Hooper, L; Summerbell, CD; Higgins, JP; Thompson, RL; Capps, NE; Smith, GD; Riemersma, RA; Ebrahim, S (2001) Dietary fat intake and prevention of cardiovascular disease: systematic review. BMJ (Clinical research ed), 322 (7289). pp. 757-63. ISSN 0959-8138 DOI: https://doi.org/10.1136/bmj.322.7289.757

Downloaded from: http://researchonline.lshtm.ac.uk/12621/

DOI: 10.1136/bmj.322.7289.757

Usage Guidelines

Please refer to usage guidelines at http://researchonline.lshtm.ac.uk/policies.html or alternatively contact researchonline@lshtm.ac.uk.

Available under license: Creative Commons Attribution Non-commercial http://creativecommons.org/licenses/by-nc/3.0/
Dietary fat intake and prevention of cardiovascular disease: systematic review

Lee Hooper, Carolyn D Summerbell, Julian P T Higgins, Rachel I. Thompson, Nigel E Capps, George Davey Smith, Rudolph A Riemersma, Shah Ebrahim

Abstract

Objective To assess the effect of reduction or modification of dietary fat intake on total and cardiovascular mortality and cardiovascular morbidity.

Design Systematic review.

Data sources Cochrane Library, Medline, Embase, CAB abstracts, SIGLE, CVRCT registry, and biographies were searched; trials known to experts were included.

Included studies Randomised controlled trials stating intention to reduce or modify fat or cholesterol intake in healthy adult participants over at least six months. Inclusion decisions, validity, and data extraction were duplicated. Meta-analysis (random effects methodology), meta-regression, and funnel plots were performed.

Results 27 studies (30,902 person years of observation) were included. Alteration of dietary fat intake had small effects on total mortality (rate ratio 0.98; 95% confidence interval 0.86 to 1.12). Cardiovascular mortality was reduced by 9% (0.91; 0.77 to 1.07) and cardiovascular events by 16% (0.84; 0.72 to 0.99), which was attenuated (0.86; 0.72 to 1.03) in a sensitivity analysis that excluded a trial using oily fish. Trials with at least two years' follow up provided stronger evidence of protection from cardiovascular events (0.76; 0.65 to 0.90).

Conclusions There is a small but potentially important reduction in cardiovascular risk with reduction or modification of dietary fat intake, seen particularly in trials of longer duration.

Introduction

For half a century the relation between dietary fat and cardiovascular disease, the “diet-heart” hypothesis, has been a central tenet of strategies for risk reduction in individuals and populations. Observational studies and systematic reviews of clinical trials with risk factors as end points support this relation. However, evidence of a beneficial effect in observational studies does not provide convincing evidence. For example, the protective effect of β-carotene in coronary heart disease was strongly supported by observational evidence, but large randomised controlled trials showed no protective effects on morbidity or mortality.

Previous investigators have extrapolated the reduction in coronary heart disease that might be expected from changes in blood cholesterol concentration,

even though there is direct evidence from randomised controlled trials of the effect of modification or reduction of intake of dietary fats. We therefore performed a systematic review to assess the effect of change in dietary fat intake, which would be expected to result in a lowering of cholesterol concentration, on mortality and cardiovascular morbidity, using all available randomised clinical trials. The interventions included any of the following: reduction in intake of total fat; reduction in intake of saturated fat; reduction in intake of dietary cholesterol; or a shift from saturated to unsaturated fat.

Methods

Much of the methodology has been reported previously. Briefly, we developed a search strategy to search for nutrition based randomised controlled trials on the Cochrane Library, Medline, Embase, CAB abstracts, CVRCT registry (inception of database to mid-1998), and SIGLE (January 1999). We searched bibliographies and contacted related Cochrane Review Groups and 60 experts (May 1999) for further trials. There were no language restrictions.

