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Original Scientific Paper

A meta-analysis of randomized control trials of home-based secondary prevention programs for coronary artery disease

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Background **A variety of different types of secondary prevention programs for coronary heart disease (CHD) exist. Home-based programs have become more common and may be more accessible or preferable to some patients. This review compared the benefits and costs of home-based programs with usual care and cardiac rehabilitation.**

Methods **A meta-analysis following a systematic search of 19 databases, existing reviews, and references was designed. Studies evaluated home-based interventions that addressed more than one main CHD risk factor using a randomized trial with a usual care or cardiac rehabilitation comparison group with data extractable for CHD patients only and reported in English as a full article or thesis.**

Results **Thirty-nine articles reporting 36 trials were reviewed. Compared with usual care, home-based interventions significantly improved quality of life [weighted mean difference: 0.23; 95% confidence interval (95% CI): 0.02–0.45], systolic blood pressure (weighted mean difference: −4.36 mmHg; 95% CI: −6.50 to −2.22), smoking cessation (difference in proportion: 14%; 95% CI: 0.02–0.26), total cholesterol (standardized mean difference: −0.33; 95% CI: −0.57 to −0.08), and depression (standardized mean difference: −0.33; 95% CI: −0.59 to −0.07). Effect sizes were small to moderate and trials were of low-to-moderate quality. Comparisons with cardiac rehabilitation could not be made because of the small number of trials and high levels of heterogeneity.**

Conclusion **Home-based secondary prevention programs for CHD are an effective and relatively low-cost complement to hospital-based cardiac rehabilitation and should be considered for stable patients less likely to access or adhere to hospital-based services.** ***Eur J Cardiovasc Prev Rehabil*** **17:261–270** © **2010 The European Society of Cardiology**

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Introduction

This systematic review examines the effects of home-based versus hospital-based secondary prevention programs for coronary heart disease (CHD) [1–39]. Programs provided in hospital settings are well established internationally and use multidisciplinary health care teams to address the main modifiable risk factors [40]. Such programs are beneficial [41], but patient access to them internationally is low (around 30%) [42], and is lower in groups with greater need for risk factor reduction [43]. Recent guidelines [44,45] recommend that to address these inequalities alternative models to traditional hospital programs should be used more widely. A promising means of doing this is to provide interventions directly in patients' homes.

Home-based secondary prevention interventions are formalized interventions for the secondary prevention of CHD with predominant or exclusive home-based components. These interventions can be provided in a range of ways including paper, face-to-face, electronic, or

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telephone-based methods. Although the effectiveness of secondary prevention programs is not dependent on placement in a hospital [36,46,47], more evidence is needed to identify the relative effectiveness and costs of home-based programs.

Methods

A multi-file search was undertaken to identify randomized control trials evaluating home-based interventions for patients with CHD. Nineteen indexing databases were searched using more than 100 search terms related to prevention, rehabilitation, and support services.

Only trials of secondary prevention programs for CHD with a predominant or exclusive home-based content were included. Other exclusion criteria were nonrandomized study or trial without a usual care or cardiac rehabilitation comparison group; intervention was not focused on secondary prevention (e.g. drug only intervention, heart failure management program, or intervention for other forms of atherosclerotic disease); program focused on a single risk factor (other than exercise) or was a predominantly hospital-based intervention (e.g. pre-discharge only, in-hospital, family or other medicine setting). Articles had to be published in English as a full article or thesis with original data that were extractable for CHD patients.

Study design filters were used only for databases that retrieved large numbers of records or had superior indexing, such as Medline and EMBASE. Study design filters were not used in databases that did not have adequate indexing or publication type limits. Two members of the team (A.M.C. and J.K.) independently searched the titles and abstracts of all citations against the *a priori* exclusion criteria to identify appropriate trials.

Data on outcomes for selected studies were extracted by A.M.C. and M.H. independently, and double checked by J.S. Definitions used for each outcome by the investigators were accepted. Cardiac rehabilitation interventions were hospital-based programs self-identified by authors of trials as constituting 'cardiac rehabilitation programs provided in a centralized health or community setting'. After initial extraction, 26 original investigators were contacted by T.McC. by email (based on latest addresses as found in recent articles/Google searchers) to obtain data missing from the original articles.

Data analysis was performed using Review Manager (RevMan, version 4.2.8 for Windows. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2003). Differences in effects were examined for two comparisons (intervention vs. usual care, and intervention vs. cardiac rehabilitation). For dichotomous outcomes, that is, all-cause mortality, cardiovascular (CV) death, recurrent myocardial infarction (MI), morbidity CV event (excluding transient ischemic attack/stroke), studies were combined using risk ratios (RR) with corresponding 95% confidence intervals (95% CI), with the exception of smoking, and risk differences (absolute difference in the proportion of smoking cessation). For continuous outcomes, change from baseline data were used if available, otherwise endpoint data were used. Weighted mean difference with 95% CI or standardized mean difference (SMD) with 95% CI were calculated for continuous variables with the same or different scales, respectively. Standard deviations of the effect sizes were calculated exactly from available data whenever possible. In cases in which exact values could not be obtained, standard deviations were estimated using P values, ranges, or interquartile ranges. For standard deviations of change from baseline, when a measure of correlation was absent, a correlation estimate of 0.5 was assumed.

