

# Physical activity in patients with stable coronary heart disease: an international perspective

Ralph Stewart<sup>1</sup>\*, Claes Held<sup>2</sup>, Rebekkah Brown<sup>3</sup>, Ola Vedin<sup>2</sup>, Emil Hagstrom<sup>2</sup>, Eva Lonn<sup>4</sup>, Paul Armstrong<sup>5</sup>, Christopher B. Granger<sup>6</sup>, Judith Hochman<sup>7</sup>, Richard Davies<sup>3</sup>, Joseph Soffer<sup>3</sup>, Lars Wallentin<sup>2</sup>, and Harvey White<sup>1</sup>

<sup>1</sup>Green Lane Cardiovascular Service, Auckland City Hospital, Auckland, New Zealand; <sup>2</sup>Uppsala Clinical Research Center, Uppsala, Sweden; <sup>3</sup>GlaxoSmithKline Research Triangle Park, NC, USA; <sup>4</sup>David Braley Cardiac Vascular and Stroke Research Institute, Hamilton, ON, Canada; <sup>5</sup>University of Alberta, Edmonton, AB, Canada; <sup>6</sup>Duke University Medical Center, Durham, NC, USA; and <sup>7</sup>New York University School of Medicine, New York, NY, USA

Received 28 February 2013; revised 23 May 2013; accepted 11 June 2013; online publish-ahead-of-print 6 September 2013

See page 3245 for the editorial comment on this article (doi:10.1093/eurheartj/eht363)

Aims	Despite the known benefits of regular exercise, the reasons why many coronary heart disease (CHD) patients engage in little physical activity are not well understood. This study identifies factors associated with low activity levels in individuals with chronic CHD participating in the STABILITY study, a global clinical outcomes trial evaluating the lipoprotein phospholipaseA <sub>2</sub> inhibitor darapladib.
Methods and results	Prior to randomization, 15 486 (97.8%) participants from 39 countries completed a lifestyle questionnaire. Total physical activity was estimated from individual subject self-reports of hours spend each week on mild, moderate, and vigorous exercise, corresponding approximately to 2, 4, and 8 METS, respectively. Multivariate logistic regression evaluated clinical and demographic variables for the lowest compared with higher overall exercise levels, and for individuals who decreased rather than maintained or increased activity since diagnosis of CHD. The least active 5280 subjects (34%) reported exercise of $\leq$ 24MET.h/week. A total of 7191 subjects (46%) reported less exercise compared with before diagnosis of CHD. The majority of participants were either 'not limited' or 'limited a little' walking 100 m (84%), climbing one flight of stairs (82%), or walking 1 km/ $\frac{1}{2}$ mile (68%), and <10% were limited 'a lot' by dyspnoea or angina. Variables independently associated with both low physical activity and decreasing exercise after diagnosis of CHD included more comorbid conditions, poorer general health, fewer years of education, race, and country ( $P < 0.001$ for all).
Conclusion	In this international study, low physical activity was only partly explained by cardiovascular symptoms. Potentially modi- fiable societal and health system factors are important determinants of physical inactivity in patients with chronic CHD.
Keywords	Physical activity • Exercise • Coronary artery disease • Cardiac rehabilitation

## Introduction

Regular exercise and greater physical fitness are associated with lower cardiovascular and total mortality, both in healthy populations,<sup>1–3</sup> and in patients with coronary heart disease (CHD)<sup>4</sup> and heart failure.<sup>5</sup> In meta-analyses of randomized clinical trials, exercise training after myocardial infarction improves quality of life and reduces the risk of recurrent myocardial infarction and death.<sup>6</sup> For most CHD patients, the benefits of increasing physical activity are likely to outweigh the small risk of exercise triggering myocardial infarction or sudden death.<sup>7,8</sup> Clinical practice guidelines therefore recommend that patients with CHD engage in regular moderate intensity exercise, which is usually defined as 30 min on most days of the week.<sup>9–11</sup>

Currently there are limited data on the reasons why many CHD patients are sedentary.<sup>12</sup> Coronary heart disease patients with symptoms such as angina, dyspnoea, and fatigue during exercise would be expected to engage in less exercise. Change in usual levels of physical activity could also be influenced by the psychological consequences of CHD, and by professional and other advice given to the patient. Sedentary behaviour may also partly reflect longstanding exercise

<sup>\*</sup> Corresponding author. Tel: +64 09 307 4949; ext: 23668, Fax: +64 9 630 9915, Email: rstewart@adhb.govt.nz

 $<sup>\</sup>ensuremath{\mathbb{C}}$  The Author 2013. Published by Oxford University Press on behalf of the European Society of Cardiology.

