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Oats and CVD risk markers: a systematic literature review

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Abstract

High consumption of whole-grain food such as oats is associated with a reduced risk of CVD and type 2 diabetes. The present study aimed to systematically review the literature describing long-term intervention studies that investigated the effects of oats or oat bran on CVD risk factors. The literature search was conducted using Embase, Medline and the Cochrane library, which identified 654 potential articles. Seventy-six articles describing sixty-nine studies met the inclusion criteria. Most studies lacked statistical power to detect a significant effect of oats on any of the risk factors considered: 59% of studies had less than thirty subjects in the oat intervention group. Out of sixty-four studies that assessed systemic lipid markers, thirty-seven (58%) and thirty-four (49%) showed a significant reduction in total cholesterol (2–19% reduction) and LDL-cholesterol (4–23% reduction) respectively, mostly in hypercholesterolaemic subjects. Few studies (three and five, respectively) described significant effects on HDL-cholesterol and TAG concentrations. Only three out of twenty-five studies found a reduction in blood pressure after oat consumption. None of the few studies that measured markers of insulin sensitivity and inflammation found any effect after long-term oat consumption. Long-term dietary intake of oats or oat bran has a beneficial effect on blood cholesterol. However, there is no evidence that it favourably modulates insulin sensitivity. It is still unclear whether increased oat consumption significantly affects other risk markers for CVD risk, and comprehensive, adequately powered and controlled intervention trials are required to address this question.

Key words: Oats: CVD: Risk markers: Cholesterol: Inflammation: Insulin sensitivity

High consumption of whole-grain foods is associated with a reduced risk of chronic diseases including CHD[1,2], hypertension[3] and type 2 diabetes[4,5]. Suggested mechanisms of action include reduction in serum lipid concentrations[6] and blood pressure[7], increased insulin sensitivity[8] and reduction in thrombotic and inflammatory markers[9,10]. However, the results of the two most comprehensive, well-designed randomised control trials ever conducted with whole-grain foods found no significant effects on the major risk factors for CVD[7,11].

Whole grains consumed in a western diet consist mainly of wheat, rye, maize and oats. These cereals have different chemical compositions, which could explain the different responses with regard to CVD risk markers. Research has focused on β-glucan-rich cereals such as oats for their potential effect on serum cholesterol concentration[12] and postprandial glycaemia[13], with inconsistent results.

Although numerous studies suggest that there is a beneficial effect of oat consumption on markers of CVD risk, there is a need for a rigorous assessment of the strength of this evidence. The present study aimed to systematically review the literature describing intervention studies that had investigated the effect of regular consumption of whole-grain oat-based products (including oat bran) on risk factors for CVD. The objectives of the study were (i) to summarise the extensive literature on the subject, (ii) to describe the relative strengths and weaknesses of the studies and (iii) to evaluate the need for large intervention trials.

Methods

Literature search and study selection

The methods for the present literature review have been previously described (Thies F, Masson LF, Boffetta P *et al.*,

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in this supplement). Briefly, Embase, Medline and the Cochrane library (Cochrane Central Register of Controlled Trials) were searched for articles describing intervention studies with oat-based products published before 26 November 2012. A total of 1174 articles were identified (Fig. 1). Titles and abstracts of 654 articles were reviewed independently by two reviewers who agreed that the full text should be obtained for 244 articles. A further 178 articles were then excluded, following agreement by two reviewers. Ten additional articles were identified by searching the reference lists in relevant articles obtained from the database search.

Data extraction

Data were extracted by one reviewer into pre-prepared tables and the data extraction from a random 10 % of articles was checked and agreed by a second reviewer. The primary outcomes of interest included blood lipids/lipoproteins, blood pressure, glucose and insulin.

Quality of reporting and reporting preferences

Use of the Jadad scale for reporting randomised control trials[14] to score the quality of reporting of each article, as well as the criteria for classifying studies as randomised control trials, is described elsewhere (Thies F, Masson LF, Boffetta P *et al.*, in this supplement). For studies that showed a statistically significant ($P<0{\cdot}05$) effect of oats consumption, the percentage change from baseline in the intervention group relative to the control group was the preferred measure to present. If this was not available in the article, it was calculated from the results given, and such values are indicated in the tables. Interventions that involved products with altered molecular weight of β-glucan were not included.

Results

Study characteristics

We identified seventy-six articles[7,15–89] describing sixty-nine studies that assessed the effect of oat consumption on CVD