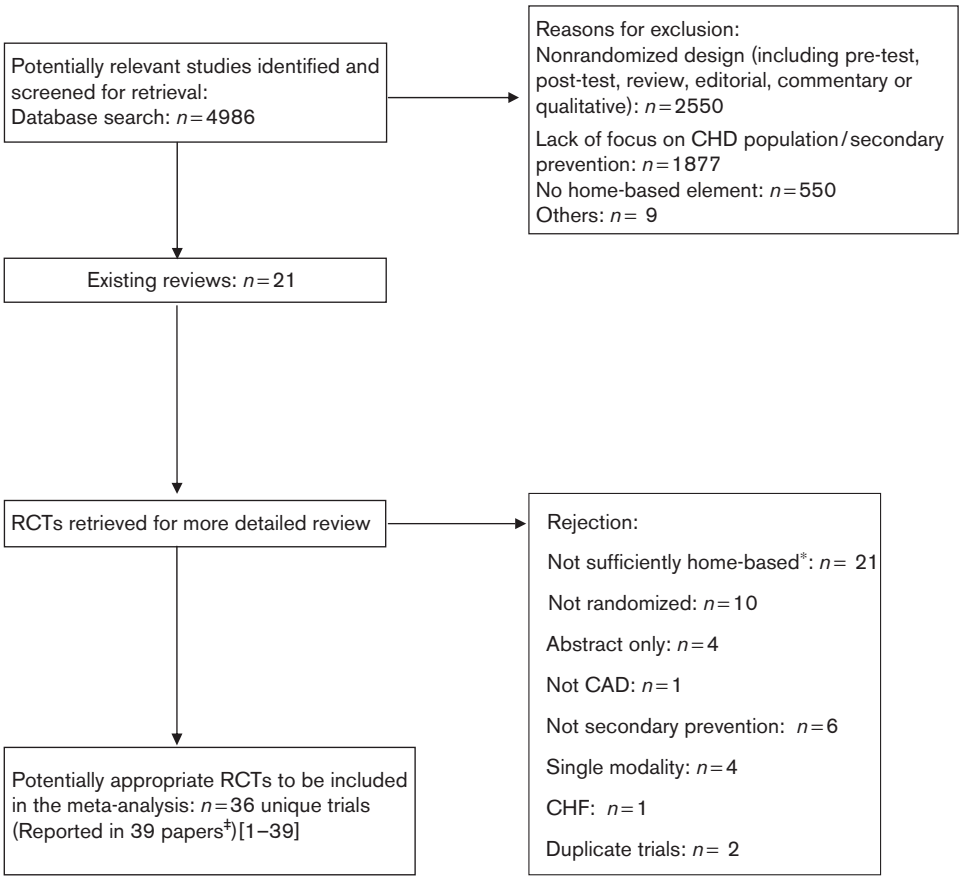
All pooling of data was done using the DerSimonian and Laird random effects model. Statistical heterogeneity was measured using I^2 statistic; based on this statistic, heterogeneity for each outcome was classified as negligible ($I^2 = 0\%$), minimal ($I^2 \leq 20\%$), moderate ($20\% < I^2 < 50\%$), or substantial ($I^2 \geq 50\%$) [48]. Subgroup analyses were conducted based on the length of the follow-up period reported (short-term and long-term, defined as less than 12 months and equal to or greater than 12 months, respectively). If the studies were too heterogeneous to combine quantitatively, qualitative analysis was done. On account of the small sample size, there was not enough statistical power to examine for publication bias using the existing methods. Measurements of quality of life varied widely between trials. It was not therefore possible to pool quality of life measures from the trials. As an alternative, the SMDs of quality of life between trials were pooled to attain an overall difference in effect.

Results

From a preliminary screening of the titles and abstracts of 4986 citations, 69 were selected for review of full articles (Fig. 1). Additional search of the titles of articles included in previous reviews of secondary prevention programs or risk factors [41,46,49–55] yielded an additional 21 citations for full review.

Further screening by A.C. and M.H. identified 39 articles (reporting 36 unique trials) [1–39] meeting the eligibility criteria (Table 1). The number of articles exceeded the number of trials as one trial [36] reported cost data in a separate article [8], one trial reported both short-term and long-term outcomes separately [2,30], and another trial reported different risk factors in different articles from the same intervention [33,34].

Fig. 1



Search process. *Programs that were nonhome-based secondary prevention or cardiac rehabilitation programs that contained minimal follow-up support at home; ‡Some overlapping cost data. CAD, coronary artery disease; CHD, coronary heart disease; CHF, congestive heart failure; RCT, randomized controlled trial.

Descriptions of programs

The trials evaluated paper-based ($n = 16$), telephone-based ($n = 12$), home-visit ($n = 5$), or electronic ($n = 2$) interventions. One trial did not state its mode of delivery [19]. Twenty trials used 'usual care' comparison groups, nine used cardiac rehabilitation comparison groups, and seven used both. Twenty-six trials evaluated comprehensive interventions (i.e. focusing on a range of modifiable CV risk factors), whereas 10 were exercise-only interventions.

Paper-based programs mostly used self-contained structured handbooks/manuals to impart risk factor information and guidance on changing physical activity, diet, and psychosocial well-being. Some of these interventions incorporated telephone backup from health professionals [8,18,20,21,28,36,37]. The most frequently researched proprietary intervention [4,8,18,20,22] was 'The Heart Manual'. Telephone-based programs involved providing remote support from health professionals to patients, predominantly through regular telephone calls supplemented with ongoing telephone contact when needed. The majority of the interventions were self-identified as being individualized [2,11,12,16,26,30,38]. Only a minority focused on exercise as opposed to comprehensive counseling on risk factor reduction [2,26,30]. Electronic-based programs were both web-based [1,31] and involved comprehensive risk factor reduction support through a combination of email communication with health professionals, web-based content, and on-line discussion. Both trials incorporated remote monitoring; either of blood pressure and heart rate [1] or health behavior change [31]. Home-visit programs varied more widely; most involved home visits from nurses [24,27,29,39], although one involved consultation with a physiotherapist [23]. These were comprehensive risk factor reduction programs provided after hospital discharge with two exceptions [23,24].

The trials reviewed were generally of short duration: 27 had follow-up of less than 12 months. Relatively few measured mortality (all-cause), recurrent acute MI, or CV-related deaths. The methodological quality of the trials was moderate to low with Jadad scores ranging

Table 1 Characteristics of the interventions reviewed [1 – 39]

