

## Online Supplemental Material

# **The prognostic significance of body mass index and metabolic parameter variabilities in predialysis chronic kidney disease: a nationwide observational cohort study**

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**Supplemental Table 1.** Risk of adverse outcomes according to baseline body mass index in predialysis CKD patients.

| Outcome                    | Baseline BMI exposure <sup>a</sup> | N                | Event | Follow-up person-years | Incidence rate (/1000PY) | Univariable model    |                      | Age, sex, and number of exams adjusted model |                      | Multivariable model <sup>b</sup> |                      |         |
|----------------------------|------------------------------------|------------------|-------|------------------------|--------------------------|----------------------|----------------------|--|----------------------|----------------------------------|----------------------|---------|
|                            |                                    |                  |       |                        |                          | HR (95% CI)          | P                    | adjusted HR (95% CI)                         | P                    | adjusted HR (95% CI)             | P                    |         |
| All-cause mortality        | Continuous                         | NA               |       |                        |                          | 0.772 (0.752, 0.792) | < 0.001              | 0.844 (0.822, 0.867)                         | < 0.001              | 0.822 (0.791, 0.854)             | < 0.001              |         |
|                            | Categorical                        | Q1 (12.33–22.59) | 21198 | 1781                   | 82119                    | 21.69                | Reference            | < 0.001                                      | Reference            | < 0.001                          | Reference            | < 0.001 |
|                            |                                    | Q2 (22.60–24.61) | 21138 | 1182                   | 82694                    | 14.29                | 0.657 (0.611, 0.707) |  | 0.703 (0.653, 0.757) |                                  | 0.702 (0.648, 0.761) |         |
|                            |                                    | Q3 (24.61–26.72) | 21130 | 950                    | 83102                    | 11.43                | 0.525 (0.485, 0.568) |  | 0.598 (0.552, 0.647) |                                  | 0.584 (0.532, 0.642) |         |
|                            |                                    | Q4 (26.73–46.43) | 21170 | 869                    | 83267                    | 10.44                | 0.479 (0.442, 0.52)  |  | 0.642 (0.591, 0.697) |                                  | 0.583 (0.519, 0.656) |         |
| Myocardial infarction      | Continuous                         | NA               |       |                        |                          | 0.963 (0.924, 1.003) | 0.07                 | 0.999 (0.959, 1.042)                         | 0.97                 | 0.901 (0.848, 0.956)             | < 0.001              |         |
|                            | Categorical                        | Q1 (12.33–22.59) | 21198 | 475                    | 81498                    | 5.83                 | Reference            | 0.10   | Reference            | 0.74                             | Reference            | 0.003   |
|                            |                                    | Q2 (22.60–24.61) | 21138 | 463                    | 82012                    | 5.65                 | 0.967 (0.851, 1.099) |  | 0.973 (0.856, 1.106) |                                  | 0.880 (0.768, 1.01)  |         |
|                            |                                    | Q3 (24.61–26.72) | 21130 | 483                    | 82369                    | 5.86                 | 1.003 (0.884, 1.139) |  | 1.037 (0.913, 1.177) |                                  | 0.863 (0.742, 1.004) |         |
|                            |                                    | Q4 (26.73–46.43) | 21170 | 418                    | 82618                    | 5.06                 | 0.866 (0.76, 0.988)  |  | 0.974 (0.853, 1.112) |                                  | 0.699 (0.579, 0.845) |         |
| Stroke                     | Continuous                         | NA               |       |                        |                          | 0.958 (0.926, 0.991) | 0.01                 | 1.007 (0.973, 1.042)                         | 0.70                 | 0.914 (0.870, 0.961)             | < 0.001              |         |
|                            | Categorical                        | Q1 (12.33–22.59) | 21198 | 706                    | 80982                    | 8.72                 | Reference            | 0.04   | Reference            | 0.61                             | Reference            | 0.002   |
|                            |                                    | Q2 (22.60–24.61) | 21138 | 660                    | 81645                    | 8.08                 | 0.926 (0.833, 1.03)  |  | 0.947 (0.852, 1.054) |                                  | 0.866 (0.772, 0.97)  |         |
|                            |                                    | Q3 (24.61–26.72) | 21130 | 684                    | 81963                    | 8.35                 | 0.956 (0.86, 1.062)  |  | 1.014 (0.912, 1.127) |                                  | 0.858 (0.757, 0.972) |         |
|                            |                                    | Q4 (26.73–46.43) | 21170 | 616                    | 82290                    | 7.49                 | 0.857 (0.77, 0.955)  |  | 1.001 (0.897, 1.116) |                                  | 0.737 (0.631, 0.862) |         |
| Kidney replacement therapy | Continuous                         | NA               |       |                        |                          | 0.837 (0.812, 0.864) | < 0.001              | 0.806 (0.782, 0.832)                         | < 0.001              | 0.852 (0.813, 0.894)             | < 0.001              |         |
|                            | Categorical                        | Q1 (12.33–22.59) | 21198 | 1092                   | 80429                    | 13.58                | Reference            | < 0.001                                      | Reference            | < 0.001                          | Reference            | < 0.001 |
|                            |                                    | Q2 (22.60–24.61) | 21138 | 789                    | 81571                    | 9.67                 | 0.709 (0.647, 0.777) |  | 0.672 (0.613, 0.736) |                                  | 0.752 (0.68, 0.831)  |         |
|                            |                                    | Q3 (24.61–26.72) | 21130 | 741                    | 82024                    | 9.03                 | 0.661 (0.602, 0.726) |  | 0.605 (0.551, 0.664) |                                  | 0.695 (0.619, 0.78)  |         |
|                            |                                    | Q4 (26.73–46.43) | 21170 | 654                    | 82277                    | 7.95                 | 0.582 (0.528, 0.641) |  | 0.521 (0.473, 0.575) |                                  | 0.612 (0.528, 0.709) |         |

HR = hazard ratio, CI = confidence interval

<sup>a</sup> The ranges of the BMI values in the quartile grades are presented within the parentheses.

<sup>b</sup> Multivariable model was adjusted for age, sex, number of exams, current-smoking, drinking alcohol, regular physical activity, low income state, history of diabetes mellitus, hypertension, dyslipidemia, cancer, chronic lung disease, waist circumference, fasting glucose, systolic BP, diastolic BP, high-density lipoprotein, baseline eGFR, presence of dipstick albuminuria, and eGFR variability during the exposure assessment period.

**Supplemental Table 2.** Risk of adverse outcomes according to body mass index variability by other indexes in predialysis CKD patients.

