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Fitness predicts long-term survival after a cardiovascular event: a prospective cohort study

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ABSTRACT

Objectives: To identify the role of fitness, fitness change, body mass index and other factors in predicting long-term (>5 years) survival in patients with coronary heart disease.

Design: Cohort study of patients with coronary heart disease recruited from 1 January 1993 to 31 December 2002, followed up to March 2011 (1 day to 18 years 3 months, mean 10.7 years).

Setting: A community-based National Health Service (NHS) cardiac rehabilitation programme serving the Basingstoke and Alton area in Hampshire, UK.

Participants: An unselected cohort of NHS patients, 2167 men and 547 women aged 28–88 years, who attended the rehabilitation programme following acute myocardial infarction, an episode of angina or revascularisation, and had a baseline fitness test.

Main outcome measures: Cardiovascular mortality and all-cause mortality.

Results: A high level of fitness ($VO_2 \geq 22$ mL/kg/min for men, $VO_2 \geq 19$ mL/kg/min for women) at completion of the programme was associated with decreased all-cause death, as was a prescription for statins or aspirin, and female gender. Increase in all-cause mortality was associated with higher age and ACE inhibitors prescription. Higher risk of cardiovascular mortality was associated with increasing age, prescriptions for ACE inhibitor, and diagnosis of myocardial infarction or angina as compared with the other diagnoses.

Conclusions: Prior fitness and fitness improvement are strong predictors of long-term survival in patients who have experienced a cardiac event or procedure. Some secondary prevention medications make a significant contribution to reducing all-cause mortality and cardiovascular mortality in these patients. This study supports public health messages promoting fitness for life.

Strengths and limitations of this study

- Unselected cohort of patients registered in a National Health Service cardiac rehabilitation centre.
- All data collected by one individual.
- Long-term follow-up of participants; mean 10 years 8 months.
- Effect of missing data examined using multiple imputations.
- Dietary factors, postrehabilitation exercise and medications unknown; height and ethnicity not routinely recorded throughout.

INTRODUCTION

We report the long-term mortality of an unselected cohort of patients who have experienced a coronary event or procedure. While many studies have reported on the effects of treatment and other factors on short-term case fatality,[1–4] there is little evidence published on the role of fitness, fitness change, depression and anxiety, and other factors which may be associated with the long-term survival of individuals who have experienced a coronary event (eg, myocardial infarction (MI)) or procedure (eg, coronary artery bypass graft (CABG), percutaneous coronary intervention (PCI)).[5–10] In addition, the relative importance of two modifiable factors, fitness and body mass index (BMI), has yet to be fully explored.

Coronary heart disease remains the leading cause of mortality in the UK, with coronary heart disease accounting for 18% of all deaths in men and 13% in women.[11] Nevertheless, the UK has been experiencing dramatic falls in death rates from coronary heart disease in recent years[12] due to the fall in smoking prevalence[13] and improvements in the treatment, particularly secondary prevention.[14]

In this analysis, we investigated the factors that influenced long-term survival after a coronary event. We were particularly interested in the effects of fitness, body weight and depression.

METHODS

Setting and participants

We used data collected by one of us (ST) on patients recruited between 1 January 1993 and 31 December 2002 through the Basingstoke and Alton (Hampshire, UK) cardiac rehabilitation programme[15–17] with follow-up to 30 March 2011. The cohort was unselected, included all National Health Service (NHS) referrals, and participants have now been followed for 1 day to 18 years and 3 months providing 11 871 person-years of follow-up. Recruitment to the cohort was undertaken typically 2 –6 weeks after their index coronary event.[18 19] NHS patients in the area served by the rehabilitation centre were routinely referred to this programme following an acute MI, episode of unstable angina or revascularisation. The only other inclusion criterion for the study was that the patients had to be registered with the cardiac rehabilitation programme. This resulted in an unselected cohort of 2714 patients.

The phase III programme —offered at Basingstoke and Alton cardiac rehabilitation centre—assessed patients for physical and psychological health at the beginning and at the end of the programme. They began a supervised aerobic exercise class once or twice a week, with home aerobic exercises in between. The supervised sessions comprised circuit training for 40 min, with those patients needing to rest between different aerobic exercises switching to strength and endurance exercises for 'active recovery'. Patients graduated from the exercise programme when they could complete the circuit without needing active recovery. Besides the exercise programme,[20] a health education and stress management component was offered to which patients' spouses or partners were also invited. This component covered relaxation techniques and a health education programme (understanding coronary heart disease, cholesterol, healthy eating, blood pressure, the benefits of regular physical activity, smoking advice, cardiac medications), and stress management.

Data

Dates and causes of death were provided by the Office for National Statistics. All patients who attended the programme and had baseline fitness measured were included in the primary analysis. Data collected included whether the programme was completed, diagnosis, comorbidity, family history, occupation, date of birth, age, gender, smoking history, resting heart rate, cholesterol level, triglycerides level, postcode and from 1998, height. At both recruitment and on completion records were made of each patient's weight, blood pressure, fitness, anxiety and depression[21 22] (as measured by Hospital Anxiety and Depression Scale[17 23]), current smoking habit and medications (ACE inhibitor, aspirin, β-blocker, statins).

We calculated changes in weight, fitness, anxiety and depression from the entry and exit values for each individual. Since height was not routinely recorded throughout, BMI was available for only 889 patients; so, for the primary analysis, we categorised baseline weight into under 78 kg, 78–93 kg and over 93 kg for men, and under 68 kg, 68–80 kg and over 80 kg for women; these categories were labelled I, II and III, respectively, for brevity. These approximate to the normal, overweight and obese categories for men and women of average height (176 cm and 164 cm, respectively; British National Formulary) and the average age of this cohort. The index of multiple deprivation was ascertained from postcode, occupation was coded under nine headings (see table 1), and age was categorised into under 50, 50–59, 60–69 and 70 years and over. The Modified D'Hoore comorbidity index is designed to assess non-coronary comorbidity specifically in the outpatient cardiac rehabilitation environment, rather than in the acute setting,[24] and was calculated for each patient based on the recorded comorbidities.

Up to August 1995, fitness was assessed on a bicycle ergometer with ECG monitoring and measurement of estimated peak workload. After that date, exercise tests were performed on a treadmill—without using a handrail, using either the Bruce protocol[25] or, the modified Bruce protocol, for frail or elderly patients.[26] Peak exercise tolerance was expressed as the predicted oxygen uptake (VO_2peak) in mL/kg/min, from the known oxygen cost of bicycling at different workloads.[27] The same end points were used as for bicycle tests and VO_2peak predicted on the assumption that each 1 min of the Bruce protocol uses 1 MET (metabolic equivalent —or 3.5 mL O_2/kg/min), and that the first three stages of the modified Bruce protocol each use 1 MET. VO_2peak<15 mL/kg/min was categorised as low fitness, VO_2peak>22 mL/kg/min as high fitness, and the in-between readings as medium fitness for males (categories established for cardiac rehabilitation by Kavanagh *et al* [28 29]); for females VO_2peak<13 mL/kg/min was categorised as low fitness, VO_2peak>19 mL/kg/min as high fitness,and the in-between values were categorisedas medium.[28 30]

Depression and anxiety were categorised into none, borderline and depressed or anxious using a Hospital Anxiety and Depression Scale score below 8 to suggest no depression or anxiety, 8–10 to suggest borderline, and a score over 10 to suggest clinical depression or clinical anxiety.[23]

We are confident that all deaths in UK have been captured and the loss to follow-up will have been minimal, perhaps due to deaths which occurred abroad and were not reported to the study.

