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FULL RESEARCH PAPER
Exercise physiology & testing

Physical activity and physical fitness in prediction of all-cause mortality and age at death in European extinct cohorts of middle-aged men followed for 60 years

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Aims A study of the power of physical activity (Phyac) and physical fitness (Fitscore) in predicting very long-term all-cause mortality and age at death (AD) is missing.

Methods and results A total of 5482 middle-aged men were examined with measurement of several risk factors and followed for 60 years until the virtual extinction of cohorts. Phyac in three classes was estimated from their type of work while Fitscore was derived from the linear combinations of levels of arm circumference, heart rate, and vital capacity computed as a factor score by principal components analysis. The predictive power of these characteristics (adjusted for five traditional cardiovascular risk factors) was made by Cox models (for all-cause mortality) and multiple linear regression models (for AD). Single levels of the three indicators of fitness were highly related to the three levels of Phyac and of Fitscore. High levels of both Phyac and of Fitscore forced into the same models were associated with lower all-cause mortality and higher AD. The predictive power of Fitscore was systematically better than that of Phyac. Hazard ratios (high vs. low) for all-cause mortality were 0.85 (Phyac) and 0.70 (Fitscore). The coefficients (all significant) were 2.25 years (Phyac) and 3.79 of AD by Fitscore. Fitscore was independently and significantly predictive of all-cause mortality for both the first and second 30-year follow-up periods.

Conclusion Phyac and Fitscore are related, and both showed important predictive power for all-cause mortality and AD. The role of Fitscore was more powerful, and both characteristics seem to be expressions of health status.

Lay summary

- Objectively measured physical fitness derived from linearly combined arm circumference, heart rate, and vital capacity (Fitscore) may represent an improvement over classes of physical activity (Phyac) estimated from the type of work performed. What was comparatively assessed among 5482 middle-aged men examined with measurement of several risk factors and followed for 60 years until the virtual extinction of cohorts.
- Arm circumference, heart rate, and vital capacity were highly related to the three levels of Phyac and of Fitscore. High levels of both Phyac and of Fitscore were associated with lower all-cause mortality and higher age at death (AD). The predictive power of Fitscore was systematically better than that of Phyac, and comparing high vs. low Phyac and Fitscore, there was a statistically significant difference in all-cause mortality risk and AD, respectively, 0.85 of hazard and 2.25 years (for Phyac) and 0.70 of hazard and 3.79 years (for Fitscore).
- Physical fitness is reportedly defined as the ability to carry out daily tasks with vigour and alertness, without undue fatigue and with ample energy to enjoy leisure-time pursuits and to meet unforeseen emergencies, and might thus help to better assess the long-term risk of all-cause mortality and higher AD when Fitscore based on arm circumference, heart rate, and vital capacity are in the

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upper tertile. This is an improvement over Phyac that is reportedly defined as any bodily movement produced by skeletal muscles that results in energy expenditure. This study shows that Fitscore should be applied in day-to-day clinical/preventive cardiology practice.

Keywords Physical activity • Physical fitness • Mortality from all-causes • Age at death • Extinct cohorts

Introduction

Old[1] and recent[2] reviews provide evidence of the beneficial role of physical activity on health. These findings were confirmed in long-term observations of the Seven Countries Study, mainly in relation to all-cause mortality and age at death (AD), the latter being a useful metric when study populations are extinct or nearly so.[3–5] However, the classification was based only on the apparent engagement at work but despite its rough characteristics, it performed in a rather good way.

Frequently, the term and concept of physical activity are confused with that of physical fitness and others. We follow a classical definition of physical activity as 'any bodily movement produced by skeletal muscles that results in energy expenditure'[1] while physical fitness is 'the ability to carry out daily tasks with vigour and alertness, without undue fatigue and with ample energy to enjoy leisure-time pursuits and to meet unforeseen emergencies'.[1] Physical fitness is partly inherited but is influenced by habitual physical activity. A number of contributions tended to study the relationship of physical activity and physical fitness considered together with cardiovascular health and disease and all-cause mortality.[6–16] References quoted here actually involve also some other indirect contributions still related to this basic issue.

The purpose of this analysis is to explore the possible relationship of physical activity classification by occupation with physical fitness and their independent and joint role in prediction of all-cause mortality and of AD among unique European cohorts of middle-aged men followed for 60 years until extinction.

