                    | 1.15 (0.85, 1.51)               | 1.11 (0.89, 1.39)               | 1.23 (0.84, 1.79)              |
| <b>rs1544410 (<i>BsmI</i>)</b>  |                                                      |                                 |                                 |                                |
| CC (n=3,831)                    | 1 (ref.)                                             | 1 (ref.)                        | 1 (ref.)                        | 1 (ref.)                       |
| CT (n=5,267)                    | 1.02 (0.89, 1.17)                                    | 1.12 (0.89, 1.41)               | 0.98 (0.82, 1.17)               | 1.08 (0.80, 1.46)              |
| TT (n=1,845)                    | 1.23 (1.04, 1.46)                                    | 1.16 (0.86, 1.55)               | 1.23 (0.99, 1.54)               | 1.44 (1.01, 2.05)              |
| <b>rs2228570 (<i>FokI</i>)</b>  |                                                      |                                 |                                 |                                |
| AA (n=1,667)                    | 1 (ref.)                                             | 1 (ref.)                        | 1 (ref.)                        | 1 (ref.)                       |
| AG (n=5,171)                    | 0.92 (0.77, 1.09)                                    | 1.01 (0.76, 1.36)               | 0.96 (0.76, 1.21)               | 1.04 (0.72, 1.52)              |
| GG (n=4,105)                    | 0.97 (0.81, 1.16)                                    | 1.02 (0.75, 1.38)               | 1.05 (0.83, 1.33)               | 1.07 (0.72, 1.57)              |
| <b>rs731236 (<i>TaqI</i>)</b>   |                                                      |                                 |                                 |                                |
| AA (n=3,882)                    | 1 (ref.)                                             | 1 (ref.)                        | 1 (ref.)                        | 1 (ref.)                       |
| AG (n=5,252)                    | 1.03 (0.89, 1.18)                                    | 1.06 (0.85, 1.33)               | 0.98 (0.82, 1.18)               | 1.09 (0.81, 1.47)              |
| GG (n=1,809)                    | 1.23 (1.03, 1.46)                                    | 1.17 (0.88, 1.57)               | 1.21 (0.97, 1.52)               | 1.41 (0.99, 2.02)              |

HR was adjusted for age (continuous), sex (female, male), ethnic (White people, non-White people [including Black people, Asian people, and multiethnic participants]), the Townsend Deprivation Index (continuous), education (College/University degree, A levels/AS levels or equivalent or O levels/GCSEs or equivalent or other professional qualifications, none of the above), employed (yes, no), smoking status (never, past, current), drinking status (never, 1-2 times/week, 3-4 times/week,  $\geq 5$  times/week), healthy diet (yes, no), use of multivitamin/mineral supplements (yes, no), total physical activity level (MET-minutes /week, continuous), time spend outdoors in summer (continuous, hours/day), season of blood drawn (March to May, June to August, September to November, December to February), estimated glomerular filtration rate (eGFR,  $\leq 90$ ,  $>90$  mL/min/1.73 m<sup>2</sup>), BMI (continuous), history of hypertension (yes, no), and hypercholesterolemia (yes, no), diabetic medication (no insulin or pills, only diabetes pills, or insulin and/or others), diabetes duration ( $\leq 3$ , 3-10 years,  $>10$  years), HbA<sub>1c</sub> ( $<7\%$ ,  $\geq 7\%$  [ $<53$ , or  $\geq 53$  mmol/mol]), genotype measurement batch, and ten principal components of ancestry.