In the main analysis, baseline categories of fitness, depression and anxiety were used as predictors. In order to test whether an improvement in fitness, depression and anxiety categories influenced survival, and whether these depend on baseline categories, we defined variables fitness, anxiety and depression where a scale of 1–7 captured each starting category and the improvement or deterioration (see online supplementary table S6, which details the categories). Very few patients started in the highest fitness category and then deteriorated over the course of the programme (5 men); so we

Table 1 Baseline values for patients at recruitment to cardiac rehabilitation programme

	Male		Female		Total	
Number (n)	1320	(86.3%)	209	(13.7%)	1529	(100%)
Mean years of follow-up (SD)	11.3	(3.8)	11.1	(3.6)	11.3	(3.7)
Mean age in years (SD)	61.0	(9.4)	62.9	(9.0)	61.3	(9.4)
	n	Per cent	n	Per cent	n	Per cent
Age (years)						
<50	158	11.9	19	9.1	177	11.5
50–59	405	30.7	50	23.9	455	29.8
60–69	500	37.9	85	40.7	585	38.3
>70	257	19.5	55	26.3	312	20.4
Diagnostic category						
MI	673	51.0	108	51.7	781	51.1
CABG	382	28.9	51	24.4	433	28.4
PCI	124	9.4	22	10.5	146	9.5
MI+PCI	56	4.3	7	3.3	63	4.1
Angina	61	4.6	19	9.1	80	5.2
Other cardiac diagnoses	24	1.8	2	1.0	26	3.8
Smoking history						
Never smoked	347	26.3	93	44.4	440	28.8
Not for >10 years	430	32.6	30	14.4	460	30.1
Not for 1–10 years	56	4.2	9	4.3	65	4.3
Recent quitter	407	30.8	64	30.6	471	30.8
Current smoker	80	6.1	13	6.3	93	6.0
D'Hoore comorbidity score						
None	968	73.3	141	67.5	1109	72.5
1 (least)	150	11.4	22	10.5	172	11.2
2	168	12.7	42	20.1	210	13.7
3	21	1.6	3	1.4	24	1.6
4 (most)	13	1.0	1	0.5	14	1.0
Diagnosis of diabetes	158	12.0	29	13.9	187	12.2
Family history of CHD	613	46.4	115	55.0	728	47.6
Weight at baseline						
I: <78 kg men; <68 kg women	519	39.3	95	45.5	614	40.2
II: 78–93 kg men; 68–80 kg women	565	42.8	69	33.0	634	41.5
III: >93 kg men; >80 kg women	236	17.9	45	21.5	281	18.3
Medications						
ACE inhibitor						
No	665	50.4	88	42.1	753	49.2
Yes	655	49.6	121	57.9	776	50.7
Aspirin						
No	45	3.4	12	5.7	57	3.7
Yes	1275	96.6	197	94.3	1472	96.3
Statin						
No	455	34.5	57	27.3	512	33.5
Yes	865	65.5	152	72.7	1017	66.5
β-blockers						
No	727	55.1	108	51.7	835	54.6
Yes	593	44.9	101	48.3	694	45.4
Occupation						
Managers and senior officials	236	17.9	16	7.6	252	16.5
Professional occupations	143	10.8	11	5.3	154	10.1
Associate professional	145	11.0	25	12.0	170	11.1
Administrative and secretarial	125	9.5	67	32.1	192	12.6
Skilled trade	362	27.4	13	6.2	375	24.5
Personal service	23	1.7	34	11.5	47	3.1
Sales and customer	26	2.0	16	7.6	42	2.7
Process, plant and machines	155	11.7	12	5.7	167	10.9
Elementary occupations	105	8.0	25	12.0	130	8.5

Continued

Table 1 Continued

	Male		Female		Total	
Fitness						
High baseline	588	44.6	53	25.4	641	41.9
Mid baseline	511	38.7	77	36.8	588	38.5
Low baseline	221	16.7	79	37.8	300	19.6
Depression						
Not depressed	1162	88.0	160	76.6	1322	86.5
Borderline	113	8.6	36	17.2	149	9.7
Depressed	45	3.4	13	6.2	58	3.8
Anxiety						
Not anxious	930	70.5	122	58.4	1052	68.8
Borderline	251	19.0	42	20.1	293	19.2
Anxious	139	10.5	45	21.5	184	12.0
Median VO_2 mL/kg/min (10th, 90th centile)	21.0	(13.1, 29.7)	15.5	(8.4, 24.5)	20.1	(11.0, 29.2)

CABG, coronary artery bypass graft; CHD, coronary heart disease; MI, myocardial infarction; PCI, percutaneous coronary intervention.

combined this category with the 'no change' category. There were no patients who deteriorated after having started in the mid-fitness category; therefore, we omitted this category and were finally left with five categories. We defined survival time as the period between the date the participant joined the programme and the date of death. In the survival analyses, we considered all-cause mortality and cardiovascular mortality, with non-cardiovascular deaths treated as censored in the latter analysis.

Statistical analysis

We used Cox proportional hazards models[31] starting with the subset of variables that were found to be significant predictors (at 5% level) of all-cause mortality in the univariate analyses. We employed a backward stepwise selection algorithm to find the model with minimum Akaike Information Criterion (AIC),[32] retaining age and gender as the minimum model. All analyses were carried out in R statistical software.[33] The primary model (model A) was based on 1529 cases with complete data, including a baseline fitness test. Two secondary models were also produced. One used the 1029 cases with complete data—including a baseline and end fitness test—to study the effects of fitness change (model B) on long-term survival. The other used the 889 cases with a baseline fitness test and a baseline BMI measurement to evaluate the relative effect of BMI and fitness (model C) on long-term survival.

Since there was a large amount of missing data, we assessed the credibility of the complete-case model. Analysis of a complete-case data set alone cannot be expected to give reliable estimates of model coefficients without making assumptions about the missing data.[34] We compared HRs from the complete-case analysis with those from an analysis of all data after replacement of missing values with imputed data. Multiple imputation was performed in the R package MICE (Multivariate Imputation using Chained Equations)[33] providing 20 completed data sets with values imputed where these were missing. The optimised model was then built with each of these 20 data sets, and pooled estimates of model coefficients and variances calculated using the rules devised by Little and Rubin[34] for comparison. There were no known reasons to believe that the data were missing other than at random, except in the case of the end fitness data. Reasons for end fitness to be missing included referral for cardiac surgery and poor health; a Student t test confirmed that time to death for these individuals differed from those with end fitness observations.

RESULTS

Patient characteristics

Of the 2964 patients with coronary heart disease recorded on the database, 160 did not attend any part of the rehabilitation programme, 1 of them had a MI suspected to be secondary to anorexia nervosa, another was 18-year-old probably a miscode, and 88 did not have a fitness assessment at entry to the programme; this left 2714 patients. A total of 2054 patients completed the programme[17]; the main reasons for not completing the programme were patient preference, referral for cardiac surgery, poor health or death. Those without complete end fitness data included the ones who were taken to a different heart rate at the final fitness test, most of whom were on a β-blocker for which the dose had been changed or who were tested at a different time of day, and those who were tested using a different test protocol.[17] The mean follow-up for those with complete data was 11 years 4 months.