Type	Study	Size (*n*)	Population	Setting	Mean age (years)	Duration (months)	Content of intervention
Article/manual	Jolly *et al.* [18]	525	After AMI, coronary revascularization or CABG	UK	60.3	1.5, 2, 2.25, or 3	'Heart Manual' introduced to patients on an individual basis in hospital or on a home visit. Risk factor counseling and support provided by telephone at 3 weeks, and three other visits took place at 6 weeks and 12 weeks. Contact could be made with rehabilitation nurse, if necessary
Article/manual	Dalal *et al.* [8]; Taylor *et al.* [36]	104	Hospitalized for AMI	UK	60.6	2–2.5	Patients given Heart Manual to use over 6 weeks. Cardiac rehabilitation nurse made one home visit in 1st week after discharge followed up by telephone calls over 6 weeks (typically one call in weeks 2, 3, 4, and 6)
Article/manual	Senuzun *et al.* [28]	60	Treated for CHD in a cardiology unit and eligible for cardiac rehabilitation	Turkey	53	3	Manual/Audio Visual-based aerobic exercise program with additional telephone support with health professional around goals, monitoring of progress and feedback; supplemented by one preliminary group counseling session; offered to literate patients only
Article/manual	Vale *et al.* [37]	792	With CABG, PCI, AMI, or unstable angina, coronary angiography with planned revascularization	Australia	58	6	Manual-based program in combination with individualized telephone calls at 2 weeks, one call every 6 weeks by coach. Used COACH program to provide support for risk factor reduction, incorporating process of continuous improvement to obtain results of risk factors, education regarding targets, monitoring of progress. Patients able to contact coach at any time by telephone
Article/manual	Lewin *et al.* [21]	142	From family medical practices prescribed nitrates over the previous year; no angina for over 1 year	UK	67	6	Manual: 'Angina-Plan' with audio-based tape for relaxation; some additional face-to-face counselling at start regarding misconceptions and follow-up telephone calls at 1, 4, 8, and 12 weeks to monitor progress
Article/manual	Clark *et al.* [7]	570	Women with cardiac disease (any condition involving the heart requiring regular treatment)	USA	72	12	Home workbook (PRIDE) supplemented with weekly community-based group meetings of women with health educator and peer leader over 4 weeks to learn self-regulation skills with physical activity as focus
Article/manual	Bell [4]	149	After AMI	UK	58	3	Participants used Heart Manual, and were contacted four times (2 weeks, 4 weeks, 7 weeks, and 18/19 weeks) post-AMI around progress, risk factor change and psychosocial well-being
Article/manual	Brosseau *et al.* [5]	80	At high risk after cardiac surgery	Canada	58.5	2	Patients received home aerobic training program, which was progressive and individualized. All participants were called twice in 1st week, once in 2nd week, and once every 2 weeks until 8th week
Article/manual	Linden [22]	41	Admitted to a CCU	UK	61.5	1.5	Heart Manual provided 2–3 days post-AMI; nurse follow-up and counseling after 1, 3, and 6 weeks given to both intervention and control
Article/manual	Brown *et al.* [6]	24	Males after elective CABG with no access to cardiac rehabilitation	Canada	55	3	Written, structured program for a progressive walking program. Patients kept a log of distance walked, duration and HR before and at the end of exercise. Logs were reviewed at 6 and 12 weeks
Article/manual	Heller *et al.* [17]	450	Age <70 years with confirmed AMI admitted to hospital	Australia	59	6	Intervention included letter to GP (benefits of ASA/β-blockers) and three mail-out packages focusing on nutrition/exercise/smoking cessation; specific target for fat reduction with contract agreement; letters of encouragement with additional contracts regarding diet improvements
Article/manual	Sparks *et al.* [32]	52	Eligible for cardiac rehabilitation	USA	52	3	Individualized aerobic exercise program given as supplement to risk factor counseling as part of cardiac rehabilitation
Article/manual	Lewin *et al.* [20]	176	Aged ≤ 80 years hospitalized after AMI	UK	55	12	'Heart Manual' including education, home-based exercise program, and audio tape-based stress management. Audiotape also provided to spouses; additional support offered to both groups 1, 3, and 6 weeks post-AMI through telephone or home visit
Article/manual	Taylor *et al.* [34]	210	Men aged ≤ 70 years hospitalized for AMI	USA	52	6	Individualized prescription for aerobic exercise from trained nurse
Article/manual	DeBusk *et al.* [9]	127	Men aged ≤ 70 years discharged with AMI	USA	53	6	Written home-based exercise program; containing information on benefits of exercise, exercises, recognizing worsening angina and changes in health; supplemented with initial specialist consultation and remove monitoring of intensity and health status
Article/manual	Miller *et al.* [25]	198	Males hospitalized for AMI	USA	52.9	2 or 5.5–6.5	Stationary cycling based on 70–85% of peak HR. ECG transmitted to nurse. Patients recorded exercise logs that were mailed to nurse every 2 weeks
Electronic	Zutz *et al.* [1]	15	On a waiting list for cardiac rehabilitation living within 60 km of site. No specific disease conditions mentioned	Canada	58	3	Intervention delivered through Web; included HR/BP monitoring Online intake forms (medical, risk factor, and lifestyle forms), one-on-one chat sessions at 12 weeks with RN case manager, exercise specialist, and dietician; weekly slide-based exercise presentations. Expert group chat sessions
Electronic	Southard *et al.* [31]	104	CHD or CHD and heart failure identified by hospital or primary care records	USA	62	6	Internet-based intervention with education modules, e-mail communication with case manager and dietician, optional on-line discussion group and entry of health behavior data to monitor self-progress

Table 1 (*continued*)

Type	Study	Size (*n*)	Population	Setting	Mean age (years)	Duration (months)	Content of intervention
Telephone	Hanssen *et al.* [16]	288	Hospitalized for confirmed AMI	Norway	60	6	Individualized telephone support (weekly for first 4 weeks, then 6, 8, and 12 weeks; last call at 25th week) to support patient coping about lifestyle change and risk reduction; incorporating goal setting, emotional support, information on risk reduction and emotional support
Telephone	Mittag *et al.* [26]	343	Confirmed AMI, CABG or PCI eligible for CR	Germany	59	12	Individualized patient support by nurse-provided telephone calls provided monthly over 1 year supplemented with manual; both relating to risk factor reduction and cardiac ailments; based on cognitive theory
Telephone	Wu *et al.* [38]	54	Males after CABG surgery	Taiwan	61	3	Exercise program individualized based on stress test. Patients asked to keep exercise log. Program updated by office or telephone consultation every 2 weeks by rehabilitation nurses
Telephone	Arthur *et al.* [2]; Smith *et al.* [30]	242	After CABG surgery	Canada	63	6	Individualized exercise program based on ACSM guidelines and VO_{2max} test. Patients asked to keep exercise log, and were telephoned every 2 weeks by exercise specialist
Telephone	Gallagher *et al.* [12]	196	Women hospitalized for: AMI, CABG, Angina, PCI	Australia	67	1.5	Individualized nurse-delivered counseling (1, 2, 3, and 6 weeks postdischarge) to promote self-management and psychosocial adjustment; included goal setting for risk factor reduction and benefits of rehabilitation; aimed to improve control, self-efficacy and increase knowledge
Telephone	Frasure-Smith *et al.* [11]	1376	Admitted to hospitals with AMI not related to coronary procedures	Canada	59	12	Individualized contact by experienced nurses monthly for 1 year; patients responded to questionnaire (anxiety, depression, impairment scale); if score low or readmitted, project RN provided additional home visits to evaluate patient's needs
Telephone	Taylor *et al.* [35]	585	Admitted to hospital aged $\leq$ 70 years with confirmed AMI	USA	57	6 min	Initial screening and risk factor reduction counseling in hospital, followed by provision of work book on range of risk factors, relaxation audiotape for stress management and supplementary nurse assessment and counseling by telephone
Telephone	Fletcher *et al.* [10]	88	Males with CAD aged $\leq$ 73 years with physical impairment	USA	62	6	Participants provided with wheelchair ramp and rollers and telephone ECG. Instructed to exercise 5days/week for a total of 100 min. Also received diet instruction
Telephone	Gortner and Jenkins [15]	156	Patients (married) who had undergone cardiac surgery (bypass and valve)	USA	58	1	Telephone follow-up for 4 weeks around recovery, risk factor reduction, physical activity coaching and spousal concerns; initial counseling around family coping and conflict resolution
Telephone	Beckie [3]	74	Scheduled for CABG surgery after hospital discharge	Canada	NR	1.5	Telephone education and support program after CABG involving discussion between specialist cardiac rehabilitation nurse and patient; four to six calls after 1 week postdischarge during the following 6 weeks
Telephone	Gortner *et al.* [14]	67	Patients (married) who had undergone cardiac surgery (bypass and valve)	USA	62	1	Telephone follow-up for 4 weeks around recovery, risk factor reduction, physical activity coaching and spousal concerns; initial counseling around family coping and conflict resolution
Telephone	Garding *et al.* [13]	51	Confirmed first time AMI admitted to hospital	Canada	NR	2	Telephone-base education done by two cardiac rehab nurses and one non-specialized nurse (mean = 3 calls per patient) to address individual learning needs and education around risk factors
Home-visit	Sinclair *et al.* [29]	324	Discharged from hospital with AMI and aged $\geq$ 65 years	UK	73	2	At least two home visits (1–2 and 6–8 weeks postdischarge) from trained support staff nurse to encourage patients around compliance, support for risk factor reduction, advice on stress, exercise, smoking cessation and diet, increase social interaction. Visits supplemented by telephone support and manual
Home-visit	Robertson *et al.* [27]	68	Discharged from hospital with AMI	Canada	NR	1	Weekly visit for 4 weeks from critical care nurse providing support and education around risk factor reduction
Home-visit	Marchionni *et al.* [23]	270	Referred to CR by intensive care units after AMI and aged >45 years	Italy	NR	14	Supervised instructions in hospital around exercise with individualized exercise prescription followed by weekly physical therapist visits to adjust exercise prescription
Home-visit	Young [39]	146	Elevated cardiac markers for AMI	Canada	68	2	Disease management program containing education, follow up and support for risk factor reduction received a minimum of 6 home care visits from cardiac nurse
Home visit	McHugh *et al.* [24]	98	On waiting list for CABG surgery	UK	62	8	Educational intervention of 1–2 h provided alternately by specialist nurse/community nurse team to reduce risk factors, improve knowledge and reduce distress using motivational techniques provided to patients waiting for CABG surgery; utilized guidelines
Other	Kugler *et al.* [19]	52	Males with their 1st AMI and entered the CR 7–14 weeks post-MI	USA	NR	2	Mode of delivery unclear. Both Intensive and less intensive home-program evaluated