**Supplementary Table 4.** Multivariable-adjusted HRs (95% CIs) for associations between serum 25(OH)D concentrations and diabetic microvascular complications among patients with T2D according to different genotypes of VDR polymorphisms

|                                | Composite microvascular complications |                          |                                 | Diabetic retinopathy |                          |                                 | Diabetic nephropathy |                          |                                 | Diabetic neuropathy |                          |                                 |
|--------------------------------|---------------------------------------|--------------------------|---------------------------------|----------------------|--------------------------|---------------------------------|----------------------|--------------------------|---------------------------------|---------------------|--------------------------|---------------------------------|
|                                | Cases                                 | HR (95% CI) <sup>a</sup> | <i>P</i> <sub>interaction</sub> | Case                 | HR (95% CI) <sup>a</sup> | <i>P</i> <sub>interaction</sub> | Cases                | HR (95% CI) <sup>a</sup> | <i>P</i> <sub>interaction</sub> | Cases               | HR (95% CI) <sup>a</sup> | <i>P</i> <sub>interaction</sub> |
| <b>rs7975232 (<i>Apal</i>)</b> |                                       |                          | 0.841                           |                      |                          | 0.959                           |                      |                          | 0.552                           |                     |                          | 0.406                           |
| CC (n=2,486)                   | 224                                   | 0.85 (0.61, 1.19)        |                                 | 77                   | 0.68 (0.39, 1.19)        |                                 | 136                  | 0.90 (0.58, 1.39)        |                                 | 45                  | 0.72 (0.34, 1.51)        |                                 |
| AC (n=5,397)                   | 510                                   | 0.67 (0.54, 0.83)        |                                 | 193                  | 0.76 (0.53, 1.08)        |                                 | 283                  | 0.54 (0.40, 0.72)        |                                 | 118                 | 0.67 (0.43, 1.04)        |                                 |
| AA (n=3,060)                   | 318                                   | 0.75 (0.58, 0.99)        |                                 | 113                  | 0.74 (0.47, 1.17)        |                                 | 191                  | 0.61(0.43, 0.86)         |                                 | 74                  | 0.84 (0.48, 1.47)        |                                 |
| <b>rs1544410 (<i>BsmI</i>)</b> |                                       |                          | 0.274                           |                      |                          | 0.159                           |                      |                          | 0.286                           |                     |                          | 0.600                           |
| CC (n=3,831)                   | 350                                   | 0.78 (0.60, 1.01)        |                                 | 121                  | 0.65 (0.42, 1.01)        |                                 | 208                  | 0.83 (0.59, 1.18)        |                                 | 73                  | 0.69 (0.40, 1.21)        |                                 |
| CT (n=5,267)                   | 489                                   | 0.72 (0.58, 0.90)        |                                 | 190                  | 1.02 (0.71, 1.45)        |                                 | 275                  | 0.52 (0.39, 0.69)        |                                 | 110                 | 0.71 (0.45, 1.12)        |                                 |
| TT (n=1,845)                   | 213                                   | 0.65 (0.46, 0.91)        |                                 | 72                   | 0.42 (0.23, 0.75)        |                                 | 127                  | 0.63 (0.41, 0.97)        |                                 | 54                  | 0.74 (0.37, 1.50)        |                                 |
| <b>rs2228570 (<i>FokI</i>)</b> |                                       |                          | 0.329                           |                      |                          | 0.533                           |                      |                          | 0.362                           |                     |                          | 0.751                           |
| AA (n=1,667)                   | 174                                   | 0.80 (0.56, 1.16)        |                                 | 60                   | 0.65 (0.35, 1.22)        |                                 | 97                   | 0.67 (0.41, 1.10)        |                                 | 36                  | 1.55 (0.67, 3.58)        |                                 |
| AG (n=5,171)                   | 478                                   | 0.76 (0.61, 0.95)        |                                 | 179                  | 0.81 (0.56, 1.16)        |                                 | 276                  | 0.68 (0.50, 0.91)        |                                 | 110                 | 0.65 (0.41, 1.02)        |                                 |
| GG (n=4,105)                   | 400                                   | 0.70 (0.54, 0.89)        |                                 | 144                  | 0.72 (0.48, 1.08)        |                                 | 237                  | 0.58 (0.42, 0.79)        |                                 | 91                  | 0.72 (0.43, 1.20)        |                                 |
| <b>rs731236 (<i>TaqI</i>)</b>  |                                       |                          | 0.244                           |                      |                          | 0.158                           |                      |                          | 0.245                           |                     |                          | 0.637                           |
| AA (n=3,882)                   | 354                                   | 0.78 (0.61, 1.02)        |                                 | 126                  | 0.67 (0.44, 1.03)        |                                 | 211                  | 0.82 (0.58, 1.17)        |                                 | 74                  | 0.73 (0.42, 1.27)        |                                 |
| AG (n=5,252)                   | 491                                   | 0.71 (0.57, 0.88)        |                                 | 184                  | 0.98 (0.68, 1.41)        |                                 | 277                  | 0.51 (0.39, 0.68)        |                                 | 111                 | 0.71 (0.45, 1.12)        |                                 |
| GG (n=1,809)                   | 207                                   | 0.67 (0.47, 0.94)        |                                 | 73                   | 0.45 (0.25, 0.80)        |                                 | 122                  | 0.64 (0.41, 1.00)        |                                 | 52                  | 0.75 (0.36, 1.55)        |                                 |

