Physical functional health predicts the incidence of coronary heart disease in the European Prospective Investigation into Cancer-Norfolk prospective population-based study

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Background Little is known about the relationship between physical functional health and long-term risk of coronary heart disease (CHD) independently of known risk factors in a general population.

Methods Men and women aged 40–79 years at baseline who completed a health and lifestyle questionnaire and attended a health examination during 1993–97 participating in the European Prospective Investigation into Cancer-Norfolk who were free of myocardial infarction (MI), stroke and cancer were included. Eighteen months later, physical functional health was assessed using physical component summary (PCS) scores of Short-Form 36-item questionnaire (SF-36). The incidence of CHD was ascertained by death certification and hospital record linkage up to March 2008.

Results A total of 14,222 men and women were included in the study. There were 389 incident CHD (total person-years = 126,896 years). People who reported better physical functional health had significantly lower risk of CHD. Using Cox proportional hazard models adjusting for age, sex, body mass index, cholesterol, systolic blood pressure, smoking, alcohol consumption, physical activity, diabetes, family history of MI, social class and aspirin usage, it was found that men and women who were in the top quartile of SF-36 PCS had half the risk of CHD [relative risk (RR) = 0.46; 95% confidence interval (CI) = 0.32–0.65] compared with the people in the bottom quartile. The relationships remained essentially unchanged after excluding incident CHD within the first 2 years of follow-up (RR = 0.48; 95% CI = 0.33–0.70).
Conclusions  Physical functional health predicts subsequent CHD risk independently of known risk factors in a general population. People with poor physical functional health may benefit from targeted preventive interventions.

Keywords  Coronary heart disease, physical functional health, Short-Form 36 (SF-36), physical component summary score

Introduction  Coronary heart disease (CHD) remains the number one cause of death in Western societies, and the global burden of cardiovascular disease is expected to rise. In the USA alone, each year approximately 1.1 million persons have myocardial infarction (MI). Early identification and appropriate management of people who are at risk of developing CHD has huge potential in reducing global burden of cardiovascular diseases.

The Short-Form 36-item questionnaire (SF-36) is a widely used and well-validated questionnaire that assesses an individual’s self-reported physical and mental functional health. The physical component summary (PCS) score or physical functional health of SF-36 measures an individual’s capability to perform physical tasks such as carrying grocery, walking, etc. Although it was originally designed to assess the efficacy of treatment(s) provided from the patients’ perspective, recent evidence suggests that physical functional health may also serve as a predictor of objective health outcomes such as mortality and chronic disabling condition such as stroke, independently of known risk factors.

In this study, we examine the relationship between self-reported physical functional health measured by PCS scores of SF-36 and incidence of CHD in a large British prospective population-based study.

Methods

Study sample  The participants were 14,222 men and women, aged 40–79 years at baseline, drawn from the Norfolk, UK, component of the European Prospective Investigation into Cancer (EPIC-Norfolk). The EPIC-Norfolk is a prospective population-based study, described in detail elsewhere. Briefly, the participants were recruited from age–sex registers of general practices. As virtually 100% of people in the UK are registered with general practitioners through the National Health Service, the age–sex registers form a population-based sampling frame. From the inception of the EPIC-Norfolk cohort, data collection was broadened to enable the examination of a wider range of determinants of chronic diseases including CHD. The Norfolk cohort was comparable with national population samples with respect to characteristics including anthropometry, blood pressure (BP) and lipids, but with a lower prevalence of current smokers. The Norwich Local Research Ethics Committee approved the study.

There were a total of 30,445 people who consented to participate (40% of the eligible general population). The majority (99.6%) of people was British White Caucasians. After excluding people who had not attended the first health check (4846), those who did not have SF-36 data (10,910), and prevalent stroke (455), MI (977) and cancer (1642) at baseline, the current report is based on 14,222 participants aged 40–79 years at baseline. Not all who attended the first health check provided SF-36 data and vice versa. Comparison between participants who completed the SF-36 and those who did not, showed no material difference, though statistically significantly different due to large numbers was found for age, sex, body mass index (BMI), systolic BP and cholesterol level (see Appendix in Supplementary data available at IJE online).