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/3.0/), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com

patterns which predate the diagnosis of CHD. Social, economic, and cultural factors may also be important. A better understanding of the relative importance of these various factors may help inform the development of more effective interventions.

The aim of this study was to determine the degree to which sedentary behaviours are related to an individual's general health, to symptoms that develop during exercise, and to broader societal factors associated with education level, race, and country of residence. The study population is the large international cohort of patients with stable CHD participating in the Stabilisation of Atherosclerotic Plaque By Initiation of Darapladib Therapy (STABILITY) trial.<sup>13</sup>

## **Methods**

#### **Study population**

The STABILITY trial is a global outcomes trial designed to determine whether darapladib, a specific inhibitor of lipoprotein associated phospholipase A2 (Lp-PLA2) will reduce the risk of cardiovascular death, myocardial infarction, and stroke in patients with chronic CHD.<sup>13</sup> In total, 15 828 subjects from 39 countries were randomized. All patients had chronic stable CHD, defined as prior myocardial infarction, prior coronary revascularization, or multi-vessel CHD confirmed by coronary angiography. In addition, patients had to meet at least one of the following cardiovascular risk criteria: age  $\geq$  60 years; diabetes mellitus requiring pharmacotherapy; HDL-cholesterol <1.03 mmol/; current or previous smoker defined as  $\geq 5$  cigarettes per day on average; significant renal dysfunction (estimated glomerular filtration rate  $\geq$  30 and < 60 mL/ min per 1.73 m<sup>2</sup> or urine albumin:creatinine ratio  $\geq$  30 mg albumin/g creatinine); or polyvascular disease (CHD and cerebrovascular disease or CHD and peripheral arterial disease). More detailed descriptions of the study design and population have been published previously.<sup>13,14</sup>

#### **Data collection**

At baseline, in addition to a detailed medical history, physical examination, and fasting blood samples, participants were invited to complete a lifestyle questionnaire. The questions related to physical activity, based on the International Physical Activity Questionnaire,<sup>15</sup> were completed by 15 486 (97.8%) subjects.

#### **Evaluation of physical activity**

Each subject was asked to estimate the number of hours spent undertaking 'mild,' 'moderate,' and 'vigorous' physical activity during a typical week. Examples of mild activity were easy walking, yoga, Tai Chi, and mild house work. Moderate exercise included fast walking, jogging, aerobics, gardening, bicycling, dancing, swimming, or house cleaning. Examples of vigorous physical activity were running, lifting heavy objects, playing strenuous sports or strenuous work. The total amount of physical activity was estimated in MET (metabolic equivalent) hours/week from the self-reported time undertaking mild (2 METS), moderate (4 METS), and vigorous intensity (8 METS) physical activity during an average week.<sup>15</sup> In separate questions, subjects were asked to indicate whether they undertook any 'moderate intensity' physical activity during work and separately during leisure time. To evaluate a change in exercise pattern, each participant was asked 'Comparing your current lifestyle to your lifestyle before your first heart problem do you exercise "less now," "about the same," or "more now"".

#### **Evaluation of symptoms during exercise**

Subjects were asked whether they were limited 'a little' or 'a lot' in the following activities; walking 100 m; climbing one flight of stairs; and

walking 1 km. To estimate the overall degree of limitation, a score was calculated from the summed responses to five activities (no limitation, limited a little '1' and limited a lot '2,' or '1 do not do this activity' '1'). Subjects also indicated whether physical activity was 'not limited,' limited 'a little' or 'a lot' by chest discomfort or tightness, shortness of breath, fatigue or tiredness, muscle weakness, dizziness, or arthritis.

#### General health, co-morbidities, and mood

Subjects rated their general health as poor, fair, good, very good, or excellent. Current and past co-morbidities were recorded on the baseline case report form. The number of the following co-morbidities, each associated with reduced physical activity, was determined; multi-vessel CHD, prior heart failure, renal dysfunction, diabetes type 1 or 2, peripheral vascular disease, chronic obstructive pulmonary disease or asthma, obstructive sleep apnoea, and prior stroke. To evaluate depression, participants were asked 'Have you felt sad, low in your spirits or depressed?' and 'Have you lost interest in hobbies, work or activities that previously gave you pleasure?' Those who responded to either question 'always' or 'often' were classified as being 'depressed.'<sup>16</sup>

#### Race groups, country, and education

In a pre-specified grouping, individuals were classified to one of the following race or ethnic groups: (i) White (White/Caucasian/European Heritage/Arabic/North African Heritage and not Hispanic/Latino ethnicity; (ii) White and Hispanic/Latino; (iii) Black (African American/ African Heritage); (iv) Central/South/South East Asian; (v) East Asian/ Japanese; and (iv) other including indigenous peoples (American Indian/Alaskan Native/Native Hawaiian/Other Pacific Islander), and 113 patients who checked more than one category.