Methods

Population and measurements

The Seven Countries Study cohorts were those of East Finland, West Finland, Zutphen in the Netherlands, Crevalcore and Montegiorgio in Italy, and Crete and Corfu Islands in Greece, for a total of 5482 men, representing virtually the selected population of men aged 40–59 years at entry. All cohorts were located in rural communities and engaged in comparable farming or forest occupations, except Zutphen, a small commercial town in the Netherlands. The overall participation rate at entry examination was around 95% of all men between those ages. Details of these cohorts can be found elsewhere.[17,18]

The variables used for analysis were: (i) working physical activity classification (Phyac) derived from the occupation or type of work determined by a few non-standardized questions and classified as low, intermediate, and high (corresponding to sedentary, moderate, and vigorous); leisure-time physical activity was not considered since it was practically absent among men of rural communities in the early 1960s; and (ii) indicators of physical fitness were: (a) arm circumference (in mm) following the technique reported in the world health organisation (WHO) cardiovascular survey methods (CSM)[19] with the crude measurement adjusted for the contribution of subcutaneous tissue using a formula that included the triceps skinfold thickness[20] representing muscle mass; (b) heart rate (in beats/min) derived from a standard resting electrocardiogram (ECG), an indicator of cardiocirculatory fitness; and (c) vital capacity (in L/m^2) following the technique reported in the WHO-CSM[19] using the best value of two attempts, a respiratory indicator of fitness. In Zutphen, the Netherlands, the vital capacity was taken a few years after the entry examination and estimates computed by regressing the measurements on age to reach the levels of the entry date.

Fitness score (Fitscore) was derived from the combination of arm circumference, heart rate, and vital capacity (arbitrary units) computed as described below in Statistical analysis. The authors are aware that the term is probably not appropriate since the variable derives from functional parameters likely related to fitness score but not measuring its real properties. However, it was adopted to identify these characteristics as used in this analysis.

Other variables used as possible confounders in the multivariate predictive analysis were: (i) age in years, to the nearest birthday; (ii) average number of cigarettes smoked per day (*n*/day) (preliminary analyses showed that ex-smokers could be reasonably classified as non-smokers); (iii) body mass index (kg/m^2) following the measurement technique reported in the WHO-CSM[19]; (iv) systolic blood pressure (mmHg) measured in supine position at the end of a physical examination, using a mercury sphygmomanometer, following the technique reported in the WHO-CSM[19] with the average of two measurements taken 1 min apart; and (v) serum cholesterol (mg/dL) measured in casual blood samples following the technique by Anderson and Keys.[21] About 4 per 1000 of the above measurements were missing and were imputed by multivariate normal procedure.

Endpoints for testing the predictive power of Phyac and Fitscore were (1) all-cause mortality and (2) AD in those who died after 60 years of follow-up, corresponding to virtual extinction of the population samples. After 60 years, out of 5482 men examined at entry, 5471 had died, 3 were still alive, and 8 were lost to follow-up and censored at defined times.

Statistical analysis

Phyac was used as defined and classified into three classes (low, intermediate, high). Fitscore is a score of fitness derived from the three indexes of fitness (arm circumference, heart rate, vital capacity) fed in a principal component analysis and expressed individually by the consequent factor score. Factor score coefficients were 0.6433 for arm circumference, −0.1404 for heart rate, and 0.6812 for vital capacity. Fitscore was presented both as continuous and discrete variables (that is divided into three tertiles).

Mean baseline levels of Phyac and Fitscore were computed in the various countries together with those of arm circumference, heart rate and vital capacity and of risk factors used as confounding variables in the multivariate models and then compared in the three classes of Phyac and tertile classes of Fitscore.

Tests of predictive power were made as follows: (1) Kaplan–Meier survival vs. all-cause mortality separately in Phyac 3 original classes; and in three tertiles of Fitscore distribution; (2) cumulative incidence for all-cause mortality separately in Phyac 3 original classes; and in three tertiles of Fitscore distribution; (3) mean levels of AD distributed in the three original classes of Phyac and in three tertile classes of Fitscore reported in histograms; and (4) Cox proportional hazards models for all-cause mortality were run with the three levels of Phyac (using low level as the reference class) and Fitscore (expressed as a single continuous variable). A similar model was run with Fitscore expressed in tertile classes to facilitate comparison with the three classes of Phyac; (5) Cox proportional hazards models for all-cause mortality were replicated for two time blocks of 30 years (i.e. 0–30 and 31–60 years) to describe the time relation of Phyac and Fitscore at different time horizons as a function of baseline measurements; (6) multiple linear regression models with AD as the endpoint were run with the three levels of Phyac and continuous measures of Fitscore. A similar model was run with Fitscore expressed in tertiles to facilitate comparison with the three classes of Phyac; and (7) comparison of mean levels (by *t*-test) of the three baseline fitness indexes (arm circumference, heart rate, and vital capacity) for those who died during the first 30 years vs. those who died in the second 30 years of follow-up.

