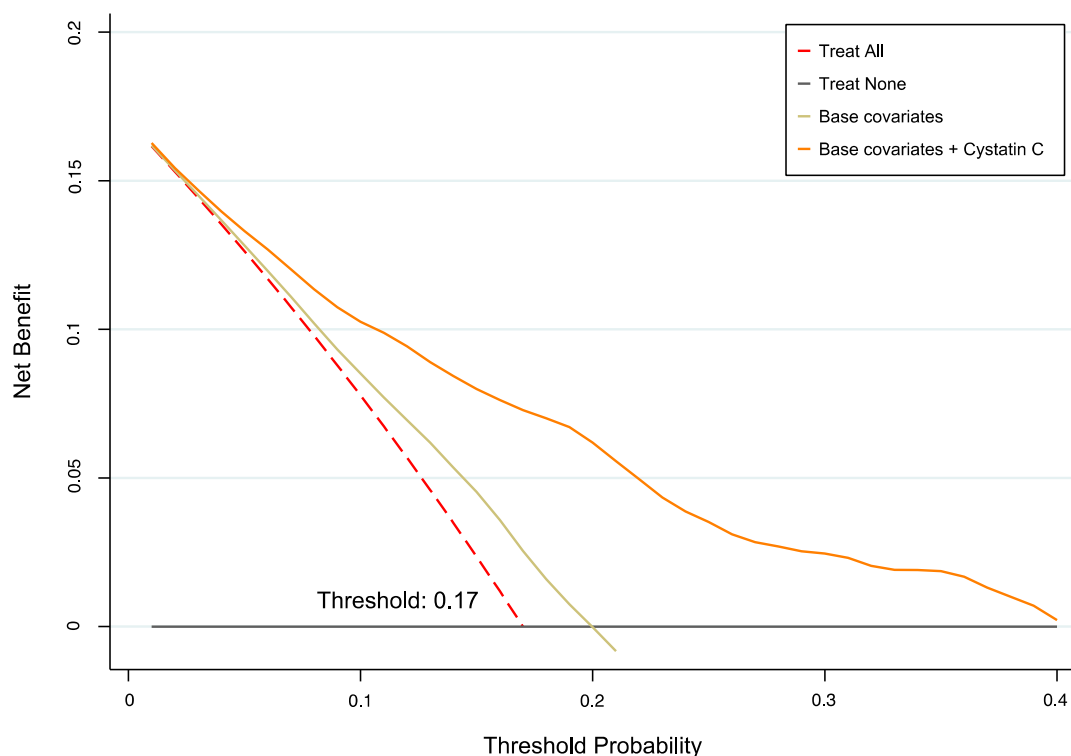
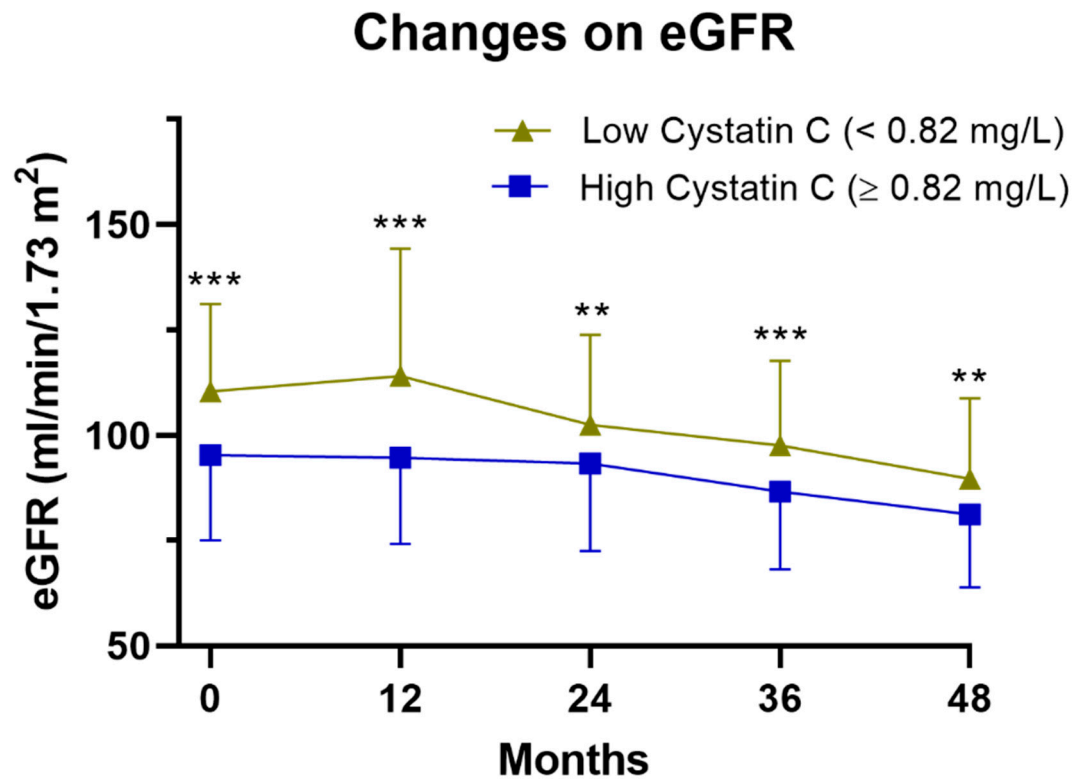