HR was adjusted for age (continuous), sex (female, male), ethnic (White people, non-White people [including Black people, Asian people, and multiethnic participants]), the Townsend Deprivation Index (continuous), education (College/University degree, A levels/AS levels or equivalent or O levels/GCSEs or equivalent or other professional qualifications, none of the above), employed (yes, no), smoking status (never, past, current), drinking status (never, 1-2 times/week, 3-4 times/week,  $\geq 5$  times/week), healthy diet (yes, no), use of multivitamin/mineral supplements (yes, no), total physical activity level (MET-minutes /week, continuous), time spend outdoors in summer (continuous, hours/day), season of blood drawn (March to May, June to August, September to November, December to February), estimated glomerular filtration rate (eGFR,  $\leq 90$ ,  $>90$  mL/min/1.73 m<sup>2</sup>), BMI (continuous), history of hypertension (yes, no), and hypercholesterolemia (yes, no), diabetic medication (no insulin or pills, only diabetes pills, or insulin and/or others), diabetes duration ( $\leq 3$ , 3-10 years,  $>10$  years), HbA1c ( $<7\%$ ,  $\geq 7\%$  [ $<53$  nmol/L,  $\geq 53$  nmol/L]), genotype measurement batch, and ten principal components of ancestry. <sup>a</sup> HR indicated the risk for per one unit increment in serum 25(OH)D concentration.

**Supplementary Table 5.** Stratified analyses of the associations between serum 25(OH)D concentrations and composite diabetic microvascular complications among patients with T2D

