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Cardiovascular medication, physical activity and mortality: cross-sectional population study with ongoing mortality follow up

Emmanuel Stamatakis,[1,2] PhD; Mark Hamer,[1,3] PhD; Paola Primatesta, PhD, MD[1,4]

[1] Department of Epidemiology and Public Health, University College London, UK.
[2] National Institute for Health Research Fellow
[3] Senior Research Associate
[4] Honorary Senior Clinical Lecturer

Correspondence: Emmanuel Stamatakis, Ph.D., Department of Epidemiology and Public Health, University College London, 1-19 Torrington Place, London WC1E 6BT, UK.
Tel: (44) 20 7679 1721, e-mail: e.stamatakis@ucl.ac.uk

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ABSTRACT

Objective: to establish physical activity levels in relation to cardiovascular medication and to examine if physical activity is associated with benefit independently of medication among individuals with no diagnosis of cardiovascular disease (CVD).

Design: Cross-sectional surveys in 1998 and 2003 with ongoing mortality follow up.

Setting: Household-based interviews in England and Scotland.

Participants: Population samples of adults aged 35 and over living in households, respondents of the Scottish Health Survey and the Health Survey for England.

Main outcome measure: Moderate to vigorous physical activity (MVPA) levels and CVD mortality.

Results: Fifteen percent (N=3,116) of the 20,177 respondents (8,791 men); were prescribed at least one cardiovascular medication. Medicated respondents were less likely than those unmedicated to meet the physical activity recommendations (OR:0.89, 95%CI: 0.81 to 0.99, p=0.028). The mean follow up (±SD) was 6.6 (2.3) years. There were 1,509 any-cause deaths and 427 CVD deaths. Increased physical activity was associated with all-cause and CVD mortality among both unmedicated (all-cause mortality HR for those with ≥150 min/wk of MVPA compared with those who reported no MVPA): 0.58, 95%CI: 0.48 to 0.69, p<0.001) ; CVD mortality: 0.65, 0.46 to 0.91, p=0.036) and medicated respondents (all-cause death: 0.54, 0.40 to 0.72, p<0.001; CVD death: 0.46 (0.27 to 0.78, p=0.008).

Conclusions: Although physical activity protects against premature mortality among both medicated and unmedicated adults, cardiovascular medication is linked with lower uptake of health enhancing physical activity. These results highlight the importance of physical activity in the primary prevention of CVD over and above medication.

Keywords: physical activity, cardiovascular disease, medication, mortality, primary prevention

INTRODUCTION

Regular physical activity is widely accepted as playing a crucial role in cardiovascular disease (CVD) primary prevention [1 2 3 4] and accumulating evidence also supports its role in secondary prevention.[5 6 7] However, medications for primary prevention are often prescribed with little attention to lifestyle modification.[8] The physical activity behaviours of participants taking medications have not been widely studied, although recent evidence has shown participation in walking and vigorous activities is inversely associated with the use of antidiabetic, antihypertensive, and lipid lowering medications.[9 10] These data suggest that medication may act as a barrier to physical activity because patients might be unsure about possible contraindications or feel that they will not gain additional protective benefit from exercise over and above that of medication.

There is little available data regarding the potential interaction of medication in relation to physical activity and CVD mortality risk. In men referred for exercise testing an exercise capacity of 5 metabolic equivalents (MET) or more was associated with higher survival rates both in users and nonusers of beta blockers[6] and in a similar study adjustment for cardiovascular medications did not impact on the association between exercise capacity and CVD mortality.[7] We are, however, unaware of any work that has attempted to compare the relative protective effects of physical activity and medication in a non-clinical (i.e. undiagnosed) general population sample at varying degrees of risk.

The aim of the present study was to 1) establish physical activity levels in non-clinical general population participants prescribed cardiovascular medications compared to none-medicated; 2) examine the association between physical activity and CVD mortality in medicated and non-medicated non-clinical participants and thus establish if physical activity is associated with benefit independently of medication. For these analyses we used data from the Scottish and English Health Surveys that contains detailed information about physical activity, medication use, and medical history of CVD.