In all tests of predictive power (*Tables 3*, *4*, and *5*), the confounding variables (age, cigarette smoking, body mass index, systolic blood pressure, and serum cholesterol) were forced in the models together with the dummy variables for countries (Finland as reference). In all the above analyses data from cohorts belonging to the same country were combined since their characteristics were similar. Replicas of Tables A1, A2, and A3 with the exclusion of confounding risk factors are given in the Appendix.

Table 1 Baseline risk factors expressed as mean and (standard deviation) for continuous variables or proportion (%) and (standard error) for discrete variables

n	Finland 1677	The Netherlands 878	Italy 1712	Greece 1215	Total 5482	*P* of ANOVA or χ^2
Occupational physical activity						
Low Phyac, %	10.2 (0.7)	24.1 (1.4)	9.7 (0.7)	17.7 (1.1)	13.9 (0.5)	<0.0001
Intermediate Phyac, %	15.7 (0.9)	64.6 (1.6)	22.1 (1.0)	33.7 (1.4)	29.5 (0.6)	<0.0001
High Phyac, %	74.1 (1.1)	11.3 (1.1)	68.2 (1.1)	48.6 (1.4)	56.6 (0.7)	<0.0001
Fitness indicators						
Arm circumference, mm	255.0 (19.8)	266.5 (20.3)	268.6 (23.6)	260.9 (22.6)	262.4 (22.5)	<0.0001
Heart rate, beats/min	67.7 (13.0)	72.6 (12.6)	71.3 (12.9)	64.6 (12.6)	68.9 (13.1)	<0.0001
Vital capacity, L/m^2	1.60 (0.24)	1.47 (0.13)	1.64 (0.24)	1.36 (0.20)	1.54 (0.24)	<0.0001
Confounding factors						
Age, years	49.4 (5.5)	49.9 (5.5)	49.1 (5.1)	49.3 (5.6)	49.3 (5.4)	0.2706
Body mass index, kg/m^2	23.7 (3.2)	24.0 (2.7)	25.2 (3.7)	23.1 (3.2)	24.1 (3.4)	<0.0001
Systolic blood pressure, mmHg	143.9 (20.7)	144.4 (19.8)	143.6 (21.0)	136.2 (20.5)	142.2 (20.8)	<0.0001
Cigarettes, *n*/day	10.7 (10.2)	9.8 (8.4)	8.7 (9.5)	11.3 (11.5)	10.1 (10.1)	<0.0001
Serum cholesterol, mg/dL	261.0 (52.0)	235.5 (44.4)	201.7 (40.8)	205.4 (42.8)	226.2 (52.2)	<0.0001
60-Year all-cause death rate, %	99.9 (0.1)	99.8 (0.2)	99.8 (0.1)	99.8 (0.1)	99.7 (0.06)	0.9702
60-Year age at death, years	72.3 (11.3)	74.3 (10.7)	74.5 (11.4)	78.1 (10.6)	74.6 (11.3)	<0.0001

Last lines give 60-year all-cause death rates and age at death.

Table 2 Mean values of indicators of fitness in three classes of Phyac and of Fitscore

Variable	Phyac class 1 *N* 764	Phyac class 2 *N* 1617	Phyac class 3 *N* 3100	ANOVA
Arm circumference, mm	256.5 (24.6)	263.9 (22.6)	263.1 (21.6)	$P < 0.0001$
Heart rate, beats/min	73.7 (14.4)	70.7 (13.2)	66.8 (12.3)	$P < 0.0001$
Vital capacity, L/m^2	1.44 (0.24)	1.49 (0.22)	1.59 (0.24)	$P < 0.0001$
Fitscore, arbitrary units	−0.50 (1.05)	−0.12 (0.92)	0.18 (0.97	$P < 0.0001$
	Fitscore 1	**Fitscore 2**	**Fitscore 3**	**ANOVA**
Arm circumference, mm	244.8 (17.8)	262.8 (15.5)	279.6 (18.8)	$P < 0.0001$
Heart rate, beats/min	71.2 (14.2)	68.6 (12.9)	67.0 (11.8)	$P < 0.0001$
Vital capacity, L/m^2	1.34 (0.19)	1.53 (0.16)	1.73 (0.20)	$P < 0.0001$

Phyac: class 1 = low; class 2 = intermediate; class 3 = high; three tertile classes of Fitscore: class 1 = low; class 2 = intermediate; class 3 = high.

The packages used were NCSS 12 for basic statistical analysis, Excel Professional Plus 2021 for graphs, and Medcalc 22-016 or R for histograms.

Results

Baseline variables and death rates

Baseline mean levels of the variables used in the analysis are given as reference in *Table 1*. They reflect the sizable difference across countries mainly for serum cholesterol as reported elsewhere.[17,18] The proportion of all deaths was similar across countries in extinct population samples while large differences were seen for AD as documented elsewhere.[4,5] Phyac showed an excess of vigorous physical activity due to the rural occupations in six cohorts out of seven.