|                              | Serum 25(OH)D concentrations (nmol/L) |                                |                                |                             | <i>P</i> interaction | Natural log-transformed<br>25(OH)D |
|------------------------------|---------------------------------------|--------------------------------|--------------------------------|-----------------------------|----------------------|------------------------------------|
|                              | < 25.0                                | 25.0-49.9                      | 50.0-74.9                      | ≥ 75.0                      |                      |                                    |
| <b>Age, years</b>            |                                       |                                |                                |                             | 0.708                |                                    |
| ≤60                          | 137/1,823<br>1 (ref.)                 | 227/3,257<br>0.94 (0.75, 1.17) | 69/1,572<br>0.59 (0.43, 0.81)  | 12/411<br>0.42 (0.23, 0.78) |                      | 0.75 (0.60, 0.92)                  |
| >60                          | 172/1,148<br>1 (ref.)                 | 407/3,402<br>0.77 (0.64, 0.93) | 268/2,370<br>0.74 (0.60, 0.92) | 78/726<br>0.71 (0.53, 0.96) |                      | 0.76 (0.65, 0.89)                  |
| <b>Sex</b>                   |                                       |                                |                                |                             | 0.306                |                                    |
| Female                       | 123/1,248<br>1 (ref.)                 | 255/2,568<br>0.94 (0.75, 1.17) | 111/1,432<br>0.74 (0.56, 0.98) | 29/409<br>0.68 (0.44, 1.05) |                      | 0.80 (0.66, 0.98)                  |
| Male                         | 186/1,723<br>1 (ref.)                 | 379/4,091<br>0.77 (0.64, 0.93) | 226/2,510<br>0.68 (0.55, 0.86) | 61/728<br>0.64 (0.47, 0.89) |                      | 0.72 (0.61, 0.85)                  |
| <b>BMI, kg/m<sup>2</sup></b> |                                       |                                |                                |                             | 0.165                |                                    |
| <30                          | 112/1,196<br>1 (ref.)                 | 208/2,791<br>0.72 (0.56, 0.92) | 157/2,030<br>0.68 (0.52, 0.91) | 43/702<br>0.50 (0.34, 0.75) |                      | 0.70 (0.57, 0.85)                  |
| ≥30                          | 197/1,775<br>1 (ref.)                 | 426/3,868<br>0.92 (0.77, 1.10) | 180/1,912<br>0.72 (0.58, 0.91) | 47/435<br>0.86 (0.61, 1.21) |                      | 0.80 (0.68, 0.94)                  |
| <b>Smoking status</b>        |                                       |                                |                                |                             | 0.182                |                                    |
| Current/ past                | 172/1,462<br>1 (ref.)                 | 344/3,406<br>0.79 (0.65, 0.96) | 200/2,130<br>0.69 (0.55, 0.87) | 52/633<br>0.61 (0.43, 0.85) |                      | 0.69 (0.59, 0.82)                  |
| Never                        | 135/1,481<br>1 (ref.)                 | 286/3,224<br>0.86 (0.69, 1.07) | 136/1,808<br>0.71 (0.54, 0.93) | 38/503<br>0.70 (0.47, 1.04) |                      | 0.80 (0.66, 0.97)                  |

|                                  |           |                   |                   |                   |                   |
|----------------------------------|-----------|-------------------|-------------------|-------------------|-------------------|
| <b>Physical activity level</b>   |           |                   |                   |                   | 0.030             |
| <150 MET minutes/week            | 191/1,712 | 326/3,448         | 149/1,763         | 39/478            |                   |
|                                  | 1 (ref.)  | 0.76 (0.63, 0.92) | 0.66 (0.52, 0.84) | 0.70 (0.48, 1.01) | 0.68 (0.57, 0.81) |
| ≥150 MET-minutes/week            | 83/944    | 228/2,586         | 162/1,891         | 47/591            |                   |
|                                  | 1 (ref.)  | 0.90 (0.69, 1.17) | 0.81 (0.60, 1.08) | 0.67 (0.45, 1.00) | 0.83 (0.67, 1.03) |
| <b>Diabetes duration (years)</b> |           |                   |                   |                   | 0.325             |
| ≤3                               | 80/1,145  | 141/2,547         | 97/1,534          | 29/438            |                   |
|                                  | 1 (ref.)  | 0.72 (0.54, 0.96) | 0.78 (0.56, 1.10) | 0.77 (0.48, 1.23) | 0.77 (0.59, 0.99) |
| >3                               | 215/1,620 | 463/3,725         | 226/2,210         | 59/632            |                   |
|                                  | 1 (ref.)  | 0.86 (0.73, 1.02) | 0.66 (0.54, 0.82) | 0.62 (0.45, 0.85) | 0.72 (0.62, 0.84) |
| <b>HbA<sub>1c</sub></b>          |           |                   |                   |                   | 0.512             |
| <7% (<53 nmol/L)                 | 154/1,736 | 330/4,228         | 201/2,697         | 61/824            |                   |
|                                  | 1 (ref.)  | 0.78 (0.64, 0.95) | 0.71 (0.56, 0.90) | 0.67 (0.48, 0.93) | 0.75 (0.64, 0.90) |
| ≥7% (≥53 nmol/L)                 | 155/1,235 | 301/2431          | 134/1,245         | 28/295            |                   |
|                                  | 1 (ref.)  | 0.89 (0.73, 1.10) | 0.71 (0.54, 0.91) | 0.61 (0.40, 0.94) | 0.75 (0.62, 0.90) |