METHODS

Design and Sample

The Health Survey for England (HSE) and Scottish Health Survey (SHS) are repeated cross-sectional general population studies examining individuals living in households in each country. This study included respondents of the 1998 and 2003 SHS and the 1998 HSE. Unless otherwise stated, the methodologies described below refer to all three surveys. HSE and SHS samples were selected using multi-stage stratified probability design to give a representative sample of the target populations. Stratification was based on geographical areas and not on individual characteristics: postcode sectors selected at the first stage and household addresses selected at the second stage. Further details on sample design and sample selection can be found elsewhere.[11 12] All surveys were linked to NHS administrative mortality data up to September 2006. This analysis considered respondents who consented to their death records being flagged (94% in HSE, and 91-92% in SHS). Diagnoses for primary cause of death was recorded using the *International Classification of Diseases*, Ninth (ICD-9) and Tenth (ICD-10) Revisions. CVD codes were 390-459 for ICD-9 and I01-I99 for ICD-10. Ethical approval had been granted by the Local Research Ethics Councils prior to each survey year data collection.

Variables

Height and weight were measured by trained interviewers using standard protocols.[11] Computer-assisted personal interviewing (CAPI) modules assessed respondents' demographics, health status and history of disease, and health behaviours. Psychological health was assessed using the General Health Questionnaire (GHQ, 12-item version).[13] In a separate visit, qualified nurses collected and coded information on prescribed medication. The nurses also measured respondents' blood pressure three times following five minutes of rest. In this study we computed blood pressure as the average of the second and third reading. Cardiovascular medication was defined using the British National Formulary classification[14] and it included positive inotropic drugs, anti-arrhythmics, diuretics, beta- blockers, ACE inhibitors, calcium-channel blockers, nitrates, anticoagulants, antiplatelets, and lipid-regulating drugs. Physical activity questions included frequency (number of days in the last 4 weeks) and duration (minutes per day) of participation in intense domestic activity (e.g. housework, DIY, gardening, restoration work), walking for any purpose, and any recreational exercise, (e.g. cycling, swimming, aerobics, callisthenics, gym exercises, dancing, team sports, racket sports). Occupational physical activity level was assessed by questions on the nature of respondents' occupation. The criterion validity of the physical activity questionnaire has been demonstrated in a recent study on 106 English adults from the general population (45 men) where the output of accelerometers (worn for two non-consecutive weeks over a month period) was compared against a slightly modified version of the above questions.[15] The questionnaire appeared to be a valid measure of time spent in moderate to vigorous physical activity, (ICC r=0.47 for men p=0.03; r=0.43 for women, p=0.02). In terms of test-retest reliability, the coefficients of time spent in moderate to vigorous physical activity were 0.89 for men ($p<0.001$) and 0.76 in women ($p<0.001$). These questions have demonstrated excellent convergent validity in grading a plethora of biochemical and physiological CVD risk factors physical activity level.[27] In the present study we only considered moderate to vigorous intensity activity (MVPA; ≥ 3 METS),[16] which concurs with current public health recommendations for physical activity in the prevention of CVD. MVPA volume was calculated as number of days multiplied by time per day in each activity type. Total volume was averaged to minutes per week and it was grouped in relation to the current physical activity recommendations ($\geq$30 MVPA minutes/day, ≥ 5 days/week).[17]

Variable handling and statistical analysis

In all analyses described below, we excluded respondents with established cardiovascular disease defined as doctor-diagnosed coronary heart disease (angina or myocardial infarction) and stroke, thereby minimising the chances that altered physical activity behaviour is due to the diagnosis.

We used likelihood ratios to examine univariable relationships of categorical confounders with medication and Mann-Whitney tests to examine differences between medicated and unmedicated respondents in continuous variables.

In the first main analysis we examined the cross-sectional association between medication use (exposure variable) and physical activity behaviour (outcome). Logistic regression was used to examine if being on cardiovascular medication (no/yes) predicts adherence to the physical activity recommendations. In the second main analysis we examined the prospective association between physical activity (exposure) and all-cause and cardiovascular mortality (outcome). The Cox

proportional hazards model was used with months as the time scale to estimate the risk of death from any cause or cardiovascular cause by MVPA levels (no MVPA, 1-150mins/wk, ≥150mins/wk) for each physical activity type or total physical activity. Separate Cox models were developed for medicated and unmedicated respondents. The proportional hazards assumption was examined by comparing the cumulative hazard plots grouped on exposure, although no appreciable violations were noted. Test for linear trend was obtained by entering the categorical variables as continuous parameters in the models. Person-years for each participant were calculated as the interval between the baseline recruitment, when physical activity was assessed, to death. For individuals who survived data were censored to September 2006. Respondents who died during the first year of follow-up were excluded to minimise the chances of reduced physical activity due to prediagnosed /prodromal illness that could obscure the examined associations.