ACSM, American College of Sports Medicine; AMI, acute myocardial infarction; ASA, Aspirin; BP, blood pressure; CABG, coronary artery bypass graft; CAD, Coronary artery disease; CCU, coronary care unit; CHD, coronary heart disease; CR, cardiac rehabilitation; GP, general practitioner; HR, heart rate; NR, not recorded; PCI, percutaneous coronary intervention; RN, registered nurse.

from 1 to 3 (Table 2). Most trials (24 of 36) did not clearly describe allocation concealment and eight did not adequately describe the services provided to the comparator arm.

Although two trials were restricted to women only, the mean proportion of women in the trials was 24%. Twenty-three trials had no age-based exclusion criteria, 11 trials had upper age limit criteria (at a mean age of 73 years), and two trials had criteria intended to exclude patients who were not older adults [7,23]. Most trials did not include any breakdown of the ethnic status of participants (71% of trials). In those that did record this, representation of participants categorized as being from ethnic minorities was 19% (± 18.9%, range: 3–58%).

Table 2 Methodological quality of trials

Study	Jaded score	Described as randomized	Method of randomization described and appropriate	Allocation concealment	Adequate description of usual care
Jolly *et al.* [18]	3	Yes	Yes	Adequate	Yes
Dalal *et al.* [8]; Taylor *et al.* [36]	3	Yes	Yes	Adequate	Yes
Senuzun *et al.* [28]	1	Yes	Unclear	Unclear	No
Vale *et al.* [37]	3	Yes	Yes	Adequate	Yes
Lewin *et al.* [21]	2	Yes	No	Unclear	Yes
Clark *et al.* [7]	3	Yes	Yes	Unclear	Yes
Bell [4]	3	Yes	Yes	Unclear	Yes
Brosseau [5]	2	Yes	No	Unclear	Yes
Linden [22]	2	Yes	No	Inadequate	Yes
Brown *et al.* [6]	1	Yes	No	Unclear	Yes
Heller *et al.* [17]	1	Yes	No	Unclear	No
Sparks *et al.* [32]	1	Yes	Unclear	Unclear	Yes
Lewin *et al.* [20]	2	Yes	Unclear	Adequate	Yes
Taylor *et al.* [34]	2	Yes	Unclear	Unclear	Yes
DeBusk *et al.* [9]	2	Yes	Unclear	Unclear	Yes
Miller *et al.* [25]	1	Yes	No	Unclear	Yes
Zutz *et al.* [1]	2	Yes	No	Unclear	No
Southard *et al.* [31]	3	Yes	Yes	Unclear	No
Hanssen *et al.* [16]	3	Yes	Yes	Unclear	Yes
Mittag *et al.* [26]	3	Yes	Yes	Unclear	Yes
Wu *et al.* [38]	1	Yes	No	Unclear	No
Arthur *et al.* [2]; Smith *et al.* [30]	2	Yes	No	Unclear	Yes
Gallagher *et al.* [12]	2	Yes	No	Unclear	Yes
Frasure Smith *et al.* [11]	3	Yes	Yes	Adequate	Yes
Taylor *et al.* [35]	2	Yes	Unclear	Unclear	No
Fletcher *et al.* [10]	2	Yes	No	Unclear	Yes
Gortner and Jenkins [15]	2	Yes	No	Unclear	Yes
Beckie [3]	1	Yes	Unclear	Unclear	Yes
Gortner *et al.* [14]	1	Yes	Unclear	Unclear	No
Garding *et al.* [13]	1	Yes	No	Unclear	No
Sinclair *et al.* [29]	3	Yes	Yes	Adequate	Yes
Robertston *et al.* [27]	3	Yes	Yes	Adequate	Yes
Marchionni *et al.* [23]	1	Yes	No	Adequate	Yes
Young [39]	3	Yes	Yes	Adequate	Yes
McHugh *et al.* [24]	2	Yes	Unclear	Unclear	Yes
Kugler *et al.* [19]	2	Yes	No	Unclear	No

The effectiveness of interventions was compared against usual care and/or provider-based cardiac rehabilitation programs. Usual care was defined as normal health care and/or risk factor management at the time the trial was undertaken without supplementary secondary prevention intervention. Cardiac rehabilitation was defined as dedicated secondary prevention programs provided by health professionals in an acute (hospital) or community care provider setting.