HR was adjusted for age (continuous), sex (female, male), ethnic (White people, non-White people [including Black people, Asian people, and multiethnic participants]), the Townsend Deprivation Index (continuous), education (College/University degree, A levels/AS levels or equivalent or O levels/GCSEs or equivalent or other professional qualifications, none of the above), employed (yes, no), smoking status (never, past, current), drinking status (never, 1-2 times/week, 3-4 times/week, ≥5 times/week), healthy diet (yes, no), use of multivitamin/mineral supplements (yes, no), total physical activity level (MET-minutes /week, continuous), time spend outdoors in summer (continuous, hours/day), season of blood drawn (March to May, June to August, September to November, December to February), estimated glomerular filtration rate (eGFR, ≤90, >90 mL/min/1.73 m<sup>2</sup>), BMI (continuous), history of hypertension (yes, no), and hypercholesterolemia (yes, no), diabetic medication (no insulin or pills, only diabetes pills, or insulin and/or others), diabetes duration (≤3, 3-10 years, >10 years), HbA<sub>1c</sub> (<7%, ≥7% [ $<53$  nmol/L,  $\geq 53$  nmol/L])). The strata variable was not included in the model when stratifying by itself.

**Supplementary Table 6.** Multivariable-adjusted HRs (95% CIs) of diabetic microvascular complications according to serum 25(OH)D concentrations among patients with T2D after excluding outcomes occurred within 2 years of follow up

|                                              | Serum 25(OH)D concentrations (nmol/L) |                   |                   |                   | <i>P</i> <sub>trend</sub> | Natural log-transformed<br>25(OH)D |
|----------------------------------------------|---------------------------------------|-------------------|-------------------|-------------------|---------------------------|------------------------------------|
|                                              | < 25.0                                | 25.0-49.9         | 50.0-74.9         | ≥ 75.0            |                           |                                    |
| <b>Composite microvascular complications</b> | 265/2,927                             | 559/6,584         | 301/3,906         | 80/1,127          |                           |                                    |
|                                              | 1 (ref.)                              | 0.85 (0.73, 1.00) | 0.74 (0.61, 0.89) | 0.68 (0.52, 0.89) | <0.001                    | 0.77 (0.68, 0.88)                  |
| <b>Diabetic retinopathy</b>                  | 95/2,927                              | 202/6,584         | 114/3,906         | 23/1,127          |                           |                                    |
|                                              | 1 (ref.)                              | 0.90 (0.70, 1.16) | 0.81 (0.60, 1.10) | 0.56 (0.34, 0.92) | 0.023                     | 0.76 (0.61, 0.95)                  |
| <b>Diabetic nephropathy</b>                  | 162/2,927                             | 337/6,584         | 174/3,906         | 47/1,127          |                           |                                    |
|                                              | 1 (ref.)                              | 0.80 (0.66, 0.97) | 0.66 (0.52, 0.83) | 0.61 (0.43, 0.87) | <0.001                    | 0.71 (0.60, 0.85)                  |
| <b>Diabetic neuropathy</b>                   | 62/2,927                              | 101/6,584         | 63/3,906          | 14/1,127          |                           |                                    |
|                                              | 1 (ref.)                              | 0.72 (0.51, 1.00) | 0.74 (0.49, 1.10) | 0.59 (0.32, 1.12) | 0.131                     | 0.80 (0.60, 1.09)                  |