Both analyses were adjusted for age, sex, occupational physical activity (sedentary, light, moderate or vigorous), body mass index (BMI) class (under 18.5, 18.5-25, 25-30, 30-40, and over 40 kg/m^2), the Registrar General's social-occupational class (I,II, III nonmanual, III manual, IV, V), ethnicity (white, black, south Asian, other) non-CVD related long-standing illness (no/yes), marital status (single/never married, married, separated/divorced/windowed), smoking status (never smoked, ex regular smoker, ex-occasional smoker, current smoker), parental cause of death (cardiovascular, diabetes, other), frequency of alcohol drinking (5-7, 1-4 times a week, 1-2 times a month or less), GHQ12 score (0, 1-4, over 4) , self-reported health status (very good/good, fair, bad/very bad) and doctor-diagnosed diabetes (no/yes). All analyses were also adjusted for hypertension (no/yes), which was defined either as self reported doctor-diagnosed or as having a survey reading ≥140 mmHg systolic and ≥90 mmHg diastolic. Analyses were also adjusted for type and number of prescribed CVD medicines (none, one, 2-3, >3) when appropriate.

All physical activity interviews were completed. Respondents with missing information on medication (n=709) were considered as unmedicated. Missing values of the covariables were dummy-coded as "other" so that cases with missing values were not dropped from the Cox models. BMI was the covariable with the largest number of missing values (n=2115) followed by alcohol (n=2091) and social class (n=414).

RESULTS

Response rates (% of eligible) were 76% in SHS 1998 and 60% in 2003 and 69% in HSE 1998. We considered 22,671 respondents initially, although respondents with existing doctor diagnosed coronary heart disease (angina or myocardial infarction) or stroke (n=2,494) were excluded, leaving 20,177 respondents that were entered in the cross-sectional analysis (8,791 men; 3,116 on cardiovascular medications). Following exclusion of 135 cases that died in the first year of follow up, 20,042 cases were entered in the longitudinal analysis, corresponding to 133,434 person years of follow up. A summary of sociodemograpghic characteristics, mortality, disease status, and physical activity information by medication status is shown in Table 1. Medicated respondents were older and had a higher BMI (and a greater proportion had a BMI over $30kg/m^2$) than those unmedicated, and were more likely to be white, from manual social class, to have a non-CVD long-standing illness (non-CVD related), and have at least one parent who died of CVD causes. Non-medicated respondents were

more likely to have never smoked and be married/cohabiting. In terms of CVD-related disease status, medicated respondents were more likely to report doctor-diagnosed diabetes and hypertension and more likely to have a high blood pressure reading than those unmedicated. We also summarised the sample characteristics by physical activity status (supplemental web Table 1). Respondents not meeting the physical activity recommendations were older and had a higher BMI (and a greater proportion had a BMI over 30kg/m^2) than those meeting the recommendations, and were more likely to be non-white, from manual social class, to have a non-CVD long-standing illness (non-CVD related), to have at least one parent who died of CVD causes, to be inactive at work, and to have a GHQ-12 score of over 4. Respondents meeting the recommendations were more likely to have never smoked, to drink on five or more occasions per week, and to be married/cohabiting. In terms of CVD-related disease status, respondents not meeting the physical activity recommendations were more likely to report doctor-diagnosed diabetes and hypertension and more likely to have a high blood pressure reading than those unmedicated

Supplemental Web Table 1: Sample characteristics by physical activity status. Respondents aged 35 and over with no doctor diagnosis of coronary heart disease (angina or myocardial infarction) or stroke.

