Interventions to achieve long-term weight loss in obese older people

A systematic review and meta-analysis

Key words: Obesity, older, weight loss, meta-analysis

Running title: Weight loss in obese older adults

Conflicts of interest: None to declare

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Abstract

Purpose – The prevalence of obesity is increasing rapidly in older adults. Information is required about what interventions are effective in reducing obesity and influencing health outcomes in this age group.

Design – Systematic review and meta-analysis

Data sources – Thirteen databases were searched, earliest date 1966 to December 2008, including Medline, CINAHL, PsycInfo, the Cochrane database and EMBASE.

Study selection – We included studies with participants' mean age≥ 60y, mean body mass index≥ 30 kg/m ^{2}, with outcomes at a minimum of 1 year. Data were independently extracted by two reviewers and differences resolved by consensus.

Data extraction – Nine eligible trials were included. Study interventions targeted diet, physical activity and mixed approaches. Populations included patients with coronary artery disease, diabetes mellitus and osteoarthritis.

Results - Meta-analysis (7 studies) demonstrated a modest but significant weight loss of 3.0 kg (95% CI 5.1 to 0.9) at 1 year. Total cholesterol (4 studies) did not show a significant change; -0.36 mmol/L (95% CI -0.75 to 0.04). There was no significant change in HDL, LDL or triglycerides. In one study recurrence of hypertension or cardiovascular events were significantly reduced (hazard ratio 0.65, 95% CI 0.50 to 0.85). Six minute walk test did not change significantly in one study. Health related quality of life significantly improved in one study but did not improve in a second study.

Conclusions - Although modest weight reductions were observed, there is a lack of high quality evidence to support the efficacy of weight loss programmes in older people.

Key Points:

- Obesity levels are rising in the over 60s.
- Weight loss interventions in older people has not been well studied.
- Weight loss programmes have a modest effect in those aged 60 and over.
- There is a dearth of high-quality evidence for obesity interventions in this age group.
- Further trial evidence about effects of intentional weight loss is needed, particularly for older old people, examining effects on markers of vascular risk, quality of life, physical function, cardiovascular events and death.

Introduction

Obesity is recognised as a major health problem amongst children, younger adults and middle-aged adults in the developed world and increasingly in rapidly industrialising countries[1]. The prevalence of obesity [body mass index (BMI)≥30kg/m ^{2}] in the US is currently between 30 and 35% in both middle aged adults (40-59 years) and in older adults (>60 years)[2]. Obesity in older adults is also increasing rapidly in other industrialised countries; England has seen a rapid increase in the number of older adults with obesity – rising from 16% of women and 15% of men aged 75 and over in 1994[3] to 27% and 18% respectively in 2006. In younger people, obesity is well known to be associated with adverse cardiovascular outcomes, osteoarthritis, type 2 diabetes mellitus and reduced exercise capacity[4]. All of these problems are prevalent in older people, and contribute to the high burden of disease and functional impairment.

Compared to younger people, there appears to have been very little research aimed at reducing obesity in older adults. There is evidence that modest degrees of overweight (BMI 25-29.9 kg/m^2) are not associated with increased mortality in older people[5]; indeed the optimum BMI for older adults is higher than for younger people. However, a recent meta-analysis of cohort studies found an association between BMI≥30kg/m ^{2} and mortality in older people (RR 1.10, 95% CI 1.06-1.13)[5]. Similar findings are evident when using more detailed anthropometric measures to circumvent the inaccuracies of BMI measurement in older people; older males with increased waist circumference showed increased mortality after adjustment for mid-arm muscle circumference[6]. The effects of obesity may be reversible even in older people; a

large cohort study suggested that perceived intentional weight loss confers a significant reduction in all-cause mortality in males aged 56-75 years[7].

Losing weight is difficult, and interventions that work in younger adults cannot be assumed to translate successfully into an older population, where low muscle mass and consequent physical frailty, osteoporosis, comorbid disease and cultural differences may increase risk and prevent benefits seen in younger people from translating into health gains in older people. It is likely that sustained weight loss is required to produce meaningful changes in health outcomes, particularly for cardiovascular disease. We therefore systematically reviewed the evidence for interventions designed to produce sustained weight loss in obese older adults to inform current practice.