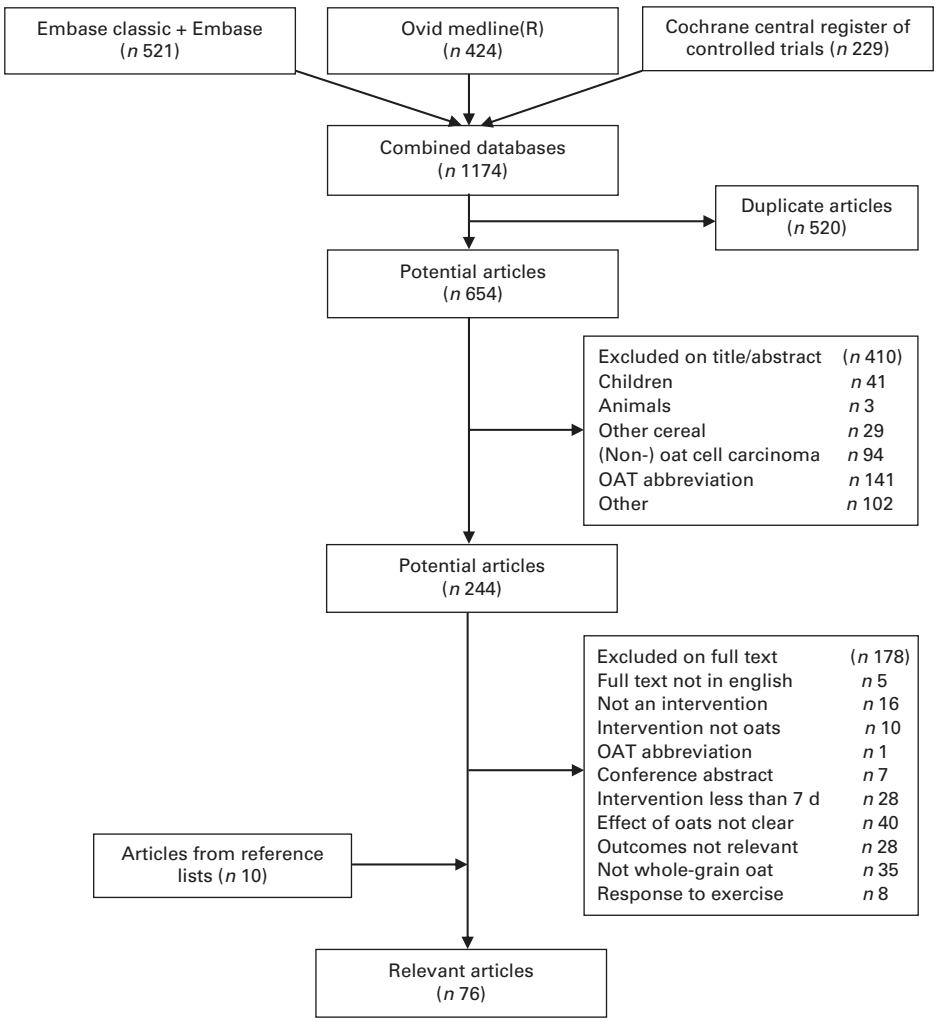

Fig. 1. Flow diagram of article selection.

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risk factors (Fig. 1). Online Web Tables S1–S3 describe the characteristics of these sixty-nine studies with less than thirty subjects (forty-one studies, 59%), between thirty and fifty-nine subjects (seventeen studies, 25%), and at least sixty subjects (eleven studies, 16%) in the oat intervention group, respectively. These tables are sub-grouped according to the quality of reporting of the articles: forty-six articles (61%) had a low quality of reporting, and thirty articles (39%) had a high quality of reporting.

Over half (54%) of the studies were carried out in North America (thirty-four in the USA and three in Canada). Six studies were carried out in Australia, five in Sweden, four each in the UK and New Zealand, three in Finland, two in the Netherlands, and one each in Austria, France, Germany, Denmark, China, Mexico and Brazil. One multicentre study was carried out in sites in Canada, the UK and Australia.

Lipids

Tables 1–3 show the results of sixty-four studies that assessed the blood lipid response to oat intervention in studies with less than thirty subjects, thirty to fifty-nine subjects or at least sixty subjects, respectively, in the oat intervention group. Of these sixty-four studies, thirty-seven (58%) and thirty-four (53%) studies identified a statistically significant reduction in total cholesterol and LDL-cholesterol, respectively, mostly in hypercholesterolaemic subjects; the rest of the studies found no significant response. This significant reduction ranged from 2 to 19% for total cholesterol and from 4 to 23% for LDL-cholesterol. In the eleven studies that contained at least sixty subjects in the oat intervention group, a higher proportion of studies found significant reductions in total cholesterol and LDL-cholesterol (eight studies (73%) and seven studies (64%), respectively), but the magnitude of these reductions was more conservative: 3–6% for total cholesterol and 4–8% for LDL-cholesterol (Table 3).

Three studies found that oat consumption significantly increased HDL-cholesterol levels by 4–11%. The ratios of total cholesterol:HDL-cholesterol and of LDL-cholesterol: HDL-cholesterol were reduced significantly in three studies (by 2–7%) and in five studies (by 9–21%), respectively. Five studies found a statistically significant reduction in TAG concentrations (by 11–24%) following oat-based intervention.

There is currently no evidence that oat consumption influences concentrations of HDL_2 and HDL_3 subfractions[18,45,49,83], intermediary density lipoprotein (IDL) cholesterol[18], VLDL cholesterol[15,18,23,24,33,41,42,57,62,87], or LDL, HDL or VLDL particle size[49].

Blood pressure

Table 4 shows that three[41,55,75] of twenty-five studies found that oat consumption significantly reduced systolic blood pressure by 4–6%. Two of these studies[41,55] had less than thirty subjects in the oat intervention group. Pins *et al.*[75] found that 73% of participants receiving treatment for hypertension were able to stop or reduce their medication by one-half after 6 weeks of consuming oats compared with 42% in the wheat-based cereal (control) group ($P<0{\cdot}05$). In addition, participants in the oat intervention group whose medication was not reduced had a significant 4% decrease in systolic blood pressure in comparison with the control group. The other twenty-two studies found no significant effect of oat consumption on systolic blood pressure.