	Moderate to vigorous physical activity status (minutes per week)		
	<150	**≥150‡**	**p**
Demographics			
N	11132	9045	
Survey (% Scottish Health Survey)	49.7	52.2	<0.001∫
Mean Age (±SD)	56.8 (13.8)	50.5 (11.5)	<0.001∫∫
Sex (% male)	42.2	45.2	<0.001∫
Ethnicity (% white)*	97.0	97.9	<0.001∫
Social Class (% manual)*	54.1	48.1	<0.001∫
Mean Body mass index, kg/m^2 (±SD)	27.6 (5.1)	26.8 (4.4)	<0.001∫∫
Body mass index (% >30kg/m^2)*	24.1	17.9	<0.001∫
Marital Status (% married/cohabiting)*	62.6	68.6	<0.001∫
Smoking Status (% never smoked)*	39.0	43.1	<0.001∫
Alcohol (% drinking on 5 days a week or more)*	19.6	21.3	<0.001∫
Non-cardiovascular long standing illness (%)	50.3	35.3	<0.001∫
Parental cause of death (% cardiovascular causes)	29.5	27.5	0.002∫
General Household Questionnaire (% with a score > 4)*	16.1	11.3	<0.001∫
Disease status			
Doctor-diagnosed hypertension	26.2	17.7	<0.001∫
Doctor-diagnosed diabetes (Type 1 or 2)	4.1	1.9	<0.001∫
High blood pressure (based on survey recording only†)	10.5	7.7	<0.001∫
Moderate-to-vigorous physical activity			
Mean time (±SD) (minutes/week)	33.1 (42.1)	569.5 (570.6)	<0.001∫∫
Occupational physical activity level (% inactive)*	70.1	56.4	<0.001∫

‡Synonymous to meeting the current physical activity recommendations; † ≥140 mmHg systolic & ≥90 mmHg systolic; ∫Based on 2-tailed Likelihood Ratio Tests; ∫∫ Based on 2-tailed Mann-Whitney Tests* Only one key category of the variable is shown

Table 2 shows use of specific cardiovascular medication types by physical activity level among medicated respondents. Use of positive inotropic drugs, diuretics, nitrates and other anti-anginal, calcium channel blockers, and anti-coagulant drugs was higher among respondents not meeting the physical activity recommendations while the opposite was true for lipid-regulating drugs. When comparing medicated with

unmedicated respondents, medicated respondents reported significantly less MVPA time, and were more likely to have a sedentary occupation.

Table 1: Sample characteristics by cardiovascular medication status. Respondents aged 35 and over with no doctor diagnosis of coronary heart disease (angina or myocardial infarction) or stroke.

	Unmedicated	**Medicated**	**p**
Demographics			
N	17061	3116	
Survey (% Scottish Health Survey)	50.4	53.2	0.04[∫]
Mean Age (±SD)	52.1 (12.6)	64.5 (11.7)	<0.001[∫∫]
Sex (% male)	44.4	39.2	<0.001[∫]
Ethnicity (% white)*	97.3	97.8	0.026[∫]
Social Class (% manual)*	50.8	54.7	<0.001[∫]
Mean Body mass index, kg/m^2 (±SD)	26.9 (4.6)	29.2 (5.3)	<0.001[∫∫]
Body mass index (% >30kg/m^2)*	19.1	33.6	<0.001[∫]
Marital Status (% married/cohabiting)*	65.9	61.9	<0.001[∫]
Smoking Status (% never smoked)*	28.2	18.0	<0.001[∫]
Alcohol (% drinking on 5 days a week or more)*	20.4	20.3	<0.001[∫]
Non-cardiovascular long standing illness (%)	39.7	64.9	<0.001[∫]
Parental cause of death (% cardiovascular causes)	27.0	37.5	<0.001[∫]
General Household Questionnaire (% with a score > 4)[*]	13.9	14.2	0.760[∫]
Mortality			
Died (any cause) (%)	5.9	15.9	<0.001[∫]
N	1012	497	
Died (cardiovascular causes) (%)	1.5	5.5	<0.001[∫]
N	257	170	
Died within first 12 months of follow-up (%)	0.5	1.5	<0.001[∫]
N	88	47	
Person-years	114653	18863	
Disease status			
Doctor-diagnosed hypertension	13.4	71.9	<0.001[∫]
Doctor-diagnosed diabetes (Type 1 or 2)	1.9	10.0	<0.001[∫]
High blood pressure (based on survey recording only[†])	8.1	14.1	<0.001[∫]
Moderate-to-vigorous physical activity			
None (%)	21.9	38.8	<0.001[∫]
<150 minutes/week week (%)	30.5	31.1	
≥150 minutes/week week (%)	47.5	30.0	<0.001[∫]
Mean time (±SD) (minutes/week)	291.8 (479.7)	173.9 (374.7)	<0.001[∫∫]
Occupational physical activity level (% inactive)*	60.4	83.2	<0.001[∫]

[†] ≥140 mmHg systolic & ≥90 mmHg systolic; [∫] Based on 2-tailed Likelihood Ratio Tests; [∫∫] Based on 2-tailed Mann-Whitney Tests[*] Only one key category of the variable is shown

(Table 1). The multivariable-adjusted analyses presented in Table 3 show that even when potential confounders and health status were taken into account, medicated respondents were less likely than those unmedicated to meet the physical activity recommendations (p=0.028).