Methods

We conducted a systematic review using a prespecified protocol, devised according to the guidelines of the Cochrane Collaboration. We included randomised controlled trials in which weight loss was a primary aim of the intervention, for which follow-up data at a minimum of one year were available, in which the mean age of groups was 60 years or greater and the mean baseline BMI was ≥ 30 kg/m^2. We included trials with placebo or no intervention for the control group, and trials comparing active intervention groups. No language restrictions were used. We excluded studies in which weight loss was a coincidental change produced by another type of intervention.

Data sources and search strategy

We searched 13 electronic databases, earliest date 1966 until 2001[8], five electronic databases from 2001 - December 2008 (Medline, CINAHL, Psycinfo, the Cochrane database and EMBASE), and handsearched four obesity and geriatrics journals. Full details of the search strategies have been published previously[6]. We used weight loss, weight maintenance and obesity related terms customised to each database.

Outcomes

We sought the following outcomes: weight, BMI, total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, fasting glucose, glycosylated haemoglobin (HbA1c), blood pressure. We also sought information on deaths, hospitalisations, morbidity, quality of life, measures of physical function and exercise capacity, and dropouts. We collected data on age, sex, social class, smoking status, dwelling place, disease state and source of trial funding.

Data extraction and quality assessment

Data were abstracted by two researchers independently, and discrepancies were resolved by consensus. Clarification of data was obtained by correspondence with trialists. Values for standard deviations of change in weight, blood pressure and lipids were imputed if not available from trial reports, based on previously published algorithms[8]. Where BMI was recorded but not weight, we imputed weight based on height data from the NHANES III dataset[9]. Study quality was assessed by two reviewers independently, and disagreements resolved by consensus. Allocation

concealment, description of dropouts, availability of intention to treat analysis, blinding and baseline comparability of groups were assessed.

Data synthesis and analysis

Meta-analysis was undertaken where results could be quantitatively combined, using RevMan 4.2 software (Cochrane Collaboration). I^2 tests for heterogeneity across analyses were performed, and possible sources of heterogeneity were explored. Random effects models were used for all analyses.

Results

Selection of trials

Reports of 649 potentially eligible studies were retrieved for further scrutiny (Figure 1). The vast majority were ineligible for inclusion; reasons included mean age of groups <60 years, weight reduction not a primary aim of the study; design other than randomised controlled trial; mean baseline BMI <30 kg/m^2, and follow-up less than 12 months.

Description of the interventions

Table 1 gives details of the nine studies included in the review. With one exception[10] the included trials were all carried out in the USA; most studies targeted patients with a specific disease entity (diabetes mellitus, coronary artery disease, osteoarthritis). Studies were a mixture of single centre and multicentre trials, with some interventions conducted in community or primary care settings, and some in secondary care settings. All studies examined patients who were living in the

community rather than in institutional settings. Only two of the studies had a mean baseline BMI of >35kg/m^2 [11,12]. One trial[11] targeted black and white adults with diabetes living in medically underserved rural communities.

All the trials provided dietary advice, with the exception of the PATH trial, which provided physical activity advice[17,18]. In two trials it was not clear whether this was low fat dietary advice[10,14]. Two trials did not report giving physical activity advice[10,15], and three trials provided facilities for undertaking physical activity[12,13,17,18].

Study quality

The quality of study design and reporting was variable. All studies reported random allocation and some studies specified intention to treat analysis in their protocols, but insufficient detail was given in most published reports to decide whether there was adequate allocation concealment. Only 2/9 studies clearly performed intention to treat analyses; insufficient detail was given in 3/9. Most studies gave numbers of withdrawals, but only four gave reasons for withdrawal or dropout. Baseline treatment and control groups were well balanced in all nine studies. Although it is usually not possible to blind patients to the intervention employed in weight loss studies, only one study clearly reported that the team in charge of patients' usual care was blinded to the intervention, or that those measuring outcomes were blinded to treatment group.

Meta-analysis results

Weight

The overall weighted mean difference change in weight comparing intervention and control groups at 12 months was -3.0 kg (95% CI -5.1 to -0.9, *P*=.005); results are displayed in Figure 2. Significant statistical heterogeneity was evident (I^2=89%; *P*<.001). *Post hoc* grouping of the trials according to the type of intervention appears to suggest that trials which provided physical activity advice with dietary advice appeared to provide greater weight loss. Omission of the two studies for which weight change was extrapolated from BMI change[15,16] gave a change in weight of -3.3 kg (95% CI -5.8 to -0.8, *P*=.009).

