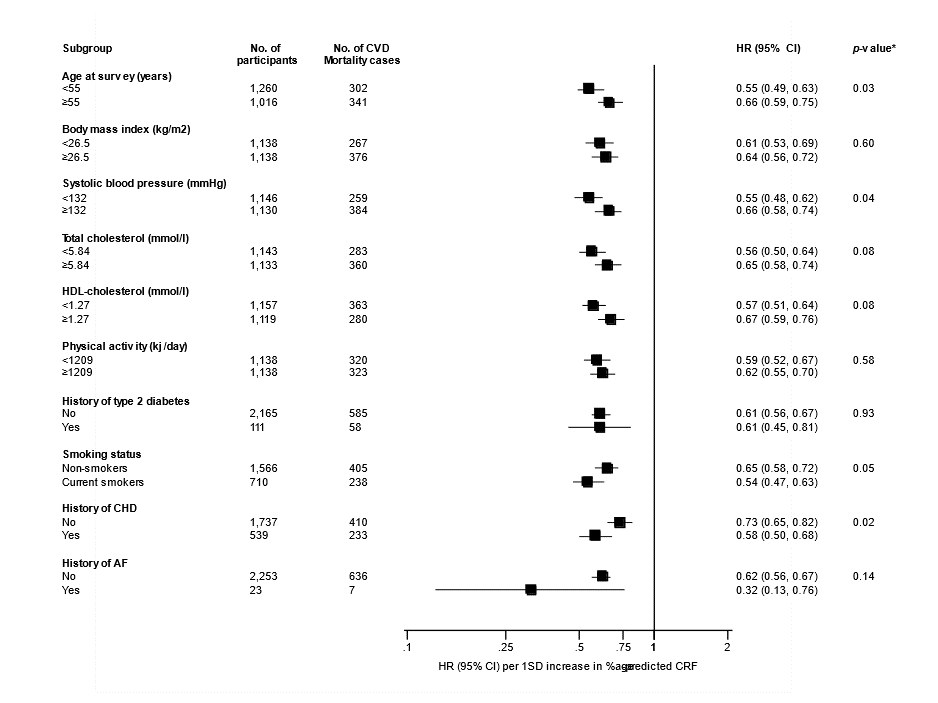
**SUPPLEMENTARY MATERIAL**

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| --- | --- |
| **Supplementary Material 1** | STROBE Statement |
| **Supplementary Material 2** | Association of %age-predicted CRF with CVD mortality in clinically relevant subgroups |
| **Supplementary Material 3** | Association between percentage of age-predicted CRF and risk of CVD mortality, on excluding the first 5 years of follow-up |
| **Supplementary Material 4** | Association between CRF and risk of cardiovascular mortality |
| **Supplementary Material 5** | Risk discrimination and reclassification upon addition of %age-predicted CRF and absolute CRF to a CVD mortality risk prediction model containing conventional risk factors |

**Supplementary Material 1.** STROBE Statement

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| --- | --- | --- | --- |
| **Section/Topic** | Item # | Recommendation | Reported on page # |
| **Title and abstract** | 1 | (*a*) Indicate the study’s design with a commonly used term in the title or the abstract | Page 1 |
| (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found | Page 2 |
| Introduction | | |  |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported | Page 3-4 |
| Objectives | 3 | State specific objectives, including any pre-specified hypotheses | Page 3-4 |
| Methods | | |  |
| Study design | 4 | Present key elements of study design early in the paper | Study design and participants |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | Study design and participants |
| Participants | 6 | (*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up | Study design and participants |
| (*b*)For matched studies, give matching criteria and number of exposed and unexposed | Not applicable |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | Methods |
| Data sources/ measurement | 8\* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | Methods |
| Bias | 9 | Describe any efforts to address potential sources of bias | Statistical analyses |
| Study size | 10 | Explain how the study size was arrived at | Statistical analyses |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | Statistical analyses |
| Statistical methods | 12 | (*a*) Describe all statistical methods, including those used to control for confounding | Statistical analyses |
| (*b*) Describe any methods used to examine subgroups and interactions | Statistical analyses |
| (*c*) Explain how missing data were addressed | Not applicable |
| (*d*) If applicable, explain how loss to follow-up was addressed | Not applicable |
| (*e*) Describe any sensitivity analyses | Statistical analyses |
| Results | | |  |
| Participants | 13\* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed | Study design and participants |
|  |  | (b) Give reasons for non-participation at each stage | Study design and participants |
|  |  | (c) Consider use of a flow diagram | Not applicable |
| Descriptive data | 14\* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders | Results; Table 1 |
|  |  | (b) Indicate number of participants with missing data for each variable of interest |  |
|  |  | (c) Summarise follow-up time (eg, average and total amount) | Results |
| Outcome data | 15\* | Report numbers of outcome events or summary measures over time | Results |
| Main results | 16 | (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included | Results; Table 2; Figures 1; Supplementary Materials 2-5 |
|  |  | (*b*) Report category boundaries when continuous variables were categorized | Results; Table 2; Figures 1; Supplementary Materials 2-5 |
|  |  | (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period |  |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses | Results; Supplementary Materials 2-3 |
| Discussion |  |  |  |
| Key results | 18 | Summarise key results with reference to study objectives | Discussion - Summary of main findings |
| **Limitations** |  |  |  |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | Discussion |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results | Discussion |
| Other information |  |  |  |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | Page 15 |

**Supplementary Material 2.** Association of %age-predicted CRF with CVD mortality in clinically relevant subgroups



Hazard ratios were adjusted for smoking status, history of diabetes, systolic blood pressure, total cholesterol and high-density lipoprotein cholesterol; %age-predicted, percentage of age-predicted; AF, atrial fibrillation; CHD, coronary heart disease; CI, confidence interval; CVD, cardiovascular disease; HDL, high-density lipoprotein; HR, hazard ratio; \*, *P*-value for interaction; cut-offs used for age, body mass index, systolic blood pressure, total cholesterol, high-density lipoprotein cholesterol; and physical activity are median values.