Glucose and insulin

Blood glucose levels changed significantly in response to oat consumption in five out of twenty-one studies (Table 5). Glucose levels increased in three[37,51,59] of these studies relative to the comparison group or baseline, and glucose levels decreased in the other two studies[52,75]. Four of these five studies had less than thirty subjects in the oat intervention group, and the other study, with n 45 in the oat intervention group, found a 13% decrease in glucose after 12 weeks of an oat-rich diet compared with the control group who consumed wheat cereals[75].

Fifteen out of sixteen studies found no significant effect of oats on insulin concentrations. One relatively small study with twenty-two participants found that high-molecular weight oat bran significantly increased insulin concentrations by 23% compared with baseline[52]. None of the studies that measured glucose:insulin ratio[51], HbA1c[15,35], homeostasis model assessment[7,41,66], quantitative insulin sensitivity check index (QUICKI)[7], insulin sensitivity[41,49,50,55] or the acute insulin response to glucose[49] found a significant effect of oat consumption on these variables. One study found that glucose effectiveness decreased in the oat intervention group by 5% but increased in the wheat intervention group by 19% ($P=0{\cdot}03$ for interaction)[49].

Other outcomes

None of the studies that measured C-reactive protein[7,25,44,77,82,88], lipoprotein(a) (Lp(a))[28,79], fibrinogen[20] or IL-6[7] found a significant effect of oat consumption on these variables. There is also a lack of evidence for a beneficial effect of oats on endothelial function[70–72].

One study[44] reported measuring plasma homocysteine and found that concentrations were reduced by 16% in response to 12 weeks of oat bran. A Danish study found that plasminogen activator inhibitor-I and factor VII levels decreased significantly by 27 and 7%, respectively, following a 2-week oat bran *v.* a low-fibre diet[33], but no other studies reported measuring these outcomes. Another study measured serum NEFA that increased by 19% after consuming 35–50 g/d of oat bran for 4 weeks, relative to the group consuming an oat bran-free diet[79].

Discussion

Lipids/lipoproteins

The present systematic review supports the results of observational studies suggesting that increased oat consumption

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Table 1. Oats and blood lipids (studies with <30 subjects in the oat intervention group)