Post hoc subgroup analysis was also performed grouping studies into those with a defined weight loss or calorie restriction and those without such a goal. Studies with a clearly defined weight loss goal[10-12,14] showed a change in weight of -4.0 kg (95% CI -7.3 to -0.7), compared with -1.3 kg (95% CI -2.9 to 0.3, *P*<.001 for difference) in those without a defined goal[15-17].

Data from the ADAPT study were not incorporated into the meta-analysis, as data were collected at 18 months from randomisation. This study showed a 12.8 kg fall in mean weight in the intervention group, compared with a 2.3 kg fall in the control group. (difference -10.5 kg, 95% CI -16.4 to -4.6). Toobert[16] reported weight change at 24 months, with a reduction of 2.8 kg (95% CI -7.8 to 2.2) compared with the control group; somewhat smaller than the 5.4 kg difference seen at 12 months. TONE[14] reported weight outcomes at 18, 24 and 30 months, showing a reduction compared with the control group of -4.6 kg (95% CI -5.6 to -3.6) at 18 months, -4.5

kg (95% CI -5.6 to -3.4) at 24 months, and -4.9kg (-6.5 to -3.4) at 30 months. Results from the DPP study[19] were also not incorporated into the meta-analysis as the analysis was performed over 3.2 years rather than at a discrete timepoint; the weight-loss intervention group lost a mean of 6.4 kg over the study, compared to a 0.2 kg reduction in the placebo arm (*P*<.001)

Lipids

Data on change in total cholesterol at 12 months were available from four studies [10,15,16,18]; the overall weighted mean difference comparing intervention and control groups at one year was -0.36 mmol/L (95% CI -0.75 to 0.04, *P*=.08). Results are shown in Figure 3. Again, significant heterogeneity was detected (I^2=77%, *P*=.004). Omitting one study[16] with an anomalous change in cholesterol in the control group at 12 months (data checked with author) gave an overall difference in change of -0.18 mmol/L (95% CI -0.44 to 0.08, *P*=.17) with lower heterogeneity (I^2=52%, p=0.13). This study also provided follow up data at 24 months; total cholesterol had risen by 0.31 mmol/L (95% CI -0.54 to 1.16) relative to the control group at this timepoint.

Data on weighted mean difference changes in LDL and HDL cholesterol and triglycerides at 12 months were available from two studies[16,18]. The difference in change in LDL cholesterol between intervention and control groups was -0.04 mmol/L (95% CI -0.25 to 0.18, *P*=.74, I^2=0%), the difference in HDL cholesterol was 0.04 mmol/L (95% CI -0.04 to 0.12, *P*=.37, I^2=0%), and for triglycerides was 0.44 mmol/L (95% CI -0.55 to 1.43, *P*=.39, I^2 =83%)

Blood pressure

Blood pressure data were available from the TONE[14] study and one other smaller study[16]. In TONE, blood pressure medication withdrawal started 90 days after commencing the intervention. At this point, the weight loss group showed a reduction of 4.0/1.1 mmHg in blood pressure, whereas the usual care group showed a reduction of 0.8/0.8 mmHg (reported $P<.001$ for difference in systolic BP change), and antihypertensives could be stopped successfully in 87% of the usual care group compared with 93% of the weight loss group. Data for blood pressure one year or more after randomisation were not presented, but follow-up in TONE for recurrence of hypertension or cardiovascular events continued for a median period of 29 months[14]. In the other study[16], there were no significant differences in either systolic or diastolic blood pressure between intervention and control groups at 12 months or 24 months.

Exercise capacity

One study (ADAPT)[13] reported changes in six-minute walk distance at 18 months in patients with osteoarthritis. Distance walked in the control group fell by 4.7m, and increased by 9.7m in the intervention group; a statistically and clinically non-significant difference[20]. In postmenopausal women[17], an exercise-based programme increased maximal oxygen uptake by 11.7% in the intervention group compared with 0.7% in the control group at 12 months (reported $P<.001$)

Glycaemic control

One study contained data on change in HbA1c at 12 months in patients with diabetes[15]. There was no difference in change between groups (mean HbA1c fell

from 7.9% to 7.8% in both groups, reported *P*=.42). The incidence of new onset diabetes in the DPP study[19] was considerably lower in the intervention group than in the control group (adjusted hazard ratio 0.50, 95%CI 0.29 to 0.89)

Mortality, morbidity and hospitalisation

Mortality and hospitalisations were not reported for any studies except TONE[14]. In the TONE study the reported hazard ratio for the primary end point (recurrence of hypertension or cardiovascular events) was 0.65 (95% CI, 0.50 to 0.85) for those randomised to weight loss alone compared with controls. One trial[16] reported a significant improvement in chest pain frequency, but not duration or severity in the intervention group over two years.