All-cause mortality

Home-based intervention compared with usual care

Home-based intervention [4,10,11,37] (four trials, 2510 patients) did not improve mortality over usual care (RR: 1.22, 95% CI: 0.83–1.80). There was no evidence of significant statistical heterogeneity between the trials ($P = 0.85$, $I^2 = 0\%$). However, there was only 17% power to detect a 20% relative risk reduction (RRR), as this analysis is based on only 100 deaths in 2510 patients.

Home-based intervention compared with cardiac rehabilitation

The relative effect on all-cause mortality was similar between home-based and cardiac rehabilitation programs [4,8,18,29,30,39] (six trials, RR: 1.08, 95% CI: 0.73–1.60) and there was no evidence of statistical heterogeneity between trials ($P = 0.80$, $I^2 = 0\%$). However, there was only 18% power to detect a 20% RRR, as this analysis is based on only 97 deaths in 1548 patients.

Cardiovascular events

Home-based intervention compared with usual care

Home-based intervention [11,17,22,25,31] (five trials, 2078 patients) reduced risk of CV events (excluding stroke, transient ischemic attack, and heart failure) by 9%; however, this did not reach statistical significance (RR: 0.91, 95% CI: 0.78–1.05). There was no evidence of significant statistical heterogeneity between the trials ($P < 0.47$, $I^2 = 0\%$). However, there was only a 73% power to detect a 20% RRR, as this analysis is based on only 447 deaths in 2078 patients.

Home-based intervention compared with cardiac rehabilitation

Although the pooled data suggested that there were no significant differences with home-based interventions [18,25,39] (three trials, 778 patients) compared with cardiac rehabilitation in reducing CV events (RR: 0.90, 95% CI: 0.33–2.43), there was substantial statistical heterogeneity ($P < 0.0001$, $I^2 = 89.7\%$). One trial [39]

reported a statistically significant benefit in the home-based arm, but it differed from the two negative trials as it involved six home visits to patients from a cardiac nurse and was supplemented by referral to specialist care. This specialist care and more intensive support may have contributed to its favorable results.

Quality of life

Only one trial identified a significant improvement in quality of life [2]; this trial compared a home-based program with cardiac rehabilitation.

Home-based intervention compared with usual care

The summative weighted mean difference in quality of life for the five trials reporting quality of life [4,16,20,24,31] (644 patients) was 0.23 (95% CI: 0.02–0.45), suggesting that quality of life was improved in those patients exposed to the home-based intervention. Significant improvements were particularly evident in short-term effects (three trials, 391 patients, follow-up < 12 months, SMD: 0.37, 95% CI: 0.17–0.57), but not long-term effects (two trials 253 patients, ≥ 12 months, SMD: 0, −2.25 to 0.25).

Home-based intervention compared with cardiac rehabilitation

The summative mean difference for the five trials reporting quality of life [2,4,7,8,30] (1070 patients) was 0.13 (95% CI: −0.03 to 0.30) using data for short-term and long-term outcomes (< 12 months and ≥ 12 months). This represents a nonsignificant quality-of-life improvement. Effects were significant in the short term

Table 3 Effects on risk factors in the interventions reviewed (compared with usual care)

Risk factor	Home versus usual care	Heterogeneity	Possible explanation of heterogeneity
Systolic blood pressure (rest)[a]	−4.36 mmHg ($n=1095$; 95% CI: −6.50 to −2.22) [1,4–6,10,24,28,37]	$P=0.53$ $I^2=0\%$	NA
Smoking cessation[a]	DP: 14% ($n=1660$; 95% CI: 0.02–0.26) [4,16,17,22,24,37]	$P<0.000001$ $I^2=84.0\%$	Intervention intensity and length
Total cholesterol[a] (≤ 12 months)	SMD: −0.33 ($n=995$; 95% CI: −0.57 to −0.08) five trials [1,10,24,28,37]	$P=0.17$ $I^2=37.4\%$	Intervention intensity
BMI	WMD: −0.46 ($n=1063$; 0.66 to −0.29) [1,4,24,28,31]	$P=0.51$ $I^2=0\%$	NA
Depression[a]	SMD: −0.33 ($n=2332$; 95% CI: −0.59 to −0.07) [4,11,20,21,37]	$P<0.0001$ $I^2=85.7\%$	Population and measurement differences
METS achieved on testing	WMD: 0.96 METS ($n=197$; 95% CI: −0.24 to 2.16) [1,5,25,28]	$P=0.0009$ $I^2=81.9\%$	Program length and exercise type

CI, confidence interval; DP, difference in proportion; METS, metabolic equivalents; NA, not applicable; SMD, standardized mean difference; WMD, weighted mean difference. [a]Significant improvement in favor of home-based programs.

Table 4 Effects on risk factors in the interventions reviewed (compared with cardiac rehabilitation)

Risk factor	Home versus CR	Heterogeneity	Possible explanation of heterogeneity
Systolic blood pressure (rest)	−4.43 mmHg ($n=860$; 95% CI: −10.23 to 1.38) [4,8,18,26]	$P=0.01$ $I^2=72.4\%$	Intervention type and length
Smoking cessation	DP: 5% ($n=942$; 95% CI: −0.04 to 0.14) [4,8,18,26]	$P=0.05$ $I^2=61.4\%$	Unclear
Total cholesterol	SMD: −0.11 ($n=966$; 95% CI: −0.11 to 0.32) [4,8,18,26]	$P=0.07$ $I^2=58.2\%$	Findings
BMI	WMD: −0.30 ($n=800$; 95% CI: −0.73 to 0.13) [4,8,18,30]	$P=0.40$ $I^2=0\%$	NA
Depression	SMD: 0.06 ($n=1576$; 95% CI: −0.15 to 0.04) [2,4,7,8,18,26]	$P=0.75$ $I^2=0\%$	NA
WHR	WMD: −0.02 ($n=446$; 95% CI: −0.04 to 0.00) [2,4,30]	$P=0.11$ $I^2=55\%$	Unclear
METS	WMD: 0.23 ($n=596$; 95% CI: −0.34 to 0.81) [2,8,25,30]	$P=0.01$ $I^2=72.9\%$	Findings

CI, confidence interval; CR, cardiac rehabilitation; DP, difference in proprotion; METS, metabolic equivalents; NA, not applicable; SMD, standardized mean difference; WHR, waist hip ratio; WMD, weighted mean difference.