Comparison	Cholesterol					TAG	Reference
	Total	LDL	HDL	Total:HDL	LDL:HDL		
Low reporting quality							
Oat bran *v.* wheat bran	NS	NS	NS	–	NS	NS	Abrahamsson *et al.*[15]
100 g/d oat bran *v.* control diet	19 % ↓	23 % ↓	NS	–	–	19 %* ↓	Anderson *et al.*[16]
25 g/d oat bran *v.* baseline	5 % ↓	9 % ↓	NS	–	–	NS	Anderson *et al.*[17]
Oat bran *v.* wheat bran	8 %* ↓	7 %* ↓	NS	–	NS	NS	Anderson *et al.*[18], Bridges *et al.*[19]
Oat bran *v.* wheat bran bread	NS	NS	NS	–	–	NS	Bremer *et al.*[20]
28 g/d oatmeal *v.* 28 g/d farina	NS	NS	NS	–	–	NS	Davidson *et al.*[21]
28 g/d oat bran *v.* 28 g/d farina	NS	NS	NS	–	–	NS	
56 g/d oatmeal *v.* 28 g/d farina	NS	NS	NS	–	–	NS	
56 g/d oat bran *v.* 28 g/d farina	10 %* ↓	17 %* ↓	NS	–	–	NS	
84 g/d oatmeal *v.* 28 g/d farina	8 %* ↓	11 %* ↓	NS	–	–	NS	
84 g/d oat bran *v.* 28 g/d farina	8 %* ↓	12 %* ↓	NS	–	–	NS	
LFLC *v.* LFLC and oat bran *v.* oat bran *v.* processed oat bran	NS	–	NS	NS	–	–	Demark-Wahnefried *et al.*[22]
50 g/d oat bran *v.* baseline	12 % ↓	–	–	7 %* ↓	–	–	
40 g/d oat bran *v.* low-fibre diet	NS	NS	NS	–	–	NS	Dubois *et al.*[23]
100 g/d oat bran *v.* rice bran	NS	NS	NS	–	NS	NS	Hegsted *et al.*[24]
Oat bran bread *v.* strawberries	NS	NS	NS	NS	–	NS	Jenkins *et al.*[25]
125 g/d rolled oats *v.* control diet	NS	–	NS	–	–	NS	Judd & Truswell[26]
Oat bran muffins (immediate) *v.* no oat bran muffins	NS	NS	NS	NS	–	–	Kahn *et al.*[27]
100 g/d oat bran *v.* baseline	8 % ↓	10 % ↓	NS	–	–	NS	Kelley *et al.*[28]
Oat *v.* wheat (bread and cookies)	NS	NS	NS	NS	–	NS	Kerckhoffs *et al.*[29]
Oat *v.* wheat (orange juice)	4 % ↓	7 % ↓	NS	5 % ↓	–	NS	
100 g/d oat bran *v.* baseline	13 % ↓	14 % ↓	NS	–	–	NS	Kirby *et al.*[30]
Toasted oat bran *v.* control	NS	–	–	–	–	NS	Kretsch *et al.*[31], Calloway & Kretsch[32]
Untoasted oat bran *v.* control	NS	–	–	–	–	NS	
Oat bran *v.* low-fibre diet	10 %* ↓	NS	NS	–	–	12 %* ↓	Kristensen & Bugel[33]
Oat-based cereal *v.* wheat cereal	NS	NS	NS	–	–	NS	Maki *et al.*[34]
100 g/d oat bran *v.* low-fibre diet	9 %* ↓	–	–	–	–	NS	Marlett *et al.*[36]
Oat bran *v.* high-amylose starch	NS	NS	NS	–	–	11 %* ↓	Noakes *et al.*[37]
Oat bran *v.* low-amylose starch	NS	NS	NS	–	–	16 %* ↓	
0·75–1 l/d oat milk *v.* cow's milk	NS	NS	NS	–	–	NS	Onning *et al.*[38]
0·75–1 l/d oat milk *v.* soya milk	NS	NS	NS	–	–	NS	
28 g/d oat bran *v.* no supplement	NS	NS	9 %* ↑	NS	NS	NS	Robitaille *et al.*[39]
Oat bran *v.* wheat bran	18 %* ↓	22 %* ↓	NS	–	14 %* ↓	NS	Romero *et al.*[40]
Oat bran *v.* psyllium	NS	NS	NS	–	NS	NS	
45 g/d oats *v.* without 45 g/d oats	10 %* ↓	12 %* ↓	NS	–	–	NS	Saltzman *et al.*[41]
77 g/d oat bran *v.* baseline	6 % ↓	7 %* ↓	NS	–	–	–	Spiller *et al.*[42]
77 g/d oat bran *v.* 15 g/d guar gum	5 %* ↑	11 %* ↑	NS	–	–	NS	
50 g/d oat bran or oat-free diet	NS	NS	–	–	–	NS	Stewart *et al.*[43]
150 g/d rolled oats *v.* baseline	5 %* ↓	14 % ↓	NS	–	–	NS	Turnbull & Leeds[45]
Oat bran *v.* wheat bran	4 % ↓	6 % ↓	NS	–	–	NS	Whyte *et al.*[46]
Oat bran *v.* wheat flour	9 % ↓	12 % ↓	NS	–	–	NS	Zhang *et al.*[47]
High reporting quality							
5–6 g/d oat bran β-glucan *v.* 8–9 g/d oat bran β-glucan *v.* high fibre, no oat bran β-glucan	NS	NS	NS	–	–	NS	Beck *et al.*[48]
Oatmeal and oat bran *v.* wheat-based cereal	NS	11 %* ↓	NS	NS	21 %* ↓	NS	Davy *et al.*[49,50]
60 g/d oat cookies *v.* baseline	NS	–	–	–	–	NS	Conceicao de Oliveira *et al.*[51]
High MW oat bran *v.* baseline	NS	NS	NS	–	NS	NS	Frank *et al.*[52]
Low MW oat bran *v.* baseline	NS	NS	NS	–	NS	NS	
84 g/d oat bran *v.* rice starch	13 %* ↓	13 %* ↓	NS	–	14 %* ↓	NS	Gerhardt & Gallo[53]
84 g/d oat bran *v.* rice bran	NS	NS	NS	–	NS	NS	
34 g/d oat bran *v.* wheat bran and whole-wheat flour or wheat bran, whole-wheat flour and 17 g/d oat bran combined	5 %* ↓	NS	NS	–	–	15 %* ↓	Gold & Davidson[54]
Oat cereal *v.* low fibre cereal	11 %* ↓	18 %* ↓	NS	–	–	NS	Keenan *et al.*[55]
Oat bran *v.* wheat bran	6 % ↓	7 %* ↓	NS	–	–	NS	Kestin *et al.*[56]
Oat bran *v.* rice bran	4 % ↓	5 %* ↓	NS	–	–	NS	
100 g/d oat bran *v.* refined wheat	NS	NS	NS	–	–	–	Swain *et al.*[57]
50 g/d oat bran *v.* baseline	NS	NS	NS	–	–	NS	Uusitupa *et al.*[58,59]

LFLC, low-fat, low-cholesterol diet; MW, molecular weight.
*% change from baseline relative to comparison group estimated.

Table 2. Oats and blood lipids (studies with thirty to fifty-nine subjects in the oat intervention group)

Comparison	Cholesterol					TAG	Reference
	Total	LDL	HDL	Total:HDL	LDL:HDL		
Low reporting quality							
Kilned oats *v.* baseline (A)†	NS	–	NS	–	–	NS	Kemppainen *et al.*[60]
Unkilned oats *v.* baseline (B)	NS	–	NS	–	–	24 %* ↓	
0 *v.* 30 *v.* 60 *v.* 90 g/d oat bran	NS	NS	NS	–	–	–	Leadbetter *et al.*[61]
55 g high-fibre oat bran *v.* run-in	NS	NS	11 %* ↑	–	9 %* ↓	NS	Mackay & Ball[62]
55 g low-fibre oat bran *v.* run-in	NS	NS	11 %* ↑	–	10 %* ↓	NS	
Oat bran crispies *v.* no oat cereal	2 % ↓	5 % ↓	NS	NS	NS	NS	Poulter *et al.*[63]
57 g/d instant oats *v.* usual intake	5 %* ↓	5 %* ↓	NS	–	–	NS	Van Horn *et al.*[64]
NCEP and oat bran *v.* NCEP	6 %* ↓	9 %* ↓	NS	–	–	NS	Winblad *et al.*[65]
NCEP and oat bran *v.* washout	NS	9 %* ↓	NS	–	–	NS	
High reporting quality							
Oats (high) *v.* oats, rice and wheat (low) *v.* corn, rice and wheat bars	NS	NS	NS	NS	–	NS	Charlton *et al.*[66]
Oat bran *v.* wheat bran	6 %* ↓	9 %* ↓	NS	–	–	NS	Kashtan *et al.*[68]
Uncooked whole oats *v.* baseline	5 %* ↓	7 %* ↓	NS	–	–	NS	Katz *et al.*[72]
Oatbran *v.* wheat bran	NS	6 %* ↓	NS	–	9 %* ↓	NS	Lepre & Crane[73]
Oat milk *v.* rice milk	6 %* ↓	6 %* ↓	NS	–	NS	NS	Onning *et al.*[74]
Oatmeal and Oat Squares *v.* wheat cereal and Kellogg's Crispix	11 %* ↓	12 %* ↓	NS	–	–	NS	Pins *et al.*[75]
Muesli with oat β-glucan *v.* wheat fibre	3 % ↓	5 % ↓	NS	2 % ↓	–	NS	Theuwissen & Mensink[76]
Oats/soya and oats/milk *v.* wheat/soya and wheat/milk	4 %* ↓	6 %* ↓	NS	–	–	–	Van Horn *et al.*[78]

