

Supplementary Table 1: ATC-coding

| Group level | Individual level | ATC codes | 1 DDD (mg) |
|----------------------|-------------------------|------------------------------------------------------|-------------------|
| Selective | Nebivolol | C07AB12, C07BB12 | 5 |
| | Bisoprolol | C07AB07, C07AB57, C07BB07, C07FB07 | 10 |
| | Atenolol | C07AB03, C07BB03, C07CB03, C07CB53, C07DB01, C07FB03 | 75 |
| | Metoprolol | C07AB02, C07AB52, C07BB02, C07BB52, C07CB02, C07FB02 | 150 |
| Non-selective | Carvedilol | C07AG02 | 37.5 |
| | Propranolol | C07AA05, C07BA05, C07FA05 | 160 |
| | Sotalol | C07AA07, C07AA57, C07BA07 | 160 |
| | Pindolol | C07AA03, C07CA03 | 15 |

Supplementary Table 2: Baseline characteristics of excluded populations due to missing values for exposure, covariates, and outcomes.

| Characteristic | Full study population n=3451 | Excluded from 6MWT analyses n=964 | Excluded from cycling analyses n=1166 |
|------------------------------------|-----------------------------------------|--------------------------------------------------|------------------------------------------------------|
| Age, years (mean, SD) | 59.8 (8.3) | 60.4 (8.4) | 60.7 (8.4) |
| Women (n, %) | 1676 (48.6) | 450 (46.7) | 502 (43.1) |
| BMI, kg m ⁻¹ (mean, SD) | 27.1 (4.4) | 27.7 (4.9) | 27.8 (4.9) |
| T2DM† | 975 (28.3) | 367 (38.1) | 429 (36.8) |
| Education (%)* | | | |
| Low | 1133 (32.8) | 362 (37.6) | 438 (37.6) |
| Med | 953 (27.6) | 239 (24.8) | 288 (24.7) |
| High | 1288 (37.3) | 286 (29.7) | 363 (31.1) |
| Missing | 77 (2.2) | 77 (8.0) | 77 (6.6) |
| Smoking status (%) | | | |
| Never | 1170 (33.9) | 264 (27.4) | 331 (28.4) |
| Former | 1749 (50.7) | 456 (47.3) | 570 (48.9) |
| Current | 469 (13.6) | 181 (18.8) | 202 (17.3) |
| Missing | 63 (1.8) | 63 (6.5) | 63 (5.4) |

† Determined by an oral glucose tolerance test (OGTT). A fasting plasma glucose level of ≥ 7.0 mmol/l (126mg/dl) or a two-hour plasma glucose level ≥ 11.1 mmol/l (200mg/dl) were defined as T2DM according to the World Health Organisation (WHO) guidelines. Others were defined as non-T2DM.

* Low=no education, primary education not completed, primary education, lower vocational education; medium = intermediate vocational education, higher secondary education; high = higher professional education, university education).

Abbreviations: SD = Standard Deviation, BMI = Body Mass Index, T2DM = Type 2 Diabetes

Supplementary Table 3: Cross-table of participants categorized into tertiles based on outcomes during six minute walk test and cycle ergometer test.

| | 6-minute walk test distance <560 meters | 6-minute walk test distance 560-620 meters | 6-minute walk test distance >620 meters |
|------------------------------------------------------------------------------------------|-----------------------------------------------------------|-----------------------------------------------------------|-----------------------------------------------------------|
| | n=(%) | n=(%) | n=(%) |
| Cycle test output ≤ 1.9 $W_{\max} \text{ kg}^{-1}$ | 408 (59.13) | 198 (27.58) | 89 (12.43) |
| Cycle test output 1.9- 2.37 $W_{\max} \text{ kg}^{-1}$ | 192 (27.83) | 277 (38.58) | 228 (31.84) |
| Cycle test output $\geq 2.37 W_{\max} \text{ kg}^{-1}$ | 90 (13.04) | 243 (33.84) | 399 (55.73) |

Supplementary Text 1: Submaximal cycle ergometer test

In this study, the estimated maximum power output (W_{\max}) was used as an objective measure of cardiorespiratory fitness (CRF).^{1,2,3} W_{\max} was estimated from a graded submaximal exercise protocol performed on a cycle ergometer system (CASETTM version 6.6 in combination with e-bike, GE-Healthcare, Milwaukee, WI, USA). The protocol consisted of at most 7 two-minute exercise stages, with an increase in external work load of 25 W between stages. At the end of each stage, heart rate (HR) and rate of perceived exertion (RPE) were recorded. RPE was measured using the 15-point Borg scale, an interval scale ranging from 6 ('no exertion at all') up to 20 ('maximal exertion').^{4,5} The exercise protocol was considered as 'completed' when HR reached $\geq 85\%$ of the age-predicted maximum HR ($220 - \text{age}$) or when a RPE ≥ 17 was scored by the participant (or when 7 stages were completed without reaching target HR or RPE).

A linear relationship between power output and HR and RPE was assumed^{2,6}. Submaximal values of HR and RPE with workload from each stage were extrapolated to 100% of maximum HR or a RPE of 20 and corresponding workload (W_{\max}) using individual linear regression models. W_{\max} was calculated from HR values if the test was completed based on HR, i.e. HR $\geq 85\%$ of estimated HR_{max} ($W_{\max\text{HR}85\%}$; n=1,358). W_{\max} was calculated from RPE values if the test was completed based on RPE, i.e. RPE ≥ 17 ($W_{\max\text{RPE}17}$; n=631). In addition to the completed tests, W_{\max} from uncompleted tests was calculated from HR if $\geq 75\%$ of HR_{max} was achieved ($W_{\max\text{HR}75\%}$; n=667; $W_{\max\text{HR}75\%} + W_{\max\text{HR}85\%} = W_{\max\text{HR}}$; n=2,025) and W_{\max} was calculated from RPE values if an RPE ≥ 15 was scored ($W_{\max\text{RPE}15}$; n=798; $W_{\max\text{RPE}15} + W_{\max\text{RPE}17} = W_{\max\text{RPE}}$; n=1,429). Tests where both 75% of HR_{max} and RPE ≥ 15 were not achieved were considered as invalid. Both approaches (i.e. estimating W_{\max} from HR and RPE values) provide similar estimates of W_{\max} . Details on the protocol and procedures have been described previously.⁷

Supplementary References

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