**Supplementary Figure S1. DCA plot to assess the clinical consequences of screening patients for the risk of RKFD using Cystatin C in addition to base covariates.** Y-axis is the net benefit of the decision strategy. Net benefit was defined as the net proportion of subjects with RKFD in whom a prediction model would provide benefit without applying a prediction model to subjects with good outcomes. For the subjects who did not develop RKFD (black line), forecasting with a combination of Cystatin C and base covariates did not yield a net benefit. When considering those who developed RKFD (grey), clear net benefits were seen for risk thresholds from 40 to 60%, forecasting that a combination of Cystatin C and base covariates (orange line) was beneficial. The net benefit was calculated as  $((\text{proportion of true positives}) - (\text{proportion of false positives})) \times \text{pt} / (1 - \text{pt})$ , where pt is the threshold probability.

**Abbreviations:** DCA, decision curve analysis; RKFD, rapid kidney function decline



**Supplementary Figure S2.** Changes in eGFR according to the serum levels of cystatin C during the study



**Abbreviations:** eGFR, estimated glomerular filtration rate; RKFD, rapid kidney function decline; UACR, urine albumin-to-creatinine ratio

\*\* P value < 0.01

\*\*\* P value < 0.001

**Supplementary Table S1. Social psychology variables of the study population**

|                       | Total<br>(n=200) | RKFD<br>(n=100) | No RKFD<br>(n=100) | <i>p</i> value |
|-----------------------|------------------|-----------------|--------------------|----------------|
| Education level       |                  |                 |                    | 0.77           |
| Illiterate, n         | 18 (9.1%)        | 7 (7.1%)        | 11 (11.2%)         |                |
| Elementary school, n  | 47 (23.9%)       | 27 (27.3%)      | 20 (20.4%)         |                |
| Junior high school, n | 39 (19.8%)       | 20 (20.2%)      | 19 (19.4%)         |                |
| Senior high school, n | 64 (32.5%)       | 30 (30.3%)      | 34 (34.7%)         |                |
| Undergraduate, n      | 26 (13.2%)       | 13 (13.1%)      | 13 (13.3%)         |                |
| Postgraduate, n       | 3 (1.5%)         | 2 (2.0%)        | 1 (1.0%)           |                |
| Substance use         |                  |                 |                    |                |
| Smoking, n            | 23 (11.6%)       | 10 (10.1%)      | 13 (13.0%)         | 0.52           |
| Betel nut, n          | 4 (2.0%)         | 3 (3.1%)        | 1 (1.0%)           | 0.31           |
| Alcohol, n            | 37 (21.3%)       | 17 (19.1%)      | 20 (23.5%)         | 0.48           |
| Dietary habits        |                  |                 |                    | 0.88           |
| Non-vegetarian, n     | 164 (82.4%)      | 82 (82.8%)      | 82 (82.0%)         |                |
| Vegetarian, n         | 35 (17.6%)       | 17 (17.2%)      | 18 (18.0%)         |                |