**Supplementary Material 3.** Association between percentage of age-predicted CRF and risk of CVD mortality, on excluding the first 5 years of follow-up

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| --- | --- | --- | --- | --- | --- | --- | --- |
| **Percentage of age-predicted exercise capacity** | **Events/**  **Total** | **Model 1** |  | **Model 2** |  | **Model 3** |  |
|  |  | HR (95% CI) | *P-*value | HR (95% CI) | *P*-value | HR (95% CI) | *P*-value |
| Per 1 SD increase | 223 / 2,171 | 0.65 (0.59 to 0.71) | <.001 | 0.73 (0.66 to 0.81) | .001 | 0.74 (0.67 to 0.82) | <.001 |
| Quartile 1 | 215 / 543 | ref |  | ref |  | ref |  |
| Quartile 2 | 161 / 543 | 0.65 (0.53 to 0.80) | <.001 | 0.77 (0.62 to 0.95) | .02 | 0.78 (0.63 to 0.97) | .03 |
| Quartile 3 | 107 / 543 | 0.42 (0.33 to 0.53) | <.001 | 0.53 (0.41 to 0.68) | <.001 | 0.55 (0.43 to 0.71) | <.001 |
| Quartile 4 | 106 / 542 | 0.40 (0.31 to 0.51) | <.001 | 0.52 (0.40 to 0.68) | <.001 | 0.55 (0.42 to 0.71) | <.001 |

CI, confidence interval; CRF, cardiorespiratory fitness; CVD, cardiovascular disease; HR, hazard ratio; ref, reference; SD, standard deviation

Model 1: Adjusted for smoking status, history of type 2 diabetes, systolic blood pressure, total cholesterol and high-density lipoprotein-cholesterol

Model 2: Model 1 plus body mass index, fasting plasma glucose, alcohol consumption, prevalent coronary heart disease, use of cholesterol medication, prevalent atrial fibrillation, total physical activity and socioeconomic status

Model 3: Model 2 plus high-sensitivity C-reactive protein

**Supplementary Material 4.** Association between CRF and risk of cardiovascular mortality

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| --- | --- | --- | --- | --- | --- | --- | --- |
| **CRF (ml/min)** | **Events/**  **Total** | **Model 1** |  | **Model 2** |  | **Model 3** |  |
|  |  | HR (95% CI) | *P-*value | HR (95% CI) | *P*-value | HR (95% CI) | *P*-value |
| Per 1 SD increase | 643 / 2,276 | 0.69 (0.63 to 0.76) | <.001 | 0.70 (0.63 to 0.78) | <.001 | 0.71 (0.64 to 0.79) | <.001 |
| Quartile 1 | 254 / 573 | ref |  | ref |  | ref |  |
| Quartile 2 | 176 / 565 | 0.60 (0.50 to 0.73) | <.001 | 0.63 (0.51 to 0.77) | <.001 | 0.63 (0.52 to 0.78) | <.001 |
| Quartile 3 | 104 / 569 | 0.39 (0.31 to 0.49) | <.001 | 0.40 (0.31 to 0.51) | <.001 | 0.40 (0.32 to 0.52) | <.001 |
| Quartile 4 | 109 / 569 | 0.47 (0.37 to 0.60) | <.001 | 0.48 (0.37 to 0.62) | <.001 | 0.50 (0.38 to 0.64) | <.001 |

CI, confidence interval; CRF, cardiorespiratory fitness; HR, hazard ratio; ref, reference; SD, standard deviation

Model 1: Adjusted for age, smoking status, history of type 2 diabetes, systolic blood pressure, total cholesterol and high-density lipoprotein-cholesterol

Model 2: Model 1 plus body mass index, fasting plasma glucose, alcohol consumption, prevalent coronary heart disease, use of cholesterol medication, prevalent atrial fibrillation, total physical activity and socioeconomic status

Model 3: Model 2 plus high-sensitivity C-reactive protein

**Supplementary Material 5.** Risk discrimination and reclassification upon addition of %age-predicted CRF and absolute CRF to a CVD mortality risk prediction model containing conventional risk factors

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| --- | --- | --- |
| **Discrimination** | **%age-predicted CRF** | **CRF** |
| C-index (95% CI): conventional risk factors | 0.6797 (0.6550 to 0.7043) | 0.7086 (0.6846 to 0.7327) |
| C-index (95% CI): conventional risk factors plus exposure | 0.7240 (0.6998 to 0.7482) | 0.7326 (0.7085 to 0.7567) |
| C-index change (95% CI) | 0.0443 (0.0237 to 0.0650) | 0.0240 (0.0095 to 0.0385) |
| *p*-value | <.001 | .001 |
| *p*-value for difference in -2 log likelihood | <.001 | <.001 |
|  |  |  |
| **Reclassification** |  |  |
| Net reclassification index (95% CI) | 22.27% (16.72 to 27.82) | 5.56% (1.27 to 9.86) |
| *p*-value | <.001 | .01 |
|  |  |  |
| Integrated discrimination index (95% CI) | 0.0534 (0.0430 to 0.0638) | 0.0303 (0.0227 to 0.0380) |
| *p*-value | <.001 | <.001 |

The model with conventional risk factors included age, systolic blood pressure, history of type 2 diabetes, total cholesterol, high-density lipoprotein cholesterol and smoking. Age was not included in the model for %age-predicted CRF

%age-predicted CRF, percentage of age-predicted cardiorespiratory fitness; CVD, cardiovascular disease