| Metabolic parameter      | Outcome                    | Variability independent of mean exposure | N        | Event | Follow-up person-years | Incidence rate (/1000PY) | Univariable model    |                      | Age, sex, and number of exams adjusted |                      | Multivariable model <sup>a</sup> |                      |        |
|--------------------------|----------------------------|--|----------|-------|------------------------|--------------------------|----------------------|----------------------|--|----------------------|----------------------------------|----------------------|--------|
|                          |                            |  |          |       |                        |                          | HR (95% CI)          | P                    | adjusted HR (95% CI)                   | P                    | adjusted HR (95% CI)             | P                    |        |
| Standard deviation       | All-cause mortality        | Continuous                               | NA       |       |                        |                          | 1.309 (1.275, 1.344) | <0.001               | 1.262 (1.229, 1.295)                   | <0.001               | 1.193 (1.162, 1.225)             | <0.001               |        |
|                          |                            | Categorical                              | Q1 (low) | 21159 | 882                    | 82887                    | 10.64                | Reference            |  | Reference            |                                  | Reference            |        |
|                          |                            |  | Q2       | 21159 | 936                    | 83387                    | 11.22                | 1.051 (0.959, 1.152) | <0.001                                 | 1.092 (0.996, 1.197) | <0.001                           | 1.064 (0.971, 1.167) | <0.001 |
|                          |                            |  | Q3       | 21159 | 1115                   | 83214                    | 13.40                | 1.255 (1.149, 1.371) |  | 1.256 (1.15, 1.372)  |                                  | 1.163 (1.064, 1.271) |        |
|                          | Q4 (high)                  |  | 21159    | 1849  | 81694                  | 22.63                    | 2.131 (1.966, 2.309) |                      | 1.953 (1.801, 2.117)                   |                      | 1.666 (1.535, 1.807)             |                      |        |
|                          | Myocardial infarction      | Continuous                               | NA       |       |                        |                          | 1.133 (1.087, 1.181) | <0.001               | 1.112 (1.067, 1.159)                   | <0.001               | 1.067 (1.024, 1.112)             | 0.002                |        |
|                          |                            | Categorical                              | Q1 (low) | 21159 | 401                    | 82326                    | 4.87                 | Reference            |  | Reference            |                                  | Reference            |        |
|                          |                            |  | Q2       | 21159 | 408                    | 82762                    | 4.93                 | 1.009 (0.879, 1.158) | <0.001                                 | 1.026 (0.894, 1.178) | <0.001                           | 1.004 (0.874, 1.153) | 0.016  |
|                          |                            |  | Q3       | 21159 | 468                    | 82490                    | 5.67                 | 1.161 (1.016, 1.326) |  | 1.157 (1.012, 1.322) |                                  | 1.097 (0.96, 1.254)  |        |
|                          | Q4 (high)                  |  | 21159    | 562   | 80918                  | 6.95                     | 1.426 (1.255, 1.621) |                      | 1.356 (1.192, 1.543)                   |                      | 1.199 (1.053, 1.365)             |                      |        |
|                          | Stroke                     | Continuous                               | NA       |       |                        |                          | 1.127 (1.089, 1.166) | <0.001               | 1.096 (1.059, 1.134)                   | <0.001               | 1.056 (1.021, 1.093)             | 0.002                |        |
|                          |                            | Categorical                              | Q1 (low) | 21159 | 582                    | 81965                    | 7.10                 | Reference            |  | Reference            |                                  | Reference            |        |
|                          |                            |  | Q2       | 21159 | 608                    | 82368                    | 7.38                 | 1.039 (0.927, 1.164) | <0.001                                 | 1.063 (0.949, 1.191) | <0.001                           | 1.047 (0.935, 1.174) | 0.015  |
|                          |                            |  | Q3       | 21159 | 663                    | 82124                    | 8.07                 | 1.136 (1.016, 1.27)  |  | 1.13 (1.011, 1.263)  |                                  | 1.079 (0.965, 1.207) |        |
|                          | Q4 (high)                  |  | 21159    | 813   | 80422                  | 10.11                    | 1.425 (1.282, 1.586) |                      | 1.32 (1.186, 1.47)                     |                      | 1.184 (1.063, 1.319)             |                      |        |
|                          | Kidney replacement therapy | Continuous                               | NA       |       |                        |                          | 1.142 (1.107, 1.178) | <0.001               | 1.19 (1.153, 1.228)                    | <0.001               | 1.060 (1.027, 1.094)             | <0.001               |        |
| Categorical              |                            | Q1 (low)                                 | 21159    | 696   | 81911                  | 8.50                     | Reference            |                      | Reference                              |                      | Reference                        |                      |        |
|                          |                            | Q2                                       | 21159    | 742   | 82293                  | 9.02                     | 1.059 (0.955, 1.175) | <0.001               | 1.055 (0.951, 1.171)                   | <0.001               | 0.961 (0.866, 1.067)             | <0.001               |        |
|                          |                            | Q3                                       | 21159    | 840   | 81924                  | 10.25                    | 1.206 (1.091, 1.333) |                      | 1.232 (1.114, 1.362)                   |                      | 1.004 (0.908, 1.111)             |                      |        |
|                          | Q4 (high)                  | 21159                                    | 998      | 80174 | 12.45                  | 1.473 (1.337, 1.623)     |                      | 1.663 (1.509, 1.833) |  | 1.178 (1.068, 1.3)   |                                  |                      |        |
| Coefficient of variation | All-cause mortality        | Continuous                               | NA       |       |                        |                          | 1.366 (1.331, 1.403) | <0.001               | 1.296 (1.262, 1.33)                    | <0.001               | 1.199 (1.167, 1.231)             | <0.001               |        |
|                          |                            | Categorical                              | Q1 (low) | 21159 | 847                    | 82941                    | 10.21                | Reference            |  | Reference            |                                  | Reference            |        |
|                          |                            |  | Q2       | 21158 | 879                    | 83492                    | 10.53                | 1.027 (0.935, 1.129) | <0.001                                 | 1.068 (0.971, 1.173) | <0.001                           | 1.035 (0.941, 1.137) | <0.001 |
|                          |                            |  | Q3       | 21160 | 1104                   | 83188                    | 13.27                | 1.296 (1.185, 1.417) |  | 1.297 (1.186, 1.419) |                                  | 1.171 (1.07, 1.281)  |        |
|                          | Q4 (high)                  |  | 21159    | 1952  | 81561                  | 23.93                    | 2.349 (2.167, 2.547) |                      | 2.068 (1.907, 2.244)                   |                      | 1.662 (1.53, 1.806)              |                      |        |
|                          | Myocardial infarction      | Continuous                               | NA       |       |                        |                          | 1.14 (1.094, 1.188)  | <0.001               | 1.113 (1.068, 1.16)                    | <0.001               | 1.072 (1.028, 1.117)             | 0.001                |        |
|                          |                            | Categorical                              | Q1 (low) | 21159 | 410                    | 82362                    | 4.98                 | Reference            |  | Reference            |                                  | Reference            |        |
|                          |                            |  | Q2       | 21158 | 388                    | 82885                    | 4.68                 | 0.937 (0.816, 1.077) | <0.001                                 | 0.959 (0.834, 1.102) | <0.001                           | 0.943 (0.82, 1.083)  | 0.003  |
|                          |                            |  | Q3       | 21160 | 470                    | 82465                    | 5.70                 | 1.141 (1, 1.303)     |  | 1.145 (1.002, 1.307) |                                  | 1.093 (0.956, 1.248) |        |