Quality of life

Two studies reported effects on the SF-36 quality of life measure. In one study[21], overall health-related quality of life improved by 3.6 points in the intervention group but worsened by 0.8 points in the control group at 12 months (reported *P*=.02). In the other[22], physical health scores improved by 0.8 points in the control group and 3.0 points in the diet group; corresponding values for mental health scores were 0.8 and 1.2 points respectively. None of these latter changes were reported as reaching statistical significance.

Economic outcomes

One trial of dietary advice estimated costs at US$137/participant[15].

Discussion

Key findings

Our systematic review shows a modest but significant reduction in weight with weight loss interventions in older, obese people. No clinically significant improvement was seen in cholesterol levels, and data were insufficient to draw conclusions regarding the effect of weight loss interventions on other cardiovascular risk factors, exercise capacity, or quality of life. Results for weight loss and change in cholesterol showed significant heterogeneity, which may have related to whether physical activity was included in the intervention. Studies with explicit goals for weight reduction or calorie restriction produced greater weight loss than those without explicit goals.

Two previous systematic reviews have been published examining weight reduction interventions in older people. In one, short-term interventions of six to twelve months were also included[23], but studies showing a reduction in weight of <2 kg were excluded, potentially biasing the results. This review concluded that clinically important benefits may be achievable in patients with diabetes, osteoarthritis and coronary artery disease. The second review[24] had similar inclusion criteria to the current review, but included fewer studies, and did not attempt to meta-analyse the results. A similar spread of weight reductions was noted compared with the current review.

Strengths and weaknesses

Although we believe that our search strategy has included all eligible papers, it is possible that unpublished studies exist that have not been included. Handsearching of

recent abstracts did not reveal any further studies however. The participants enrolled in the included studies did not appear to have a high burden of comorbid disease in comparison to many older people; baseline data regarding physical and psychosocial function were however lacking. Inadequate reporting and heterogenous outcome times and measures hampered our ability to combine data into meta-analysis; the results should therefore be treated with caution. Although anthropometric measures of adiposity may provide a more sensitive measure of response to interventions, these data were not available for most of the included studies.

Study findings in context

A variety of weight reduction approaches have been shown to be effective in younger patients, with a mean reduction of 5kg in weight at 12 months for low-fat diets[8]. In younger patients, epidemiological modelling suggests that intentional weight loss is associated with up to a 20% reduction in all-cause mortality in women[8]; this result was not seen in men with intentional weight loss. Concern exists that obesity may be protective against death in some diseases that are very common in older people, including coronary artery disease and heart failure – the so-called 'obesity paradox'[23]. Our analysis is unable to shed further light on this issue; only the TONE study reported deaths and cardiovascular events, and numbers were too small to draw conclusions on death rates from this single study. Furthermore, it is probably unreasonable to expect to detect changes in markers of cardiovascular disease, exercise capacity and quality of life without first achieving a significant, sustained reduction in weight.

The paucity of trials conducted in older people is striking; indeed even those studies that we included had a mean age between 60 and 69 years. There is therefore virtually no evidence to guide practice in people older than this. Equally striking is the paucity of outcome data that addresses issues directly relevant to older people – exercise capacity, physical function and quality of life. Such data are essential if the overall impact of interventions on health status is to be determined, as opposed to a narrow effect on risk factors for disease. No studies of pharmacological interventions for weight loss in older people were found for inclusion in this review; results from the large SCOUT trial of sibutramine in high cardiovascular risk people should provide additional data in this area, although very few patients aged over 75 years were randomised[24].

Future directions

Trials of weight loss interventions in older people are badly needed. Such trials should incorporate approaches to behavioural modification grounded in psychological theory and tailored to older people, and need to take account of multiple comorbidities in older people. Trials will need to include much older people than previously, and should actively seek to include patients with extensive comorbidities. Baseline details need to include information on cognition, deprivation, physical function, social support and comorbid disease. Although weight, cardiovascular risk factors, and clinical outcomes such as cardiovascular events should be measured, patient-centred outcomes will also be needed[25]. Such an approach is necessary to ensure not only that the evidence base is relevant to typical older people with obesity, but that it can be seen to be relevant – by patients, healthcare providers and policymakers.