**Abbreviations:** RKFD, rapid kidney function decline

**Supplementary Table S2. NRI and IDI analyses for the role of Cystatin C in stratifying individuals into high or low risk categories (re-classification).**

| Model                   | Model with Cystatin C |
|-------------------------|-----------------------|
| Freq (Row percent)      | reclassification(%)   |
| Subjects without RKFD   |                       |
| decreased probabilities | 61                    |
| increased probabilities | 39                    |
| Total                   | 100                   |
| Subjects with RKFD      |                       |
| decreased probabilities | 29                    |
| increased probabilities | 71                    |
| Total                   | 100                   |
| Combined data           |                       |
| Total                   | 100                   |

NRI(Categorical): 0.6571, *P*-value: 0.0001

Standard error: 0.1690

IDI: 0.26, *P*-value: < 0.001

Standard error: 0.031

**Abbreviations:** IDI, integrated discrimination improvement; NRI, net reclassification improvement.

**Supplementary Table S3. Subgroup analysis of RKFD compared with low (< 0.82 mg/L) and high levels ( $\geq 0.82$  mg/L) of cystatin C**

|                        | HR (95%CI)        | p-value          | Wald test(unweighted) |
|------------------------|-------------------|------------------|-----------------------|
| Age, years             |                   |                  | <b>&lt;0.001</b>      |
| ≤60                    | 5.66 (2.56-12.51) | <b>&lt;0.001</b> |                       |
| >60                    | 2.08 (1.09-3.95)  | <b>0.026</b>     |                       |
| Gender                 |                   |                  | <b>&lt;0.001</b>      |
| Female                 | 2.86 (1.78-4.60)  | <b>&lt;0.001</b> |                       |
| Male                   | 3.43 (1.41-8.34)  | <b>0.007</b>     |                       |
| Hypertension           |                   |                  | <b>&lt;0.001</b>      |
| no                     | 3.48 (2.05-5.89)  | <b>&lt;0.001</b> |                       |
| yes                    | 3.09 (1.45-6.55)  | <b>0.003</b>     |                       |
| Diabetes               |                   |                  | <b>&lt;0.001</b>      |
| no                     | 3.29 (2.09-5.19)  | <b>&lt;0.001</b> |                       |
| yes                    | 1.43 (0.52-3.96)  | 0.491            |                       |
| Metabolic syndrome     |                   |                  | <b>&lt;0.001</b>      |
| no                     | 3.46 (2.02-5.90)  | <b>&lt;0.001</b> |                       |
| yes                    | 2.22 (1.15-4.26)  | <b>0.017</b>     |                       |
| Cardiovascular disease |                   |                  | <b>&lt;0.001</b>      |
| no                     | 2.99 (1.93-4.63)  | <b>&lt;0.001</b> |                       |
| yes                    | 7.63 (1.27-45.91) | <b>0.026</b>     |                       |
| Gout                   |                   |                  | <b>&lt;0.001</b>      |
| no                     | 3.07 (2.00-4.71)  | <b>&lt;0.001</b> |                       |
| yes                    | 1.63 (0.27-9.85)  | 0.592            |                       |

**Abbreviation:** HR, hazard ratio

Values in bold are statistically significant ( $p < 0.05$ )

**Supplementary Table S4. Sensitivity analysis for risk estimation of cystatin C < 0.82 mg/L.**

|                                 | Unadjusted       |                  | Adjusted           |                  |
|---------------------------------|------------------|------------------|--------------------|------------------|
|                                 | HR (95%CI)       | p-value          | HR (95%CI)         | p-value          |
| Different PS modeling           |                  |                  |                    |                  |
| With IPTW (n= 200)              | 2.61 (1.76-3.87) | <b>&lt;0.001</b> | 5.65 (2.69-11.88)  | <b>&lt;0.001</b> |
| With stratification (n= 200)    | 2.42 (1.57-3.71) | <b>&lt;0.001</b> | 5.54 (2.62-11.73)  | <b>&lt;0.001</b> |
| With overlap weighting (n= 200) | 2.53 (1.70-3.75) | <b>&lt;0.001</b> | 5.53 (2.65-11.53)  | <b>&lt;0.001</b> |
| 1:1 PSM (n= 144)                | 2.63 (1.68-4.13) | <b>&lt;0.001</b> | 10.32 (3.25-32.74) | <b>&lt;0.001</b> |

**Abbreviations:** HR, hazard ratio; IPTW, inverse probability of treatment weighting;  
PS, propensity score; PSM propensity score matching  
Values in bold are statistically significant (p < 0.05)