|                          | Q4 (high)                  |  | 21159    | 571   | 80784                  | 7.07                     | 1.421 (1.252, 1.613) |                      | 1.332 (1.172, 1.514)                   |                      | 1.191 (1.046, 1.356)             |                      |        |
|                          | Stroke                     | Continuous                               | NA       |       |                        |                          | 1.128 (1.09, 1.168)  | <0.001               | 1.09 (1.053, 1.128)                    | <0.001               | 1.056 (1.020, 1.093)             | 0.002                |        |
|                          |                            | Categorical                              | Q1 (low) | 21159 | 584                    | 82010                    | 7.12                 | Reference            |  | Reference            |                                  | Reference            |        |
|                          |                            |  | Q2       | 21158 | 610                    | 82452                    | 7.40                 | 1.038 (0.927, 1.163) | <0.001                                 | 1.07 (0.955, 1.199)  | <0.001                           | 1.06 (0.946, 1.187)  | 0.015  |
|                          |                            |  | Q3       | 21160 | 652                    | 82111                    | 7.94                 | 1.114 (0.997, 1.246) |  | 1.115 (0.997, 1.247) |                                  | 1.075 (0.961, 1.202) |        |
|                          | Q4 (high)                  |  | 21159    | 820   | 80308                  | 10.21                    | 1.436 (1.291, 1.597) |                      | 1.304 (1.172, 1.452)                   |                      | 1.189 (1.067, 1.325)             |                      |        |
|                          | Kidney replacement therapy | Continuous                               | NA       |       |                        |                          | 1.183 (1.147, 1.221) | <0.001               | 1.242 (1.203, 1.282)                   | <0.001               | 1.068 (1.035, 1.103)             | <0.001               |        |
| Categorical              |                            | Q1 (low)                                 | 21159    | 647   | 82054                  | 7.89                     | Reference            |                      | Reference                              |                      | Reference                        |                      |        |
|                          |                            | Q2                                       | 21158    | 751   | 82392                  | 9.12                     | 1.154 (1.039, 1.282) | <0.001               | 1.128 (1.016, 1.254)                   | <0.001               | 0.989 (0.89, 1.099)              | <0.001               |        |
|                          |                            | Q3                                       | 21160    | 834   | 81897                  | 10.18                    | 1.291 (1.165, 1.431) |                      | 1.32 (1.191, 1.463)                    |                      | 1.067 (0.963, 1.183)             |                      |        |
|                          | Q4 (high)                  | 21159                                    | 1044     | 79959 | 13.06                  | 1.667 (1.511, 1.839)     |                      | 1.903 (1.725, 2.1)   |  | 1.199 (1.085, 1.325) |                                  |                      |        |
| Actual real variability  | All-cause mortality        | Continuous                               | NA       |       |                        |                          | 1.291 (1.258, 1.325) | <0.001               | 1.236 (1.204, 1.269)                   | <0.001               | 1.179 (1.148, 1.210)             | <0.001               |        |
|                          |                            | Categorical                              | Q1 (low) | 21158 | 877                    | 83157                    | 10.55                | Reference            |  | Reference            |                                  | Reference            |        |
|                          |                            |  | Q2       | 21160 | 953                    | 83298                    | 11.44                | 1.083 (0.988, 1.187) | <0.001                                 | 1.072 (0.978, 1.175) | <0.001                           | 1.057 (0.964, 1.159) | <0.001 |
|                          |                            |  | Q3       | 21159 | 1179                   | 82982                    | 14.21                | 1.347 (1.234, 1.47)  |  | 1.308 (1.198, 1.428) |                                  | 1.207 (1.105, 1.317) |        |
|                          | Q4 (high)                  |  | 21159    | 1773  | 81745                  | 21.69                    | 2.064 (1.903, 2.238) |                      | 1.824 (1.681, 1.979)                   |                      | 1.6 (1.474, 1.737)               |                      |        |
|                          | Myocardial infarction      | Continuous                               | NA       |       |                        |                          | 1.128 (1.082, 1.175) | <0.001               | 1.101 (1.057, 1.148)                   | <0.001               | 1.060 (1.017, 1.105)             | 0.006                |        |
|                          |                            | Categorical                              | Q1 (low) | 21158 | 399                    | 82571                    | 4.83                 | Reference            |  | Reference            |                                  | Reference            |        |
|                          |                            |  | Q2       | 21160 | 411                    | 82699                    | 4.97                 | 1.027 (0.895, 1.178) | <0.001                                 | 1.022 (0.89, 1.173)  | <0.001                           | 0.997 (0.869, 1.145) | 0.03   |
|                          |                            |  | Q3       | 21159 | 481                    | 82259                    | 5.85                 | 1.209 (1.059, 1.381) |  | 1.19 (1.042, 1.359)  |                                  | 1.13 (0.989, 1.291)  |        |
|                          | Q4 (high)                  |  | 21159    | 548   | 80968                  | 6.77                     | 1.403 (1.234, 1.597) |                      | 1.306 (1.147, 1.487)                   |                      | 1.163 (1.02, 1.326)              |                      |        |
|                          | Stroke                     | Continuous                               | NA       |       |                        |                          | 1.118 (1.08, 1.157)  | <0.001               | 1.078 (1.042, 1.116)                   | <0.001               | 1.042 (1.007, 1.079)             | 0.02                 |        |
|                          |                            | Categorical                              | Q1 (low) | 21158 | 590                    | 82220                    | 7.18                 | Reference            |  | Reference            |                                  | Reference            |        |
|                          |                            |  | Q2       | 21160 | 614                    | 82273                    | 7.46                 | 1.04 (0.929, 1.164)  | <0.001                                 | 1.038 (0.927, 1.162) | <0.001                           | 1.018 (0.909, 1.14)  | 0.09   |
|                          |                            |  | Q3       | 21159 | 657                    | 81891                    | 8.02                 | 1.118 (1.001, 1.25)  |  | 1.092 (0.977, 1.22)  |                                  | 1.043 (0.933, 1.166) |        |
|                          | Q4 (high)                  |  | 21159    | 805   | 80495                  | 10.00                    | 1.396 (1.255, 1.552) |                      | 1.256 (1.129, 1.398)                   |                      | 1.134 (1.018, 1.263)             |                      |        |
|                          | Kidney replacement therapy | Continuous                               | NA       |       |                        |                          | 1.099 (1.066, 1.134) | <0.001               | 1.158 (1.123, 1.195)                   | <0.001               | 1.052 (1.019, 1.086)             | 0.002                |        |
| Categorical              |                            | Q1 (low)                                 | 21158    | 712   | 82136                  | 8.67                     | Reference            |                      | Reference                              |                      | Reference                        |                      |        |
|                          |                            | Q2                                       | 21160    | 791   | 82104                  | 9.63                     | 1.111 (1.004, 1.23)  | <0.001               | 1.078 (0.974, 1.193)                   | <0.001               | 1.02 (0.922, 1.129)              | 0.002                |        |
|                          |                            | Q3                                       | 21159    | 846   | 81697                  | 10.36                    | 1.196 (1.083, 1.322) |                      | 1.235 (1.118, 1.364)                   |                      | 1.011 (0.915, 1.118)             |                      |        |
|                          | Q4 (high)                  | 21159                                    | 927      | 80365 | 11.53                  | 1.339 (1.214, 1.476)     |                      | 1.548 (1.403, 1.708) |  | 1.18 (1.068, 1.303)  |                                  |                      |        |