There were 1529 cases (56.3%) which were complete in all the 36 variables that were significant in the univariate analysis and became the starting point for the primary analysis (model A), see figure 1. Patient characteristics for these are given in table 1. There were 1029 cases (38%) which were complete in the variables used in the primary analysis and also had observations

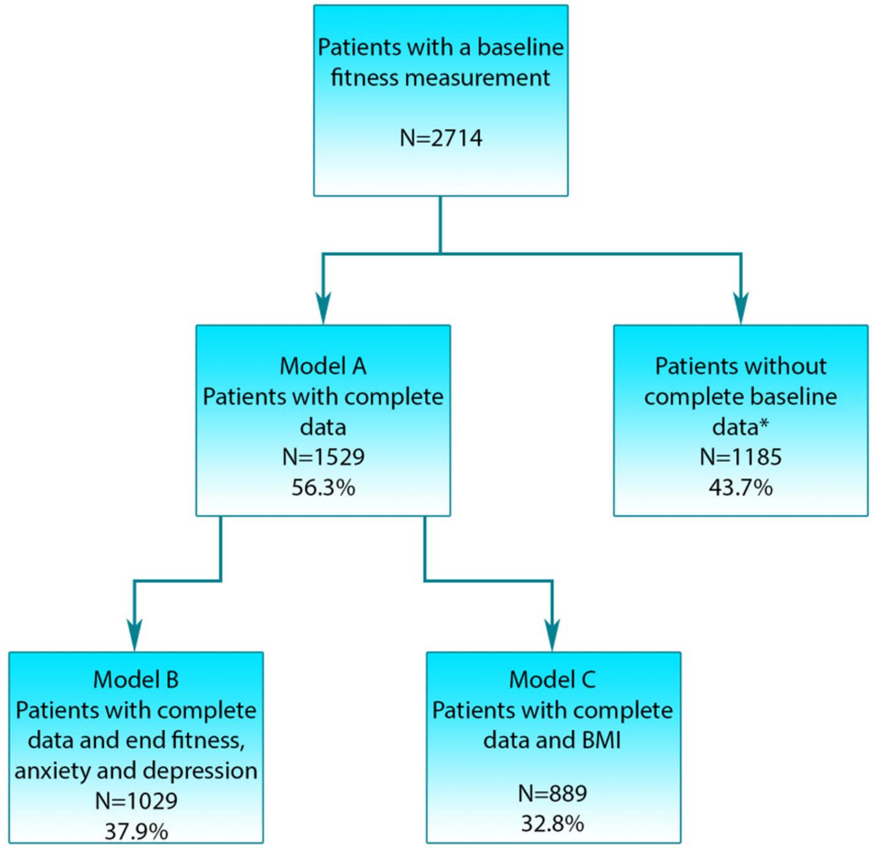

Figure 1 The number of patients* with missing data in individual variables of interest varied, with fitness after the programme missing in 48.5% of cases, and the remaining variables missing data ranging between 0% and 29.4%. Details of variables and numbers, and percentage of missing observations are provided in online supplementary table S1 (BMI, body mass index).

for fitness, depression and anxiety at the end of the programme, allowing us to assess the impact of changes in these variables on survival (model B). Patient characteristics for these are given in online supplementary table S5. There were 889 cases (32.8%) for which it was possible to calculate BMI and were complete in the other variables (model C). Patient characteristics for these are given in online supplementary table S7.

Women (13.7%) had a higher mean age. The most common reason for referral to the programme was acute MI (51.1%). Nearly half the women had never smoked compared with just under one-third of the men, and close to one-third of both genders had recently given up smoking. Around half of all patients had a family history of coronary heart disease and over 70% were free from non-coronary comorbidity, although a higher proportion of the women had diabetes. The men had a higher mean fitness than the women, and the percentage of men in the high-fitness category at recruitment was twice that of the women. At completion, 67% of the men and 41% of the women were in the high-fitness category, with one-fifth of the patients having improved from the mid-fitness category. Median fitness was improved by a similar amount in both genders, and high fitness was the largest group at completion.

There was little evidence of clinical depression in this cohort, and most of those whose scores suggested a borderline category improved by programme completion (83%), as did almost all of the few whose scores at recruitment suggested clinical depression (83%). There was more anxiety, although the rates were not high. Again, the majority who began in the borderline category improved, as did a significant proportion of those starting in the clinical anxiety category, but the proportion of women who remained in the clinical anxiety class was three times that of the men. The maximum recorded comorbidity score was 7 (very high), but only 2.6% of participants had a comorbidity score of 3 or more (see online supplementary table S2 for scoring details).[24]

Survival

During the course of the study and follow-up, 385 participants (25.2%) died and of these deaths, 192 (49.9%) were from cardiovascular causes.

For model A, the primary proportional hazards model, the significant predictors of all-cause mortality are presented in table 2. In this model, age was the most important predictor of all-cause mortality, with risk of death increasing with age. The next most important predictor was fitness category at recruitment, with the fittest patients having the lowest risk. Risk increased with comorbidity, and aspirin and statins prescriptions reduced risk. MI was the diagnosis carrying the greatest risk, including MI with PCI, angina and other cardiac diagnoses. CABG and PCI alone were much lower risk diagnoses. Those with a lower resting heart rate were at a lower risk of mortality. Higher systolic blood pressure was also a risk indicator. ACE inhibitor prescription was

Table 2 All-cause survival model A (using only baseline fitness, anxiety and depression categories), ordered by importance of variables to the model (1529 cases, 385 deaths)

Model term	Complete cases HR	95% CI Lower	95% CI Upper	Imputed data HR
Age category(years)				
<50	1.00	–	–	1.00
50–59	2.13	1.17	3.88	2.04
60–69	3.85	2.15	6.89	3.09
>70	7.96	4.38	14.44	6.12
Fitness at baseline				
High baseline	1.00	–	–	1.00
Mid baseline	1.54	1.16	2.05	1.75
Low baseline	2.47	1.78	3.42	2.67
D'Hoore comorbidity				
None	1.00	–	–	1.00
1 (least)	1.23	0.91	1.66	1.74
2	1.42	1.08	1.86	1.40
3	1.35	0.68	2.66	1.96
4 (most)	4.50	2.13	9.50	2.09
Statins				
Yes	0.72	0.57	0.89	0.74
No	1.00	–	–	1.00
Aspirin				
Yes	0.52	0.35	0.78	0.63
No	1.00	–	–	
Systolic blood pressure before: each 1 mm Hg reduction	0.995	0.993	0.999	0.998
ACE inhibitor				
Yes	1.26	1.01	1.57	1.18
No	1.00	–	–	1.00
Resting heart rate	1.007	1.000	1.014	1.007
Diagnostic category				
MI	1.00	–	–	1.00
CABG	0.69	0.54	0.89	0.69
PCI	0.53	0.32	0.88	0.67
MI+PCI	0.84	0.44	1.65	0.79
Angina	0.87	0.54	1.39	0.84
Other cardiac diagnoses	0.99	0.44	2.25	0.93
Gender				
Male	1.0	–	–	1.00
Female	0.79	0.59	1.06	0.69

CABG, coronary artery bypass graft; MI, myocardial infarction; PCI, percutaneous coronary intervention.