Measurements  Study participants completed a baseline health and lifestyle questionnaire and attended a clinic at the study baseline during 1993–97. Height, weight and BP were measured by trained staff using standardized protocols. Means of two measures of systolic BP were used. Non-fasting blood samples were taken. Serum total cholesterol was measured on fresh samples with the RA 1000 (Bayer Diagnostics, Basingstoke, UK).

Participants were asked ‘Have you ever smoked as much as one cigarette a day for as long as a year?’ and ‘Do you smoke cigarettes now?’ in the baseline questionnaire and classified as current or ex-smokers, or those who had never smoked. A four-level physical activity index (level I = inactive, II = moderately inactive, III = moderately active and IV = active) was derived from the EPIC-validated short physical activity questionnaire. The detailed description of this physical activity questionnaire had been previously reported. This index was validated against heart rate monitoring with individual calibration in two independent studies.

Alcohol consumption derived from the question ‘How many alcoholic drinks do you have each week?’ with four separate categories of drinks. A unit of alcohol (~8 g) was defined as a half pint of
beer, cider or lager; a glass of wine; a single unit of spirits (whisky, gin, brandy or vodka); or a glass of sherry, port, vermouth or liqueurs. Total alcohol consumption was estimated as the total units of drinks consumed in a week.

At baseline, they were also asked, ‘Has a doctor ever told you that you have any of the following?' followed by a list of conditions to obtain baseline prevalent illnesses, which included stroke, heart attack, cancer and diabetes. Family history of MI was ascertained from the question ‘Have any of your immediate family had any of the following conditions?’ that included ‘heart attack’. Social class was classified according to the Registrar General’s occupation-based classification [I = professionals, II = managerial and technical occupations, III = skilled workers (non-manual and manual), IV = partly skilled workers and V = unskilled manual workers]. Social classes I, II and III non-manual were re-categorized as ‘non-manual’ and III manual, IV and V as ‘manual’. Aspirin use was ascertained by a question ‘Have you taken aspirin continuously for 3 months or more?’.

Eighteen months later, the surviving participants were asked to complete, by mail, a psychosocial questionnaire that included the anglicized version of the SF-36 (UK SF-36). This assessment included eight dimensions (subscales) of health: physical functioning, social functioning, role limitation due to physical problems, mental health, energy/vitality, pain and general health perception.

Briefly, scores for each dimension are obtained by summing of scores from individual relevant responses concerned with that particular health dimension. For each health dimension (subscale), the raw scores were transformed into a scale from 0 to 100; score 0 represents poor health and 100 represents good health for each subscale. Scoring on the 0 to 100 metric provides with a score that represents the percentage of the total possible score that the participant received. This score is computed by (i) subtracting the lowest possible raw score from the participant’s actual raw score, (ii) dividing this number by the possible raw score range and (iii) multiplying this number by 100.

PCS scores were derived according to algorithms specified by the original developers. They were created by aggregating across the eight SF-36 subscales after transforming to z-scores and multiplying by their respective factor score coefficients and standardized as T-scores with mean 50 and standard deviation (SD) 10. Three scales (physical functioning, role-physical and bodily pain) correlate most highly with the physical component and contribute most to the scoring of the PCS measure.

### Outcome measures

Complete follow-up of the study sample was achieved using death certification at the UK Office of National Statistics and hospital record linkage with vital status ascertained for the whole cohort. Incident cases of CHD were identified by the Tenth Revision of the International Classification of Diseases (ICD 10) code I10–I17.9. The follow-up period commenced from time of completion of the SF-36 (18 months after baseline) and until date of MI or 31 March 2008, as the end of follow-up date.

### Statistical analyses

Statistical analyses were performed using SPSS for Windows Version 14.0 (SPSS Inc., Chicago, IL, USA). We used Cox proportional hazards model to determine the overall and sex-specific independent association of physical functional health with incident CHD adjusting first for age (Model A); secondly for age and sex (Model B); thirdly for age, sex, systolic BP, BMI and cholesterol level (Model C); fourthly, additionally adjusting for lifestyle behaviours including smoking status, alcohol consumption and physical activity (Model D); fifthly, additionally adjusting for history of diabetes and family history of MI (Model E); then including occupational social class (Model F) and finally additionally adjusting for prior aspirin use (Model G).

To address the reverse causality issue, we excluded all those who had CHD within the first 2, 4 and 6 years of follow-up and constructed further models (Models H, I and J) controlling for all of the above-mentioned variables (as in Model G).