Table 5 Costs for interventions (where provided)

Study	Cost saving (Y/N)	Data-led conclusion (Y/N)	Cost per patient of home intervention (inflationary adjustment)	Amount of costs saved (total cost of reduced hospitalizations minus cost of home program/per patient)
Jolly *et al.* [18]	N	Y	$330 ($336)	NR
DeBusk *et al.* [9]	Y	NR	$328 ($592)	NR
Lewin *et al.* [20]	Y	N	$50 ($68)	NR
Southard *et al.* [31]	Y	Y	$453 ($495)	$965 per patient
Mittag *et al.* [26]	Y	N	NR	NR
Taylor *et al.* [33]	Neutral	Y	NR	NR
Robertson *et al.* [27]	Y	Y	$312 ($356)	$178.62 per patient
Marchionni *et al.* [23]	Y	Y	$179 ($196)	NR

NR, not recorded; Y/N, yes/no.

(two trials, 346 patients, SMD: 0.28, 95% CI: 0.06–0.50), but this difference did not persist in the long term (SMD: 0.06, 95% CI: −0.13 to 0.25).

Coronary heart disease risk factors

Significant benefits of home-based programs over usual care were evident in resting systolic blood pressure, cholesterol levels, smoking cessation rates, and depression scores (Table 3). The effects on other risk factors were positive, but nonsignificant. No differences in the effect on risk factors were evident compared with cardiac rehabilitation (Table 4).

Costs

Eight trials provided costs (Table 5) [9,18,20,23,26,27,31,36]; six reported that interventions were 'cost saving' [9,20,23,26,27,31], though only three of these studies presented data to support this conclusion [23,27,31]. The costs of home-based interventions were modest and averaged around US$300 for each patient adjusting for inflation.

Discussion

Home-based interventions for the secondary prevention of CHD showed a number of benefits on the quality of life and atherosclerotic risk factors compared with usual care. Individually, reductions in risk factors were moderate, but, in combination, would lead to clinically important reductions in risk [56,57].

Home-based programs showed a 14% superior smoking cessation rate than usual care. Smoking cessation in patients with CV disease lowers mortality risk by around 46% in men and women [58]. The home-based interventions also reduced total cholesterol. Although differences in recording in the trials prevented the synthesis of these data beyond the calculation of standardized mean change, changes of 1 mmol/l total cholesterol in patients with CHD represent a high relative risk reduction and are associated with the reduced risk of cardiac death and nonfatal MI by 18–28% [59]. The 4 mmHg reduction in systolic blood pressure found in home-based programs should reduce subsequent CV events by up to 20% [59]. As around half of all patients with CHD are hypertensive [60], these reductions are clinically important. Similarly, reductions in depression were small, but significant because depression after MI is common and doubles the risk of adverse events [61].

On account of the small number of trials and their heterogeneous nature there was inadequate trial data to establish whether home-based secondary prevention programs are as effective as traditional hospital-based programs. Future trials should be carried out to determine this.

This review is limited by the small number and relatively short-term follow-up of the trials, and low mortality and morbidity rates. Thus, although we showed beneficial changes in risk factors, larger studies with longer follow-up are required to confirm the improvements in the major clinical endpoints because it takes around 2 years for mortality benefits from secondary prevention programs to emerge [41]. In addition, participants in the trials were younger and, compared with clinical populations, were likely to be more motivated and have fewer comorbidities [41]. Furthermore, despite contact with original trial authors, we were unable to comprehensively define the care provided to the control arms. As with most systematic reviews, we confined our search to published trials in English. Although it was not feasible to statistically evaluate the possibility of publication bias because of the relatively small number of trials, published studies may be a subset of all the trials conducted on this topic. Issues remained with regard to the comparability of trials, and statistical heterogeneity was evident in many of the syntheses performed. Heterogeneity in meta-analyses can be caused by sampling error, known or unknown differences in intervention, and population or methodological differences between the trials [48,62,63]. For example, this review included interventions that were defined as either 'secondary prevention' or 'cardiac rehabilitation' and/or differed in potentially salient characteristics such as mode of provision, duration, and health care personnel involved. However, because of the small number of trials, it was not possible to examine the effects of these factors or to explain the differences in

outcomes. Future trials should attempt to examine the influence of such factors. These trials should be adequately described to allow for rigorous subanalyses or sensitivity analysis.

Although most patients with CHD do not achieve lifestyle, risk factor, and therapeutic targets for secondary prevention [64], the low likelihood of harm associated with secondary prevention interventions and the relatively low costs involved, home-based secondary prevention programs are a viable and effective method of secondary prevention that may circumvent some of the common problems associated with patient access for some populations. Given the marked reductions in participation associated with increasing distance of residency from a cardiac rehabilitation centre and the inability to compare home-based with hospital-based programs, home-based programs offer a promise for individuals less likely to access hospital-based cardiac rehabilitation. Until further high-quality evidence accrues, the relative effectiveness of home-based programs over hospital-based programs remains uncertain. Patients who are frail, clinically complex, or with multiple comorbidities that are often absent from trials of secondary prevention interventions, should continue to receive close supervision [41].