The inclusion criteria were adequate randomisation; usual or control diet or placebo group; stated aim of intervention was reduction or modification of intake of dietary fat or cholesterol, unless the intervention was exclusively omega 3 fatty acids; intervention was not multifactorial; the intervention group were not children, acutely ill, or pregnant; the intervention (diet provided or supplementation) continued for at least six months; and data on mortality or cardiovascular morbidity were available.

Our primary outcomes of interest were effects of intervention on total mortality, cardiovascular mortality, combined cardiovascular events (including all available data on cardiovascular deaths, non-fatal myocardial infarction, stroke, angina, heart failure, peripheral vascular disease, angioplasty, and coronary artery bypass grafting), and quality of life. Event data were included only when they occurred during provision of diet or supplement (when these were provided) or...
while randomisation and blinding were maintained (in dietary advice trials).

Inclusion was assessed independently by two assessors (LH, RLT) and differences were resolved by discussion, with, if necessary, a third reviewer (RAR). Data extracted independently in duplicate (by LH and RLT) included type of participants, interventions, and outcomes; characteristics of trial quality; numbers of events; total patient years in trial; and data on potential effect modifiers. Effect modifiers included participants’ baseline risk of cardiovascular disease, trial duration, mode of intervention, change in intake of dietary fats, and serum cholesterol concentration achieved.

Criteria for assessment of trial quality included method of randomisation, physician blinding, participant blinding, and any systematic difference in care between the intervention groups.

We used meta-analysis to explore the primary hypothesis, which was that reduction or modification of dietary fat intake affects mortality, cardiovascular mortality, and cardiovascular events. We examined the effects of duration of intervention, initial level of cardiovascular risk and dietary fat intake, type of intervention, and changes in intake of total, saturated, monounsaturated, and polyunsaturated fats and blood cholesterol concentration using subgrouping of trials and meta-regression. We excluded trials that aimed to alter omega 3 intake as the method of action (if any) is probably different from any action caused by the reduction in intake of total or saturated fats—that is, it does not primarily lower low density lipoprotein cholesterol.

Treatment effect was measured as a rate ratio and meta-analysis performed as a weighted average of log rate ratios. The meta-analysis used random effects methodology within S-PLUS. Meta-analysis pools results of individual trials with weighting so that results with higher precision (related to sample size) contribute more to the combined outcome. We used the STATA command metareg for random effects meta-regression. Meta-regression investigates the effect of one or more study characteristics on the size of treatment effect, taking precision into account. A genuine relation may be inferred (for example, if the extent of reduction in total fat achieved by the intervention is associated with the degree of reduction in mortality) when a slope is significantly different from zero. We used funnel plot asymmetry to detect any bias in the trials retrieved.

Results

Study characteristics

We identified 27 studies, comprising 40 distinct intervention arms over 30 902 person years of observation. A table with details of all 27 studies can be found on the BMJ’s website. Figure 1 gives a flow chart of studies assessed and excluded at various stages of the review. Table 1 gives details of extracted data. We found almost no data on quality of life or levels of trans fats. The κ statistic for inter-rater agreement on inclusion or exclusion of potential trials was 0.61.

Reduction or modification of dietary fat intake

The pooled rate ratio for total mortality was 0.98 (95% confidence interval 0.86 to 1.12), which indicates little, if any, effect (fig 2). The data on cardiovascular mortality indicate a slight (9%) protection from modification of intake of dietary fat (0.91; 0.77 to 1.07) (fig 3) and a 16% reduction in cardiovascular events (0.84; 0.72 to 0.99) (fig 4). A funnel plot of effect size versus sample size did not show any evidence of bias (data not shown).

The Oslo diet-heart trial provided some oily fish (a source of omega 3 fatty acids) to participants in the intervention group. Exclusion of the results of this trial attenuated the rate ratios for all three main outcomes (total mortality 1.02 (0.91 to 1.14); cardiovascular mortality 0.94 (0.79 to 1.11); combined cardiovascular events 0.86 (0.72 to 1.03)).

Figure 5 shows the results of the meta-analyses, subgroupings, and sensitivity analyses performed. Table 2 shows the results of the meta-regressions.