All numerical data were entered as continuous variables and ordinal data as categorical variables. Initial analyses were performed using SF-36 PCS quartile categories. As there was a continuous inverse dose–response relationship, the analyses were repeated using every 10-point (~1 SD) increase in SF-36 PCS as the predictor variable. We also explored the association between SF-36 PCS and fatal and non-fatal CHD adjusting for confounders (Model G).

### Results

After exclusion of participants with prevalent MI, stroke and cancer, a total of 14,222 participants aged 40–79 years at the time of study enrolment were included in the current report. There were a total of 389 incident CHD cases (fatal = 102; 26.2%) during the follow-up (total person-years = 126,896 years, mean follow-up = 8.9 years).

Table 1 shows the sample characteristics by quartiles of SF-36 PCS scores. Quartile 1 represents the bottom 25% and quartile 4 represents the top 25%. The corresponding SF-36 PCS scores for quartiles 1, 2, 3 and 4 were 5.20–43.50, 43.51–51.00, 51.01–55.10 and 55.11–72.10, respectively. Participants who reported better physical functional health (those in a higher quartile) were significantly younger, more likely to be men, had lower BMI, cholesterol level and systolic
BP. The proportion of participants who smoked, with history of diabetes and family history of MI, and prior aspirin usage was significantly lower in those participants who were in the top quartile compared with those in the bottom quartile. People in the top quartile are more likely to be physically active and less likely to be from lower occupational social class background. Weekly alcohol consumption differed statistically significantly between top and bottom quartiles. The average alcohol consumption, however, was well within the recommended weekly limit for the UK population. The unadjusted rates for CHD were 4.5, 3.0, 2.1 and 1.2% during the follow up for quartiles 1, 2, 3 and 4, respectively.

Table 2 shows the relative risks (RRs) and their corresponding 95% confidence intervals (CIs) for having a diagnosis of CHD by quartiles of PCS scores of SF-36, first for all, and then for men and women separately. In all models, the results were consistent. Participants with highest SF-36 PCS scores (quartile 4), as compared with the lowest (quartile 1), had significant RR reduction (54%) for incident CHD during the follow-up ($RR = 0.46; 95\% CI = 0.32–0.65$) in the fully adjusted model controlling for age, sex, BMI, cholesterol, systolic BP, smoking, alcohol consumption, physical activity, diabetes, family history of MI, social class and aspirin usage (Model G; Figure 1). Exclusion of CHD diagnosed within first 2 years of

| Table 1 Sample characteristics of 14,222 men and women by quartile of SF-36 PCS |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|
| Q1 (5.20–43.50) | Q2 (43.51–51.00) | Q3 (51.01–55.10) | Q4 (55.11–72.10) |
| N = 3555 | N = 3586 | N = 3558 | N = 3523 |
| Age (years) | 61.4 (9.0) | 59.0 (8.9) | 57.0 (8.6) | 54.3 (8.2) |
| Age (years) | 64.1 (9.0) | 61.6 (8.9) | 59.6 (8.6) | 56.9 (8.2) |
| Sex | | | | |
| Male | 1435 (40.4) | 1648 (46.0) | 1673 (47.0) | 1561 (44.3) |
| Female | 2120 (59.6) | 1938 (54.0) | 1885 (53.0) | 1962 (55.7) |
| BMI (kg/m²) | 27.1 (4.4) | 26.4 (3.8) | 25.9 (3.5) | 25.2 (3.2) |
| Cholesterol (mmol/l) | 6.3 (1.2) | 6.2 (1.1) | 6.1 (1.1) | 6.1 (1.2) |
| Systolic BP (mmHg) | 138 (19) | 136 (18) | 134 (18) | 131 (17) |
| Smoking | | | | |
| Current | 402 (11.3) | 366 (10.2) | 342 (9.6) | 344 (9.8) |
| Former | 1615 (45.4) | 1531 (42.7) | 1432 (40.2) | 1301 (36.9) |
| Never smoked | 1538 (43.3) | 1689 (47.1) | 1784 (50.1) | 1878 (53.3) |
| Alcohol (units/week) | 6.1 (9.1) | 7.4 (9.5) | 7.5 (9.3) | 7.8 (9.3) |
| Diabetes (yes) | 104 (2.9) | 75 (2.1) | 54 (1.5) | 28 (0.8) |
| Physical activity | | | | |
| Inactive | 1301 (36.6) | 996 (27.8) | 822 (23.1) | 652 (18.5) |
| Moderately inactive | 1012 (28.5) | 1074 (29.9) | 1080 (30.4) | 1031 (29.3) |
| Moderately active | 706 (19.9) | 855 (23.8) | 926 (26.0) | 943 (26.8) |
| Active | 536 (15.1) | 661 (18.4) | 730 (20.5) | 897 (25.5) |
| Social class | | | | |
| I | 193 (5.4) | 259 (7.2) | 318 (8.9) | 309 (8.8) |
| II | 1201 (33.8) | 1323 (36.9) | 1437 (40.4) | 1472 (41.8) |
| III non-manual | 655 (18.4) | 626 (17.5) | 583 (16.4) | 551 (15.6) |
| III manual | 828 (23.3) | 804 (22.4) | 697 (19.6) | 742 (21.1) |
| IV | 518 (14.6) | 470 (13.1) | 419 (11.8) | 368 (10.4) |
| V | 160 (4.5) | 104 (2.9) | 104 (2.9) | 81 (2.3) |
| Aspirin use (yes) | 432 (12.2) | 257 (7.2) | 197 (5.5) | 105 (3.0) |
| Family history of MI (yes) | 1413 (39.7) | 1327 (37.0) | 1281 (36.0) | 1224 (34.7) |
| Incidence of CHD (number, crude rate) | 163 (4.5) | 110 (3.0) | 73 (2.1) | 43 (1.2) |