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References

1. Haslam D, Sattar N, Lean M. ABC of obesity. Obesity--time to wake up. BMJ 2006; 333: 640-2.

2. Ogden CL, Carroll MD, Curtin LR, McDowell MA, Tabak CJ, Flegal KM. Prevalence of overweight and obesity in the United States, 1999-2004. JAMA 2006; 295: 1549-55.

3. Craig R, Mindell J. Health Survey for England 2006. Vol 1: Cardiovascular disease and risk factor in adults. The Information Centre for Health and Social Care 2008.

4. Lean M, Gruer L, Alberti G, Sattar N. ABC of obesity. Obesity--can we turn the tide? BMJ 2006; 333: 1261-4.

5. Janssen I, Mark AE. Elevated body mass index and mortality risk in the elderly. Obes Rev 2007; 8: 41-59.

6. Wannamethee SG, Shaper AG, Lennon L, Whincup PH. Decreased muscle mass and increased central adiposity are independently related to mortality in older men. Am J Clin Nutr 2007; 86: 1339-46.

7. Wannamethee SG, Shaper AG, Lennon L. Reasons for intentional weight loss, unintentional weight loss, and mortality in older men. Arch Intern Med 2005; 165: 1035-40.

8. Avenell A, Broom J, Brown TJ *et al*. Systematic review of the long-term effects and economic consequences of treatments for obesity and implications for health improvement. Health Technol Assess 2004; 8(21): 1-182.

9. Third National Health and Nutrition Examination Survey (2001) [www document]. URL: http://www.cdc.gov/nchs/nhanes.htm (accessed 9th February 2009).

10. Mengham LH, Morris BF, Palmer CR, White AJS. Is intensive dietetic intervention effective for overweight patients with diabetes mellitus? A randomised controlled trial in a general practice. Pract Diab International 1999; 16: 5-8.

11. Mayer-Davis EJ, D'Antonio AM, Smith SM *et al*. Pounds off with empowerment (POWER): a clinical trial of weight management strategies for black and white adults with diabetes who live in medically underserved rural communities. Am J Public Health 2004; 94: 1736-42.

12. Villareal DT, Shah K, Banks MR, Sinacore DR, Klein S. Effect of weight loss and exercise therapy on bone metabolism and mass in obese older adults: a one-year randomised controlled trial. J Clin Endocrinol Metab 2008; 93: 2181-7.

13. Messier SP, Loeser RF, Miller GD *et al*. Exercise and dietary weight loss in overweight and obese older adults with knee osteoarthritis: the Arthritis, Diet, and Activity Promotion Trial. Arthritis Rheum 2004; 50: 1501-10.

14. Whelton PK, Appel LJ, Espeland MA *et al*. Sodium reduction and weight loss in the treatment of hypertension in older persons: a randomized controlled trial of nonpharmacologic interventions in the elderly (TONE). TONE Collaborative Research Group. JAMA 1998; 279: 839-46.

15. Glasgow RE, La Chance PA, Toobert DJ, Brown J, Hampson SE, Riddle MC. Long-term effects and costs of brief behavioural dietary intervention for patients with diabetes delivered from the medical office. Patient Educ Couns 1997; 32: 175-84.

16. Toobert DJ, Glasgow RE, Radcliffe JL. Physiologic and related behavioral outcomes from the Women's Lifestyle Heart Trial. Ann Behav Med 2000; 22: 1-9.

17. Irwin ML, Yasui Y, Ulrich CM *et al*. Effect of exercise on total and intra-abdominal body fat in postmenopausal women: a randomized controlled trial. JAMA 2003; 289: 323-30.

18. Frank LL, Sorensen BE, Yasui Y, Tworoger SS, Schwartz RS, Ulrich CM. Effects of exercise on metabolic risk variables in overweight postmenopausal women: a randomized clinical trial. Obes Res 2005; 13: 615-25.

19. Diabetes Prevention Program Research Group. Crandall J, Schade D, Ma Y *et al*. The influence of age on the effects of lifestyle modification and metformin in the prevention of diabetes. J Gerontol A Med Sci 2006; 61A: 1075-81.

20. Perera S, Mody SH, Woodman RC, Studenski SA. Meaningful change and responsiveness in common physical performance measures in older adults. J Am Geriatr Soc 2006; 54: 743-9.

21. Bowen DJ, Fesinmeyer MD, Yasui Y *et al*. Randomized trial of exercise in sedentary middle aged women: effects on quality of life. Int J Behav Nutr Phys Act 2006; 3: 34.