Countries were classified as high income, upper middle income, or lower middle income according to the World Bank classification.<sup>17</sup> No low income countries were included in the study. Because the number of subjects from lower middle income countries was small, lower and upper middle income countries were combined for the analysis.

Years of formal education completed were defined as 'none or 1-8 years,' '9-12 years,' and either 'trade school' or 'college/university.'

#### Statistical analysis

Data collected at baseline assessment and before randomization are included. To summarize relations between physical activity and other variables, total physical activity in MET.h/week was divided into tertiles.  $\chi^2$  tests were used to assess associations between physical activity tertiles and change in exercise since CHD diagnosis, level of limitation by symptoms, and demographic factors including age, sex, and time since CHD diagnosis.  $\chi^2$  tests were also used to assess associations between change in exercise since CHD diagnosis and level of limitation by symptoms. Two-sided *P*-values were generated for descriptive purposes only.

Logistic regression models were used to assess differences in the lowest tertile vs. the highest two tertiles in physical activity and for subjects who decreased compared with those who did not change or increased their level of exercise after a diagnosis of CHD. Factors included were age, sex, level of limitation during exercise, general health, number of co-morbidities, mood, obesity, country, race group, country income level, and years of education. Backwards selection was used to remove factors not statistically significant at the 0.10 level to provide the final multivariate models.

All statistical analyses were conducted in SAS version 9.1. The bubble plot was produced in R version 2.15.2.

## Results

Exercise levels for subjects in the lowest, middle, and highest tertile of overall physical activity are given in Table 1. Almost half of the study participants were exercising less compared with before the diagnosis of CHD. Overall, more subjects reported moderate or greater intensity exercise during leisure than at work, but only 33% of subjects were currently working. Differences in physical activity levels by age and sex were small, and there was no association with time since CHD diagnosis.

#### Importance of symptoms

Subjects reporting low physical activity were more likely to be limited 'a lot' by common daily activities such as walking 100 m or 1 km, and climbing one flight of stairs than those who were more active (Table 2). However, most sedentary subjects did not report 'a lot' of limitation with these activities. The least active subjects were more likely to be limited 'a lot' by symptoms, the most common of which were fatigue, shortness of breath, and arthritis. However, for the least active tertile, only 12% of subjects were limited 'a lot' by shortness of breath compared with 7% for the most active tertile (P < 0.001). Seven percent of the least active tertile reported they were limited 'a lot' by chest discomfort or tightness, compared with 5% of the most active tertile of subjects (Table 2).

#### Variables associated with low physical activity

Increasing age and being male were associated with low physical activity in both the unadjusted and fully adjusted models (Table 3). Low physical activity was also associated with more frequently

reported limitation by symptoms during exercise, poorer selfreported general health, and a larger number of co-morbidities. The strength of these associations was weaker in the fully adjusted model with the exception of sex. There was a modest association between depressed mood and low physical activity, but not in the fully adjusted model. Obesity was associated with lower physical activity, in both the unadjusted and adjusted models.

The majority of subjects (65%) had never participated in a cardiac rehabilitation programme, and these subjects were more likely to report taking less exercise. Living in a lower or upper middle income country compared with a high income country was associated with higher odds ratio for low physical activity in the unadjusted but not in the adjusted model. This may be the result of collinearity between this parameter and country. East Asian/Japanese races had more than twice the odds ratio for low physical activity compared with Whites.

### Change in activity since diagnosis of coronary heart disease

Overall, 46% of subjects had reduced their level of exercise compared with before the diagnosis of CHD, while 34% had increased their physical activity (Table 3). Factors associated with a greater likelihood of decreasing exercise since diagnosis of CHD were similar to those for low physical activity. The strongest associations with reduced activity were for poorer self-reported health and symptoms during exercise. Living in a middle compared with a high income country was also strongly associated with a greater likelihood of decreasing exercise. There were also modest independent associations for Asian and Black race groups.