P-values indicate the level of significance between all quartiles. Data are presented as mean (SD) for continuous variables and number (%) for categorical variables.

aAge at the time of completion of SF-36.
follow-up (Model H) attenuated the results only slightly (RR = 0.48; 95% CI = 0.33–0.70). Sensitivity analysis after excluding people with known diabetes, as the prevalence of diabetes was hugely different between physical functional quartiles (2.9% in Q1 and 0.8% in Q4), did not alter the results (RR = 0.46; 95% CI = 0.32–0.66).

Table 3 shows the RR reductions and their corresponding 95% CIs for having CHD by every 10-point increase of SF-36 PCS scores (1-SD equivalent) controlling for age, sex (in sex-combined analyses), BMI, cholesterol, systolic BP, smoking status, alcohol consumption, physical activity, history of diabetes and family history of MI, social class and prior aspirin
usage. Every increase in 10 points (1-SD equivalent) of SF-36 PCS score was associated with significant RR reduction of 24% (RR = 0.76; 95% CI = 0.69–0.84). The relationships between SF-36 PCS and CHD remained consistent when fatal and non-fatal CHD were examined separately. The RRs were 0.78 and 0.75, respectively, for fatal and non-fatal CHD with every increase in 1 SD (10 points) of SF-36 PCS score, showing risk reductions of 22 and 25%, respectively (Table 3).

Similar to the findings in Table 2, exclusion of CHD diagnosed within first 2 years of follow-up attenuated the results only slightly and RR reduction remained highly significant (RR = 0.79; 95% CI = 0.71–0.87). Further models excluding initial 4 and 6 years of follow-up (Models C and D) showed similar results.

Discussion

Self-reported physical functional health assessed by SF-36 was inversely related to risk of incident CHD independently of known risk factors in a general population free of known heart attack, stroke and cancer at the baseline. The strengths of our study include a prospective design, a study population drawn from the community, case ascertainment using objective death certificates and hospital record linkage data and the ability to adjust for known biological, social and lifestyle risk factors for both physical functional health and CHD.

In constructing SF-36, symptoms and problems that are specific to a particular condition were not included. The comparison with other longer measures such as Sickness Impact Profile and Health Insurance Experiment battery, however, showed that the SF-36 includes eight of the most frequently represented health concepts. The plausible mechanisms by which baseline physical functional health predicts subsequent risk of CHD is unclear. Future studies should look for plausible explanations of the associations.

In the current study, the RR reduction for every increase in 10 points of SF-36 PCS score (1-SD increase) was found to be 21% in men (RR = 0.79, 95% CI = 0.70–0.89) and 27% in women (RR = 0.73, 95% CI = 0.62–0.87). There was some attenuation of RR in both men and women after excluding early CHD (18 and 25%, respectively). Interestingly, these findings are similar to our previous report for the relationship between physical functional health and stroke incidence. This consistent finding of relationship between physical functional health and...
subsequent cardiovascular and cerebrovascular conditions raises an interesting hypothesis that maintenance or prevention of decline in physical functional health in ageing populations may have added benefit in prevention of cardiovascular diseases.