HR = hazard ratio, CI = confidence interval

<sup>a</sup> Multivariable model was adjusted for age, sex, number of exams, current-smoking, drinking alcohol, regular physical activity, low income state, history of diabetes mellitus, hypertension, dyslipidemia, cancer, chronic lung disease, baseline body mass index, waist circumference, fasting glucose, systolic BP, diastolic BP, high-density lipoprotein, baseline eGFR, presence of dipstick albuminuria, and eGFR variability during the exposure assessment period.

The P values for the correlation (by Pearson's correlation) between other body mass index variability indices with variation independent mean were P = 0.974 (standard deviation), P < 0.001 (coefficient of variation), and P < 0.001 (average real variability), respectively.

**Supplemental Table 3.** Interaction term analysis results for the subgroup analysis.

| <b>Variable to divide subgroups</b>      | <b>Outcome</b>             | <b>Interaction term P values in the multivariable model <sup>a</sup></b> |
|--|----------------------------|--|
| Sex                                      | All-cause mortality        | 0.09   |
|  | Myocardial infarction      | 0.20   |
|  | Stroke                     | 0.84   |
|  | Kidney replacement therapy | 0.66   |
| Baseline BMI $\geq 25$ kg/m <sup>2</sup> | All-cause mortality        | 0.03   |
|  | Myocardial infarction      | 0.88   |
|  | Stroke                     | 0.41   |
|  | Kidney replacement therapy | 0.04   |
| Baseline diabetes mellitus               | All-cause mortality        | 0.32   |
|  | Myocardial infarction      | 0.19   |
|  | Stroke                     | 0.71   |
|  | Kidney replacement therapy | 0.001  |
| eGFR $< 60$ mL/min/1.73 m <sup>2</sup>   | All-cause mortality        | 0.79   |
|  | Myocardial infarction      | 0.47   |
|  | Stroke                     | 0.75   |
|  | Kidney replacement therapy | 0.01   |
| BMI slope                                | All-cause mortality        | 0.08   |
|  | Myocardial infarction      | 0.70   |
|  | Stroke                     | 0.64   |
|  | Kidney replacement therapy | 0.16   |

BMI = body mass index, KRT = kidney replacement therapy

<sup>a</sup> Interaction term with the variable dividing the subgroup and the variability of BMI (VIM quartile) was included in the multivariable model adjusted for adjusted for age, sex, number of exams, current-smoking, drinking alcohol, regular physical activity, low income state, history of diabetes mellitus, hypertension, dyslipidemia, cancer, chronic lung disease, baseline body mass index, waist circumference, fasting glucose, systolic BP, diastolic BP, high-density lipoprotein, baseline eGFR, presence of dipstick albuminuria, and eGFR variability during the exposure assessment period.