Table I	Physical activity	levels in the STABIL	ITY study population
---------	-------------------	----------------------	----------------------

	Least active	Intermediate activity	Most active
	<24 MET.h/week	26 to 56 MET.h/week	>58 MET.h/week
Number of subjects	5280	5055	5151
Age, mean $\pm$ standard deviation, years	64.6 <u>+</u> 9.6	64.8 ± 9.2	63.7 <u>+</u> 9.1
Male, %	83	80	81
Time since CHD diagnosis, mean $\pm$ SD, months	$52 \pm 56$	54 <u>+</u> 57	53 <u>+</u> 54
Exercise			
Total exercise, MET.h/week	14 (6, 18)	40 (32, 46)	90 (70, 122)
Mild-intensity activity (2 METS), h/week	8 (4, 14)	18 (12, 28)	28 (14, 42)
Moderate-intensity activity (4 METS), h/week	0 (0, 8)	16 (8, 28)	44 (32, 80)
Vigorous-intensity activity (8 METS), h/week	0 (0, 0)	0 (0, 0)	8 (0, 40)
$\geq$ 10MET.h/week moderate or vigorous activity (%)	16	74	100
Some moderate-intensity exercise during leisure time (%)	10	23	38
Some moderate-intensity exercise at work (%)	7	8	19
Change in exercise since CHD diagnosis (%)			
Less now	55	47	38
About the same	30	31	40
More now	15	22	22

Results are mean  $\pm$  standard deviation (SD), median (inter-quartile range), or % of group. Differences between groups have P < 0.001, except for gender and time since CHD diagnosis. Statistical tests were not performed for the number of exercise h/week. CHD, coronary heart disease.

	Low physical activity	Intermediate physical activity	Most physically active	Decreased exercise since CHD diagnosis	Same exercise since CHD diagnosis	Greater exercise since CHD diagnosis
Number of subjects	5280	5055	5151	7191	5244	3014
Limited during activities (%)						
Walking 100 m	30	22	18	32	17	13
Climbing one flight of stairs	42	34	28	44	28	23
Walking 1 km or half mile	46	41	38	53	34	26
Limited by symptoms (%)						
Dypsnoea	53	50	47	60	42	38
Chest pain or tightness	39	38	35	49	28	27
Fatigue	62	61	61	72	53	51
Arthritis	38	38	44	46	34	32
Muscle weakness	44	40	41	51	35	32
Dizziness	27	26	23	33	18	19

#### Table 2 Relationships between physical activity and symptoms during exercise

The proportion of subjects who report being limited either 'a little' or 'a lot' during the activity or by the symptoms is given.

All differences between all groups have P < 0.001 by  $\chi^2$  test.

CHD, coronary heart disease.

## Table 3 Predictors of low physical activity and of taking less exercise compared with before diagnosis of coronary heart disease