NCEP, National Cholesterol Education Program.
* % change from baseline relative to comparison group estimated.
† Group A started using kilned oats and group B started using unkilned oats.

has a beneficial effect on serum cholesterol concentration, particularly in hypercholesterolaemic subjects. This is consistent with Ripsin *et al.*'s[90] rigorous meta-analysis that concluded that about 3 g/d of soluble fibre from oat products can lower total cholesterol by 0·13 to 0·16 mmol/l, with a greater reduction in individuals with higher initial cholesterol concentrations. A 1% reduction in total cholesterol or LDL-cholesterol is associated with a 2–3% or 1% decreased risk, respectively, of CHD[91]. The magnitude of the effect found in the present review (3–6% for total cholesterol and 4–8% for LDL-cholesterol when considering studies with a sufficient sample size) would translate to a 6–18% decrease in CHD risk, which would equate to a substantial health benefit at a population level. However, increased oat consumption does not seem to significantly benefit other systemic lipid/lipoprotein markers associated with CVD risk, such as serum TAG and HDL-cholesterol concentration.

Lipoprotein particle number and size, particularly for LDL, are possibly strong predictors of CVD[92] and could provide an independent measure of atherogenicity, which may be superior to total cholesterol determination. However, only a few studies evaluated the effect of oat intervention on the size and concentration of lipoprotein particles, with inconclusive results. More evidence is needed to establish whether increased oat consumption favourably affects the lipoprotein particle profile.

Blood pressure

Few studies found a significant effect of increased oat consumption on blood pressure. However, none of the studies carried out to date was adequately powered to rigorously evaluate the effect of oats or oat bran on this outcome. Furthermore, blood pressure results from these studies were most likely averaged from only two or three consecutive measurements. Such methodology, recommended by the British Hypertension Society, might be useful to identify hypertensive subjects but does not represent a precise method for measuring blood pressure, as recently suggested[7].

Tighe *et al.*[7] found a significant reduction in systolic blood pressure after 12 weeks intervention with whole grain (wheat or oats plus wheat) compared with a refined cereals group. Blood pressure was measured using additional consecutive readings until the last three measurements varied by less than 8%, and a significant reduction would not have been identified using the conventional method of measuring blood pressure. This demonstrates the requirement for all types of intervention trials (pharmaceutical, supplement, food-based, lifestyle interventions, etc.) where blood pressure is an outcome to adopt procedures designed to accurately measure blood pressure rather than those used for diagnostic classification. The best method to accurately measure blood pressure is to carry out 24-h ambulatory measurements. Thus, adequately powered and controlled intervention trials are required to determine the effects of oats on blood pressure.

Glucose and insulin

Impaired fasting glycaemia and impaired glucose tolerance are major risk factors for type 2 diabetes, and are strongly associated with an increased risk of CVD and all-cause mortality[93]. The present review indicates that interventions with oats or oat bran do not affect fasting glycaemia or insulin concentration.

Table 3. Oats and blood lipids (studies with ≥60 subjects in the oat intervention group)

Comparison	Cholesterol					TAG	Reference
	Total	LDL	HDL	Total:HDL	LDL:HDL		
Low reporting quality							
Oat bran *v.* no added oat bran	4 %* ↓	6 %* ↓	NS	–	–	NS	Berg *et al.*[79]
90 g/d oat cereal *v.* corn cereal	6 %* ↓	8 %* ↓	NS	–	–	NS	Karmally *et al.*[80]
Oat bran cereal and CNA *v.* CNA	NS	NS	NS	NS	–	NS	Keenan *et al.*[81]
Oat bran cereal *v.* baseline	NS	NS	NS	NS	–	NS	
Oat cereal *v.* low-fibre foods	3 % ↓	4 % ↓	NS	–	–	NS	Maki *et al.*[82]
Whole-wheat foods and oats *v.* whole-wheat foods	NS	NS	NS	–	–	NS	Tighe *et al.*[7]
56 g oatmeal or no oat products	NS	NS	NS	–	–	NS	Van Horn *et al.*[83]
100 g/d oatmeal *v.* wheat noodles	4 %* ↓	5 %* ↓	4 %* ↑	–	–	NS	Zhang *et al.*[84]
High reporting quality							
90 g oat cereal *v.* cornflakes	4 % ↓	4 % ↓	NS	–	–	NS	Johnston *et al.*[85]
Oat bran cereal *v.* wheat cereal	6 % ↓	8 % ↓	NS	–	–	–	Keenan *et al.*[86]
Oat bran *v.* no oat products	NS	–	–	–	–	–	Van Horn *et al.*[87]
Oatmeal *v.* no oat products	3 % ↓	–	–	–	–	–	
Oat bran *v.* oatmeal *v.* no oat products	NS	NS	NS	–	–	NS	
Oat bran *v.* wheat bran cereal	4 % ↓	6 % ↓	NS	NS	–	NS	Wolever *et al.*[88]

CNA, controlled-release nicotinic acid.
* % change from baseline relative to comparison group estimated.