Table 3 Optimised cardiovascular survival model A (using only baseline fitness, anxiety and depression categories), ordered by importance of variables to the model (1529 cases, 192 cardiovascular deaths)

Model term	Complete cases HR	95% CI Lower	95% CI Upper	Imputed data HR
Fitness				
High baseline	1.00	–	–	1.00
Mid baseline	1.83	1.20	2.79	2.34
Low baseline	4.06	2.58	6.39	4.26
Statin				
Yes	0.45	0.33	0.61	0.51
No	1.00	–	–	
Age (years)				
<50	1.00	–	–	1.00
50–59	1.58	0.76	3.31	1.53
60–69	2.63	1.30	5.35	2.39
>70	4.00	1.93	8.28	3.77
Diagnostic category				
MI	1.00	–	–	1.00
CABG	0.60	0.42	0.85	0.62
PCI	0.26	0.09	0.70	0.49
MI+PCI	1.05	0.42	2.62	0.74
Angina	0.85	0.46	1.53	0.72
Other cardiac diagnoses	0.79	0.25	2.49	0.99
Aspirin				
Yes	0.47	0.28	0.78	0.57
No	1.00	–	–	1.00
Gender				
Male	1.00	–	–	1.00
Female	0.73	0.48	1.10	0.62
ACE inhibitor				
Yes	1.42	1.04	1.94	1.36
No	1.00	–	–	1.00

CABG, coronary artery bypass graft; MI, myocardial infarction; PCI, percutaneous coronary intervention.

associated with higher risk; the most likely reason for this is that at the time these drugs were being prescribed the ACE inhibitors were only given to individuals at high risk. That is, the users of ACE inhibitors will have been at higher risk than non-users before starting to use the medication. After adjusting for other factors, gender was not a statistically significant predictor of mortality. The significant terms from the cardiovascular mortality model are detailed in table 3. Fitness category at baseline was the strongest predictor of cardiovascular mortality, with higher fitness associated with lower risk. A prescription for statins cut the risk of cardiovascular mortality by more than half in this cohort. Age was the next most significant predictor of mortality, with risk increasing with age as expected. As with all-cause mortality, a diagnosis of MI carried the highest associated risk of mortality, with MI+PCI, angina and other cardiac diagnoses having an equally high mortality risk. A prescription for ACE inhibitor was associated with higher risk.

The all-cause mortality for model B, the cohort having complete data including end depression anxiety and fitness, is detailed in online supplementary table S3. In model B, age was the strongest predictor of risk for all-cause mortality, followed by the combination of fitness category at recruitment, and whether the patient improved or maintained that fitness, with highest risk attributed to those who began in the low-fitness category. Mean VO_2peak change was 3.81 VO_2 mL/kg/min

(SD 3.38). There was no statistically significant difference (assessed at the 5% level) between those who began in the mid-fitness category and improved to high fitness and those who began in the high-fitness category and maintained high fitness. However, those who did not improve sufficiently to move up from the mid-fitness category had significantly higher risk; improvement to a mid-fitness from low-fitness category did not significantly reduce risk, although a significant difference in risk is evident between low and medium fitness for the patients whose category did not change. Having a prescription for statins or having a prescription for aspirin was each associated with a lower risk of mortality. A prescription for ACE inhibitors was associated with a higher risk of mortality.

The cardiovascular mortality for model B is detailed in online supplementary table S4. Fitness was the most powerful predictor of cardiovascular mortality, low baseline and failure to improve being powerful predictors of cardiovascular mortality. A prescription for statins was important, with those having a prescription having one-third the risk of those without. After fitness, age was the most important factor, with those over 70 years at higher risk of cardiovascular death. Aspirin was associated with lower risk of mortality.

The all-cause and cardiovascular mortality for model C, with BMI as a prognostic factor, is detailed in online supplementary tables S8 and S9. Model C was very similar to the primary model. Notably, while BMI was a predictor of mortality in the univariate analysis, in the presence of a fitness assessment it ceased to be statistically significant. This suggests that an assessment of fitness may be a better prognosis of survival than a measure of obesity in people with coronary disease.

Imputed data

The HRs derived from the pooled imputed data (shown in tables 2 and 3) are reassuringly very similar to those from the complete-cases model, both in size and direction, indicating that missing data has not significantly modified the inferences we report.

DISCUSSION

We set out to discover which factors predict mortality in an unselected cohort of patients attending cardiac rehabilitation. We found that having a good level of fitness before a coronary event or procedure confers a survival advantage. Also, individuals who increase fitness during cardiac rehabilitation could increase life expectancy, even if they were already moderately fit.

Four major strengths of this study are that there was a long follow-up period, the participants were unselected, fitness was assessed at entry into rehabilitation, and all the data were collected in routine clinical practice by one physiotherapist (ST) using a consistent fitness delivery programme. The data reported here are derived from a single NHS centre, with a consistent delivery of the programme spanning 18 years (average follow-up 11.5 years). Since all patients registered in the programme with a baseline fitness test were included, the participants represent a realistic sample of the population of people who are likely to access cardiac rehabilitation.

The majority of trials of cardiac rehabilitation have followed participants for 2 years or less,[17] and of the studies that have reported on long-term survival, very few consider fitness as a possible explanatory variable.[13 14 35] However, a recent Canadian study of a similar duration to ours, but which followed a selected cohort of patients,[30] also found that baseline fitness and fitness improvement were associated with reduced all-cause mortality. The authors selected a group of patients who had undergone cardiac catherisation procedures, had completed a 12-week exercise-based cardiac rehabilitation course, had returned 12 weeks later for a repeated assessment, and had survived for at least 6 months from the date of catherisation. There were no missing data. The study participants were of a similar age range and gender balance as those in our study, but their baseline fitness was higher.

Our findings were based on routinely collected clinical data in an unselected group of patients, with inevitably some missing data. However, we have been able to demonstrate the robustness of our models using established statistical methods. Physical fitness was assessed indirectly using predicted, not measured, oxygen uptake. Over the course of the study, two different methods of estimating fitness were used. However, we ensured that only patients whose fitness was assessed by the same method at the beginning and the end of cardiac rehabilitation programme were included in the variable measuring change in fitness. Furthermore, method of fitness assessment was not statistically significant in the survival models. The methods of fitness assessment are typical of the pragmatic methods used in such NHS settings.[36] Patients who did not have a baseline measure of fitness were excluded, diminishing the generalisability of the results. Some of these individuals will have been the frailest patients. Lower VO_2peak estimated from a treadmill test can indicate more severe cardiovascular disease as well as lower fitness, and it may be that those patients with low fitness also have more severe cardiovascular disease.