**Supplemental Table 4.** Risk of adverse outcomes according to body mass index variability in predialysis CKD patients stratified by sex.

| Subgroup | Outcome                    | BMI variability independent of mean exposure |           | N     | Event | Follow-up person-years | Incidence rate (/1000PY) | Univariable model    |         | Age, sex, and number of exams adjusted model |         | Multivariable model <sup>a</sup> |         |
|----------|----------------------------|--|-----------|-------|-------|------------------------|--------------------------|----------------------|---------|--|---------|----------------------------------|---------|
|          |                            |  |           |       |       |                        |                          | HR (95% CI)          | P       | adjusted HR (95% CI)                         | P       | adjusted HR (95% CI)             | P       |
| Male     | All-cause mortality        | Continuous                                   |           | NA    |       |                        |                          | 1.402 (1.355, 1.45)  | < 0.001 | 1.305 (1.262, 1.349)                         | < 0.001 | 1.198 (1.158, 1.24)              | < 0.001 |
|          |                            | Categorical                                  | Q1 (low)  | 11397 | 547   | 44438                  | 12.31                    | Reference            | < 0.001 | Reference                                    | < 0.001 | Reference                        | < 0.001 |
|          |                            |  | Q2        | 11096 | 603   | 43672                  | 13.81                    | 1.116 (0.994, 1.253) |         | 1.159 (1.032, 1.301)                         |         | 1.119 (0.997, 1.257)             |         |
|          |                            |  | Q3        | 10421 | 690   | 40656                  | 16.97                    | 1.376 (1.23, 1.54)   |         | 1.359 (1.214, 1.52)                          |         | 1.209 (1.08, 1.353)              |         |
|          |                            |  | Q4 (high) | 8751  | 1072  | 33196                  | 32.29                    | 2.638 (2.38, 2.924)  |         | 2.187 (1.972, 2.425)                         |         | 1.719 (1.546, 1.911)             |         |
|          | Myocardial infarction      | Continuous                                   |           | NA    |       |                        |                          | 1.169 (1.103, 1.238) | < 0.001 | 1.138 (1.074, 1.205)                         | < 0.001 | 1.088 (1.027, 1.153)             | 0.004   |
|          |                            | Categorical                                  | Q1 (low)  | 11397 | 227   | 44116                  | 5.15                     | Reference            | < 0.001 | Reference                                    | < 0.001 | Reference                        | 0.02    |
|          |                            |  | Q2        | 11096 | 231   | 43310                  | 5.33                     | 1.032 (0.859, 1.239) |         | 1.058 (0.881, 1.271)                         |         | 1.033 (0.86, 1.242)              |         |
|          |                            |  | Q3        | 10421 | 239   | 40305                  | 5.93                     | 1.15 (0.959, 1.379)  |         | 1.153 (0.961, 1.382)                         |         | 1.087 (0.906, 1.304)             |         |
|          |                            |  | Q4 (high) | 8751  | 270   | 32839                  | 8.22                     | 1.604 (1.345, 1.914) |         | 1.484 (1.243, 1.771)                         |         | 1.298 (1.084, 1.554)             |         |
|          | Stroke                     | Continuous                                   |           | NA    |       |                        |                          | 1.13 (1.077, 1.185)  | < 0.001 | 1.09 (1.039, 1.143)                          | < 0.001 | 1.054 (1.004, 1.106)             | 0.03    |
|          |                            | Categorical                                  | Q1 (low)  | 11397 | 331   | 43911                  | 7.54                     | Reference            | < 0.001 | Reference                                    | < 0.001 | Reference                        | 0.13    |
|          |                            |  | Q2        | 11096 | 350   | 43071                  | 8.13                     | 1.077 (0.927, 1.251) |         | 1.117 (0.961, 1.299)                         |         | 1.102 (0.948, 1.281)             |         |
|          |                            |  | Q3        | 10421 | 339   | 40117                  | 8.45                     | 1.121 (0.963, 1.304) |         | 1.127 (0.968, 1.311)                         |         | 1.074 (0.923, 1.251)             |         |
|          |                            |  | Q4 (high) | 8751  | 363   | 32673                  | 11.11                    | 1.478 (1.273, 1.715) |         | 1.328 (1.144, 1.542)                         |         | 1.200 (1.031, 1.397)             |         |
|          | Kidney replacement therapy | Continuous                                   |           | NA    |       |                        |                          | 1.234 (1.188, 1.282) | < 0.001 | 1.244 (1.197, 1.292)                         | < 0.001 | 1.066 (1.026, 1.108)             | 0.001   |
|          |                            | Categorical                                  | Q1 (low)  | 11397 | 474   | 43750                  | 10.83                    | Reference            | < 0.001 | Reference                                    | < 0.001 | Reference                        | < 0.001 |
|          |                            |  | Q2        | 11096 | 535   | 42866                  | 12.48                    | 1.149 (1.015, 1.3)   |         | 1.113 (0.983, 1.26)                          |         | 0.967 (0.854, 1.095)             |         |
|          |                            |  | Q3        | 10421 | 575   | 39725                  | 14.47                    | 1.337 (1.184, 1.51)  |         | 1.314 (1.164, 1.484)                         |         | 1.081 (0.957, 1.221)             |         |
|          |                            |  | Q4 (high) | 8751  | 652   | 32184                  | 20.26                    | 1.889 (1.679, 2.127) |         | 1.921 (1.707, 2.162)                         |         | 1.182 (1.047, 1.335)             |         |
| Female   | All-cause mortality        | Continuous                                   |           | NA    |       |                        |                          | 1.405 (1.345, 1.467) | < 0.001 | 1.277 (1.223, 1.333)                         | < 0.001 | 1.188 (1.138, 1.241)             | < 0.001 |
|          |                            | Categorical                                  | Q1 (low)  | 9762  | 300   | 38502                  | 7.79                     | Reference            | < 0.001 | Reference                                    | < 0.001 | Reference                        | < 0.001 |
|          |                            |  | Q2        | 10063 | 275   | 39827                  | 6.90                     | 0.885 (0.751, 1.042) |         | 0.906 (0.769, 1.067)                         |         | 0.874 (0.742, 1.03)              |         |
|          |                            |  | Q3        | 10738 | 415   | 42527                  | 9.76                     | 1.248 (1.076, 1.448) |         | 1.187 (1.023, 1.377)                         |         | 1.091 (0.94, 1.266)              |         |
|          |                            |  | Q4 (high) | 12408 | 880   | 48364                  | 18.20                    | 2.338 (2.051, 2.666) |         | 1.849 (1.62, 2.11)                           |         | 1.515 (1.325, 1.732)             |         |
|          | Myocardial infarction      | Continuous                                   |           | NA    |       |                        |                          | 1.128 (1.063, 1.198) | < 0.001 | 1.083 (1.02, 1.15)                           | 0.009   | 1.048 (0.987, 1.113)             | 0.124   |
|          |                            | Categorical                                  | Q1 (low)  | 9762  | 183   | 38245                  | 4.78                     | Reference            | < 0.001 | Reference                                    | 0.005   | Reference                        | 0.049   |
|          |                            |  | Q2        | 10063 | 157   | 39582                  | 3.97                     | 0.827 (0.669, 1.024) |         | 0.84 (0.679, 1.04)                           |         | 0.833 (0.673, 1.031)             |         |
|          |                            |  | Q3        | 10738 | 231   | 42156                  | 5.48                     | 1.141 (0.94, 1.385)  |         | 1.12 (0.922, 1.36)                           |         | 1.084 (0.893, 1.317)             |         |
|          |                            |  | Q4 (high) | 12408 | 301   | 47943                  | 6.28                     | 1.311 (1.091, 1.576) |         | 1.175 (0.977, 1.413)                         |         | 1.07 (0.887, 1.29)               |         |
|          | Stroke                     | Continuous                                   |           | NA    |       |                        |                          | 1.142 (1.087, 1.2)   | < 0.001 | 1.086 (1.034, 1.141)                         | 0.001   | 1.054 (1.003, 1.107)             | 0.04    |
|          |                            | Categorical                                  | Q1 (low)  | 9762  | 253   | 38097                  | 6.64                     | Reference            | < 0.001 | Reference                                    | 0.006   | Reference                        | 0.18    |
|          |                            |  | Q2        | 10063 | 260   | 39388                  | 6.60                     | 0.994 (0.836, 1.181) |         | 1.012 (0.851, 1.204)                         |         | 1.004 (0.844, 1.194)             |         |
|          |                            |  | Q3        | 10738 | 313   | 41990                  | 7.45                     | 1.121 (0.95, 1.323)  |         | 1.096 (0.929, 1.294)                         |         | 1.062 (0.9, 1.254)               |         |
|          |                            |  | Q4 (high) | 12408 | 457   | 47633                  | 9.59                     | 1.446 (1.24, 1.686)  |         | 1.263 (1.083, 1.474)                         |         | 1.158 (0.99, 1.354)              |         |
|          | Kidney replacement therapy | Continuous                                   |           | NA    |       |                        |                          | 1.219 (1.153, 1.289) | < 0.001 | 1.237 (1.169, 1.308)                         | < 0.001 | 1.083 (1.023, 1.146)             | 0.006   |
|          |                            | Categorical                                  | Q1 (low)  | 9762  | 172   | 38303                  | 4.49                     | Reference            | < 0.001 | Reference                                    | < 0.001 | Reference                        | 0.02    |
|          |                            |  | Q2        | 10063 | 219   | 39530                  | 5.54                     | 1.233 (1.01, 1.506)  |         | 1.191 (0.975, 1.454)                         |         | 1.056 (0.864, 1.29)              |         |
|          |                            |  | Q3        | 10738 | 257   | 42171                  | 6.09                     | 1.356 (1.118, 1.644) |         | 1.324 (1.091, 1.606)                         |         | 1.045 (0.861, 1.269)             |         |
|          |                            |  | Q4 (high) | 12408 | 392   | 47773                  | 8.21                     | 1.837 (1.536, 2.198) |         | 1.889 (1.579, 2.26)                          |         | 1.274 (1.063, 1.527)             |         |

HR = hazard ratio, CI = confidence interval

<sup>a</sup> Multivariable model was adjusted for age, sex, number of exams, current-smoking, drinking alcohol, regular physical activity, low income state, history of diabetes mellitus, hypertension, dyslipidemia, cancer, chronic lung disease, baseline body mass index, waist circumference, fasting glucose, systolic BP, diastolic BP, high-density lipoprotein, baseline eGFR, presence of dipstick albuminuria, and eGFR variability during the exposure assessment period.