Duration of follow up, initial level of cardiovascular risk, type of intervention, and dietary fat intake at baseline

We obtained results for specific length of time on diet, initial level of cardiovascular risk, or mode of intervention through subgrouping of trials. Trials in which the mean length of follow up exceeded two years showed somewhat larger reductions in combined cardiovascular events (0.76 (0.65 to 0.90) vs 0.96 (0.75 to 1.23) than trials of less than two years’ duration). When we excluded data from the Oslo diet-heart study, the rate ratio for combined cardiovascular events for trials with mean follow up longer than two years was not altered (0.77; 0.62 to 0.96). Total mortality was not substantially influenced by mean follow up.

The relation between mean follow up and cardiovascular events was further explored through meta-regression. The negative slope (in rate ratio) ν
Mean follow up time, slope –0.096; –0.190 to –0.002) suggests fewer cardiovascular events at longer mean follow up times in the groups with reduced or modified fat intake.

Trials with participants at high initial cardiovascular risk suggested very similar levels of protection from combined cardiovascular events (rate ratio 0.84; 0.70 to 0.99) as did trials with participants at low cardiovascular risk (0.82; 0.56 to 1.20). Neither the method of dietary modification (by diet advice, advice plus a supplement, or diet provided) nor the initial level of intake of dietary fat influenced rate ratios.

### Changes in fat intake and blood cholesterol concentration

We used meta-regression to explore the effects on total mortality and combined cardiovascular events of changing the proportion of energy from total fat and of altering serum cholesterol concentrations. Meta-regressions also explored the relation between change in proportion of saturated fat, polyunsaturated fat, and monounsaturated fat on cardiovascular events. These suggested that total mortality and cardiovascular events were reduced as energy from fat, and as serum cholesterol concentrations, fell. Similarly, cardiovascular