Phyac and Fitscore vs. indicators of fitness

Table 2 shows increasing levels of arm circumference and vital capacity across the three classes of Phyac while the reverse was the case for heart rate. The mean levels of Fitscore were significantly different in the three classes of Phyac. The same picture is seen in the relationship of the three fitness indexes in the tertile classes of Fitscore. The arm circumference gradient across Phyac classes is neither very large nor monotonic. The associations of the Fitscore components with the overall score are useful for understanding but of course much larger just because they are components. Moreover, it is interesting that heart rate is somewhat more closely related to Phyac than to Fitscore and its components. In all cases, analysis of variance (ANOVA) was highly significant for heterogeneity.

Mean levels of age at death in classes of Phyac and Fitscore

Figure 1 shows that the discrimination across the three classes of Fitscore (tertiles) is similar in Phyac classes, confirmed by the *P* values of ANOVA (both < 0.0001).

Table 3 Multivariate models predicting all-cause mortality (Cox) as a function of Phyac (three classes) and Fitscore (continuous or discrete) adjusted for age, cigarette smoking, body mass index, systolic blood pressure, serum cholesterol, and country

	Coefficient	*P* value	Hazard ratio	95% CI
Cox model predicting all-cause mortality with Fitscore as continuous variable				
Phyac 1	Reference	—	—	—
Phyac 2	−01 330	0.0028	0.88	0.80 0.96
Phyac 3	−0.1347	0.0025	0.87	0.80 0.95
Fitscore continuous	−0.1920	0.0001	0.83	0.80 0.95
Cox model predicting all-cause mortality with Fitscore as discrete variable				
Phyac 1	Reference	—	—	—
Phyac 2	−0.1394	0.0017	0.87	0.78 0.93
Phyac 3	−0.1637	0.0025	0.85	0.78 0.93
Fitscore 1	References	—	—	—
Fitscore 2	−0.2655	0.0001	0.77	0.72 0.82
Fitscore 3	−0.3631	0.0001	0.70	0.64 0.75

Baseline alive = 5482; baseline age = 40–59; dead = 5471. Phyac classes: Phyac 1 = low; Phyac 2 = intermediate; Phyac 3 = high. Fitscore classes: Fitscore 1 = low; Fitscore 2 = intermediate; Fitscore 3 = high.
95% CI, confidence intervals.

Prediction of 60-year mortality and age at death by Phyac and Fitscore

Figure 2 shows Kaplan–Meier survival curves for three classes of Phyac, with clear separations of curves of low vs. intermediate plus high levels of Phyac, the last two largely overlapping and still associated with a strongly significant *P* value of log rank χ^2. In contrast, the curves for the three classes of Fitscore, instead, showed a clear separation across the three classes again with a strong significant level for *P* of log rank χ^2. Also, curves for cumulative incidence (*Figure 3*) suggested a better separation across the classes of Fitscore than those of Phyac.

In *Table 3*, the Cox model with all-cause mortality as an endpoint suggested a significant 'protective' role for both high and intermediate levels of Phyac and of Fitscore (continuous). Hazard ratios for Fitscore were more favourable ('protective') than those for Phyac. A clearer picture of the situation is given by the Cox model run with Fitscore in three classes that allowed a better comparison with the three classes of Phyac. In all cases, hazard ratios from Fitscore were more 'favourable' than those from Phyac. In fact, the *t*-test of coefficients (Phyac 2 vs. Fitscore 2 and Phyac 3 vs. Fitscore 3) showed higher and significant differences in both comparisons.

Table 4 reports the Cox models for total mortality, dealing with two subsequent follow-up periods of 30 years, showing that entry levels of Fitscore were significantly predictive for both periods, which was not the case for Phyac.

In *Table 5*, similar findings were seen for the multiple linear regression (MLR) models predicting AD, where Phyac showed an increase of AD of 1.6 and 1.7 years for intermediate and high levels vs. low levels. The coefficient for 1 (arbitrary) unit of Fitscore was >2. All the coefficients were statistically significant. The model with Fitscore in tertile classes further increased the role of Fitscore with the direct comparison of the three classes of Phyac that also increased the magnitude of coefficients. In general, the performance of Fitscore was better than that of Phyac. The *t*-test of coefficients (Phyac 2 vs. Fitscore 2 and Phyac 3 vs. Fitscore 3) showed a higher and significant difference only comparing the coefficients of Phyac 3 vs. Fitscore 3.