Attaining a fitness level of $VO_2 \geq 22$ mL/kg/min for men and $VO_2 \geq 19$ mL/kg/min for women in the early months following a cardiac event or procedure is associated with improved long-term survival. For comparison, a man aged 60+ with a VO_2peak of 26.1–32.2 mL/kg/min is considered reasonably fit and 32.3–36.4 mL/kg/min, as very fit;[37] so these fitness categories are not very demanding. High fitness at recruitment to the rehabilitation programme was likely to reflect high fitness before a coronary event or procedure, but there was no statistically significant difference between patients who improved from moderate fitness at

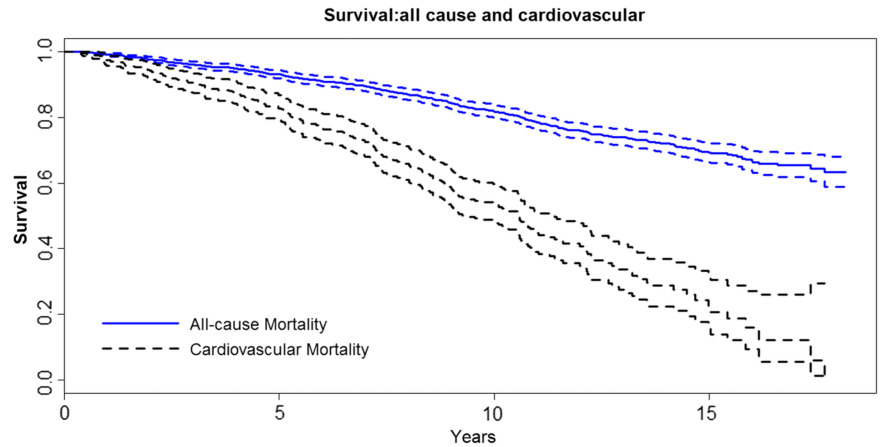

Figure 2 Kaplan-Meier survival curves for all-cause and cardiovascular mortality. The plot is for the entire observation period and the dashed lines are 95% CIs.

recruitment to high fitness at programme completion and those who maintained high fitness from recruitment. Since we have followed these patients for a mean of 10.7 years, and have no information on what their levels of exercise or fitness were during those years, it is even more striking that a brief snapshot of their past fitness should show such a strong effect on long-term survival. If long-term data on fitness were available, it may be that the effect would prove to be even stronger. Measured VO_2peak was found to be a predictor of long-term mortality of men and women in Canada in the earlier decades, without consideration of change in fitness; even moderate fitness conferred a 50% reduction in cardiac mortality.[28 29]

Having adjusted for fitness, BMI does not appear to affect all-cause or cardiovascular mortality in patients with cardiovascular disease, which is consistent with other studies.[10 30 38–40] These findings are in line with those of a recent large European cohort study which examined reported physical activity and measures of obesity as predictors of all-cause mortality, and concluded that physical inactivity 'is responsible for more than twice as many deaths as general obesity'.[40]

Using medications for secondary prevention, particularly aspirin and statins, in the early weeks after a cardiac event or procedure appears to reduce long-term mortality from cardiovascular causes and all-causes. This confirms previous findings.[14] Given that we have no information on adherence or changes to medication after completion of the programme, the strong effect of secondary preventative medication is striking. Analysis of data sets with information on the long-term use of medications might show an even stronger effect. Preoperative risk factors which are good predictors of short-term outcomes have been found to contribute little information to the prediction of long-term survival in patients with CABG.[7] Traditional predictors of early survival in patients with CABG over the age of 65 years do not affect long-term survival,[10] but late mortality is increasingly associated with chronic diseases and health behaviours. Long-term prognosis after hospital admission for MI is improving.[41] In the majority of previous studies, differences between cardiovascular mortality and all-cause mortality were not considered, and nor were secondary prevention medications, fitness or anxiety and depression considered as predictors of survival.

Health may be expected to be generally better in an affluent area, such as the one selected for this study, than in a deprived geographical area; thus these results may not be fully generalisable to other settings. Patients who never attended or attended but did not have a baseline assessment of fitness are excluded from this analysis, but they may form part of the population of patients typically experiencing a cardiac event or procedure,

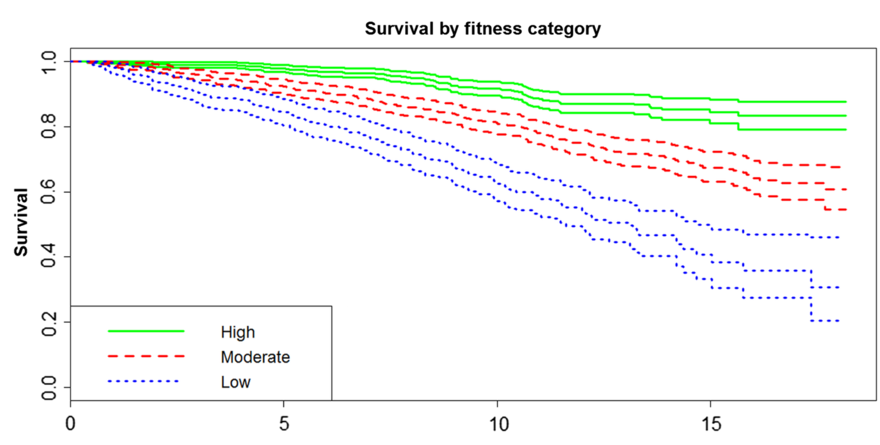

Figure 3 Kaplan-Meier survival curves for all-cause and cardiovascular mortality by baseline fitness group. The plot is for the entire observation period with 95% CIs.

potentially diminishing the generalisability of the results. Some of these individuals will have been the frailest patients, and excluding them also explains the initial period of no deaths seen in the Kaplan-Meier plot (figures 2 and 3). Other limitations include unknown dietary factors, postrehabilitation exercise and medications.

However, our study shows that fitness level in the early weeks after a cardiac event or procedure was equally important for cohorts with a wider range of initial fitness than previous studies, a wider age range, those having significant comorbidities and including women. This analysis contributes to the body of research seeking to identify risk factors for long-term mortality in patients with coronary heart disease.

CONCLUSIONS

Pre-existing fitness or improvement in fitness within the early months after a coronary event or procedure predicts long-term survival of patients. Fitness interventions should take precedence over weight loss interventions.

Secondary prevention medications contribute significantly to improved long-term survival in all-cause and cardiovascular mortality even when there is no information on how long the medications were used, suggesting that the effect is very strong. Patients having coronary artery bypass surgery and PCI have a significantly higher long-term survival from cardiovascular mortality than do patients with a MI or angina. Promotion of fitness after a coronary event or procedure may extend life expectancy.

Contributors MT, FG, NP and MJB contributed to the study design. ST and HB collected the data. ST was involved in editing and data preparation. MJB and NP performed the analysis. MT, ST and MJB contributed to the first draft of the manuscript. SW read and critically appraised several versions of the manuscript. MJB had full access to the data in the study. MJB is the guarantor. All the authors critically revised the manuscript for important intellectual content, and approved the final version to be published.

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Competing interests None declared.

Ethics approval Approval for this study was granted in 2001 from the North and Mid Hampshire Local Research Ethics Committees reference 354/B.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement The permanent URL for this dataset will be: http://wrap.warwick.ac.uk/70379.