### Table 1 Outcome data from included trials of diet and health for control/intervention groups

<table>
<thead>
<tr>
<th>Included trial arm</th>
<th>Person years of observation</th>
<th>Total mortality</th>
<th>CVD mortality</th>
<th>Combined CVD events</th>
<th>Events included in combined CVD events</th>
</tr>
</thead>
<tbody>
<tr>
<td>BDIT pilot studies</td>
<td>1138/986</td>
<td>3†</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Diet and resnotification (DART)</td>
<td>1917/1923</td>
<td>112/111</td>
<td>100/101</td>
<td>147/136</td>
<td>CV deaths (including stroke) plus non-fatal MI</td>
</tr>
<tr>
<td>Diet and gallstones</td>
<td>19/11</td>
<td>0</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>German fat reduced</td>
<td>25/26</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>CV deaths, non-fatal MI, stroke</td>
</tr>
<tr>
<td>Glasgow diet in hypertension</td>
<td>34/33</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>CV deaths</td>
</tr>
<tr>
<td>Glasgow weight loss</td>
<td>22/24</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>CV deaths, non-fatal MI, stroke</td>
</tr>
<tr>
<td>Kentucky low fat</td>
<td>56/105</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>CV deaths, fatal and non-fatal MI, stroke</td>
</tr>
<tr>
<td>Kuopio</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Fat modified (American Heart Association)</td>
<td>6/20</td>
<td>0</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Fat modified (low fat)</td>
<td>6/20</td>
<td>0</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Fat modified (monosaturated)</td>
<td>6/20</td>
<td>0</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Linoleic enrichment</td>
<td>48/34</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>CV deaths, non-fatal MI, stroke</td>
</tr>
<tr>
<td>London corn/olive</td>
<td>22/41</td>
<td>0.5/5</td>
<td>0.5/5</td>
<td>5.5/15</td>
<td>CV deaths, non-fatal MI, angina, stroke</td>
</tr>
<tr>
<td>Olive</td>
<td>22/38</td>
<td>0.5/3</td>
<td>0.5/3</td>
<td>5.5/11</td>
<td>CV deaths, non-fatal MI, angina, stroke</td>
</tr>
<tr>
<td>London low fat</td>
<td>393/374</td>
<td>24/20</td>
<td>20/17</td>
<td>42 / 38</td>
<td>CV deaths, non-fatal MI, stroke</td>
</tr>
<tr>
<td>Low fat in breast cancer</td>
<td>171/170</td>
<td>At least 2†</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Maitopidy diet</td>
<td>4/5</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>CV deaths</td>
</tr>
<tr>
<td>Minnesota coronary</td>
<td>415/493</td>
<td>248/269</td>
<td>157/157</td>
<td>128/134</td>
<td>Total MI, sudden death, stroke</td>
</tr>
<tr>
<td>MRC soy</td>
<td>715/751</td>
<td>31/29</td>
<td>25/27</td>
<td>74/82</td>
<td>CV deaths, total MI</td>
</tr>
<tr>
<td>Multicentre study on fat reduction (MSFAT)</td>
<td>56/59</td>
<td>0</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>National diet-heart study</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Farbault 1, B</td>
<td>18/52</td>
<td>—</td>
<td>0</td>
<td>0</td>
<td>Total MI, peripheral vascular events</td>
</tr>
<tr>
<td>Farbault 1, C</td>
<td>18/49</td>
<td>—</td>
<td>0</td>
<td>0</td>
<td>Total MI, peripheral vascular events</td>
</tr>
<tr>
<td>Farbault 1, E</td>
<td>18/53</td>
<td>—</td>
<td>0</td>
<td>0</td>
<td>Total MI, peripheral vascular events</td>
</tr>
<tr>
<td>Open 1st, B</td>
<td>120/358</td>
<td>—</td>
<td>0</td>
<td>0.3/0</td>
<td>Total MI, peripheral vascular events</td>
</tr>
<tr>
<td>Open 1st, C</td>
<td>120/361</td>
<td>—</td>
<td>0</td>
<td>0.3/4</td>
<td>Total MI, peripheral vascular events</td>
</tr>
<tr>
<td>Open 1st, X</td>
<td>120/50</td>
<td>—</td>
<td>0</td>
<td>0.3/1</td>
<td>Total MI, peripheral vascular events</td>
</tr>
<tr>
<td>Open 2nd, BC</td>
<td>59/112</td>
<td>—</td>
<td>0</td>
<td>1.3/0</td>
<td>Total MI, peripheral vascular events</td>
</tr>
<tr>
<td>Open 2nd, F</td>
<td>59/74</td>
<td>—</td>
<td>0</td>
<td>1.3/1</td>
<td>Total MI, peripheral vascular events</td>
</tr>
<tr>
<td>Open 2nd, G</td>
<td>59/70</td>
<td>—</td>
<td>0</td>
<td>1.3/0</td>
<td>Total MI, peripheral vascular events</td>
</tr>
<tr>
<td>Open 2nd, X</td>
<td>22/22</td>
<td>—</td>
<td>0</td>
<td>0</td>
<td>Total MI, peripheral vascular events</td>
</tr>
<tr>
<td>Oslo diet-heart</td>
<td>885/895</td>
<td>65/48</td>
<td>52/38</td>
<td>91/66</td>
<td>Total MI, sudden death, stroke, angina</td>
</tr>
<tr>
<td>Oxford retinopathy</td>
<td>1160/1160</td>
<td>34†</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Sollentuna diet</td>
<td>19/20</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>Total MI, CV deaths, stroke</td>
</tr>
<tr>
<td>Stanford weight</td>
<td>42/42</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>CV deaths</td>
</tr>
<tr>
<td>St Thomas’ atherosclerosis regression (STARS)</td>
<td>88/91</td>
<td>3/1</td>
<td>3/1</td>
<td>20/8</td>
<td>CV deaths, non-fatal MI, angina, stroke, CABG, angiplasty</td>
</tr>
<tr>
<td>Sydney diet-heart</td>
<td>1011/939</td>
<td>28/39</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Toronto polyp prevention</td>
<td>204/198</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>CV deaths</td>
</tr>
<tr>
<td>Turk weight</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Mixed</td>
<td>21/41</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>CV deaths, non-fatal MI, angina, stroke, heart failure, angioplasty, CABG</td>
</tr>
<tr>
<td>Vegetarian</td>
<td>21/38</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>CV deaths, non-fatal MI, angina, stroke, heart failure, angioplasty, CABG</td>
</tr>
<tr>
<td>Veterans administration</td>
<td>1544/1588</td>
<td>177/174</td>
<td>58/44</td>
<td>122/97</td>
<td>Sudden death, definite MI, definite stroke, angina, peripheral vascular events</td>
</tr>
<tr>
<td>Veterans diet and skin cancer</td>
<td>125/123</td>
<td>2/0</td>
<td>2/0</td>
<td>2/0</td>
<td>CV deaths</td>
</tr>
<tr>
<td>Total, all trials</td>
<td>15096/15808</td>
<td>30 902</td>
<td>662/669 (1430)</td>
<td>419/393 (812)</td>
<td>643/573 (1216)</td>
</tr>
<tr>
<td>Total, high risk participants</td>
<td>5053/5054</td>
<td>10 (107)</td>
<td>265/255 (320)</td>
<td>201/192 (333)</td>
<td>385/336 (721)</td>
</tr>
</tbody>
</table>