**Supplemental Table 5.** Risk of adverse outcomes according to body mass index variability in predialysis CKD patients stratified by baseline body mass index  $\geq 25$  kg/m<sup>2</sup>.

| Subgroup                        | Outcome                    | BMI variability independent of mean exposure |           | N     | Event | Follow-up person-years | Incidence rate (/1000PY) | Univariable model    |         | Age, sex, and number of exams adjusted model |         | Multivariable model <sup>a</sup> |         |
|---------------------------------|----------------------------|--|-----------|-------|-------|------------------------|--------------------------|----------------------|---------|--|---------|----------------------------------|---------|
|                                 |                            |  |           |       |       |                        |                          | HR (95% CI)          | P       | adjusted HR (95% CI)                         | P       | adjusted HR (95% CI)             | P       |
| BMI $\geq 25$ kg/m <sup>2</sup> | All-cause mortality        | Continuous                                   |           | NA    |       |                        |                          | 1.268 (1.213, 1.326) | < 0.001 | 1.269 (1.214, 1.326)                         | < 0.001 | 1.21 (1.158, 1.266)              | < 0.001 |
|                                 |                            | Categorical                                  | Q1 (low)  | 10578 | 352   | 41638                  | 8.45                     | Reference            | < 0.001 | Reference                                    | < 0.001 | Reference                        | < 0.001 |
|                                 |                            |  | Q2        | 9767  | 319   | 38633                  | 8.26                     | 0.974 (0.837, 1.133) |         | 1.033 (0.888, 1.203)                         |         | 1.011 (0.868, 1.176)             |         |
|                                 |                            |  | Q3        | 9303  | 423   | 36671                  | 11.54                    | 1.361 (1.182, 1.568) |         | 1.442 (1.252, 1.662)                         |         | 1.347 (1.169, 1.552)             |         |
|                                 |                            |  | Q4 (high) | 8173  | 515   | 31807                  | 16.19                    | 1.921 (1.678, 2.2)   |         | 1.947 (1.698, 2.232)                         |         | 1.697 (1.479, 1.947)             |         |
|                                 | Myocardial infarction      | Continuous                                   |           | NA    |       |                        |                          | 1.097 (1.031, 1.168) | 0.004   | 1.1 (1.033, 1.171)                           | 0.003   | 1.061 (0.996, 1.13)              | 0.07    |
|                                 |                            | Categorical                                  | Q1 (low)  | 10578 | 212   | 41328                  | 5.13                     | Reference            | 0.003   | Reference                                    | 0.004   | Reference                        | 0.08    |
|                                 |                            |  | Q2        | 9767  | 172   | 38369                  | 4.48                     | 0.871 (0.712, 1.065) |         | 0.897 (0.734, 1.098)                         |         | 0.883 (0.722, 1.08)              |         |
|                                 |                            |  | Q3        | 9303  | 204   | 36334                  | 5.61                     | 1.092 (0.901, 1.323) |         | 1.121 (0.924, 1.359)                         |         | 1.066 (0.879, 1.292)             |         |
|                                 |                            |  | Q4 (high) | 8173  | 205   | 31496                  | 6.51                     | 1.27 (1.048, 1.539)  |         | 1.282 (1.057, 1.556)                         |         | 1.149 (0.946, 1.396)             |         |
|                                 | Stroke                     | Continuous                                   |           | NA    |       |                        |                          | 1.086 (1.031, 1.143) | 0.002   | 1.082 (1.027, 1.14)                          | 0.003   | 1.046 (0.993, 1.102)             | 0.09    |
|                                 |                            | Categorical                                  | Q1 (low)  | 10578 | 300   | 41151                  | 7.29                     | Reference            | 0.01    | Reference                                    | 0.02    | Reference                        | 0.33    |
|                                 |                            |  | Q2        | 9767  | 275   | 38170                  | 7.20                     | 0.988 (0.839, 1.163) |         | 1.03 (0.874, 1.213)                          |         | 1.016 (0.862, 1.197)             |         |
|                                 |                            |  | Q3        | 9303  | 300   | 36169                  | 8.29                     | 1.137 (0.969, 1.335) |         | 1.173 (1, 1.377)                             |         | 1.123 (0.957, 1.319)             |         |
|                                 |                            |  | Q4 (high) | 8173  | 287   | 31371                  | 9.15                     | 1.256 (1.069, 1.477) |         | 1.246 (1.059, 1.467)                         |         | 1.123 (0.953, 1.324)             |         |
|                                 | Kidney replacement therapy | Continuous                                   |           | NA    |       |                        |                          | 1.185 (1.127, 1.246) | < 0.001 | 1.238 (1.176, 1.303)                         | < 0.001 | 1.088 (1.034, 1.146)             | 0.001   |
|                                 |                            | Categorical                                  | Q1 (low)  | 10578 | 289   | 41246                  | 7.01                     | Reference            | < 0.001 | Reference                                    | < 0.001 | Reference                        | < 0.001 |
|                                 |                            |  | Q2        | 9767  | 290   | 38219                  | 7.59                     | 1.081 (0.918, 1.272) |         | 1.051 (0.893, 1.238)                         |         | 0.84 (0.712, 0.991)              |         |
|                                 |                            |  | Q3        | 9303  | 318   | 36176                  | 8.79                     | 1.255 (1.07, 1.472)  |         | 1.283 (1.094, 1.505)                         |         | 1.037 (0.883, 1.218)             |         |
|                                 |                            |  | Q4 (high) | 8173  | 361   | 31248                  | 11.55                    | 1.66 (1.422, 1.937)  |         | 1.878 (1.607, 2.195)                         |         | 1.21 (1.033, 1.418)              |         |
| BMI < 25 kg/m <sup>2</sup>      | All-cause mortality        | Continuous                                   |           | NA    |       |                        |                          | 1.391 (1.346, 1.438) | < 0.001 | 1.289 (1.247, 1.332)                         | < 0.001 | 1.164 (1.125, 1.203)             | < 0.001 |
|                                 |                            | Categorical                                  | Q1 (low)  | 10581 | 495   | 41301                  | 11.99                    | Reference            | < 0.001 | Reference                                    | < 0.001 | Reference                        | < 0.001 |
|                                 |                            |  | Q2        | 11392 | 559   | 44867                  | 12.46                    | 1.035 (0.917, 1.168) |         | 1.065 (0.944, 1.202)                         |         | 1.035 (0.917, 1.168)             |         |
|                                 |                            |  | Q3        | 11856 | 682   | 46513                  | 14.66                    | 1.219 (1.086, 1.369) |         | 1.184 (1.054, 1.329)                         |         | 1.057 (0.941, 1.187)             |         |
|                                 |                            |  | Q4 (high) | 12986 | 1437  | 49753                  | 28.88                    | 2.414 (2.179, 2.673) |         | 2.008 (1.811, 2.226)                         |         | 1.524 (1.372, 1.694)             |         |
|                                 | Myocardial infarction      | Continuous                                   |           | NA    |       |                        |                          | 1.17 (1.107, 1.237)  | < 0.001 | 1.124 (1.064, 1.188)                         | < 0.001 | 1.084 (1.024, 1.147)             | 0.005   |
|                                 |                            | Categorical                                  | Q1 (low)  | 10581 | 198   | 41033                  | 4.83                     | Reference            | < 0.001 | Reference                                    | < 0.001 | Reference                        | 0.03    |
|                                 |                            |  | Q2        | 11392 | 216   | 44523                  | 4.85                     | 1.001 (0.826, 1.214) |         | 1.02 (0.841, 1.237)                          |         | 0.997 (0.822, 1.209)             |         |
|                                 |                            |  | Q3        | 11856 | 266   | 46127                  | 5.77                     | 1.191 (0.991, 1.431) |         | 1.175 (0.977, 1.412)                         |         | 1.123 (0.933, 1.35)              |         |
|                                 |                            |  | Q4 (high) | 12986 | 366   | 49287                  | 7.43                     | 1.54 (1.296, 1.831)  |         | 1.385 (1.164, 1.649)                         |         | 1.243 (1.04, 1.485)              |         |
|                                 | Stroke                     | Continuous                                   |           | NA    |       |                        |                          | 1.161 (1.108, 1.215) | < 0.001 | 1.101 (1.051, 1.153)                         | < 0.001 | 1.059 (1.011, 1.11)              | 0.02    |
|                                 |                            | Categorical                                  | Q1 (low)  | 10581 | 284   | 40857                  | 6.95                     | Reference            | < 0.001 | Reference                                    | < 0.001 | Reference                        | 0.03    |
|                                 |                            |  | Q2        | 11392 | 335   | 44290                  | 7.56                     | 1.087 (0.928, 1.273) |         | 1.113 (0.95, 1.304)                          |         | 1.099 (0.938, 1.288)             |         |
|                                 |                            |  | Q3        | 11856 | 352   | 45937                  | 7.66                     | 1.101 (0.942, 1.288) |         | 1.082 (0.925, 1.265)                         |         | 1.038 (0.887, 1.214)             |         |
|                                 |                            |  | Q4 (high) | 12986 | 533   | 48935                  | 10.89                    | 1.569 (1.359, 1.812) |         | 1.363 (1.178, 1.576)                         |         | 1.221 (1.053, 1.417)             |         |
|                                 | Kidney replacement therapy | Continuous                                   |           | NA    |       |                        |                          | 1.165 (1.12, 1.212)  | < 0.001 | 1.229 (1.18, 1.28)                           | < 0.001 | 1.044 (1.002, 1.087)             | 0.04    |
|                                 |                            | Categorical                                  | Q1 (low)  | 10581 | 357   | 40807                  | 8.75                     | Reference            | < 0.001 | Reference                                    | < 0.001 | Reference                        | 0.17    |
|                                 |                            |  | Q2        | 11392 | 464   | 44176                  | 10.50                    | 1.199 (1.044, 1.376) |         | 1.178 (1.026, 1.352)                         |         | 1.087 (0.946, 1.249)             |         |
|                                 |                            |  | Q3        | 11856 | 514   | 45720                  | 11.24                    | 1.284 (1.122, 1.47)  |         | 1.313 (1.147, 1.503)                         |         | 1.075 (0.939, 1.231)             |         |
|                                 |                            |  | Q4 (high) | 12986 | 683   | 48710                  | 14.02                    | 1.613 (1.419, 1.834) |         | 1.868 (1.643, 2.124)                         |         | 1.16 (1.017, 1.322)              |         |