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Supplementary material

Table S1| **Missing Data. ‡ indicates that this variable was a significant predictor of all-cause mortality in a single-variable model.**

Variable	description	Missing	%
id	Unique identifier	1	0.04
Illness date	Date of the index event	0	0
Entry date	Date entered the programme	0	0
Graduate date	Date graduated from the programme	0	0
Death date	Date of death	0	0
Diagnosis ‡	A number from 1 to 8 where 1 is myocardial infarction (MI), 2 is coronary artery bypass grafting (CABG), 3 is percutaneous transluminal coronary with or without stenting, 4 is angina pectoris(AP), 5 is valve surgery (VS), 6 is other cardiac conditions e.g. cardiomyopathy, ischaemic and non-ischaemic heart failure (OC), 7 is non-cardiac conditions(NC) and 8 is myocardial infarction with percutaneous transluminal coronary angioplasty as a single episode of care,(MI+PCI).	0	0
Family History ‡	Family history, yes / no	0	0
Age ‡	Age in years	0	0
age category ‡	Age in categories: 1 is under 50, 2 is 50 to 59, 3 is 60 to 69 and 4 is 70	0	0
Sex ‡	Gender	0	0
Cholesterol	Cholesterol measurement at recruitment	537	19.8
Triglycerides	Triglycerides measurement at recruitment	787	29.0
Diabetes ‡	patient has diabetes, yes / no	0	0
Comorbidity	List of comorbidities in free text	0	0
Height	Height in Metres	1161	42.8
Weight ‡	Weight in kilogrammes at recruitment	20	0.7
Weight after ‡	Weight in kilogrammes at completion	799	29.4
weight category before ‡	A is defined as under 75kg, 75-90kg as overweight, and over 90kg as C.	20	0.7
sbp before ‡	Systolic blood pressure at recruitment	15	0.6
dbp before	Diastolic blood pressure at recruitment	26	1.0
sbp after ‡	Systolic blood pressure at completion	742	27.3
dbp after	Diastolic blood pressure at recruitment	763	28.1
vo2 before ‡	Fitness at recruitment in VO2 max	0	0
vo2 after ‡	Fitness at completion in VO2 max	1316	48.5
vo2 category before ‡	Fitness category at entry	0	0
vo2 category after ‡	Fitness category at exit	1316	48.5
anxiety before	Anxiety measured at recruitment using the hospital anxiety and depression scale (HADS). A score between 8 and 10 indicates borderline anxiety, whilst over 10 suggests clinical anxiety.	89	3.3
anxiety after ‡	Categorisation by HADS at completion	748	27.6
depression before ‡	Categorisation by HADS at recruitment	89	3.3
depression after ‡	Categorisation by HADS at completion	749	27.6
overall health before	Patient's perception of overall health at entry - one of six domains from the Dartmouth Coop / wonca charts used to assess functional health and quality of life. Only patients joining after April 1996 were assessed in this way	773	28.5
over all health after	1 (excellent) to 5(poor) patient's perception of overall health at completion	1275	47.0
life before	patient perception of life in general at recruitment	773	28.5

Table S1| **Missing Data. ‡ indicates that this variable was a significant predictor of all-cause mortality in a single-variable model.**

Variable	description	Missing	%
life after	patient perception of life in general at completion	1275	47.0
feelings before	patient perception of feelings at recruitment	773	28.5
feelings after	patient perception of feelings at completion	1275	47.0
painful tension before	patient perception of		
	painful tension at recruitment	775	28.6
painful tension after	patient perception of		
	painful tension at completion	1276	47.0
physical fitness before	patient perception of		
	physical fitness at recruitment	775	28.6
physical fitness after	patient perception of		
	physical fitness at completion	1274	46.9
social support before	patient perception of social support		
	available to them at recruitment	775	28.6
social support after	patient perception of social support at completion	1274	46.9
risk category before ‡	Risk category (high, medium, low) at recruitment	101	3.7
risk category after ‡	Risk category at exit	730	26.9
Smoking history ‡	coded 0 to 4 where 0 is never smoked, 1 is not smoked for 10 years or more, 2 is not smoked for between 1 and 10 years, 3 is recent quitter, and 4 is current smoker.	3	0.1
aspirin before ‡	Prescription for aspirin at recruitment, yes / no	1	0.04
aspirin after ‡	Prescription for aspirin at completion	671	24.7
ace before ‡	Prescription for ACE inhibitor at recruitment	1	0.04
statin before ‡	Prescription for statins at recruitment	9	0.3
statin after ‡	Prescription for statins at completion	678	25.0
full secondary			
prevention before	Prescription for aspirin and ACE inhibitors and beta blockers and statins at recruitment	1	0.04
full secondary			
prevention after ‡	Prescription for aspirin and ACE inhibitors		
resting heart rate ‡	resting heart rate at entry	7	0.3
hrateafter ‡	Heart rate after exercise	681	25.1
exercise sessions	number of exercise sessions attended to completion or drop-out	105	3.9
imd2004score ‡	Index of multiple deprivation derived from post code	114	4.2
combined total comorborbidity ‡	D'Hoore comorbidity score	0	0
occupation code ‡	Occupational Code 1-9: Managers & senior officials, Professional occupations, Associate professional, Administrative & secretarial, Skilled trade, Personal service, Sales & customer, Process, plant & machines, Elementary occupations	293	10.8
completer category‡	1 is completed the programme, 2 is started but did not complete, 3 is never started.	0	0

Risk stratification

All patients who are recruited to exercise-based CR undergo risk stratification during initial assessment. Exercise testing is a part of this process. Risk stratification enables an appropriate and individualised exercise prescription to be planned for patients that reflects the severity of cardiac illness, co-morbidity and current medical state. The American Association of Cardiovascular and Pulmonary Rehabilitation [AACVPR] was the first to lay down criteria for risk stratification.

Risk stratification criteria for cardiac patients (AACVPR 1999) LOW RISK

- Uncomplicated MI, CABG, angioplasty or atherectomy
- Functional capacity equal to or greater than 6 METS 3 or more weeks after clinical event
- No resting or exercise induced myocardial ischaemia manifested as angina and/or ST segment displacement
- No resting or exercise-induced complex arrhythmias
- No significant left ventricular dysfunction (Ejection fraction equal to or greater than 50

MODERATE RISK

- Functional capacity less than 5- 6 METS 3 or more weeks after clinical event
- Mild to moderately depressed left ventricular function (Ejection fraction 31-49
- Failure to comply with exercise prescription
- Exercise induced ST-segment depression of 1-2mm or reversible ischaemia defects (echocardiography or nuclear radiography)

HIGH RISK

- Severely depressed left ventricular function (Ejection fraction equal to or less than 30
- Complex ventricular arrhythmias at rest or appearing or increasing with exercise
- Decrease in systolic blood pressure of >15mmHg during exercise or failure to rise consistent with exercise workloads
- MI complicated by Congestive Heart Failure, cardiogenic shock and/or complex arrhythmias
- Patients with severe CHD and marked (>2mm) exercise induced ST-segment depression
- Survivor of a cardiac arrest

Co-morbidity

Table S2| **Co-morbidity Score**

Weight	Condition
1	Myocardial infarct*
	Congestive heart failure*
	Peripheral vascular disease
	Dementia
	Cerebrovascular disease †
	Chronic pulmonary disease
	Connective tissue disease
	Ulcer disease
	Mild liver disease‡
2	Hemiplegia
	Moderate/severe renal disease (end stage)
	Diabetes
	Any tumour ♣
	Leukaemia ♣
	Lymphoma ♣
3	Moderate or severe liver disease
6	Metastatic solid tumour

*Myocardial infarct and congestive heart failure were omitted from the index because they are included in the AACVPR risk stratification for events.
†includes patients with history of stroke or history of cerebrovascular disease.
‡Mild liver disease and hemiplegia were omitted from index because it could not be quantified in Zoghbi database
§Includes patients with end stage renal disease
♣ Labelled as one category (malignancy)