CVD=cardiovascular disease, CV=cardiovascular, MI=myocardial infarction, CABG=coronary artery bypass grafting.

*Events counted only once, only major event counted for each participant.
†Deaths occurred but it was not clear in which group.
which is rich in omega 3 fatty acids, seems to have
acted the effects on cardiovascular events. In this trial
reduces the incidence of combined cardiovascular
reduction or modification of intake of dietary fat
Pooled results of dietary fat trials indicate that
medium sized trial, St Thomas's atherosclerosis
at a P < 0.05, see table 2), except for that of monounsatu-
does not provide convincing (none of the slopes were different from zero
Here the slope depended heavily on one
changes that reduce clinical events are observed.
Sustained change in dietary behaviour, promoted by
long interventions, is probably necessary to achieve
and stability of atherosclerotic plaques (rather than
rapid alteration in blood coagulability), but other
mechanisms may also be operating.
It is not clear whether it is the duration of the inter-
vention or the duration of the follow up that
determines whether the intervention is effective.
Sustained change in dietary behaviour, promoted by
long interventions, is probably necessary to achieve
reduction in cardiovascular events, and lengthy follow
up is probably required before pathophysiological
time lag between the effects of dietary intervention and statins suggests a common
mechanism, perhaps through effects on the scale, type,
and stability of atherosclerotic plaques (rather than
rapid alteration in blood coagulability), but other
mechanisms may also be operating.

Initial level of cardiovascular risk
Subgrouping suggested no effect of initial level of risk on outcomes. Both high and low risk groups had
a similar level of risk reduction for combined cardiovas-
cular events. This is in contrast to results of previous
studies, though initial levels of risk in studies in this
systematic review were generally high (people in
control group at “low risk” of cardiovascular events suf-
fed 2.57 events per 100 people per year and those at
“high risk” 7.62 events per 100 people per year).
Most of the events in this review occurred in men.
Only two trials with events included women so it
may not be appropriate to generalise these results to
women.

Type of intervention
Subgrouping by mode of intervention showed no benefit
of providing the entire diet compared with dietary
advice or advice and a supplement. This was surprising
as we expected that provision of food would have a
more powerful effect on events than dietary advice
alone.