HR = hazard ratio, CI = confidence interval

<sup>a</sup> Multivariable model was adjusted for age, sex, number of exams, current-smoking, drinking alcohol, regular physical activity, low income state, history of diabetes mellitus, hypertension, dyslipidemia, cancer, chronic lung disease, baseline body mass index, waist circumference, fasting glucose, systolic BP, diastolic BP, high-density lipoprotein, baseline eGFR, presence of dipstick albuminuria, and eGFR variability during the exposure assessment period.

**Supplemental Table 6.** Risk of adverse outcomes according to body mass index variability in predialysis CKD patients stratified by the presence of diabetes mellitus.

| Subgroup | Outcome                    | BMI variability independent of mean exposure |           | N     | Event | Follow-up person-years | Incidence rate (/1000PY) | Univariable model    |         | Age, sex, and number of exams adjusted model |         | Multivariable model <sup>a</sup> |         |
|----------|----------------------------|--|-----------|-------|-------|------------------------|--------------------------|----------------------|---------|--|---------|----------------------------------|---------|
|          |                            |  |           |       |       |                        |                          | HR (95% CI)          | P       | adjusted HR (95% CI)                         | P       | adjusted HR (95% CI)             | P       |
| DM (+)   | All-cause mortality        | Continuous                                   |           | NA    |       |                        |                          | 1.309 (1.256, 1.365) | < 0.001 | 1.291 (1.239, 1.346)                         | < 0.001 | 1.221 (1.171, 1.274)             | < 0.001 |
|          |                            | Categorical                                  | Q1 (low)  | 5809  | 323   | 22600                  | 14.29                    | Reference            | < 0.001 | Reference                                    | < 0.001 | Reference                        | < 0.001 |
|          |                            |  | Q2        | 5919  | 344   | 23242                  | 14.80                    | 1.03 (0.885, 1.199)  |         | 1.078 (0.926, 1.255)                         |         | 1.044 (0.897, 1.215)             |         |
|          |                            |  | Q3        | 6196  | 471   | 24029                  | 19.60                    | 1.371 (1.19, 1.579)  |         | 1.397 (1.212, 1.609)                         |         | 1.292 (1.121, 1.49)              |         |
|          |                            |  | Q4 (high) | 7095  | 797   | 27017                  | 29.50                    | 2.075 (1.823, 2.361) |         | 2.036 (1.787, 2.319)                         |         | 1.737 (1.522, 1.982)             |         |
|          | Myocardial infarction      | Continuous                                   |           | NA    |       |                        |                          | 1.053 (0.99, 1.12)   | 0.100   | 1.045 (0.982, 1.112)                         | 0.16    | 1.015 (0.953, 1.08)              | 0.65    |
|          |                            | Categorical                                  | Q1 (low)  | 5809  | 186   | 22338                  | 8.33                     | Reference            | 0.11    | Reference                                    | 0.20    | Reference                        | 0.49    |
|          |                            |  | Q2        | 5919  | 170   | 22982                  | 7.40                     | 0.885 (0.719, 1.09)  |         | 0.893 (0.725, 1.1)                           |         | 0.876 (0.711, 1.079)             |         |
|          |                            |  | Q3        | 6196  | 196   | 23720                  | 8.26                     | 0.992 (0.812, 1.212) |         | 0.99 (0.81, 1.211)                           |         | 0.952 (0.778, 1.164)             |         |
|          |                            |  | Q4 (high) | 7095  | 250   | 26663                  | 9.38                     | 1.129 (0.934, 1.365) |         | 1.107 (0.914, 1.34)                          |         | 1.014 (0.835, 1.23)              |         |
|          | Stroke                     | Continuous                                   |           | NA    |       |                        |                          | 1.108 (1.052, 1.167) | < 0.001 | 1.094 (1.039, 1.152)                         | < 0.001 | 1.071 (1.017, 1.129)             | 0.01    |
|          |                            | Categorical                                  | Q1 (low)  | 5809  | 242   | 22198                  | 10.90                    | Reference            | < 0.001 | Reference                                    | 0.006   | Reference                        | 0.06    |
|          |                            |  | Q2        | 5919  | 245   | 22819                  | 10.74                    | 0.984 (0.824, 1.176) |         | 1.016 (0.85, 1.213)                          |         | 1.006 (0.842, 1.202)             |         |
|          |                            |  | Q3        | 6196  | 288   | 23510                  | 12.25                    | 1.124 (0.948, 1.334) |         | 1.135 (0.956, 1.347)                         |         | 1.107 (0.932, 1.314)             |         |
|          |                            |  | Q4 (high) | 7095  | 381   | 26430                  | 14.42                    | 1.324 (1.127, 1.556) |         | 1.287 (1.095, 1.514)                         |         | 1.211 (1.028, 1.427)             |         |
|          | Kidney replacement therapy | Continuous                                   |           | NA    |       |                        |                          | 1.158 (1.107, 1.212) | < 0.001 | 1.222 (1.167, 1.279)                         | < 0.001 | 1.099 (1.049, 1.151)             | < 0.001 |
|          |                            | Categorical                                  | Q1 (low)  | 5809  | 302   | 22184                  | 13.61                    | Reference            | < 0.001 | Reference                                    | < 0.001 | Reference                        | < 0.001 |
|          |                            |  | Q2        | 5919  | 315   | 22765                  | 13.84                    | 1.014 (0.866, 1.187) |         | 0.984 (0.84, 1.153)                          |         | 0.827 (0.705, 0.969)             |         |
|          |                            |  | Q3        | 6196  | 390   | 23424                  | 16.65                    | 1.226 (1.055, 1.424) |         | 1.256 (1.081, 1.46)                          |         | 1.071 (0.92, 1.245)              |         |
|          |                            |  | Q4 (high) | 7095  | 530   | 26189                  | 20.24                    | 1.499 (1.301, 1.726) |         | 1.727 (1.499, 1.991)                         |         | 1.21 (1.047, 1.399)              |         |
| DM (-)   | All-cause mortality        | Continuous                                   |           | NA    |       |                        |                          | 1.383 (1.336, 1.431) | < 0.001 | 1.279 (1.236, 1.324)                         | < 0.001 | 1.181 (1.141, 1.223)             | < 0.001 |
|          |                            | Categorical                                  | Q1 (low)  | 15350 | 524   | 60339                  | 8.68                     | Reference            | < 0.001 | Reference                                    | < 0.001 | Reference                        | < 0.001 |
|          |                            |  | Q2        | 15240 | 534   | 60257                  | 8.86                     | 1.017 (0.902, 1.148) |         | 1.053 (0.933, 1.187)                         |         | 1.028 (0.911, 1.16)              |         |
|          |                            |  | Q3        | 14963 | 634   | 59155                  | 10.72                    | 1.23 (1.095, 1.38)   |         | 1.217 (1.084, 1.366)                         |         | 1.101 (0.98, 1.237)              |         |
|          |                            |  | Q4 (high) | 14064 | 1155  | 54543                  | 21.18                    | 2.44 (2.201, 2.706)  |         | 2.203 (1.805, 2.224)                         |         | 1.607 (1.444, 1.788)             |         |
|          | Myocardial infarction      | Continuous                                   |           | NA    |       |                        |                          | 1.185 (1.121, 1.252) | < 0.001 | 1.144 (1.083, 1.209)                         | < 0.001 | 1.118 (1.057, 1.182)             | < 0.001 |
|          |                            | Categorical                                  | Q1 (low)  | 15350 | 224   | 60022                  | 3.73                     | Reference            | < 0.001 | Reference                                    | < 0.001 | Reference                        | < 0.001 |
|          |                            |  | Q2        | 15240 | 218   | 59910                  | 3.64                     | 0.971 (0.806, 1.17)  |         | 0.999 (0.829, 1.204)                         |         | 0.994 (0.825, 1.198)             |         |
|          |                            |  | Q3        | 14963 | 274   | 58741                  | 4.66                     | 1.244 (1.043, 1.484) |         | 1.247 (1.045, 1.489)                         |         | 1.212 (1.015, 1.446)             |         |
|          |                            |  | Q4 (high) | 14064 | 321   | 54120                  | 5.93                     | 1.589 (1.339, 1.884) |         | 1.442 (1.214, 1.713)                         |         | 1.351 (1.135, 1.609)             |         |
|          | Stroke                     | Continuous                                   |           | NA    |       |                        |                          | 1.118 (1.068, 1.17)  | < 0.001 | 1.064 (1.017, 1.114)                         | 0.007   | 1.045 (0.998, 1.094)             | 0.06    |
|          |                            | Categorical                                  | Q1 (low)  | 15350 | 342   | 59810                  | 5.72                     | Reference            | < 0.001 | Reference                                    | 0.03    | Reference                        | 0.17    |
|          |                            |  | Q2        | 15240 | 365   | 59640                  | 6.12                     | 1.069 (0.922, 1.239) |         | 1.099 (0.948, 1.273)                         |         | 1.098 (0.947, 1.272)             |         |
|          |                            |  | Q3        | 14963 | 364   | 58596                  | 6.21                     | 1.085 (0.936, 1.257) |         | 1.076 (0.928, 1.248)                         |         | 1.053 (0.908, 1.221)             |         |
|          |                            |  | Q4 (high) | 14064 | 439   | 53876                  | 8.15                     | 1.427 (1.238, 1.643) |         | 1.236 (1.071, 1.425)                         |         | 1.172 (1.013, 1.354)             |         |
|          | Kidney replacement therapy | Continuous                                   |           | NA    |       |                        |                          | 1.169 (1.12, 1.22)   | < 0.001 | 1.222 (1.17, 1.276)                          | < 0.001 | 1.047 (1.003, 1.094)             | 0.04    |
|          |                            | Categorical                                  | Q1 (low)  | 15350 | 344   | 59870                  | 5.75                     | Reference            | < 0.001 | Reference                                    | < 0.001 | Reference                        | 0.03    |
|          |                            |  | Q2        | 15240 | 439   | 59631                  | 7.36                     | 1.279 (1.111, 1.473) |         | 1.236 (1.073, 1.424)                         |         | 1.159 (1.006, 1.335)             |         |
|          |                            |  | Q3        | 14963 | 442   | 58472                  | 7.56                     | 1.313 (1.141, 1.512) |         | 1.325 (1.15, 1.525)                          |         | 1.056 (0.917, 1.217)             |         |
|          |                            |  | Q4 (high) | 14064 | 514   | 53769                  | 9.56                     | 1.672 (1.459, 1.917) |         | 1.887 (1.645, 2.164)                         |         | 1.207 (1.05, 1.387)              |         |

DM = diabetes mellitus, HR = hazard ratio, CI = confidence interval

<sup>a</sup> Multivariable model was adjusted for age, sex, number of exams, current-smoking, drinking alcohol, regular physical activity, low income state, history of diabetes mellitus, hypertension, dyslipidemia, cancer, chronic lung disease, baseline body mass index, waist circumference, fasting glucose, systolic BP, diastolic BP, high-density lipoprotein, baseline eGFR, presence of dipstick albuminuria, and eGFR variability during the exposure assessment period.

**Supplemental Table 7.** Risk of adverse outcomes according to body mass index variability in predialysis CKD patients stratified by baseline eGFR < 60 mL/min/1.73 m<sup>2</sup>.