Table 2: Prescribed cardiovascular medication by physical activity. Respondents with no self-reported diagnosis of coronary heart disease (angina or myocardial infarction) or stroke who are currently on cardiovascular medication.

Cardiovascular medication type	***Moderate-to-vigorous physical activity*** *(Minutes per week)*			
	<150 (%)	≥150[†] (%)	Total (%)	P[∫]
Positive Inotropic drugs	4.8	1.6	3.8	<0.001
Diuretics	46.3	40.4	44.5	0.002
Anti-arrhythmic drugs	1.7	1.3	1.5	0.435
Beta- blockers	28.0	26.9	27.7	0.527
ACE inhibitors	26.1	25.4	25.9	0.674
Nitrates, and other anti-anginal	3.4	1.7	2.9	0.07
Calcium-channel blockers	22.3	16.8	20.7	<0.001
Anticoagulants	4.5	2.2	3.9	0.001
Antiplatelet	17.9	18.1	17.9	0.912
Lipid-regulating	11.6	15.7	12.8	0.002

[†]Synonymous to meeting the current physical activity recommendations; [∫] P values are based on likelihood ratios and refer to the difference between those meeting the physical activity recommendations and those who do not

Table 3: Odds ratios and 95% confidence intervals of meeting the current physical activity recommendations by cardiovascular medication status. Respondents with no self-reported diagnosis of coronary heart disease (angina or myocardial infarction) or stroke.

	Cardiovascular medication status		
	Unmedicated (Referent) (N= 17002)	***Medicated*** (N=3104)	Trend P
Model 1[†]			
OR (95%CI)	1 (n/a)	0.72 (0.66 to 0.79)	<0.001
Model 2[††]			
OR (95%CI)	1 (n/a)	0.73 (0.67 to 0.80)	<0.001
Model 3[∫]			
OR (95%CI)	1 (n/a)	0.89 (0.81 to 0.99)	0.028

[†] Adjusted for sex and age

[††] As above plus ethnicity, social class, marital status, occupational physical activity, smoking, and general household questionnaire score

[∫] As above plus non-cardiovascular long-standing illness, self-reported general health status, doctor-diagnosed diabetes, body mass index class, and hypertension (doctor-diagnosed or based on survey readings).

n/a: no 95% confidence intervals are applicable as this is the referent category

The mean follow up (±SD) was 6.7 (2.3) and 6.1 (2.5) years for the unmedicated and medicated groups, respectively. In total there were 1,509 any-cause deaths (719 in men) and 427 CVD deaths (213 in men). As shown in Table 1, medicated respondents were more likely to die both from any cause and CVD causes.

Table 4 shows the all-cause and CVD-cause mortality hazard ratios and 95% confidence intervals (95%CI) of physical activity level compared to those who reported no MVPA. Among both unmedicated and medicated respondents, MVPA showed a dose-response relationship with all-cause mortality and adjustments for potential confounders only slightly attenuated these relationships. Meeting the physical activity recommendations was associated with similar reduction in all-cause death risk in the medicated (fully- adjusted HR: 0.54, 95%CI: 0.40-0.72) and unmedicated (HR: 0.58, 0.48-0.69) groups. Similarly, among both unmedicated and medicated groups MVPA showed a dose-response relationship with CVD mortality that persisted after adjustments for potential confounders. Meeting the physical activity recommendations was associated with a larger CVD death risk reduction in the medicated (fully- adjusted HR: 0.46, 0.27-0.78) than the unmedicated (HR: 0.65, 0.46-0.91) groups. Engagement in MVPA even below the recommended level appeared be linked to a lower risk for all-cause (unmedicated HR: 0.70, 0.60-0.82; medicated: 0.62, 0.50-0.79) and CVD death (unmedicated HR: 0.76, 0.56-1.04; medicated HR: 0.70, 0.48-1.01).
We repeated all analyses without the 709 respondents with missing values on cardiovascular medication (n=19,468) but results changed very little and we do not report them. For example, the OR (95%CI, p) for the fully adjusted model 3 in table 3 was 0.88 (0.80 to 0.98, 0.017).

Table 4: Hazard ratios and 95% confidence intervals of mortality according to moderate-to-vigorous physical activity time. Respondents with no self-reported diagnosis of coronary heart disease (angina or myocardial infarction) or stroke.