HR was adjusted for age (continuous), sex (female, male), ethnic (White people, non-White people [including Black people, Asian people, and multiethnic participants]), the Townsend Deprivation Index (continuous), education (College/University degree, A levels/AS levels or equivalent or O levels/GCSEs or equivalent or other professional qualifications, none of the above), employed (yes, no), smoking status (never, past, current), drinking status (never, 1-2 times/week, 3-4 times/week, ≥5 times/week), healthy diet (yes, no), use of multivitamin/mineral supplements (yes, no), total physical activity level (MET-minutes/week, continuous), time spend outdoors in summer (continuous, hours/day), season of blood drawn (March to May, June to August, September to November, December to February), estimated glomerular filtration rate (eGFR, ≤90, >90 mL/min/1.73 m<sup>2</sup>), BMI (continuous), history of hypertension (yes, no), and hypercholesterolemia (yes, no), diabetic medication (no insulin or pills, only diabetes pills, or insulin and/or others), diabetes duration (≤3, 3-10 years, >10 years), HbA<sub>1c</sub> (<7%, ≥7% [ $<53$  nmol/L,  $\geq 53$  nmol/L]).

**Supplementary Table 7.** Multivariable-adjusted HRs (95% CIs) of diabetic microvascular complications according to serum 25(OH)D concentrations among patients with T2D with further adjustment of CRP

|                                              | Serum 25(OH)D concentrations (nmol/L) |                   |                   |                   | <i>P</i> <sub>trend</sub> | Natural log-transformed<br>25(OH)D |
|----------------------------------------------|---------------------------------------|-------------------|-------------------|-------------------|---------------------------|------------------------------------|
|                                              | < 25.0                                | 25.0-49.9         | 50.0-74.9         | ≥ 75.0            |                           |                                    |
| <b>Composite microvascular complications</b> | 309/2,971                             | 634/6,659         | 337/3,942         | 90/1,137          |                           |                                    |
|                                              | 1 (ref.)                              | 0.83 (0.72, 0.96) | 0.71 (0.60, 0.84) | 0.66 (0.51, 0.85) | <0.001                    | 0.75 (0.66, 0.85)                  |
| <b>Diabetic retinopathy</b>                  | 114/2,971                             | 248/6,659         | 134/3,942         | 31/1,137          |                           |                                    |
|                                              | 1 (ref.)                              | 0.91 (0.72, 1.15) | 0.78 (0.59, 1.04) | 0.62 (0.40, 0.95) | 0.014                     | 0.75 (0.61, 0.92)                  |
| <b>Diabetic nephropathy</b>                  | 182/2,971                             | 367/6,659         | 183/3,942         | 49/1,137          |                           |                                    |
|                                              | 1 (ref.)                              | 0.78 (0.65, 0.94) | 0.61 (0.48, 0.77) | 0.56 (0.40, 0.79) | <0.001                    | 0.67 (0.57, 0.79)                  |
| <b>Diabetic neuropathy</b>                   | 80/2,971                              | 128/6,659         | 76/3,942          | 14/1,137          |                           |                                    |
|                                              | 1 (ref.)                              | 0.71 (0.53, 0.96) | 0.72 (0.50, 1.03) | 0.49 (0.27, 0.90) | 0.031                     | 0.77 (0.59, 1.01)                  |

HR was adjusted for age (continuous), sex (female, male), ethnic (White people, non-White people [including Black people, Asian people, and multiethnic participants]), the Townsend Deprivation Index (continuous), education (College/University degree, A levels/AS levels or equivalent or O levels/GCSEs or equivalent or other professional qualifications, none of the above), employed (yes, no), smoking status (never, past, current), drinking status (never, 1-2 times/week, 3-4 times/week, ≥5 times/week), healthy diet (yes, no), use of multivitamin/mineral supplements (yes, no), total physical activity level (MET-minutes/week, continuous), time spend outdoors in summer (continuous, hours/day), season of blood drawn (March to May, June to August, September to November, December to February), estimated glomerular filtration rate (eGFR, ≤90, >90 mL/min/1.73 m<sup>2</sup>), BMI (continuous), history of hypertension (yes, no), and hypercholesterolemia (yes, no), diabetic medication (no insulin or pills, only diabetes pills, or insulin and/or others), diabetes duration (≤3, 3-10 years, >10 years), HbA<sub>1c</sub> (<7%, ≥7% [ $<53$  nmol/L,  $\geq 53$  nmol/L]), CRP (mg/L, continuous).