Similarly, evidence to date suggests that markers for insulin resistance (homeostasis model assessment) or sensitivity that use algorithms including fasted glucose and insulin concentrations are also unchanged after intervention with oats or oat bran.

Other outcomes

Many inflammatory markers (including C-reactive protein, IL-6 and soluble intercellular adhesion molecule 1 (ICAM-1)) have been linked to CVD risk, but only high-sensitivity C-reactive protein is currently considered an independent marker of CVD risk[94]. Observational studies suggest that a high dietary fibre intake may reduce C-reactive protein levels[95,96]. However, only a few intervention studies reported the effect of long-term consumption of oats and oat bran on inflammatory markers or markers of endothelial dysfunction (von Willebrand factor, arterial stiffness and fibrinogen). None reported changes in these markers with increased oat consumption, suggesting that the benefits of oats on CVD are unlikely to be mediated by the modulation of these markers. However, more studies are needed to confirm the lack of effect, or otherwise, of oats on these putative markers.

Other systemic compounds that have been linked to an increased CVD risk include homocysteine[97], plasminogen activator inhibitor-I[98] and factor VII[99]. However, the studies that examined the effects of increased oat consumption on these markers are scarce. One study reported measuring plasma homocysteine and found that concentrations decreased by 16 % in response to 12 weeks of oat bran[44]. A Danish study[33] found that plasminogen activator inhibitor-I and factor VII levels decreased significantly by 27 and 7 %, respectively, following a 2-week oat bran *v.* a low-fibre diet. No other studies reported measuring these outcomes, which deserve further investigation.

Weight gain is associated with an increased risk of high blood pressure and hyperlipidaemia. Whilst some studies suggest that increased oat consumption may aid weight loss[16,69] and reduce waist circumference[82,84], the majority of studies reviewed herein found no significant effect of oat consumption on weight[15,17–20,22,24–26,28–30,33,36,38–40,42,45,48–50,52,55–58,60–64,66–68,73–76,79,82–85,87,88], BMI[15,39–41,43,49,50,58,60,64,78,79,84] or waist circumference[39,48–50]. In order to assess the effect of oats on body weight, it is necessary to also consider the energy and macronutrient content of the intervention diets, which is beyond the scope of the present review. Whilst oats may be used to displace other (more energy dense) foods in the diet, their effect on hunger and satiety is not clear. Although three[48,67,86] of the studies included in the present review found no significant effect of oats on satiety, hunger or appetite, positive comments from one study[48] included 'feeling more full, for longer' and 'less peaks & lows' in intake. However, satiety is an acute physiological effect of a single meal intake and does not necessarily equate to longer-term changes in dietary habits, which could result in weight loss and/or reduced weight gain. Therefore, the measurement of satiety cannot substitute for longer-term intervention studies measuring body weight and/or composition. The European Food Safety Authority Panel on Dietetic Products, Nutrition and Allergies (NDA) recently concluded that a cause-and-effect relationship has not been established between the consumption of β-glucans from oats and barley and a sustained increase in satiety leading to a reduction in energy intake[100]. However, this aspect requires further investigation.

Whilst advice to increase oat consumption is likely to have beneficial health effects, it should be noted that relatively minor side effects (which may only be initial or intermittent) may include flatulence[15,43,57,59,85], abdominal distension or bloating[20,43,57,68,73], diarrhoea or loose stools[35,57,68], and abdominal pain or cramping[48,57]. Taking such side effects into consideration, one study[43] found that 50 g/d of oat bran was considered 'acceptable long term' by 76 % of participants and 'unacceptable long term' by 24 % of participants.

Table 4. Results of studies assessing the effect of oat consumption on blood pressure