Table S3 | **Model B All-cause survival model using fitness change Optimised all-cause survival model ordered by importance of variables to the Model. Pooled hazard ratios are from multiple imputation of missing data**

		complete cases model			**Imputed data model**
Model Term		Hazard Ratio	Confidence Interval lower .95	upper .95	Pooled Hazard Ratio
Age category	under 50	1	-	-	1
	50-59	1.68	0.87	3.26	2.23
	60-69	2.42	1.27	4.58	3.65
	70+	5.42	2.82	10.41	7.77
Fitness:	High baseline, no change	1	-	-	1
	Mid baseline, improve	1.16	0.77	1.74	0.51
	Mid baseline, no change	2.31	1.60	3.35	0.85
	Low baseline, improve	2.63	1.75	3.98	0.95
	Low baseline, no change	3.77	2.42	5.85	1.33
Aspirin	Yes	0.35	0.23	0.55	0.61
	No	1	-	-	1
ACE inhibitor	Yes	1.48	1.14	1.93	1.29
	No	1	-	-	1
Statins	Yes	0.74	0.57	0.96	0.69
	No	1	-	-	1
Gender	MALE	1	-	-	1
	FEMALE	0.71	0.50	1.02	0.70

Table S4 | **Model B Cardiovascular survival model using fitness change Optimised Cardiovascular survival model ordered by importance of variables to the Model. Pooled hazard ratios are from multiple imputation of missing data**

Model Term		complete cases model			Imputed data model
		Hazard Ratio	Confidence Interval		Pooled Hazard Ratio
			lower .95	upper .95	
Fitness:	High baseline, no change	1	-	-	1
	Mid baseline, improve	1.08	0.59	2.00	0.46
	Mid baseline, no change	2.18	1.25	3.80	0.69
	Low baseline, improve	3.37	1.86	6.15	0.95
	Low baseline, no change	5.10	2.66	9.76	1.49
Statin	Yes	0.43	0.29	0.63	0.52
	No	1	-	-	1
Age category	under 50	1	-	-	1
	50-59	1.16	0.52	2.64	1.70
	60-69	1.83	0.84	4.01	3.01
	70+	3.35	1.50	7.52	5.35
Aspirin	Yes	0.36	0.20	0.65	0.57
	No	1	-	-	1
Gender:	MALE	1	-	-	1
	FEMALE	0.50	0.29	0.86	0.62
ACE inhibitor	Yes	1.59	1.08	2.33	1.41
No		1	-	-	1
Diagnostic Category	Myocardial Infarction (MI)	1	-	-	1
	Coronary Artery Bypass Graft (CABG)	0.64	0.41	0.98	0.67
	Percutaneous Coronary Intervention (PCI)	0.20	0.05	0.84	0.42
	MI + PCI	1.1	0.37	3.88	0.68
	Angina	0.95	0.48	1.88	0.68
	Other cardiac	1.00	0.24	4.15	0.90

Table S5| **Model B Baseline values for patients at recruitment to cardiac rehabilitation programme**

	Male		Female		Total	
Number	895	(86.9%)	134	(13.1%)	1029	(100%)
Mean years of follow-up (sd)	11.6	(3.9)	11.2	(3.8)	11.5	(3.9)
Mean age in years (sd)	61.1	(9.3)	63.1	(9.0)	61.3	(9.3)
	N	%	N	%	N	%
Age group under 50 years	104	11.6	14	10.5	118	11.5
Age group 50-59 years	275	30.7	29	21.6	304	29.5
Age group 60-69 years	336	37.6	52	38.8	388	37.7
Age group 70 years and over	180	20.1	39	29.1	219	21.3
Diagnostic Category						
Myocardial Infarction (MI)	456	50.9	73	54.5	529	51.4
Coronary Artery Bypass Graft (CABG)	269	30.1	34	25.4	303	29.4
Percutaneous Coronary Intervention (PCI)	81	9.1	12	9.0	93	9.0
MI + PCI	36	4.0	3	2.2	52	5.1
Angina	41	4.6	11	8.2	13	1.3
Other cardiac	12	1.3	1	0.7	39	3.8

Table S5| **Model B Baseline values for patients at recruitment to cardiac rehabilitation programme**

	Male		Female		Total	
Smoking history						
Never smoked	249	27.8	63	47.0	312	30.3
Not for 10 years+	285	31.9	19	14.2	304	29.6
Not for 1-10 years	34	3.8	4	2.9	38	3.7
Recent quitter	273	30.5	40	29.9	313	30.4
Current smoker	54	6.0	8	6.0	62	6.0
D'Hoore Co-morbidity score						
None	663	74.1	89	66.4	752	73.1
1 (least)	111	12.4	14	10.5	125	12.1
2	102	11.4	27	20.2	129	12.5
3	12	1.3	3	2.2	15	1.5
4 (most)	7	0.8	1	0.7	8	0.8
Diagnosis of diabetes	92	10.3	22	16.4	114	11.1
Family history of CHD	424	47.4	67	50.0	491	47.7
Weight at baseline						
I	402	44.9	35	26.2	440	42.8
II	354	39.67	43	32.2	397	38.6
III	139	15.53	53	39.611.	192	18.6
ACE inhibitor No	479	53.5	54	40.3	533	51.8
ACE inhibitor Yes	416	46.5	80	59.7	496	48.2
Aspirin No	31	3.5	10	7.5	41	4.0
Aspirin Yes	864	96.5	124	92.5	988	96.0
Statin No	338	37.8	43	32.1	381	37.0
Statin Yes	557	62.2	91	67.9	649	63.0
Beta blockers No	573	64.0	80	59.7	653	63.5
Beta blockers Yes	322	36.0	54	40.3	376	36.5
Occupation						
Managers & senior officials	152	17.0	11	8.2	163	15.8
Professional Occupations	98	10.9	7	5.2	105	10.2
Associate Professional	105	11.7	17	12.7	122	11.8
Administrative & secretarial	75	8.4	41	30.6	116	11.3
Skilled trade	250	27.9	7	5.2	257	25.0
Personal service	14	1.6	16	11.9	30	2.9
Sales and customer	18	2.0	10	7.5	28	2.7
Process, plant & machines	110	12.3	10	7.5	120	11.7
Elementary occupations	73	8.2	15	11.2	88	8.6

Table S6| **Model B Change from baseline at completion of the programme**

	Male		Female		Total	
	N	%	N	%	N	%
Fitness						
High baseline, no change	397	44.3	18	13.4	415	40.3
High baseline, deteriorate	5	0.6	0	0	5	0.5
Mid baseline, improve	203	22.7	28	20.9	231	22.5
Mid baseline, no change	151	16.9	25	18.7	176	17.1
Mid baseline, deteriorate	0	0	0	0	0	0
Low baseline, improve	86	9.6	20	14.9	106	10.3
Low baseline, no change	53	5.9	43	32.1	96	9.3
Depression						
Not depressed, no change	780	87.2	107	79.9	887	86.2

Table S6| **Model B Change from baseline at completion of the programme**

	Male		Female		Total	
Not depressed, deteriorate	14	1.6	2	1.5	16	1.5
Borderline, improve	62	6.9	15	11.2	77	7.5
Borderline, no change	8	0.9	2	1.5	9	0.9
Borderline, deteriorate	2	0.2	0	0	3	0.3
Depressed, improve	26	2.9	7	5.2	33	3.2
Depressed, no change	3	0.3	1	0.7	4	0.4
Anxiety						
Not anxious, no change	607	67.8	73	54.4	887	86.2
Not anxious, deteriorate	40	4.5	10	7.5	16	1.5
Borderline, improve	99	11.1	17	12.7	77	7.5
Borderline, no change	45	5.0	10	7.5	9	0.9
Borderline, deteriorate	9	1.0	0	0	3	0.3
Anxious, improve	68	7.6	11	8.2	33	3.2
Anxious, no change	27	3.0	13	9.7	4	0.4
Change VO_2 ml/kg/min Mean(sd)	3.86	(3.39)	3.51	(3.33)	3.81*	(3.38)
Median final estimated VO_2 ml/kg / min (10th, 90th	25.3	(16.3, 35.0)	18.1	(10.4, 26.8)	24.5	(15.2, 35.0)
Median change from baseline in VO_2 ml/kg / min (10th, 90th Percentiles)	3.3	(0.5, 8.1)	2.6	(0.0, 7.95)	3.2	(0.3, 8.1)

*Change in VO_2 ml/kg/min t = 36.16, df = 1028, p-value < 0.001

Model C a subset of Model A of those who also had a BMI measurement.