22. Rejeski WJ, Focht BC, Messier SP, Morgan T, Pahor M, Penninx B. Obese, older adults with knee osteoarthritis: weight loss, exercise, and quality of life. Health Psychol 2002; 21: 419-26.

23. Bales CW, Buhr G. Is obesity bad for older persons? A systematic review of the pros and cons of weight reduction in later life. J Am Med Dir Assoc 2008; 9: 302-12.

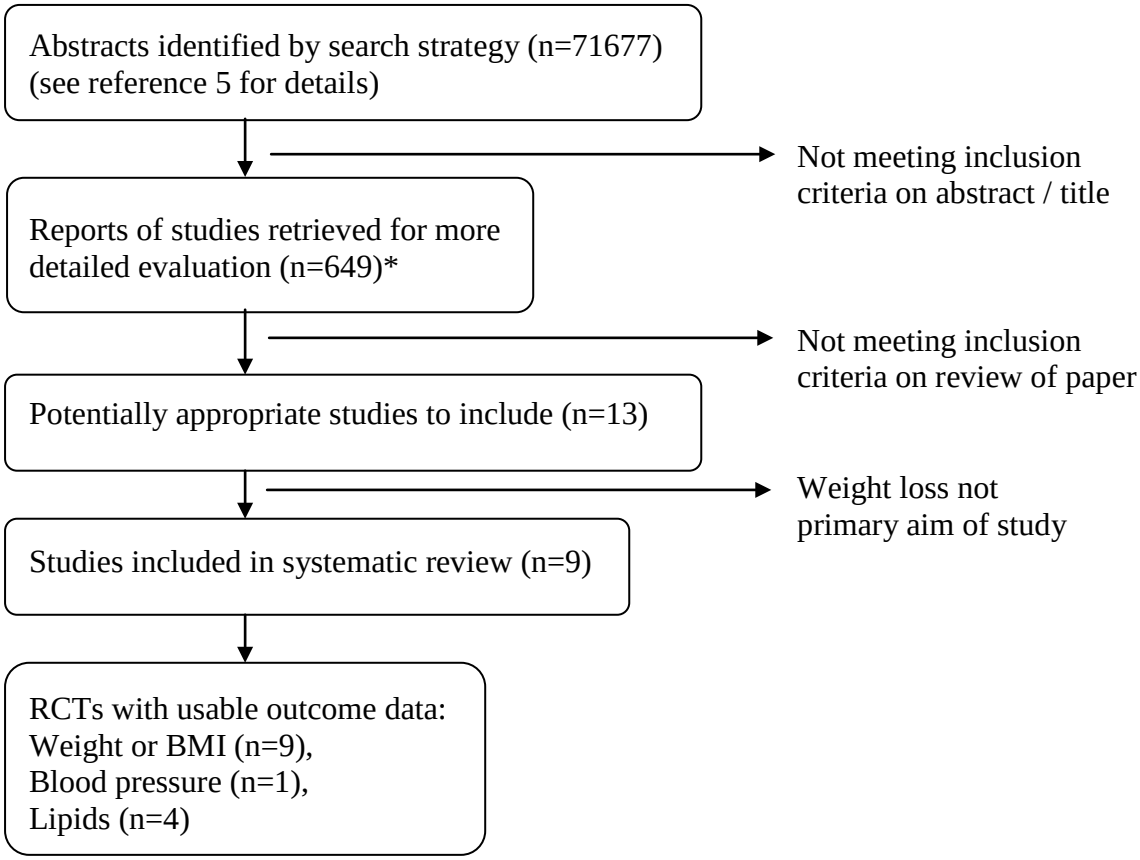
24. McTigue KM, Hess R, Ziouras J. Obesity in older adults: a systematic review of the evidence for diagnosis and treatment. Obesity 2006; 14: 1485-97.

25. Uretsky S, Messerli FH, Bangalore S *et al*. Obesity paradox in patients with hypertension and coronary artery disease. Am J Med 2007; 120: 863-70.

26. Torp-Pedersen C, Caterson I, Coutinho W *et al*; SCOUT Investigators. Cardiovascular responses to weight management and sibutramine in high-risk subjects: an analysis from the SCOUT trial. Eur Heart J 2007; 28: 2915-23.

27. Mead N, Bower P. Patient-centredness: a conceptual framework and review of the empirical literature. Soc Sci Med 2000; 51: 1087-110.