Table 4 Multivariate models predicting all-cause mortality (Cox) as a function of three classes of Phyac (class 1 = low, class 2 = intermediate, class 3 = high) and Fitscore (continuous) adjusted for age, cigarette smoking, body mass index, systolic blood pressure, serum cholesterol, and country in the first 30 and independently in the second 30 years of follow-up

Variable	Coefficient	*P* value	Hazard ratio	95% CI
Cox model predicting all-cause mortality from year 0 to year 30				
Phyac 1	Reference	—	—	—
Phyac 2	0.1944	0.0004	0.82	0.74 0.92
Phyac 3	−0.1930	0.0003	0.82	0.74 0.92
Fitscore continuous	−0.5466	0.0001	0.58	0.49 0.68
Cox model predicting all-cause mortality from year 31 to year 60				
Phyac 1	Reference	—	—	—
Phyac 2	−0.0139	0.8545	0.99	0.85 1.14
Phyac 3	−0.0259	0.7334	0.97	0.84 1.13
Fitscore continuous	−0.3754	0.0025	0.68	0.54 0.88

Baseline alive year 0 = 5482; baseline age = 40–59; dead = 3379 in years 0–30. Baseline alive year 30 = 2103; baseline year 30 age = 70–89; dead = 2092 in years 31–60.
95% CI, confidence intervals.

Table 5 Multiple linear regression models predicting age at death in 60 years as a function of three classes of Phyac and Fitscore (continuous or discrete), adjusted for age, cigarette smoking, body mass index, systolic blood pressure, serum cholesterol, and country

	Coefficient	*P* value	95% CI
Multiple linear regression model predicting age at death with Fitscore as continuous variable			
Phyac 1	Reference	—	—
Phyac 2	1.6423	0.0005	0.72 2.56
Phyac 3	1.7537	0.0002	0.85 2.66
Fitscore continuous	2.0544	0.0001	1.71 2.04
Multiple linear regression model predicting age at death with Fitscore as discrete variable			
Phyac 1	Reference	—	—
Phyac 2	1.8918	0.0001	0.97 2.81
Phyac 3	2.2547	0.0001	1.36 3.15
Fitscore 1	Reference	—	—
Fitscore 2	2.8384	0.0001	2.12 3.56
Fitscore 3	3.7901	0.0001	2.97 4.61

Baseline alive = 5482; baseline age = 40–59; dead = 5471. Phyac classes: Phyac 1 = low; Phyac 2 = intermediate; Phyac 3 = high. Fitscore classes: Fitscore 1 = low; Fitscore 2 = intermediate; Fitscore 3 = high.
95% CI, confidence intervals.

The simple *Table 6* reports mean levels of the three indexes of fitness for those who died during the first 30 years of follow-up vs. those who died during the second 30 years. For arm circumference and vital capacity, lower levels were seen in men who died early while the opposite was seen for heart rate. All comparisons were significant with *P* values of <0.0001.

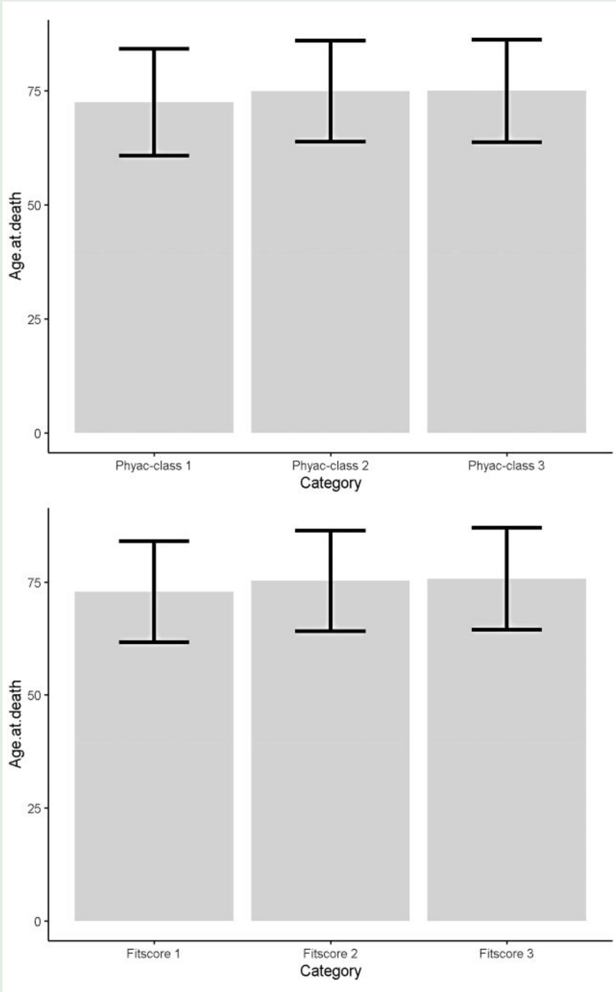

Figure 1 Mean levels of age at death in three original classes of Phyac and three tertile classes of Fitscore. Note the Fitness score tertiles limits: tertile 1 from −5.0435 to −0.3909; tertile 2 from −0.3905–0.3945; tertile 3 from 0.3953–3.8502. *P* of ANOVA for both variables < 0.0001.