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References

1 Zutz A, Andrew I, Joanna B, Scott AL. Utilization of the internet to deliver cardiac rehabilitation at a distance: a pilot study. *Telemed J E Health* 2007; **13**:323–330.
2 Arthur HM, Smith KM, Kodis J, McKelvie R. A controlled trial of hospital versus home based exercise in cardiac patients. *Med Sci Sports Exerc* 2002; **34**:1544–1550.
3 Beckie T. A supportive-educative telephone program: impact on knowledge and anxiety after coronary artery bypass graft surgery. *Heart Lung* 1989; **18**:46–55.
4 Bell J. A comparison of a multi-disciplinary home based cardiac rehabilitation programme with comprehensive conventional rehabilitation in post-myocardial infarction patients. University of London; 1998.
5 Brosseau R. Safety and feasibility of a self-monitored, home-based phase II exercise program for high risk patients after cardiac surgery. *Can J Cardiol* 1995; **11**:675–685.
6 Brown CA, Wolfe LA, Hains S, Pym J, Parker JO. Early low intensity home exercise after coronary artery bypass graft surgery. *J Cardiopulm Rehabil Prev* 1994; **14**:238–245.
7 Clark NM, Janz NK, Dodge J A, Schork MA, Fingerlin TE, Wheeler JRC, *et al.* Changes in functional health status of older women with heart disease: Evaluation of a program based on self-regulation. *J Gerontol B Psycho Sci Soc Sci* 2000; **55B**:S117–S126.
8 Dalal HM, Evans PH, Campbell JL, Taylor RS, Watt A, Read KLQ, *et al.* Home-based versus hospital-based rehabilitation after myocardial infarction: a randomized trial with preference arms Cornwall Heart Attack Rehabilitation Management Study (CHARMS). *Int J Cardiol* 2007; **192**:202–211.
9 DeBusk RF, Haskell WL, Miller NH, Miller NH, Berra K, Barr Taylor C, *et al.* Medically directed at-home rehabilitation soon after clinically uncomplicated acute myocardial infarction: a new model for patient care. *Am J Cardiol* 1985; **55**:251–257.
10 Fletcher BJ, Dunbar SB, Felner JM, Jensen BE, Almon L, Cotsonis G, *et al.* Exercise testing and training in physically disabled men with clinical evidence of coronary artery disease. *Am J Cardiol* 1994; **73**:170–174.
11 Frasure-Smith N, Lesperance F, Prince R, Verrier P, Garber RA, Juneau M, *et al.* Randomized trial of home-based psychosocial nursing intervention for patients recovering from myocardial infarction. *Lancet* 1997; **350**:473–479.
12 Gallagher R, McKinley S, Dracup K. Effects of a telephone counseling intervention on psychosocial adjustment in women following a cardiac event. *Heart Lung* 2003; **32**:79–87.
13 Garding BS, Kerr JC, Bay K. Effectiveness of a program of information and support for myocardial infarction patients recovering at home. *Heart Lung* 1988; **17**:355–362.
14 Gortner SR, Gilliss CL, Shinn JA, Sparacino PA, Rankin S, Leavitt M, *et al.* Improving recovery following cardiac surgery: a randomized clinical trial. *J Adv Nurs* 1988; **13**:649–661.
15 Gortner SR, Jenkins LS. Self-efficacy and activity level following cardiac surgery. *J Adv Nurs* 1990; **15**:1132–1138.
16 Hanssen TA, Nordrehaug JE, Eide GE, Hanestad BR. Improving outcomes after myocardial infarction: a randomized controlled trial evaluating effects of a telephone follow-up intervention. *Eur J Cardiovasc Prev Rehabil* 2007; **14**:429–437.
17 Heller RF, Knapp JC, Valenti LA, Dobson AJ. Secondary prevention after acute myocardial infarction. *Am J Cardiol* 1993; **72**:759–762.
18 Jolly K, Taylor R, Lip GYH, Greenfield S, Raftery J, Mant J, *et al.* The Birmingham Rehabilitation Uptake Maximisation Study (BRUM). Home-based compared with hospital-based cardiac rehabilitation in a multi-ethnic population: cost-effectiveness and patient adherence. *Health Technol Assess (Winchester, England)* 2007; **11**:1–118.
19 Kugler J, Dimsdale JE, Hartley LH, Sherwood J. Hospital supervised versus home exercise in cardiac rehabilitation: effects on aerobic fitness, anxiety, and depression. *Arch Phys Med Rehabil* 1990; **71**:322–325.
20 Lewin B, Robertson IH, Cay EL, Irving JB, Campbell M. Effects of self-help post myocardial infarction rehabilitation on psychological adjustment and use of health services. *Lancet* 1992; **339**:1036–1040.
21 Lewin RJP, Furze G, Robinson J, Griffiths K, Wiseman S, Pye M, *et al.* A randomized controlled trial of a self-management plan for patients with newly diagnosed angina. *B J Gen Pract* 2002; **52**:194–201.
22 Linden B. Evaluation of a home-based rehabilitation programme for patients recovering from acute myocardial infarction. *Intensive Crit Care Nurs* 1995; **11**:10–19.
23 Marchionni N, Fattirolli F, Fumagalli S, Oldridge N, Del Lungo F, Morosi L, *et al.* Improved exercise tolerance and quality of life with cardiac rehabilitation of older patients after myocardial infarction. Results of a randomized, controlled trial. *Circulation* 2003; **107**:2201–2206.
24 McHugh F, Lindsay G, Hanlon P, Hutton I, Brown MR, Morrison C. Nurse led shared care for patients on the waiting list for coronary artery bypass surgery: a randomised controlled trial. *Heart* 2001; **86**:317–323.

25 Miller NH, Haskell WL, Berra K, DeBusk RF. Home versus group exercise training for increasing functional capacity after myocardial infarction. *Circulation* 1984; **70**:645–649.

26 Mittag O, China C, Hoberg E, Juers E, Kolenda KD, Richardt G, *et al*. Outcomes of cardiac rehabilitation with versus without a follow-up intervention rendered by telephone (Luebeck follow-up trial): overall and gender-specific effects. *Int J Rehabil Res* 2006; **29**:295–302.

27 Robertson K, Kayhko K, Kekki P. A supportive-education home follow-up programme for post MI patients. *J Community Nurs* 2003; **17**:4.

28 Senuzun F, Fadiloglu C, Burke LE, Payzin S. Effects of home-based cardiac exercise program on the exercise tolerance, serum lipid values and self-efficacy of coronary patients. *Eur J Cardiol Prev Rehabil* 2006; **13**:640–645.

29 Sinclair A, Conroy S, Davies P. Post-discharge home-based support for older cardiac patients: a randomised controlled trial. *Age Ageing* 2005; **34**:338–343.

30 Smith KM, Arthur HM, McKelvie RS, Kodis J. Differences in sustainability of exercise and health-related quality of life outcomes following home or hospital-based cardiac rehabilitation. *Eur J Cardiovasc Prev Rehabil* 2004; **11**:313–319.

31 Southard B, Southard D, Nuckolls CW. Clinical trial of an Internet-based case management system for secondary prevention of heart disease. *J Cardiopulm Rehabil Prev* 2003; **23**:341–348.

32 Sparks KE, Shaw DK, Eddy D, Hanigosky P, Vantrese J. Alternatives for cardiac rehabilitation patients unable to return to a hospital-based program. *Heart Lung* 1993; **22**:298–303.

33 Taylor CB, Houston-Miller N, Ahn DK, Haskell W, DeBusk RF. The effects of exercise training programs on psychosocial improvement in uncomplicated postmyocardial infarction patients. *J Pshychosom Res* 2007; **62**:411–418.

34 Taylor CB, Houston-Miller N, Haskell W, DeBusk RF. Smoking cessation after acute myocardial infarction: the effects of exercise training. *Addict Behav* 1988; **13**:331.

35 Taylor CB, Miller NH, Smith PM, DeBusk RF. The effect of a home-based, case managed, multifactorial risk-reduction program on reducing psychological distress in patients with cardiovascular disease. *J Cardiopulm Rehabil Prev* 1997; **17**:157–162.

36 Taylor RS, Watt A, Dalal HM, Evans PH, Campbell JL, Read KL, *et al*. Home-based cardiac rehabilitation versus hospital-based rehabilitation: a cost effectiveness analysis. *Int J Cardiol* 2007; **119**:196–201.