Fig 1. Trial flow diagram



*Includes 400 reports of RCTs considered in previous HTA report[8]

Table 1. Included studies

Study	Location	N	Comorbidity	Sex	Mean age (years)	BMI (kg/m^2)	Intervention	Goal for weight loss or calorie restriction?	Extractable outcomes	Follow up (mths)	% dropout at 12 mths
Glasgow 1997[15]	USA; single secondary care centre (office based)	206	Diabetes mellitus	62% female	Ctrl: 63.1 Int: 61.7	Ctrl: 30.5 Int: 30.4	Ctrl: three and 12 month clinic appointment. Int: Counselling to remove barriers to dietary change; goal setting and problem solving at start to lower fat. Telephone follow up and repeat goal setting, follow-up 3 monthly.	No	BMI, Cholesterol HbA1c	12	16
TONE 1998[14]	USA; 4 academic secondary care centres plus community	294	Hypertension, obesity	55% female	Ctrl: 66 Int: 66	Ctrl: 31.3 Int: 31.0	Ctrl: Talks unrelated to diet or sodium restriction Int: Aim 5-10% reduction in weight, social action theory, plus advice to increase physical activity. 4 mths weekly intensive group and individual sessions; 3 mths fortnightly group meetings; then monthly group meetings	Yes	Weight	30	12
Mengham 1999[10]	UK; single primary care centre	75	Diabetes mellitus	55% female	Ctrl: 63.5 Int: 57.8	Ctrl: 31.7 Int: 31.4	Ctrl: 15 min dietetic appt every 6 mths Int: Aim 10% reduction in BMI; fortnightly dietetic and group work sessions for 3 months.	Yes	Weight, cholesterol	12	1
Toobert 2000[16]	USA; community	28	Postmenopausal, coronary heart disease	100% female	Ctrl 63 Int: 64	Ctrl: 32 Int: 32	Ctr: Usual care Int: Week long retreat; cooking classes, yoga, stress management, aerobic exercise, group support meetings. Twice weekly	No	BMI, BP, Cholesterol	24	11

							meetings for 15 months, then less frequent. Prescribed exercise 1hr 3 times/week. Vegetarian diet and <10% fat				
ADAPT 2002 [13,22]	USA; single academic centre and community	316	Osteoarthritis	72% female	Ctrl: 69 Diet: 68 Exercise: 69 Combined: 68	Ctrl: 34.5 Diet: 34.4 Exercise: 34.6 Combined: 33.9	Ctrl: Discussion groups Diet: 500 kcal/day reduction in intake, low fat, based on group dynamics and social cognitive theory initially weekly for 16 weeks then 2 weekly, maintenance months 7-18. Exercise: supervised 1hr three days a week for 4 months, then could be at home.	Yes	Weight, BMI, six min walk, quality of life	18	20
POWER 2004[11]	USA; two primary care centres	187	Diabetes mellitus	79% female	Ctrl: 62.4 Int: 59.7	Ctrl: 35.2 Int: 37.6	Ctrl: 1 session with nutritionist – aim 10% weight loss Int: Group and individual behavioural intervention with aim 10% weight loss, 25% calories from fat, 150 min/wk activity. Weekly for 4 mths, fortnightly for 2 months, monthly for 6 months. Advised to exercise 150min/week.	Yes	Weight	12	19
PATH 2005 [17,18]	USA; single secondary care centre plus community	173	Postmenopausal	100% female	Ctrl: 60.6 Int: 60.7	Ctrl: 30.5 Int: 30.4	Ctrl: Weekly stretching sessions Int: 3x/wk supervised aerobic exercise, aiming for 70% VO_2 max for 3 mths. Transition to home exercise 4x/wk plus weekly supervised exercise. No dietary advice detailed.	No	Weight, BMI Cholesterol Quality of life Maximal oxygen uptake	12	2
DPP 2006[19]	USA; multiple secondary care	648	Impaired glucose tolerance	51% female	Combined: 66.4	Ctrl: 30.8 Int: 30.5	Ctrl: Annual 30 min talk about lifestyle adjustment	Yes	Weight, diabetes	3.2 years	Unclear

	centres						Int: Aim 7% weight loss. Low fat, low calorie diet. 1 to 1 weekly lessons for 16 weeks, followed by monthly group sessions. Goal of moderate intensity physical activity for 150min/wk (unsupervised)		incidence	(mean)	
Villareal 2008[12]	USA; single secondary care centre	27	Frail, >65 years	66% female	Ctrl: 71.1 Int: 69.4	Ctrl: 39.0 Int: 38.5	Ctrl: Usual care. Instructed to avoid exercise or weight loss programmes Int: Weekly group nutrition and behaviour sessions for 1yr. Goal 10% wt loss by 6 mths; 500-750kcal deficit per day, <30% fat. Weight maintenance after 6 months. 3x/wk supervised group exercise for 1yr; 75-90% VO_2 max endurance exercise, plus 65-80% 1 rep maximum resistance exercise	Yes	Weight, markers of bone metabolism, bone mineral density	12	11