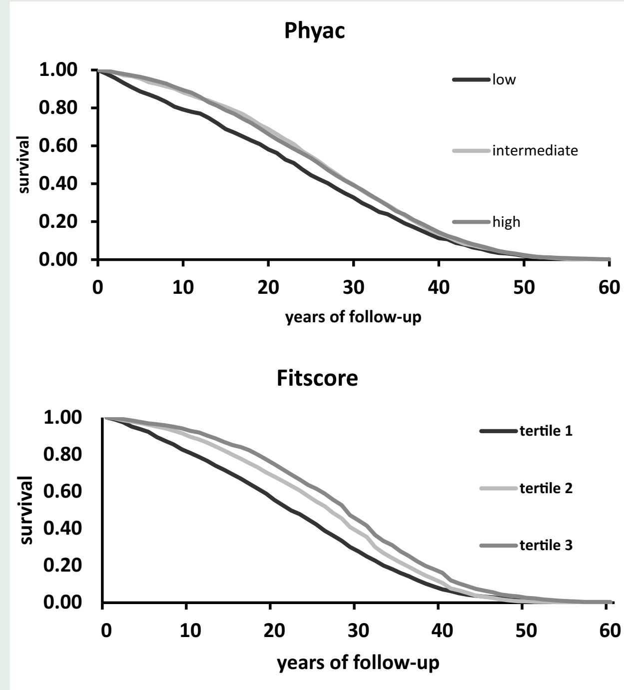

Figure 2 Kaplan–Meier survival in 60 years as a function of three classes of Phyac and three tertiles of Fitscore. *P* of log rank χ^2: Phyac = 0.0001; Fitscore < 0.0001.

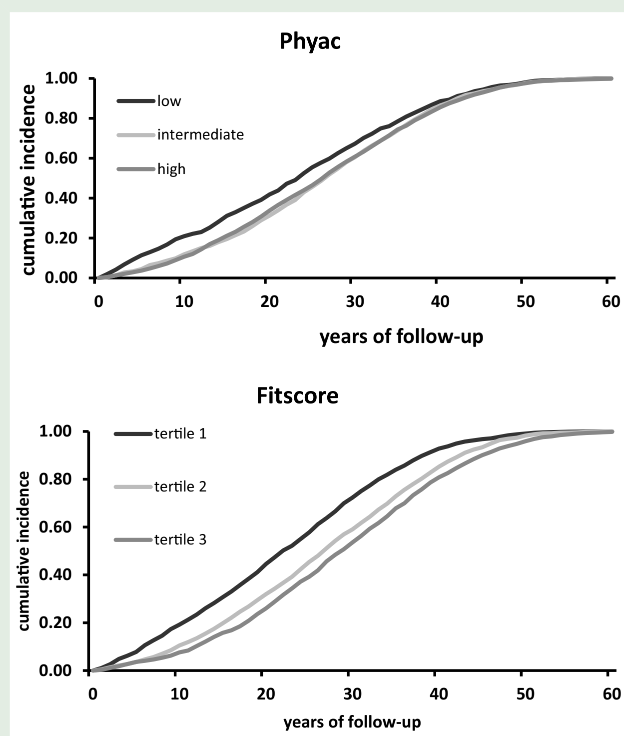

Figure 3 Cumulative incidence of all-cause mortality as a function of three levels of Phyac and three tertiles of Fitscore.

Discussion

The purpose of this analysis was an attempt to disentangle the role of physical activity from that of physical fitness in the prediction of all-cause death plus that of AD. Physical activity of occupation (Phyac), with its three levels, was significantly predictive of all-cause mortality and AD. On the other hand, Fitscore was equally or even better predictive than Phyac when fed in the same models. These findings suggest that there are some connections between Phyac and Fitscore but they are only indirect in the sense that both have a similar relationship with the three indexes of fitness. However, there were no mathematical connections between them, since Fitscore was created in an entirely different and independent way. In any case, they perform in different ways when used to predict events since Fitscore outperforms Phyac. In this process, we can exclude the presence of multicollinearity across the covariates since the tolerance was always very high.