37 Vale MJ, Jelinek MV, Best JD, Dart A, Grigg LE, Hare DLE, *et al*.; for the Coach Study Group. Coaching patients On Achieving Cardiovascular Health (COACH): a multicenter randomized trial in patients with coronary heart disease. *Arch Int Med* 2003; **163**:2775–2783.

38 Wu S, Lin YW, Chen CL, Tsai SW. Cardiac rehabilitation versus home exercise after coronary artery bypass graft surgery: a comparison of heart rate recovery. *Am J Phys Med Rehabil* 2006; **85**:711–717.

39 Young W. Evaluation of a community-based inner-city disease management program for postmyocardial infarction patients: a randomized controlled trial. *CMAJ* 2003; **169**:905–910.

40 Balady GJ, Ades PA, Comoss P, Limacher M, Pina IL, Southard D, *et al*. Core components of cardiac rehabilitation/secondary prevention programs. *Circulation* 2000; **102**:1069–1073.

41 Clark AM, Hartling L, Vandermeer B, McAlister FA. Secondary prevention program for patients with coronary artery disease: a meta-analysis of randomized control trials. *Ann Intern Med* 2005; **143**:659–672.

42 Jackson L, Leclerc J, Erskine Y, Linden W. Getting the most out of cardiac rehabilitation: a review of referral and adherence predictors. *Heart* 2005; **91**:10–14.

43 Cooper AF, Jackson G, Weinman J, Horne R. Factors associated with cardiac rehabilitation attendance: a systematic review of the literature. *Clin Rehabil* 2002; **16**:541–552.

44 Dafoe W, Arthur H, Stokes H, Morrin L, Beaton L. Universal access: but when? Treating the right patient at the right time: access to cardiac rehabilitation. *Can J Cardiol* 2006; **22**:905–911.

45 Leon AS, Franklin BA, Costa F, Balady GJ, Berra KA, Stewart KJ. Cardiac rehabilitation and secondary prevention of coronary heart disease: an American Heart Association Scientific Statement From the Council on Clinical Cardiology (Subcommittee on Exercise, Cardiac Rehabilitation, and Prevention) and the Council on Nutrition, Physical Activity, and Metabolism (Subcommittee on Physical Activity), in Collaboration With the American Association of Cardiovascular and Pulmonary Rehabilitation. *Circulation* 2005; **111**:369–376.

46 Clark AM, Hartling L, Vandermeer B, Lissel S, McAlister FA. The merits of shorter, generalist secondary prevention programs based in primary care: results from a meta regression. *Eur J Cardiovasc Prev Rehabil* 2007; **14**:538–546.

47 Wenger NK. Current status of cardiac rehabilitation. *J Am Coll Cardiol* 2008; **51**:1619–1631.

48 Higgins J, Thompson S, Deeks J, Altman D. Measuring inconsistency in meta analysis. *BMJ* 2003; **327**:557–560.

49 Shaw K, Gennat H, O'Rourke P, Del Mar C. Exercise for overweight and obesity (Review). *Cochrane Database Syst Rev* 2007; **4**:(CD003817). doi: 10.1.002/14651858.CD.003817.pub3.

50 Jolliffe JA, Rees K, Taylor RS, Thompson DR, Oldridge N, Ebrahim S. Exercise based rehabilitation for coronary heart disease (a review). Cochrane Libr 2001; Issue 4. Art. No.: CD001800. doi: 10.1002/14651858.CD001800.

51 Ashworth N, Chad K, Harrison E, Reeder B, Marshall S. Home versus center based physical activity programs in older adults. Cochrane Database Syst Rev 2005; Issue 1. Art No: CD004017. doi: 10.1002/14651858.CD004017.pub2.

52 Dusseldorp E, van Elderen T, Maes S, Meulman J, Kraajj V. A meta-analysis of psychoeducational programs for coronary heart disease patients. *Health Psychol* 1999; **18**:506–519.

53 Clark AM, Hartling L, Vandermeer B, McAlister FA. *Randomized trials of secondary prevention programs in coronary artery disease: a systematic review*. Baltimore, Maryland: Agency for Health Care Research and Quality, US Department of Health; 2005.

54 Jolly K, Taylor RS, Lip GYH, Stevens A. Home-based cardiac rehabilitation compared with centre-based rehabilitation and usual care: a systematic review and meta-analysis. *Int J Cardiol* 2006; **111**:343–351.

55 Hillsdon M, Foster C, Thorogood M. Interventions for promoting physical activity. Cochrane Database Syst Rev 2005; Issue 2 Art No: CD003180. doi: 10.1002/14651858.CD003180.pub2.

56 Khot U, Khot M, Bajzer C, Sapp SK, Ohman EM, Brener SJ, *et al*. Prevalence of conventional risk factors in patients with coronary heart disease. *JAMA* 2003; **290**:898–904.

57 Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *Lancet* 2004; **364**:937–952.

58 Wilson K, Gibson N, Willan A, Cook D. Effect of smoking cessation on mortality after myocardial infarction. *Arch Int Med* 2000; **160**:939–944.

59 De Lorgeril M, Salen P, Martin J, Monjaud I, Delaye J, Mamelle N. Mediterranean Diet, Traditional Risk Factors, and the Rate of Cardiovascular Complications After Myocardial Infarction: final Report of the Lyon Diet Heart Study. *Circulation* 1999; **99**:779–785.

60 Frazier C, Shah S, Armstrong PW, Bhapkar MV, McGuire DK, Sadowski Z, *et al*. for the SYMPHONY and the Second SYMPHONY Investigators. Prevalence and management of hypertension in acute coronary syndrome patients varies by sex: observations from the Sibrafiban versus aspirin to Yield Maximum Protection from ischemic Heart events postacute Coronary Syndromes (SYMPHONY) randomized clinical trials. *Am Heart J* 2005; **150**:1260–1267.

61 Van Melle J, de Jonge P, Spijkerman T, Tijssen JGP, Ormel J, van Veldhuisen DJ, *et al*. Prognostic Association of Depression Following Myocardial Infarction with Mortality and Cardiovascular Events: a Meta-analysis. *Psychosom Med* 2004; **66**:814–822.

62 Thompson SG. Why and how sources of heterogeneity should be investigated. In: Egger M, Davey Smith G, Altman DG, editors. *Systematic review in health care: meta analysis in context*. London: BMJ Books; 2001. pp. 157–175.

63 Sutton A, Abrams KR, Jones DR, Sheldon TA, Song F. *Methods for meta-analysis in medical research*. New York: John Wiley; 2000.

64 Kotseva K, Wood D, De Backer G, De Bacquer D, Pyorala K, Keil U, *et al*. EUROASPIRE III: a survey on the lifestyle, risk factors and use of cardioprotective drug therapies in coronary patients from 22 European countries. *Eur J Cardiovasc Prev Rehabil* 2009; **6**:121–137.