			Death from any cause						
Physical Activity (minutes/week)			**Model 1†**		**Model 2††**		**Model 3∫**		**Model 4∫∫**	
	Person-years	N/deaths	HR (95%CI)	Trend p	HR (95%CI)	Trend p	HR (95%CI)	Trend p	HR (95%CI)	Trend p
Unmedicated				<0.001		<0.001		<0.001		n/a
None (referent)	24378	452/3685								
<150	35756	256/5196	0.62 (0.53 to 0.73)		0.67 (0.57 to 0.79)		0.70 (0.60 to 0.82)			
≥150	54465	215/8091	0.46 (0.39 to 0.55)		0.54 (0.46 to 0.65)		0.58 (0.48 to 0.69)			
Medicated				<0.001		<0.001		<0.001		<0.001
None (referent)	6964	276/1175								
<150	6067	108/961	0.56 (0.45 to 0.70)		0.59 (0.47 to 0.74)		0.61 (0.49 to 0.77)		0.62 (0.50 to 0.79)	
≥150	5804	65/932	0.45 (0.34 to 0.60)		0.50 (0.38 to 0.67)		0.51 (0.39 to 0.69)		0.54 (0.40 to 0.72)	
			Death from cardiovascular causes							
Unmedicated				<0.001		0.009		0.036		n/a
None (referent)	24378	120/3685								
<150	35756	69/5196	0.68 (0.50 to 0.91)		0.72 (0.53 to 0.98)		0.76 (0.56 to 1.04)			
≥150	54465	57/8091	0.52 (0.37 to 0.73)		0.60 (0.43 to 0.85)		0.65 (0.46 to 0.91)			
Medicated				<0.001		0.001		0.005		0.008
None (referent)	6964	101/1175								
<150	6067	44/961	0.62 (0.43 to 0.88)		0.66 (0.46 to 0.95)		0.69 (0.48 to 1.00)		0.70 (0.48 to 1.01)	
≥150	5804	19/932	0.37 (0.23 to 0.62)		0.42 (0.25 to 0.69)		0.45 (0.26 to 0.75)		0.46 (0.27 to 0.78)	

* Excluding deaths that occurred during the first 12 months of follow up; † Adjusted for sex and age; †† As above plus ethnicity, social class, marital status, alcohol drinking, occupational physical activity, smoking, parental cause of death, and general household questionnaire score; ∫ As above plus non-CVD long standing illness, doctor-diagnosed diabetes, body mass index class, and hypertension (doctor-diagnosed or based on survey reading); ∫∫As above plus cardiovascular medication type (lipid-lowering, diuretics, beta blockers, ace inhibitors, calcium blockers, or other), and number of prescribed cardiovascular medicines

DISCUSSION

Follow-up mortality data from this large, cross-sectional study of a representative sample of English and Scottish adults who were free from CVD at the time of data collection demonstrate that increasing levels of physical activity are associated with lower mortality from all causes and CVD, irrespective of use of cardiovascular medications. Engaging in physical activity which corresponded to meeting the recommended level of at least 30 minutes of moderate exercise 5 days/wk was associated with approximately a 50% reduction in risk of all cause mortality in medicated and unmedicated participants. Similarly, the risk for CVD mortality was reduced by 48% and 63% in the physically active unmedicated and medicated, respectively. Smaller but still significant reductions in the risk of dying were achieved even among those whose physical engagement was below the recommended level: the hazard ratios for mortality from CVD were almost 40% and 30% lower compared to medicated and unmedicated physically inactive subjects.

The beneficial effect of physical activity on CVD risk is well documented.[3 4 5 6 18] . Physical activity can prevent or delay the development of hypertension, diabetes, hypercholesterolemia.[19] Both CVD and all cause mortality are reduced in people engaging in physical activity, in a dose-response fashion. It is therefore clear that a comprehensive programme of CVD prevention must include regular exercise. To what extent physical activity and medications for the prevention of CVD interact with each other is unclear and the existing literature is less explicit in supporting evidence of an effect of physical activity independent of the effect of medications. In previous cohort studies exercise capacity has been associated with risk of CVD mortality independent of medication use.[6 7] Several other cohort studies have shown protective effects of physical activity on CVD mortality in clinical populations such as type 2 diabetes[20] and hypertension.[21] We might speculate that participants from these clinical groups were also medicated and thus the findings are largely comparable with results from the present study. Clinical trial data also suggests that beta-adrenergic blocker medication use does not reduce the ability of participants to gain exercise training benefits such as increased cardiorespiratory fitness and improved endothelial function.[22 23] There is, however, some evidence to suggest that combinations of beta 1-selective blockers and lipid-lowering drugs are associated with a greater perception of effort during moderate intensity exercise,[24] which might act as a barrier towards physical activity in medicated individuals.