	Proportion of study participants (%)	OR for low PA (95% Cl)	OR for low PA in fully adjusted model <sup>a</sup> (95%CI)	OR for decreasing PA after CHD diagnosis (95% CI)	OR for decreasing PA after CHD diagnosis in fully adjusted model (95% CI)
Age (+10 years)	_	1.05 (1.01, 1.08)	1.05 (1.00, 1.09)	1.09 (1.05, 1.13)	1.16 (1.11, 1.22)
Male vs. Female	81	1.13 (1.03, 1.23)	1.46 (1.32, 1.62)	0.78 (0.72, 0.84)	1.24 (1.12, 1.38)
Individual health measures					
Good vs. very good general health	44	1.34 (1.20, 1.49)	1.23 (1.10, 1.39)	2.45 (2.19, 2.73)	1.78 (1.58, 2.01)
Poor/fair vs. very good health	41	1.83 (1.65, 2.04)	1.41 (1.24, 1.61)	5.88 (5.26, 6.57)	3.17 (2.78, 3.63)
Amount of limitation during exercise (score +1)	_	1.12 (1.11, 1.13)	1.11 (1.09, 1.13)	1.27 (1.25, 1.28)	1.20 (1.18, 1.22)
Number of co-morbidities (+1)	_	1.17 (1.14, 1.21)	1.10 (1.07, 1.14)	1.32 (1.28,1.35)	1.11 (1.07, 1.15)
Depressed mood (yes vs. no)	12	1.19 (1.07, 1.31)	0.91 (0.81, 1.03)	1.79 (1.62, 1.98)	1.12 (0.99, 1.27)
Obesity (BMI $>$ 30 vs. $\leq$ 30)	36	1.16 (1.08, 1.24)	1.28 (1.17, 1.39)	1.25 (1.17, 1.34)	1.14 (1.05, 1.24)
Cardiac rehabilitation					
No vs. Yes	65	1.35 (1.26, 1.45)	1.11 (1.01, 1.20)	1.47 (1.37, 1.57)	1.14 (1.05, 1.24)
Country					
Low/Middle vs. high income	30	1.56 (1.45, 1.67)	0.63 (0.49, 0.83)	2.16 (2.01, 2.31)	3.54 (2.67, 4.70)
Race/ethnic group					
Latino/Hispanic vs. white	9	2.85 (2.55, 3.18)	1.37 (1.03, 1.83)	1.44 (1.29, 1.61)	1.06 (0.78, 1.43)
Central + South + SE Asian vs. white	7	2.38 (2.10, 2.69)	1.54 (1.04, 2.29)	1.27 (1.13, 1.44)	1.79 (1.18, 2.70)
East Asian/Japanese vs. white	10	1.82 (1.63, 2.03)	3.04 (1.83, 5.67)	0.82 (0.74, 0.92)	1.28 (0.68, 2.40)
Black vs. white	2	2.24 (1.79, 2.82)	1.46 (1.10, 1.94)	1.46 (1.17, 1.83)	1.39 (1.04, 1.87)
Indigenous/other vs. white	0.7	1.20 (0.81, 1.79)	0.91 (0.59, 1.41)	0.98 (0.68, 1.43)	1.24 (0.80, 1.91)
Education					
9–12 years vs. trade/college	31	1.17 (1.08, 1.26)	1.00 (0.91, 1.09)	1.11 (1.03, 1.20)	1.02 (0.94, 1.12)
< = 8 years vs. trade/college	23	1.63 (1.50, 1.77)	1.10 (0.99, 1.23)	1.27 (1.17, 1.38)	1.15 (1.03, 1.27)

OR, odds ratio; PA, physical activity; CHD, coronary heart disease.

<sup>a</sup>The fully adjusted model includes age, gender, obesity, exercise limitation, co-morbidities, general health, mood, country income level, race, education, and country.





#### International differences

There were large international differences in proportion of subjects reporting low physical activity, with subjects living in Asia and Latin America reporting the lowest levels of physical activity. (*Figure 1*, *Table 4*) There were also large international differences in the proportion of subjects who decreased physical activity since CHD diagnosis, and in attendance at a cardiac rehabilitation programme (*Figure 2*, *Table 4*). Subjects living in Russia and several Eastern European countries reported the greatest decreases in physical activity after CHD diagnosis. Fewer subjects living in Latin America, Asian, or Eastern European Countries had attended a cardiac rehabilitation programme compared with those living in North America, Western Europe, Australia, and New Zealand.

## Discussion

In this large international study, about one-third of patients with chronic CHD reported substantially less physical activity than recommended in current guidelines.<sup>10,11</sup> Factors associated with being sedentary fell into two broad groups, those related to individual health, and those related to race group, country, and level of education. The observations are consistent with socioeconomic, general population, and/or health system-related factors being important determinants of the amount of exercise taken by patients with CHD.<sup>18</sup>

Physical activity in patients with CHD is likely to reflect longstanding patterns of exercise as well as change in physical activity since the diagnosis of CHD. In this study, about two-thirds of subjects did not attend cardiac rehabilitation, which was independently associated with both lower physical activity and a greater risk of decreasing exercise after CHD diagnosis. Cardiac rehabilitation and other interventions which increase early return to normal activities and help to maintain regular exercise after an acute coronary event are likely to reduce the proportion of CHD patients who become sedentary.<sup>19</sup> The observation of higher rates of non-attendance at cardiac rehabilitation in countries where more subjects reported decreasing physical activity after diagnosis of CHD, is further evidence supporting the importance of cultural and/or health system-related factors in influencing physical activity in CHD patients.