Comparison	Blood pressure		Reference
	Systolic	Diastolic	
<30 subjects in the oat intervention group and low reporting quality			
Oat bran *v.* wheat bran (20 g fibre)	NS	NS	Abrahamsson *et al.*[15]
65 g/8368 kJ/d (2000 kcal/d) oat bran bread *v.* 454 g/d strawberries	NS	NS	Jenkins *et al.*[25]
Oat bran, oatmeal and oat β-glucan *v.* wheat-based, low-fibre cereal and maltodextrin powder	NS	NS	Maki *et al.*[35]
45 g/d oats *v.* without 45 g/d oats	4 %* ↓	NS	Saltzman *et al.*[41]
<30 subjects in the oat intervention group and high reporting quality			
Oatmeal and oat bran *v.* wheat-based cereal	NS	NS	Davy *et al.*[50]
137 g/d oat cereal *v.* 146 g/d low-fibre cereal	6 %* ↓	NS	Keenan *et al.*[55]
95 g/d oat bran *v.* 35 g/d wheat bran	NS	NS	Kestin *et al.*[56]
95 g/d oat bran *v.* 60 g/d rice bran	NS	NS	
100 g/d oat bran *v.* refined wheat	NS	NS	Swain *et al.*[57]
50 g/d oat bran *v.* baseline	NS	NS	Uusitupa *et al.*[59]
30–59 subjects in the oat intervention group and low reporting quality			
0 *v.* 30 *v.* 60 *v.* 90 g/d oat bran	NS	NS	Leadbetter *et al.*[61]
55 g high-fibre oat bran *v.* run-in	NS	NS	Mackay & Ball[62]
55 g low-fibre oat bran *v.* run-in	NS	NS	
≥50 g/d Oat bran crispies *v.* no oat cereal	NS	NS	Poulter *et al.*[63]
57 g/d instant oats *v.* usual intake	NS	NS	Van Horn *et al.*[64]
30–59 subjects in the oat intervention group and high reporting quality			
Oats (high) *v.* oats, rice and wheat (low) *v.* corn, rice and wheat	NS	–	Charlton *et al.*[66]
OBC and Oatmeal Squares *v.* refined wheat and cornflakes	NS	NS	He *et al.*[67]
60 g/d uncooked whole oats *v.* baseline	NS	NS	Katz *et al.*[72]
60 g/d oat bran *v.* baseline	NS	NS	Lepre & Crane[73]
Oat milk deprived of insoluble fibre *v.* rice milk	NS	NS	Onning *et al.*[74]
Oatmeal and Oat Squares *v.* wheat cereal and Kellogg's Crispix	4 %* ↓	NS	Pins *et al.*[75]
Oats/soya and oats/milk *v.* wheat/soya and wheat/milk	NS	NS	Van Horn *et al.*[78]
≥60 subjects in the oat intervention group and low reporting quality			
80 g/d oat cereal *v.* low-fibre foods	NS	NS	Maki *et al.*[82]
Whole-wheat foods and oats *v.* whole-wheat foods	NS	NS	Tighe *et al.*[7]
100 g/d oatmeal *v.* wheat noodles	NS	NS	Zhang *et al.*[84]
≥60 subjects in the oat intervention group and high reporting quality			
90 g oat cereal *v.* cornflakes	NS	NS	Johnston *et al.*[85]
20 g/d oat bran cereal *v.* 21 g/d wheat bran cereal	NS	NS	Wolever *et al.*[88]

OBC, oat bran concentrate.
* % change from baseline relative to comparison group estimated.

Limitations

The majority of studies identified by the present review were relatively small and did not have sufficient power to detect an effect: only twenty-three of the seventy-six articles reviewed (30 %) described carrying out a sample size or power calculation. For many of the variables (such as total cholesterol, LDL-cholesterol, ICAM1, apo and glucose), variation among individuals has been found by other authors to be about 10–20 %. Baseline covariate adjustment should reduce this to 5–10 %. This means that sixty subjects per group should give sufficient experimental power (90 %) to detect intervention effects of 5–7 %. Even less variation is expected in total cholesterol (SD approximately 0·25 mM, range 5–6 mM), so that sixty subjects per group will provide sufficient power to detect differences of 0·2 mM. Larger sample sizes would be required to assess intervention effects on blood pressure and inflammatory markers.

Ideally, a meta-analysis would be carried out to assess whether oats have a significant effect on the outcomes reported in the present review, and if so the size of this effect. However, the authors concluded that a meaningful summary estimate could not be obtained by meta-analysis for several reasons. First, the studies were too heterogeneous. The amount and type of oat products used were varied, and the comparison/control groups included a range of different treatments, for example, refined wheat, whole-wheat products, rice bran, psyllium, farina, fruit or no control. The duration of the studies (from 2 weeks to 6 months) and the initial blood cholesterol concentration of the subjects were also varied. Secondly, many studies were considered of poor quality: 61 % of articles had a low modified Jadad score, and 59 % of studies had less than thirty subjects in the oat intervention group. Thirdly, the outcomes were reported inconsistently among studies, e.g. mean absolute difference, or percentage change, or simply a line in the text to say that there was no significant effect. Some changes were compared with a control group *v.* baseline, and some results were adjusted for confounding factors whereas others were not.

Furthermore, the present review did not consider the appropriateness of the control group, changes in body weight, energy intake and macronutrient intake during the intervention, or compliance with the intervention – all of which could impact the response to the intervention and thus a meta-analysis summary estimate. The question regarding what could be considered as an ideal control group is

Table 5. Results of studies assessing the effect of oat consumption on glucose and insulin