Present findings confirm that working physical activity classes, although defined by a simple and rough procedure, carry a good predictive power for fatal events[3–5] while the Fitscore adds something extra by being strongly predictive (thus 'protective') and to a greater extent than Phyac. Therefore, it appears logical to consider that, despite some intercorrelations, these variables represent something different, as suggested by other studies.[8,12,14–16]

Table 6 Mean levels (standard deviations) of three indexes of fitness in those who died during the first 30 years of follow-up vs. those who died in the second 30 years

Variable	Arm circumference mm	Heart rate beats/min	Vital capacity L/m²
Dead year 0–30	260.5 (23.0)	69.8 (13.5)	1.51 (0.24)
Dead year 31–60	265.4 (21.3)	67.5 (12.4)	1.58 (0.23)
P value of *t*-test	<0.0001	<0.0001	<0.0001

Measurements of Phyac and of indexes used to compute Fitscore were taken at baseline with the expectation that they could change along the way during the long follow-up. Unfortunately, later systematic measurements were not taken after entry for all variables and countries. Nevertheless, it appears that characteristics measured at year 0 are predictive of events spread along an unusual follow-up of 60 years. In particular, the Cox models segregating the first 30 from the second 30 years of follow-up add the indication of a long-term association with fatal events at least for Fitscore vs. all-cause mortality. It is not clear why the effect of Phyac does not last for a long time, but by sure there has been a sharp decline among these men who, in the majority, were farmers with heavy work and whose age after 30 years reached the range of 70–89 years. The important fact is that the Fitness score remained predictive also after the first 30 years of follow-up.

The MLR models produced the same concepts using a different, but valuable endpoint, AD, that is ideal when the follow-up reaches extinction as in this case. The same effect was seen in the univariate association of Phyac and Fitscore classes with AD.

In a paper of 2001, it was shown that a single question about physical activity (somewhat similar to our experience) was not enough sufficient to classify in a proper way people with sedentary habits.[9] Moreover, other investigators made great efforts to test different procedures in order to estimate the true time spent in physical activity.[10] In some studies, physical activity was simply classified as self-reported[16] or derived from activity pattern questionnaires[12] or from caloric expenditure[8] or, in a large review, from these and other ways like complex questionnaires or estimates of metabolic equivalents.[15]

All original studies and a large meta-analysis used exercise testing as an indicator of physical fitness when comparing physical activity with physical fitness[12,14–16] and when only physical fitness was considered.[6,7,13] As a consequence of these choices, a direct comparison of those studies and reviews with our findings is simply impossible because we could not find reports that used the same variables to define the levels of fitness as we did by combining arm circumference with heart rate and vital capacity. Only in one of the reported investigations we found indications of the beneficial effect of increasing physical activity on the levels of forced expiratory volume.[11] Nevertheless, studies that have directly tackled the problem have systematically shown that physical fitness classification is a better predictor than physical activity classification for cardiovascular and all-cause mortality[12,14–16] anticipating some of the findings of this analysis.

In a recent meta-analysis, it was shown that working physical activity is not protective vs. cardiovascular disease and total mortality,[22] and this seems true also for contributions published before 1989, while a protective role is played by leisure physical activity. The findings of our study seem to be an exception or simply belong to the minority group of that review.

The important information provided with the present investigation is the superiority, in terms of all-cause mortality risk and AD, of Fitscore vs. Phyac and this may well incite the clinical application of these findings, related to the fact that arm circumference (with the crude measurement adjusted for the contribution of subcutaneous tissue using a formula that included the triceps skinfold thickness), heart rate, and vital capacity are objective indicators of cardio-circulatory and respiratory fitness, which is a significant contribution to the current literature.[1–3,6–16] We recommend however further comparative studies to be carried out in different contexts since also Phyac may be greatly evolved nowadays that leisure-time activities are so prevalent. Finally, coronary and more in general cardiovascular death risks should also be assessed by Phyac and Fitscore in this and other populations, possibly including women that were notably absent in the Seven Countries Study.

A limitation of Fitscore relates to the need of measuring vital capacity that is more complex than only measuring arm circumference and heart rate. Thus, future studies should assess how large is the contribution of respiratory fitness measured by spirometry to the risk of cardiovascular and all-cause mortality, although indications still exist in this European population that well assessed respiratory function, adopting the ratio of forced expiratory volume (in ¾ s, rather than 1 s as of today)/vital capacity, is essential.[23] In conclusion, the three classes of occupational physical activity in the original Seven Countries Study classifications are well related to the indicators of fitness involving muscular mass (arm circumference), circulatory (heart rate), and respiratory (vital capacity) functions, thus leading to their valuable predictive power of events. The Fitscore derived from the above indicators represents another outperforming and powerful predictor of all-cause death and AD. These results may impact on day-to-day clinical/preventive cardiology practice by objectively measuring the parameters whereby Fitscore is calculated and consider them for risk assessment.