Most previous large studies on physical activity have evaluated general populations,<sup>1,3</sup> but CHD patients differ in several important respects. The risk of adverse events, especially during vigorous exercise, is greater for CHD patients. Thus while guidelines recommend 30 min of moderate or vigorous exercise each day,<sup>10,11</sup> many patients and their health advisors may be cautious about more vigorous exercise. Coronary heart disease patients are also more likely to have symptoms which limit exercise compared with a healthy general population. In the current study, poorer general health, cardiac, and non-cardiac co-morbidities and exertional symptoms were all associated with less physical activity. Despite this, the majority of those reporting low physical activity were 'not limited' or only 'limited a little' by activities which involved moderate intensity exercise. Also physical activity was most often limited by non-specific symptoms such as shortness of breath, fatigue, and weakness, and limitation by chest tightness or discomfort was less common. In clinical trials, exercise training reduces dyspnoea and fatigue, increases muscle strength, and improves angina.<sup>6,20,21</sup> It is therefore possible that lack of fitness in part explains the association between symptoms and less physical activity. Depression was associated with low physical activity, but not in the fully adjusted model. This may in part be explained by the association between depressed mood and poorer general health.<sup>22</sup>

In previous studies, leisure time physical activity has been more clearly related to lower CHD mortality than activity at work.<sup>23</sup> The majority (67%) of STABILITY study participants were not working, and a higher proportion of subjects reported moderate or greater physical activity during 'leisure time' than 'at work'. However, not all exercise was 'at work' or 'during leisure', probably reflecting exercise during usual activities of daily life. It is possible women reported greater physical exercise than men, because on average they spend more time on household chores.

	Number of subjects	World bank income classification	Attended cardiac rehabilitation (%)	Low physical activity (%)	Decreased exercise since CHD diagnosis (%)
Argentina	542	Upper middle	16	56	52
Australia	306	High	48	25	38
Belgium	202	High	56	32	33
Brazil	384	Upper middle	20	60	58
Bulgaria	222	Upper middle	22	21	88
Canada	780	High	37	38	37
Chile	195	Upper middle	12	40	63
China	369	Upper middle	89	39	32
Czech Republic	774	High	21	12	58
Denmark	102	High	50	21	23
Estonia	77	High	30	24	65
France	250	High	45	40	48
Germany	1089	High	52	20	25
Greece	187	High	1	35	26
Hong Kong	117	High	16	50	43
Hungary	410	High	33	30	52
India	398	Lower middle	13	59	44
Italy	256	High	21	38	42
Japan	318	High	14	45	49
Korea	503	High	5	42	40
Mexico	141	Upper middle	20	56	58
Netherlands	444	High	66	26	36
New Zealand	202	High	56	28	34
Norway	113	High	36	35	30
Pakistan	250	Lower middle	6	53	68
Peru	78	Upper middle	37	56	53
Philippines	219	Lower middle	20	39	46
Poland	510	High	30	30	60
Romania	411	Upper middle	8	31	73
Russia	654	Upper middle	43	22	73
Slovakia	120	High	37	25	53
South Africa	386	Upper middle	8	41	53
Spain	474	High	27	39	42
Sweden	299	High	47	29	34
Taiwan	200	High	5	35	45
Thailand	207	Upper middle	14	38	53
UK	184	High	67	31	48
Ukraine	353	Lower middle	41	28	78
USA	3102	High	48	33	39

 Table 4
 International differences in reported physical activity, decrease in exercise after coronary heart disease diagnosis, and cardiac rehabilitation attendance for STABILITY study participants assessed at baseline

CHD, coronary heart disease.

## Limitations

Physical activity may differ in a clinical trial population compared with usual CHD patients, and these differences could vary by country. STABILITY study participants had high levels of adherence to evidence-based pharmacological therapies, suggesting they were well-motivated and received good medical care.<sup>14</sup> Almost all subjects completed the lifestyle questionnaire at the baseline visit, so bias

related to non-participation within the STABILITY study would be small. Self-reporting of activity level is likely to be relatively imprecise, and for some subjects may overestimate the exercise taken. The use of standard questionnaires based on the widely used and validated International Physical Activity Questionnaire<sup>15</sup> allows comparison of diverse geographic and ethnic groups, but cultural differences in the interpretation of some questions is possible. Independent validation of the lifestyle questionnaire used in this study, including





questions related to change in physical activity was not undertaken. A threshold of 30 min of moderate or vigorous exercise on at least 5 days each week has been used in many guidelines.<sup>11</sup> In this study, mild exercise was also included because there is a graded association between exercise and mortality, with benefits from mild compared with no exercise.<sup>24</sup> Also some CHD patients are advised to avoid vigorous exercise. This analysis was undertaken prior to completion of the STABILITY trial and therefore includes only baseline data. The relationship between self-reported physical activity and morbidity and mortality in the STABILITY study population will be assessed in future.