Changes in blood cholesterol concentration
Meta-regression provided weak evidence that a greater
reduction in serum cholesterol concentrations in the
intervention group compared with the control group
resulted in a slightly greater reduction in cardiovas-
cular events and mortality.
A reduction of over 20% in total serum cholesterol
concentration can result in a 25% fall in mortality from
coronary heart disease. Within dietary trials in this
review the mean initial serum cholesterol concentration
was 5.8 mmol/l, with a fall of 0.64 mmol/l (11%).
This degree of reduction is similar to that achieved by

Discussion
Pooled results of dietary fat trials indicate that
reduction or modification of intake of dietary fat
reduces the incidence of combined cardiovascular
events by 16% (rate ratio 0.84; 95% confidence interval
0.72 to 0.99) and cardiovascular deaths by 9% (0.91;
0.77 to 1.07). No effect was seen on total mortality.
Exclusion of data from the Oslo diet study attenu-
atmed the effects on cardiovascular events. In this trial
participants in the intervention group were supplied
with oily fish, in addition to dietary advice. Oily fish,
which is rich in omega 3 fatty acids, seems to have
early fibrates, which show reductions in rates of coronary heart disease only among those at high risk. However, early fibrates seemed to increase mortality from other causes, and hence any benefit from this reduction in cholesterol concentration was outweighed by adverse effects of the drugs themselves. In dietary modification this degree of cholesterol lowering is probably of modest overall benefit.

**Methodology of the review**

In this review we aimed to find trials that modified or reduced dietary fat intake for at least six months, even when mortality and morbidity were not reported. We tried to contact trial authors to ascertain whether it was known if any deaths or cardiovascular events had occurred. For this reason, many of the included trials are small but are included in the hope of augmenting the data from larger trials and reducing bias. Although small trials cannot individually hope to achieve useful data on rare events, in meta-analysis we are increasing the power of the group of studies by pooling.

We included factorial trials (for example, the diet and reinfarction trial (DART)) when it was possible to separate out the data on the effect of change in dietary fat from the other interventions (which are randomly distributed across the fat control and intervention groups). We excluded multiple risk factor intervention trials as it is not possible to disaggregate the effects of change in dietary fat intake from other, potentially effective interventions such as increasing exercise, stopping smoking, and change in other dietary constituents. There is already a systematic review on this topic. We excluded the Lyon heart study as inclusion in our review was decided by the stated intention of the trial. This trial nowhere states the intention to reduce or modify dietary fat intake and the major effect on diet was to increase the omega 3 fat intake. We excluded the Finnish mental hospital study as it was not a truly randomised design (a cluster randomised trial with only two clusters).

Although we amassed 30 902 person years of observation, 1490 deaths, and 1216 cardiovascular events, considerable uncertainty exists over the size of effects and the means by which they were achieved given the scarcity of trials longer than two years’ duration. It is unlikely that further resources will now be forthcoming to perform a large trial of dietary modification. Consequently the evidence pooled in this review contributes all that is available to guide clinical practice and health policy on dietary manipulation. However, publication of data on deaths or cardiovascular events in the large ongoing trials of dietary fat lowering with cancer end points would augment currently available data.

**Conclusions**

In this review we have tried to separate out whether changes in individual fatty acid fractions are responsible for any benefits to health (using the technique of meta-regression). The answers are not definitive, the data being too sparse to be convincing. We are left with

---

**Table 2** Effect of modification of dietary fat intake and serum cholesterol concentration on mortality and cardiovascular outcomes, results of meta-regressions performed

<table>
<thead>
<tr>
<th>Outcome measure and test variable</th>
<th>Slope (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mortality</strong></td>
<td></td>
</tr>
<tr>
<td>Total fat</td>
<td>0.15 (-0.009 to 0.039)</td>
</tr>
<tr>
<td>Serum cholesterol</td>
<td>0.297 (-0.141 to 0.734)</td>
</tr>
<tr>
<td><strong>Cardiovascular events</strong></td>
<td></td>
</tr>
<tr>
<td>Total fat</td>
<td>0.084 (-0.012 to 0.017)</td>
</tr>
<tr>
<td>Saturated fat</td>
<td>0.059 (-0.047 to 0.064)</td>
</tr>
<tr>
<td>Polyunsaturated fat</td>
<td>0.014 (-0.034 to 0.061)</td>
</tr>
<tr>
<td>Monounsaturated fat</td>
<td>0.167 (0.046 to 0.288)</td>
</tr>
<tr>
<td>Serum cholesterol</td>
<td>0.296 (-0.094 to 0.687)</td>
</tr>
</tbody>
</table>

*In (rate ratio).
Despite decades of effort and many thousands of people randomised, it is still only limited and inconclusive evidence of the effects of modification of total, saturated, monounsaturated, or polyunsaturated fats on cardiovascular morbidity and mortality.