| Subgroup           | Outcome                    | BMI variability independent of mean exposure |           | N     | Event | Follow-up person-years | Incidence rate (/1000PY) | Univariable model    |         | Age, sex, and number of exams adjusted model |         | Multivariable model <sup>a</sup> |         |
|--------------------|----------------------------|--|-----------|-------|-------|------------------------|--------------------------|----------------------|---------|--|---------|----------------------------------|---------|
|                    |                            |  |           |       |       |                        |                          | HR (95% CI)          | P       | adjusted HR (95% CI)                         | P       | adjusted HR (95% CI)             | P       |
| Baseline eGFR < 60 | All-cause mortality        | Continuous                                   |           | NA    |       |                        |                          | 1.358 (1.321, 1.396) | < 0.001 | 1.291 (1.256, 1.327)                         | < 0.001 | 1.191 (1.158, 1.224)             | < 0.001 |
|                    |                            | Categorical                                  | Q1 (low)  | 17594 | 769   | 68941                  | 11.15                    | Reference            | < 0.001 | Reference                                    | < 0.001 | Reference                        | < 0.001 |
|                    |                            |  | Q2        | 17485 | 786   | 68984                  | 11.39                    | 1.018 (0.921, 1.124) |         | 1.051 (0.952, 1.161)                         |         | 1.014 (0.918, 1.121)             |         |
|                    |                            |  | Q3        | 17586 | 1000  | 69142                  | 14.46                    | 1.293 (1.177, 1.42)  |         | 1.283 (1.167, 1.409)                         |         | 1.151 (1.047, 1.265)             |         |
|                    |                            |  | Q4 (high) | 18084 | 1784  | 69639                  | 25.62                    | 2.302 (2.116, 2.505) |         | 2.035 (1.868, 2.216)                         |         | 1.621 (1.486, 1.769)             |         |
|                    | Myocardial infarction      | Continuous                                   |           | NA    |       |                        |                          | 1.153 (1.104, 1.205) | < 0.001 | 1.126 (1.078, 1.177)                         | < 0.001 | 1.082 (1.035, 1.131)             | < 0.001 |
|                    |                            | Categorical                                  | Q1 (low)  | 17594 | 350   | 68439                  | 5.11                     | Reference            | < 0.001 | Reference                                    | < 0.001 | Reference                        | 0.002   |
|                    |                            |  | Q2        | 17485 | 341   | 68462                  | 4.98                     | 0.971 (0.836, 1.127) |         | 0.988 (0.851, 1.147)                         |         | 0.97 (0.836, 1.127)              |         |
|                    |                            |  | Q3        | 17586 | 415   | 68503                  | 6.06                     | 1.181 (1.024, 1.361) |         | 1.177 (1.021, 1.357)                         |         | 1.122 (0.973, 1.294)             |         |
|                    |                            |  | Q4 (high) | 18084 | 520   | 68939                  | 7.54                     | 1.476 (1.289, 1.69)  |         | 1.386 (1.209, 1.588)                         |         | 1.232 (1.072, 1.415)             |         |
|                    | Stroke                     | Continuous                                   |           | NA    |       |                        |                          | 1.132 (1.092, 1.174) | < 0.001 | 1.092 (1.053, 1.133)                         | < 0.001 | 1.057 (1.019, 1.097)             | 0.003   |
|                    |                            | Categorical                                  | Q1 (low)  | 17594 | 510   | 68138                  | 7.48                     | Reference            | < 0.001 | Reference                                    | < 0.001 | Reference                        | 0.02    |
|                    |                            |  | Q2        | 17485 | 530   | 68096                  | 7.78                     | 1.039 (0.92, 1.173)  |         | 1.065 (0.943, 1.203)                         |         | 1.053 (0.932, 1.189)             |         |
|                    |                            |  | Q3        | 17586 | 567   | 68222                  | 8.31                     | 1.109 (0.984, 1.25)  |         | 1.101 (0.977, 1.241)                         |         | 1.059 (0.939, 1.194)             |         |
|                    |                            |  | Q4 (high) | 18084 | 742   | 68504                  | 10.83                    | 1.45 (1.295, 1.623)  |         | 1.314 (1.173, 1.472)                         |         | 1.193 (1.063, 1.339)             |         |
|                    | Kidney replacement therapy | Continuous                                   |           | NA    |       |                        |                          | 1.17 (1.134, 1.208)  | < 0.001 | 1.246 (1.206, 1.287)                         | < 0.001 | 1.059 (1.025, 1.094)             | < 0.001 |
|                    |                            | Categorical                                  | Q1 (low)  | 17594 | 618   | 68087                  | 9.08                     | Reference            | < 0.001 | Reference                                    | < 0.001 | Reference                        | 0.002   |
|                    |                            |  | Q2        | 17485 | 726   | 67912                  | 10.69                    | 1.176 (1.057, 1.309) |         | 1.149 (1.032, 1.28)                          |         | 0.990 (0.888, 1.102)             |         |
|                    |                            |  | Q3        | 17586 | 804   | 67885                  | 11.84                    | 1.305 (1.175, 1.449) |         | 1.351 (1.217, 1.501)                         |         | 1.059 (0.953, 1.177)             |         |
|                    |                            |  | Q4 (high) | 18084 | 995   | 68104                  | 14.61                    | 1.621 (1.466, 1.792) |         | 1.927 (1.743, 2.132)                         |         | 1.170 (1.056, 1.296)             |         |
| Baseline eGFR ≥ 60 | All-cause mortality        | Continuous                                   |           | NA    |       |                        |                          | 1.383 (1.267, 1.51)  | < 0.001 | 1.34 (1.229, 1.461)                          | < 0.001 | 1.242 (1.138, 1.355)             | < 0.001 |
|                    |                            | Categorical                                  | Q1 (low)  | 3565  | 78    | 13998                  | 5.57                     | Reference            | < 0.001 | Reference                                    | < 0.001 | Reference                        | < 0.001 |
|                    |                            |  | Q2        | 3674  | 92    | 14516                  | 6.34                     | 1.132 (0.837, 1.531) |         | 1.219 (0.901, 1.649)                         |         | 1.192 (0.881, 1.613)             |         |
|                    |                            |  | Q3        | 3573  | 105   | 14042                  | 7.48                     | 1.34 (1, 1.796)      |         | 1.44 (1.074, 1.931)                          |         | 1.337 (0.996, 1.794)             |         |
|                    |                            |  | Q4 (high) | 3075  | 168   | 11921                  | 14.09                    | 2.538 (1.94, 3.319)  |         | 2.376 (1.813, 3.115)                         |         | 1.921 (1.458, 2.532)             |         |
|                    | Myocardial infarction      | Continuous                                   |           | NA    |       |                        |                          | 1.016 (0.898, 1.148) | 0.81    | 1.011 (0.894, 1.142)                         | 0.87    | 0.983 (0.869, 1.111)             | 0.78    |
|                    |                            | Categorical                                  | Q1 (low)  | 3565  | 60    | 13922                  | 4.31                     | Reference            | 0.45    | Reference                                    | 0.61    | Reference                        | 0.70    |
|                    |                            |  | Q2        | 3674  | 47    | 14430                  | 3.26                     | 0.753 (0.514, 1.103) |         | 0.785 (0.536, 1.151)                         |         | 0.791 (0.539, 1.161)             |         |
|                    |                            |  | Q3        | 3573  | 55    | 13958                  | 3.94                     | 0.914 (0.634, 1.317) |         | 0.951 (0.66, 1.372)                          |         | 0.919 (0.636, 1.327)             |         |
|                    |                            |  | Q4 (high) | 3075  | 51    | 11844                  | 4.31                     | 1.002 (0.69, 1.455)  |         | 0.984 (0.676, 1.432)                         |         | 0.909 (0.622, 1.328)             |         |
|                    | Stroke                     | Continuous                                   |           | NA    |       |                        |                          | 1.077 (0.974, 1.191) | 0.15    | 1.066 (0.965, 1.178)                         | 0.21    | 1.036 (0.937, 1.146)             | 0.49    |
|                    |                            | Categorical                                  | Q1 (low)  | 3565  | 74    | 13870                  | 5.34                     | Reference            | 0.55    | Reference                                    | 0.60    | Reference                        | 0.81    |
|                    |                            |  | Q2        | 3674  | 80    | 14363                  | 5.57                     | 1.047 (0.763, 1.436) |         | 1.102 (0.803, 1.512)                         |         | 1.094 (0.797, 1.501)             |         |
|                    |                            |  | Q3        | 3573  | 85    | 13884                  | 6.12                     | 1.148 (0.841, 1.568) |         | 1.214 (0.888, 1.658)                         |         | 1.168 (0.854, 1.597)             |         |
|                    |                            |  | Q4 (high) | 3075  | 78    | 11802                  | 6.61                     | 1.239 (0.902, 1.703) |         | 1.199 (0.871, 1.651)                         |         | 1.102 (0.798, 1.522)             |         |
|                    | Kidney replacement therapy | Continuous                                   |           | NA    |       |                        |                          | 1.291 (1.102, 1.512) | 0.002   | 1.328 (1.132, 1.557)                         | < 0.001 | 1.199 (1.02, 1.409)              | 0.03    |
|                    |                            | Categorical                                  | Q1 (low)  | 3565  | 28    | 13967                  | 2.00                     | Reference            | < 0.001 | Reference                                    | < 0.001 | Reference                        | 0.01    |
|                    |                            |  | Q2        | 3674  | 28    | 14483                  | 1.93                     | 0.958 (0.567, 1.617) |         | 0.959 (0.568, 1.622)                         |         | 0.915 (0.541, 1.549)             |         |
|                    |                            |  | Q3        | 3573  | 28    | 14011                  | 2.00                     | 0.994 (0.589, 1.678) |         | 1.018 (0.602, 1.72)                          |         | 0.879 (0.518, 1.49)              |         |
|                    |                            |  | Q4 (high) | 3075  | 49    | 11854                  | 4.13                     | 2.078 (1.306, 3.307) |         | 2.253 (1.414, 3.589)                         |         | 1.698 (1.056, 2.729)             |         |

HR = hazard ratio, CI = confidence interval

<sup>a</sup> Multivariable model was adjusted for age, sex, number of exams, current-smoking, drinking alcohol, regular physical activity, low income state, history of diabetes mellitus, hypertension, dyslipidemia, cancer, chronic lung disease, baseline body mass index, waist circumference, fasting glucose, systolic BP, diastolic BP, high-density lipoprotein, baseline eGFR, presence of dipstick albuminuria, and eGFR variability during the exposure assessment period.