## Conclusions

In this study, the majority of sedentary CHD patients were not limited 'a lot' by symptoms, suggesting most could be more active. The observation of large international differences in activity levels, in the proportion of subjects reporting a decrease in exercise since CHD diagnosis, and in rates of attendance at cardiac rehabilitation, suggest that modifiable societal and health system-related factors are important determinants of physical inactivity in patients with CHD.

Cultural and regional geographic factors need to be considered when planning strategies to increase physical activity in CHD patients. Particularly in middle income countries, quality of life and prognosis of patients with CHD may be improved by health professionals focusing more on cardiac rehabilitation and other interventions which help to maintain or increase exercise after CHD diagnosis. Further research is needed to improve understanding of ways to overcome barriers to exercise such as the patient's, family's, or physician's concerns about risk, and to evaluate novel approaches such as with information technology to engage inactive patients and reinforce changes with regular feedback.

#### Acknowledgements

We thank all patients who participated in the STABILITY trial, as well as study nurses and investigators at 639 participating sites.

#### Funding

The STABILITY trial and the lifestyle sub-study were funded by GSK. Study design and drafting and approval of the manuscript were undertaken by the study authors. The charge for Open Access will be paid by GlaxoSmithKline, who were the sponsor for the Stability trial.

**Conflict of interest:** Rebekkah Brown, Richard Davies and Joseph Sofer are employees of GlaxoSmithKline and Ralph Stewart, Claes Held, Ola Vedin, Emil Hagstrom, Eva Lonn, Paul Armstrong, Christopher B. Granger, Judith Hochman, Lars Wallentin and Harvey White are Stability Study Investigators.

#### References

- Shiroma EJ, Lee IM. Physical activity and cardiovascular health. *Circulation* 2010;**122**: 743–752.
- Lee IM, Shiroma EJ, Lobelo F, Puska P, Blair SN, Katzmarzyk PT. Effect of physical inactivity on major non-communicable diseases worldwide: an analysis of burden of disease and life expectancy. *Lancet* 2012;**380**:219–229.
- Kodama S, Saito K, Tanaka S, Maki M, Yachi Y, Asumi M, Sugawara A, Totsuka K, Shimano H, Phashi Y, Yamada N, Sone H. Cardiorespiratory fitness as a quantitative predictor of all-cause mortality and cardiovascular events in healthy men and women: a meta-analysis. JAMA 2009;301:2024–2035.
- Kavanagh T, Mertens DJ, Hamm LF, Beyene J, Kennedy J, Corey P, Shepherd P. Prediction of long-term prognosis in 12 169 men referred for cardiac rehabilitation. *Circulation* 2002;106:666–671.
- Piepoli MF, Conraads V, Corrà U, Dickstein K, Francis DP, Jaarsma T, McMurray J, Pieske B, Piotrowicz E, Schmid JP, Anker SD, Solal AC, Filippatos GS, Hoes AW,

Gielen S, Giannuzzi P, Ponikowski PP. Exercise training in heart failure: from theory to practice. A concensus document of the Heart Failure Association and the European Association for Cardiovascular Prevention and Rehabilitaion. *Eur J Heart Fail* 2011; **13**:347–357.

- Heran BS, Chen JM, Ebrahim S, Moxham T, Oldridge N, Rees K, Thompson DR, Taylor RS. Exercise-based cardiac rehabilitation for coronary heart disease. *Cochrane Database SystRev* 2011; CD001800.
- Dahabreh IJ, Paulus JK. Association of episodic physical and sexual activity with triggering of acute cardiac events: systematic review and meta-analysis. JAMA 2011;305: 1225–1233.
- 8. Thompson PD, Franklin BA, Balady GJ, Blair SN, Corrado D, Estes NA III, Fulton JE, Gordon NF, Haskell WL, Link MS, Maron MA, Pelliccia A, Wenger NK, Willich SN, Costa F. American Heart Association Council on Nutrition, Physical Activity and Metabolism; American Heart Association Council on Clinical Cardiology: American College of Sports Medicine. Exercise and acute cardiovascular events placing the risks into perspective: a scientific statement from the American Heart Association Council on Nutrition, Physical Activity, and Metabolism and the Council on Clinical Cardiology. Circulation 2007;115:2358–2368.
- Corra U, Piepoli MF, Carre F, Heuschmann P, Hoffmann U, Verschuren M, Halcox J. Secondary prevention through cardiac rehabilitation: physical activity counselling and exercise training: key components of the position paper from the Cardiac Rehabilitation Section of the European Association of Cardiovascular Prevention and Rehabilitation. Eur Heart J 2010;31:1967–1974.
- Haskell WL, Lee IM, Pate RR, Powell KE, Blair SN, Franklin BA, Macera CA, Heath GW, Thompson PD, Bauman A. Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. *Circulation* 2007;**116**:1081–1093.
- 11. Perk J, de Backer G, Gohlke H, Graham I, Reiner Z, Verschuren WM, Albus C, Benlian P, Boysen G, Cifkova R, Deaton C, Ebrahim S, Fisher M, Germano G, Hobbs R, Hoes A, Kaadeniz S, Mezzani A, Prescott E, Ryden L, Scherer M, Syvanne M, Op Reimer WJ, Vrints C, Wood D, Zamorano JL, Zannad F. European Guidelines on cardiovascular disease prevention in clinical practice (version 2012): The Fifth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of nine societies and by invited experts). Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). *Eur J Prev Cardiol* 2012;**19**:585–667.
- Kotseva K, Wood D, De Backer G, De Bacquer D, Pyorala K, Keil U. Cardiovascular prevention guidelines in daily practice: a comparison of EUROASPIRE I, II, and III surveys in eight European countries. *Lancet* 2009;**373**:929–940.