**Supplementary Table 8.** Multivariable-adjusted HRs (95% CIs) of diabetic microvascular complications according to serum 25(OH)D concentrations among patients with T2D with further adjustment of lipid profiles

|                                              | Serum 25(OH)D concentrations (nmol/L) |                   |                   |                   | <i>P</i> <sub>trend</sub> | Natural log-transformed<br>25(OH)D |
|----------------------------------------------|---------------------------------------|-------------------|-------------------|-------------------|---------------------------|------------------------------------|
|                                              | < 25.0                                | 25.0-49.9         | 50.0-74.9         | ≥ 75.0            |                           |                                    |
| <b>Composite microvascular complications</b> | 309/2,971                             | 634/6,659         | 337/3,942         | 90/1,137          |                           |                                    |
|                                              | 1 (ref.)                              | 0.84 (0.73, 0.97) | 0.72 (0.61, 0.86) | 0.68 (0.52, 0.88) | <0.001                    | 0.77 (0.67, 0.87)                  |
| <b>Diabetic retinopathy</b>                  | 114/2,971                             | 248/6,659         | 134/3,942         | 31/1,137          |                           |                                    |
|                                              | 1 (ref.)                              | 0.90 (0.72, 1.14) | 0.77 (0.58, 1.03) | 0.61 (0.39, 0.94) | 0.013                     | 0.74 (0.60, 0.91)                  |
| <b>Diabetic nephropathy</b>                  | 182/2,971                             | 367/6,659         | 183/3,942         | 49/1,137          |                           |                                    |
|                                              | 1 (ref.)                              | 0.78 (0.65, 0.95) | 0.62 (0.49, 0.79) | 0.58 (0.41, 0.83) | <0.001                    | 0.68 (0.58, 0.81)                  |
| <b>Diabetic neuropathy</b>                   | 80/2,971                              | 128/6,659         | 76/3,942          | 14/1,137          |                           |                                    |
|                                              | 1 (ref.)                              | 0.74 (0.55, 1.00) | 0.78 (0.54, 1.12) | 0.55 (0.30, 1.02) | 0.100                     | 0.83 (0.63, 1.10)                  |

HR was adjusted for age (continuous), sex (female, male), ethnic (White people, non-White people [including Black people, Asian people, and multiethnic participants]), the Townsend Deprivation Index (continuous), education (College/University degree, A levels/AS levels or equivalent or O levels/GCSEs or equivalent or other professional qualifications, none of the above), employed (yes, no), smoking status (never, past, current), drinking status (never, 1-2 times/week, 3-4 times/week, ≥5 times/week), healthy diet (yes, no), use of multivitamin/mineral supplements (yes, no), total physical activity level (MET-minutes/week, continuous), time spend outdoors in summer (continuous, hours/day), season of blood drawn (March to May, June to August, September to November, December to February), estimated glomerular filtration rate (eGFR, ≤90, >90 mL/min/1.73 m<sup>2</sup>), BMI (continuous), history of hypertension (yes, no), and hypercholesterolemia (yes, no), diabetic medication (no insulin or pills, only diabetes pills, or insulin and/or others), diabetes duration (≤3, 3-10 years, >10 years), HbA<sub>1c</sub> (<7%, ≥7% [ $<53$  nmol/L,  $\geq 53$  nmol/L]), LDL (mmol/L, continuous), HDL (mmol/L, continuous), triglyceride (mmol/L, continuous).