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Author contribution

A.M. and P.E.P. contributed to the conception or design of the work. A.M., J.M.G., A.K., and H.T. contributed to the acquisition, analysis, or interpretation of data for the work. A.M. and P.E.P. drafted the manuscript. J.M.G., A.K., and H.T. critically revised the manuscript. All gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

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Data availability

The data and computing codes are not available for replication because the original data are not publicly available, although the Board of Directors of the Study may evaluate specific requests for dedicated analyses.

Institutional review board statement

The board of directors of the various institutions involved in data collections (12 in this case) were *de facto* playing the role of ethical committee approving the execution of the study on the basis of the local existing legislation by the date this investigation started.

Informed consent

Baseline measurements were taken before the era of the Helsinki Declaration and approval was implied in participation, while verbal or written consent was obtained for the collection of follow-up data.

Appendix

Table A1 Multivariate models predicting all-cause mortality (Cox) and as a function of Phyac (three classes) and Fitscore (continuous or discrete) unadjusted for confounding variables

	Coefficient	*P* value	Hazard ratio	95% CI
Cox model predicting all-cause mortality with Fitscore as continuous variable				
Phyac 1	Reference	—	—	—
Phyac 2	−0.1183	0.0073	0.89	0.81 0.87
Phyac 3	−0.0459	0.2650	0.96	0.88 1.04
Fitscore continuous	−0.2354	0.0001	0.79	0.77 0.79
Cox model predicting all-cause mortality with Fitscore as discrete variable				
Phyac 1	Reference	—	—	—
Phyac 2	−0.1268	0.0040	0.88	0.81 0.96
Phyac 3	−0.0674	0.1007	0.93	0.86 1.01
Fitscore 1	Reference	—	—	—
Fitscore 2	0.3237	0.0001	0.72	0.38 0.77
Fitscore 3	−0.5025	0.0001	0.61	0.57 0.65

Baseline alive = 5482; baseline age = 40–59; dead = 5471. Phyac classes: Phyac 1 = low; Phyac 2 = intermediate; Phyac 3 = high. Fitscore classes: Fitscore 1 = low; Fitscore 2 = intermediate; Fitscore 3 = high.
95% CI, confidence intervals.

Table A2 Multivariate models predicting all-cause mortality (Cox) and as a function of Phyac (three classes) and Fitscore (continuous or discrete) unadjusted for confounding variables in the first 20 and independently in the second 30 years of follow-up

	Coefficient	*P* value	Hazard ratio	95% CI
Cox model predicting all-cause mortality from year 0 to year 30				
Phyac 1	Reference	—	—	—
Phyac 2	−0.1862	0.0006	0.83	0.75 0.92
Phyac 3	−0.1042	0.0393	0.90	0.82 0.99
Fitscore continuous	−0.1309	0.0001	0.88	0.85 0.91
Cox model predicting all-cause mortality from year 31 to year 60				
Phyac 1	Reference	—	—	—
Phyac 2	0.0201	0.7888	1.02	0.88 1.18
Phyac 3	0.030	0.6509	1.03	0.90 1.19
Fitscore continuous	−0.1718	0.0001	0.84	0.80 0.88

Phyac classes: Phyac 1 = low; Phyac 2 = intermediate; Phyac 3 = high. Fitscore classes: Fitscore 1 = low; Fitscore 2 = intermediate; Fitscore 3 = high.
95% CI, confidence intervals.

Table A3 Multiple linear regression models predicting age at death in 60 years as a function of three classes of Phyac and Fitscore (continuous or discrete), unadjusted for confounding variables

	Coefficient	*P* value	95% CI
Multiple linear regression model predicting age at death with Fitscore as continuous variable			
Phyac 1	Reference	—	—
Phyac 2	1.8681	0.0002	0.90 2.84
Phyac 3	1.5044	0.0012	0.60 2.41
Fitscore continuous	1.3921	0.0001	1.09 1.70
Multiple linear regression model predicting age at death with Fitscore as discrete variable			
Phyac 1	Reference	—	—
Phyac 2	2.0053	0.0001	1.04 2.97
Phyac 3	1.7888	0.0001	0.88 2.69
Fitscore 1	Reference	—	—
Fitscore 2	2.2597	0.0001	1.53 2.99
Fitscore 3	2.6836	0.0001	1.94 2.53

Baseline alive = 5482; baseline age = 40–59; dead = 5471. Phyac classes: Phyac 1 = low; Phyac 2 = intermediate; Phyac 3 = high. Fitscore classes: Fitscore 1 = low; Fitscore 2 = intermediate; Fitscore 3 = high.
95% CI, confidence intervals.

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