- White HD, Held C, Stewart RA, Watson D, Harrington R, Budaj A, Steg PG, Cannon CP, Krug-Gourley S, Wittes J, Trivedi T, Tarka E, Wallentin L. Study design and rationale for the clinical outcomes of the STABILITY Trial (STabilisation of Atherosclerotic plaque By Initiation of darapLadlb TherapY) comparing darapladib versus placebo in patients with clinical coronary heart disease). *Am Heart J* 2010; 160:655–661.
- 14. Vedin O, Hagstrom E, Stewart R, Brown R, Krug-Gourley S, Davies R, Wallentin L, White H, Held C. Secondary prevention and risk factor target achievement in a global, high-risk population with established coronary heart disease: baseline results from the STABILITY study. *Eur J Prev Cardiol* 2012; doi: 10.1177/ 2047487312444995. Published online ahead of print 10 April 2012.
- Craig CL, Marshall AJ, Sjostrom M, Bauman AE, Booth ML, Ainsworth BE, Pratt BE, Ekeland U, Yngve A, Sallis JF, Oja P. International Physical Activity Questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc* 2003;**35**:1381–1395.
- Depression: management of depression in primary and secondary care NICE guidance. London: National Institute for Health and Clinical Excellence (NICE). [Internet]. 2004;23. Available from: http://www.nice.org.uk/guidance/index.jsp?Action= byID&o=10958 (last accessed April 30, 2013).
- How we classify countries The World Bank [Internet]. 2012. Available from: http://data.worldbank.org/about/country-classifications (last accessed April 30, 2013).
- Heath GW, Parra DC, Sarmiento OL, Andersen LB, Owen N, Goenka S, Montes F, Brownson RC. Evidence-based intervention in physical activity: lessons from around the world. *Lancet* 2012;**380**:272–281.
- Roffi M, Wenaweser P, Windecker S, Mehta H, Eberli FR, Seiler C, Fleisch M, Garachemani A, Pedrazzini GB, Hess OM, Meier B. Early exercise after coronary stenting is safe. J Am Coll Cardiol 2003;42:1569–1573.
- Heaps CL, Parker JL. Effects of exercise training on coronary collateralization and control of collateral resistance. J Appl Physiol 2011;111:587–598.
- van der Meer S, Zwerink M, van Brussel M, van der V, Wajon E, van der PJ. Effect of outpatient exercise training programmes in patients with chronic heart failure: a systematic review. *Eur J Prev Cardiol* 2012;**19**:795–803.
- Stewart RA, North FM, West TM, Sharples KJ, Simes RJ, Colquhoun DM, White HD, Tonkin AM. Depression and cardiovascular morbidity and mortality: cause or consequence? *Eur Heart J* 2003;24:2027–2037.
- Held C, Iqbal R, Lear SA, Rosengren A, Islam S, Mathew J, Yusuf S. Physical activity levels, ownership of goods promoting sedentary behaviour and risk of myocardial infarction: results of the INTERHEART study. *Eur Heart* J 2012;33:452–466.
- Wen CP, Wai JP, Tsai MK, Yang YC, Cheng TY, Lee MC, Chan HT, Tsao CK, Wu X. Minimum amount of physical activity for reduced mortality and extended life expectancy: a prospective cohort study. *Lancet* 2011;**378**:1244–1253.