The physical activity behaviours of participants taking medications have not been widely studied. The results of the present study suggested that those on medications were less physically active and also demonstrated lower odds of meeting the physical activity recommendations, even after adjusting for potential confounders. An inverse relationship between vigorous physical activity and medication use in male and female runners was also demonstrated in a recent study.[9] Several reasons for an inverse association between medication use and activity can be hypothesised. In our study those on medications were at higher CVD risk, being older, more likely to be hypertensive, diabetic, and obese. It is possible that lifelong exposure to sedentary behaviour contributes to the development of CVD risk factors that subsequently require medication. Nevertheless, the reverse might also be true: medication may act as a barrier to physical activity because patients might be unsure about possible contraindications and feel that they will not gain additional protective benefit from exercise over and above that of medication. In addition, medicated individuals may

find it perceptually more difficult to exercise although whether this is a physiological phenomena remains to be established. In any case, the low physical activity levels of the medicated respondents are surprising given that this group, by definition, had multiple contact with the health service (e.g. >70% are doctor-diagnosed hypertensives, 10% are doctor-diagnosed diabetics, medication prescriptions presumably rely on regular general practice or hospital visits). One would expect that these contacts would have offered opportunities for effective physical activity prescriptions, counselling or at least education about the benefits of exercise. Our findings are alarming and may highlight an opportunity for improvement of the primary health care services. The National Institute for Health and Clinical Excellence (NICE) has published guidance on commonly used methods to increase physical activity, including short interventions in primary care.[25] There is an imperative for Primary Care Trusts to implement such guidance so that all patients on cardiovascular medication receive appropriate physical activity interventions. Finally, we should note that a validation study of our physical activity measuring instrument in a cardiac population suggested that older people may over-estimate their activity levels.[26] If there is such a bias, the inverse association between cardiovascular medication and physical activity we observed may have been under-estimated: our medicated group was considerably older than the unmedicated one and has approximately the same age profile as the Orell et al study sample (64.5 ±11.7 Vs 65.9±7.5 years).

A number of study limitations should be highlighted. Firstly, the data relating to medication use and physical activity behaviour were collected cross-sectionally. It is therefore not possible to establish the causality and direction of the association, i.e. whether those that were more active were less ill, hence less prone to be on prescribed medications. Furthermore, it is possible that the physically active-medicated participants represent a group of individuals whose risk factors are effectively controlled by medication, thus enabling them to be more active and have less disease progression. We did not assess adherence to medication use, which might have confounded the effects of physical activity on mortality, although previous evidence showed that an exercise intervention had negligible effects on medication adherence behaviour.[24 27] Several of the measures, such as disease status, were self-reported thus it is possible that unrecognised CVD introduced bias into our results. Our definition of hypertension was based on either doctor-diagnosis or on measurements during a single household visit, thus there is a possibility for misclassification of blood pressure status. Information on dietary parameters that are largely affecting CVD death risk, such as and saturated fat intake,[28] have not been taken into account as relevant data were not collected. Lastly, we only assessed physical activity once at baseline, thus we cannot exclude the possibility that changes in this behaviour over time could have influenced our results. This limitation may have affected the precision of our estimates because physical activity levels have a tendency to decrease with age[29] and there are indications that such decreases may dilute the relationships between mortality and physical activity up to 60%.[30] An ideal research scenario to assess the independent impacts of exercise and medication on survival would be a prospective study expanding through the lifecourse that makes repeated physical activity measures at frequent intervals.

Although physical exercise is recommended for primary CVD prevention, a large proportion of adults do not engage in enough physical activity, with only approximately 20-25% of the English adult population accumulating physical non-

occupational activity at or above the recommended limits[31] and occupational physical activity levels steadily decreasing.[32] The current recommendations of the Joint British Societies on prevention of CVD[33] require high risk individuals to receive multi-factorial risk factor management based on risk reduction with both pharmacological and lifestyle intervention. The present findings strongly advocate the use of physical activity in medicated individuals for optimal CVD prevention.

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