This study was conducted as a Cochrane systematic review under the auspices of the Cochrane Heart Group, whose assistance is gratefully acknowledged. We thank Gill Clements for her comments throughout the review, all those at the Systematic Reviews Training Unit for their help and support, and all the primary advisers. GDS provided epidemiological expertise and arbitrated on study inclusion when necessary. SE and CDS were primary reviewers. HL, SLM, and SDR made all treatment decisions and carried out the review, was the principal author, and is guarantor for the paper.

Funding: LJH's work on this review was partly funded by a studentship from the Systematic Reviews Training Unit, Institute of Child Health, University of London, and Shropshire Health Authority, Shrewsbury, contributed to travel expenses. RAR is supported by the British Heart Foundation.

Competing interests: None declared.

The effectiveness of exercise as an intervention in the management of depression: systematic review and meta-regression analysis of randomised controlled trials

Debbie A Lawlor, Stephen W Hopker

Abstract

Objective To determine the effectiveness of exercise as an intervention in the management of depression.

Design Systematic review and meta-regression analysis of randomised controlled trials obtained from five electronic databases (Medline, Embase, Sports Discus, PsycLIT, Cochrane Library) and through contact with experts in the field, bibliographic searches, and hand searches of recent copies of relevant journals.

Main outcome measures Standardised mean difference in effect size and weighted mean difference in Beck depression inventory score between exercise and no treatment and between exercise and cognitive therapy.

Results All of the 14 studies analysed had important methodological weaknesses; randomisation was adequately concealed in only three studies, intention to treat analysis was undertaken in only two, and assessment of outcome was blinded in only one. The participants in most studies were community volunteers, and diagnosis was determined by their score on the Beck depression inventory. When compared with no treatment, exercise reduced symptoms of depression (standardised mean difference in effect size −1.1 (95% confidence interval −1.5 to −0.6); weighted mean difference in Beck depression inventory −7.3 (−10.0 to −4.6)). The effect size was significantly greater in those trials with shorter follow up and in two trials reported only as conference abstracts. The effect of exercise was similar to that of cognitive therapy (standardised mean difference −0.3 (95% confidence interval −0.7 to 0.1)).

Conclusions The effectiveness of exercise in reducing symptoms of depression cannot be determined because of a lack of good quality research on clinical populations with adequate follow up.

Introduction

Depression is a common and important cause of morbidity and mortality worldwide. The effect of exercise on depression has been the subject of research for several decades, and the literature on the subject is growing. In the past decade “exercise on prescription” schemes have become popular in primary care in the United Kingdom, many of which include depression as a referral criterion.

Several plausible mechanisms for how exercise affects depression have been proposed. In the developed world taking regular exercise is seen as a virtue; the depressed patient who takes regular exercise may, as a result, get positive feedback from other people and an increased sense of self worth. Exercise may act as a diversion from negative thoughts, and the mastery of a new skill may be important. Social contact may be an important mechanism, and physical activity may have physiological effects such as changes in endorphin and monoamine concentrations.

This review summarises the evidence from randomised controlled trials of the effectiveness of exercise as a treatment for depression.

Methods

Identification of the studies

We searched Medline (1966-99), Embase (1980-99), Sports Discus (1975-99), PsycLIT (1981-99), the Cochrane Controlled Trials Register, and the Cochrane Database of Systematic Reviews using the terms “exercise,” “physical activity,” “physical fitness,” “walking,” “jogging,” “running,” “cycling,” “swimming,” “depression,” “depressive disorder,” and “dysthymia.” We also examined bibliographies, contacted experts, and hand searched copies published in the 12 months to December 1999 of selected journals (for details see the longer version of this paper on the BMJ’s website).