Fig 2. Meta-analysis of change in weight at 12 months

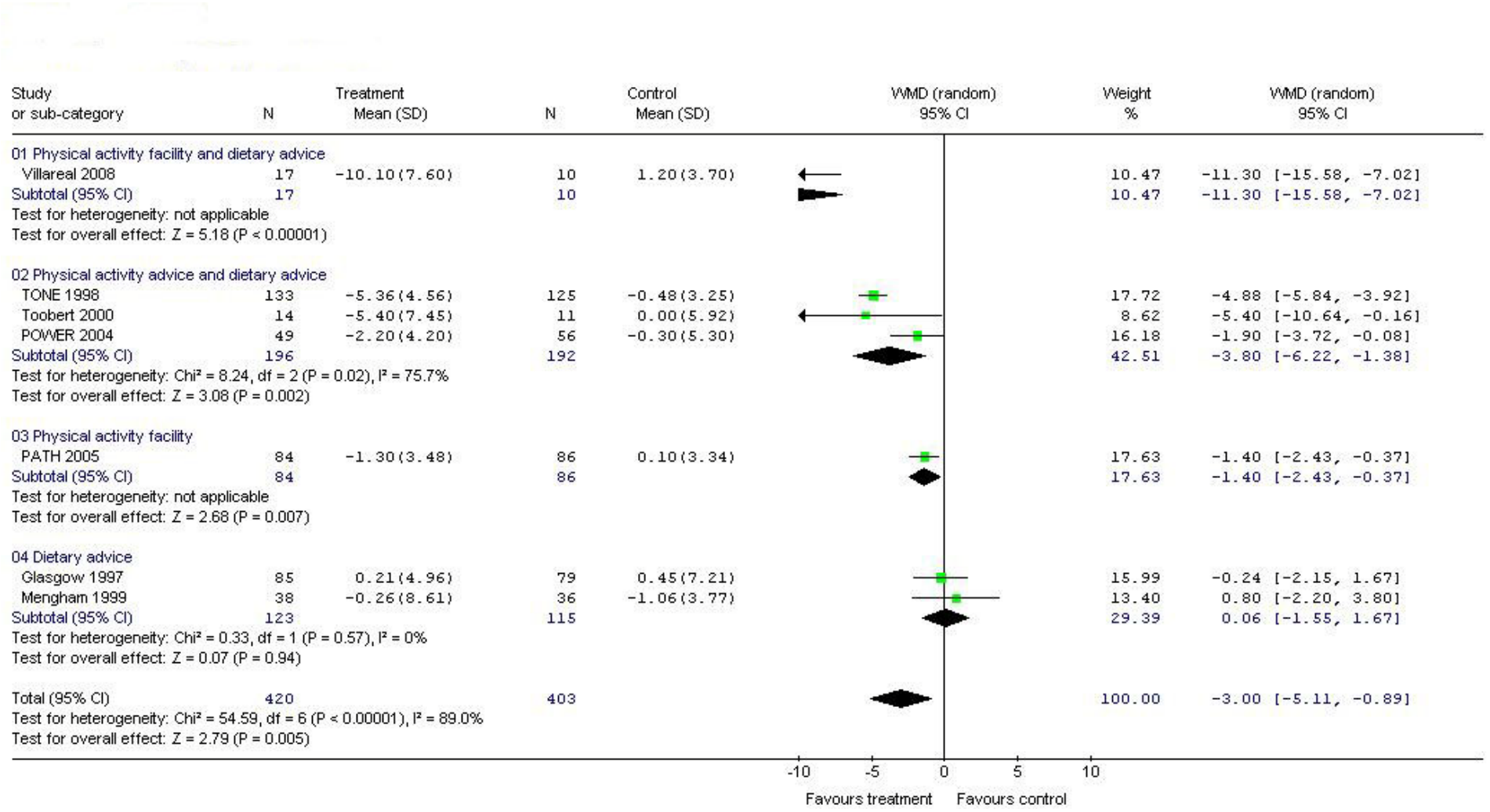


Fig 3. Meta-analysis of change in total cholesterol at 12 months