Table S7| **Model C, a subset of Model A of those who also had a BMI measurement. Baseline values for patients at recruitment to cardiac rehabilitation programme**

	Male		Female		Total	
Number	753		136		889	
Mean years of follow-up (sd)	9.8	(2.5)	9.7	(2.7)	9.8	(2.5)
Mean age in years (sd)	62.1	(9.4)	63.5	(9.1)	62.3	(9.3)
	N	%	N	%	N	%
Age group under 50 years	71	9.4	10	7.3	81	9.1
Age group 50-59 years	214	28.4	33	24.3	247	27.8
Age group 60-69 years	297	39.5	51	37.5	348	39.1
Age group 70 years and over	171	22.7	42	30.9	213	24.0
Diagnostic Category						
Myocardial Infarction (MI)	302	40.1	60	44.1	362	40.7
Coronary Artery Bypass Graft (CABG)	256	34.0	37	27.2	293	33.0
Percutaneous Coronary Intervention (PCI)	98	13.0	19	14.0	117	13.2
MI + PCI	49	6.5	7	5.1	56	6.3
Angina	26	3.5	11	8.1	47	4.2
Other cardiac	22	2.9	2	1.5	24	2.6
Smoking history						
Never smoked	197	26.2	60	44.1	257	28.9
Not for 10 years+	287	38.1	20	14.7	307	34.5
Not for 1-10 years	49	6.5	7	5.1	56	6.3
Recent quitter	181	24.0	41	30.2	222	25.0
Current smoker	39	5.2	8	5.9	47	5.3

Table S7| **Model C, a subset of Model A of those who also had a BMI measurement. Baseline values for patients at recruitment to cardiac rehabilitation programme**

	Male		Female		Total	
D'Hoore Co-morbidity score						
None	536	71.2	86	63.2	622	70.0
1 (least)	84	11.2	18	13.2	102	11.6
2	107	14.2	29	23.0	136	15.3
3	16	2.1	2	1.4	18	1.9
4 (most)	10	1.3	1	0.1	11	1.2
Diagnosis of diabetes	105	13.9	18	13.2	123	13.8
Family history of CHD	335	44.5	76	55.9	411	46.2
BMI at baseline						
BMI Normal	220	29.2	36	26.5	256	28.8
BMI Overweight	363	48.2	60	44.1	423	47.6
BMI Obese	170	22.6	40	29.4	210	23.6
ACE inhibitor No	295	39.2	49	36.0	344	38.7
ACE inhibitor Yes	458	60.8	87	64.0	545	61.3
Aspirin No	26	3.5	6	4.4	32	3.6
Aspirin Yes	727	96.5	130	95.6	857	96.4
Statin No	120	15.9	18	13.2	138	15.5
Statin Yes	633	84.1	118	86.8	751	84.5
Beta blockers No	329	43.7	57	41.9	386	43.4
Beta blockers Yes	424	56.3	79	58.1	503	56.6
Occupation						
Managers & senior officials	128	17.0	9	6.6	137	15.5
Professional Occupations	93	12.4	7	5.2	100	11.2
Associate Professional	81	10.8	16	11.8	97	10.9
Administrative & secretarial	65	8.6	43	31.6	108	12.1
Skilled trade	212	28.2	8	5.9	220	24.8
Personal service	13	1.7	18	13.2	31	3.5
Sales and customer	15	2.0	11	8.1	26	2.9
Process, plant & machines	87	11.5	7	5.1	94	10.6
Elementary occupations	59	7.8	17	12.5	76	8.5

Table S8 | **Model C, a subset of Model A of those who also had a BMI measurement. Optimised all-cause survival model ordered by importance of variables to the Model. Pooled hazard ratios are from multiple imputation of missing data**

		complete cases model			**Imputed data model**
Model Term		Hazard Ratio	Confidence Interval		Pooled Hazard Ratio
			lower .95	upper .95	
Age category	under 50	1.00	-	-	1.00
	50-59	3.052.96	0.92	10.03	1.99
	60-69	4.17	1.28	13.56	3.05
	70+	10.64	3.24	35.00	6.31
Fitness:	High baseline	1.00	-	-	1.00
	Mid baseline	1.49	1.00	2.20	1.80
	Low baseline	2.12	1.41	3.21	2.92
Smoking history	Never smoked	1.00	-	-	1.00
	Not for 10 years+	1.22	0.83	1.80	1.18
	Not for 1-10 years	1.42	0.74	2.74	1.23
	Recent quitter	1.98	1.28	3.05	1.45
	Current smoker	1.71	0.78	3.80	1.66

Table S8 | **Model C, a subset of Model A of those who also had a BMI measurement. Optimised all-cause survival model ordered by importance of variables to the Model. Pooled hazard ratios are from multiple imputation of missing data**

		complete cases model			Imputed data model
Model Term		Hazard Ratio	Confidence Interval		Pooled Hazard Ratio
			lower .95	upper .95	
Statins	Yes	0.65	0.45	0.94	0.69
	No	1.00	-	-	1.00
D'Hoore Co-morbidity score	None	1.32	0.86	2.05	1.20
	1 (least)	1.52	1.04	2.22	1.49
	2	1.68	0.76	3.71	1.90
	3	3.38	1.32	8.65	2.43
Depression at baseline	Not depressed	1.00	-	-	1.0
	Borderline	1.18	0.74	1.86	0.97
	Depressed	2.36	1.21	4.59	1.12
Gender	MALE	1.00	-	-	1.0
	FEMALE	1.00	0.67	1.49	0.76

Table S9 | **Model C, a subset of Model A of those who had a BMI measurement. Optimised Cardiovascular survival model ordered by importance of variables to the Model (889 cases, 80 cardiovascular deaths). Pooled hazard ratios are from multiple imputation of missing data**

		complete cases model			Imputed data model
Model Term		Hazard Ratio	Confidence Interval		Pooled Hazard Ratio
			lower .95	upper .95	
Fitness:	High baseline	1.00	-	-	1.00
	Mid baseline	1.90	1.00	3.60	2.47
	Low baseline	3.93	2.07	7.45	4.80
Statin	Yes	0.52	0.31	0.87	0.51
	No	1.00	-	-	1.00
Age category	under 50	1.00	-	-	1.00
	50-59	1.82	0.41	8.15	1.49
	60-69	2.60	0.61	11.10	2.18
	70+	3.64	0.84	15.85	3.57
Gender:	MALE	1.00	-	-	1.00
	FEMALE	1.06	0.61	1.869	0.64.