It may be possible to attenuate the decline in physical functional health associated with chronological age. We have shown the relationships between modifiable lifestyle behaviours such as smoking, physical activity and alcohol consumption and other potential determinants of SF-36 in the EPIC-Norfolk cohort.\textsuperscript{17–20} In this study, we also adjusted for these factors and the relationships observed appeared to be independent of these factors. It may be that SF-36, being a health profile measure, reflects the overall health status of an individual and captures the subclinical stage of a condition before it can be detected by objective measures such as a diagnosis made on the basis of a blood test result. Poor physical functional health may reflect underlying biological processes such as chronic inflammation that may relate to CHD. It is also possible that a poor score may reflect psychosocial factors such as stress, which may also influence cardiovascular risk. The PCS score of SF-36 may therefore be a potentially useful additional marker in assessing CHD risk. Our findings suggest that inclusion of physical functional health assessment in predicting cardiovascular risk may be a useful approach to better identify people at high risk of future CHD at the population level in an apparently CHD-free population. However, further studies in different populations are required to replicate these findings.

Study limitations
Underestimation of incident coronary events results towards the null, i.e. underestimation of the magnitude of the association. Using self-reported MI to exclude people with prevalent disease may have missed some prevalent CHD cases. Reverse causality is a potential major issue. People who are already ill might be more likely to be physically inactive and change their lifestyle (e.g. smoking habit) as a result of prevalent disease. To address this we excluded those with prevalent MI, stroke and cancer at baseline and also adjusted for other potential indicators of ill health such as high or low BP, cholesterol concentration, high or low BMI, diabetes mellitus and aspirin use, and also repeated the analyses excluding people with CHD diagnosed within the first 2 years of follow-up. People with angina have been shown to have impaired health-related quality of life.\textsuperscript{21} However, the exclusion of CHD incidents occurring within first 2 years of follow-up did not alter the results significantly. The residual confounding with known or unknown factors is always possible. We used only one measure at one point in time to characterize individuals and did not take into account possible changes in lifestyle or other treatment effects on the variables we examined (e.g. anti-hypertensive medication or cholesterol-lowering therapy during the study period). Nevertheless, random measurement error would probably attenuate any associations observed, so the estimated differences in risk are likely to be larger than those observed.

Because participants had to be willing to provide detailed information and participate in a long-term follow-up, the EPIC-Norfolk had modest participation rate of ~40% of the eligible population at the baseline, despite 100% follow-up rate. However, EPIC-Norfolk sample is comparable with the other representative National Surveys in the UK, with only slightly lower prevalence of smokers.\textsuperscript{3,14} The potential healthy responder bias resulting in truncation of sample distribution would probably only attenuate the findings and very unlikely to change the direction of the study results. We were not able to examine the relationship between the SF-36 PCS and incident CHD in the whole cohort. This is due to the fact that the SF-36 survey was not completed by all participants and also because we excluded anyone with missing variables that are included in the current report. Exclusion of these individuals, however, is unlikely to influence the internal relationship between physical functional health and incidence of CHD in the study population.

Conclusion
Physical functional health-related quality of life measured as PCS scores of SF-36 predicts subsequent risk of CHD independently of known risk factors in a general population without history of ischemic heart disease at baseline. The nature of the association between physical functioning and subsequent risk of CHD needs further exploration. Further studies could perhaps investigate different ethnic populations to reflect the current situation of increasing number of diverse populations in the UK. In the interim, regardless of the underlying mechanism, a poor physical function score may identify men and women in the apparently healthy general population at increased risk of a coronary event independent of classical risk factors. People with low level of SF-36 PCS may benefit most from targeted preventive interventions such as management of known risk factors and increased uptake of positive lifestyle behaviours.

Supplementary data
Supplementary data are available at IJE online.

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KEY MESSAGES

- Physical functional health-related quality of life measured as PCS scores of SF-36 predicts subsequent risk of CHD independently of known risk factors in a general population.
- Poor physical function score may identify men and women in the apparently healthy general population at increased risk of a coronary event independent of classical risk factors.

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