Comparison	Glucose	Insulin	Reference
<30 subjects in the oat intervention group and low reporting quality			
Oat bran *v.* wheat bran (20 g fibre)	NS	NS	Abrahamsson *et al.*[15]
100 g/d oat bran *v.* control diet	NS	–	Anderson *et al.*[16]
Oat bran bread *v.* wheat bran bread	NS	NS	Bremer *et al.*[20]
40 g/d oat bran diet *v.* low-fibre diet *v.*	–	NS	Dubois *et al.*[23]
100 g/d oat bran *v.* no oat bran	NS	–	Kirby *et al.*[30]
Oat bran, oatmeal and oat β-glucan *v.* wheat-based, low-fibre cereal and maltodextrin powder	NS	NS	Maki *et al.*[35]
87–121 g/d oat bran *v.* 50–74 g/d high-amylose starch diet	NS	NS	Noakes *et al.*[37]
87–121 g/d oat bran *v.* low-amylose starch diet	3 %* ↑	NS	
0·75–1 l/d oat milk *v.* cow's milk	NS	NS	Onning *et al.*[38]
0·75–1 l/d oat milk *v.* soya milk	NS	NS	
45 g/d oats *v.* without 45 g/d oats	NS	NS	Saltzman *et al.*[41]
123 g/d oat bran *v.* 54 g/d wheat bran	NS	–	Whyte *et al.*[46]
<30 subjects in the oat intervention group and high reporting quality			
5–6 g/d oat bran β-glucan *v.* 8–9 g/d oat bran β-glucan *v.* high fibre, no oat bran β-glucan	NS	NS	Beck *et al.*[48]
Oatmeal and oat bran *v.* wheat-based cereal	NS	NS	Davy *et al.*[49,50]
60 g/d oat cookies *v.* baseline	NS	NS	Conceicao de Oliveira *et al.*[51]
60 g/d oat cookies *v.* 300 g/d fruit	5 %* ↑	–	
High molecular weight oat bran *v.* baseline	3 %* ↓	23 %* ↑	Frank *et al.*[52]
Low molecular weight oat bran *v.* baseline	NS	NS	
137 g/d oat cereal *v.* 146 g/d low-fibre cereal	–	NS	Keenan *et al.*[55]
95 g/d oat bran *v.* 35 g/d wheat bran	NS	NS	Kestin *et al.*[56]
95 g/d oat bran *v.* 60 g/d rice bran	NS	NS	
50/d oat bran *v.* baseline	+4 %* ↑	NS	Uusitupa *et al.*[59]
30–59 subjects in the oat intervention group and low reporting quality			
No studies			
30–59 subjects in the oat intervention group and high reporting quality			
Oats (high) *v.* oats, rice and wheat (low) *v.* corn, rice and wheat	NS	NS	Charlton *et al.*[66]
Oat milk deprived of insoluble fibre *v.* rice milk	NS	–	Onning *et al.*[74]
Oatmeal and Oat Squares *v.* wheat cereal and Kellogg's Crispix	13 %* ↓	–	Pins *et al.*[75]
≥60 subjects in the oat intervention group and low reporting quality			
Whole wheat foods and oats *v.* whole wheat foods	NS	NS	Tighe et al.[7]
100 g/d oatmeal *v.* wheat noodles	NS	–	Zhang *et al.*[84]
≥60 subjects in the oat intervention group and high reporting quality			
20 g/d oat bran cereal *v.* 21 g/d wheat bran cereal	NS	–	Wolever *et al.*[88]

* % change from baseline relative to comparison group estimated.

important, and depends on the study aim as well as the primary outcomes of the trial. The results tables highlight the disparity of control groups used as comparators in previous studies. Guar gum, undefined control diet, usual diet, wheat- or rice-based products, β-glucan-enriched products as well as products based on specific parts of the grain such as bran and not the whole-grain product have been used. Some designs involved increasing total whole-grain intake without substitution of existing dietary components. An ideal control group should at least consider unchanged total energy intake during the intervention, substituting whole-grain food items with a similar amount of refined cereal products (white breads, etc.). The level of oats/whole-grain intake in the control group should match the lowest quartile of consumption observed in the population studied. When trials aim to identify the active parts or components of the grain, a positive control (with whole grain) should also be included. Further analysis of the studies reviewed herein is required before sufficiently homogenous studies can be chosen for inclusion in a meta-analysis to obtain both a precise and meaningful estimate of the magnitude of the effect of oat consumption on CVD risk markers.

The lack of significant effects in some studies may have been due to the factors mentioned earlier, or could be due to the fact that the response may be modified by other factors. Some studies carried out sub-group analysis or tested for interaction (effect modification), e.g. by sex[29,37,38,52,83], sex and age group[86], BMI group[35], ethnicity (Caucasians *v.* non-Caucasians)[89], genotype[59,69], amount of target dose consumed[59] and baseline total cholesterol level[40,83].

The results of such analyses were not considered in the present review; however, these need to be further assessed in larger studies with sufficient power for subgroup analyses or assessing effect modification.

The present review only considered the effect of oats on fasting lipids, glucose and insulin. However, regular consumption of oats may alter the postprandial concentrations. For example, Anderson *et al.*[18] showed that 110 g/d oat bran for 21 d significantly lowered postprandial serum total cholesterol and TAG concentrations *v.* a control diet. However, Kirby *et al.*[30] found that a similar amount of oat bran (100 g/d) for a shorter time period (at least 10 d) did not significantly affect postprandial serum total cholesterol or TAG, when measured at hourly intervals throughout the day when compared with a control diet. A 12-week trial of oat consumption significantly lowered the mean peak insulin and incremental area under the insulin curve response (both by 7 %) compared with a control group, but there was no significant change in peak glucose or incremental area under the glucose curve[35]. Other studies found that oats or oat bran did not significantly affect postprandial glucose or insulin responses[30,34,56]. The efficacy of oats and barley products to lower postprandial blood glucose concentration has been reviewed recently[13]. The author concluded that intact grain, as well as barley and oat products containing at least 4 g of β-glucan and 30–80 g of available carbohydrate can significantly reduce postprandial glucose concentrations. The health benefit of reducing postprandial glycaemia is still debatable, but a statement recently issued by the European Food Safety Authority indicates that 'the reduction of postprandial glycaemic responses (as long as insulinaemic responses are not disproportionally increased) may be a beneficial physiological effect'[100].

Conclusions

Regular consumption of oats or oat bran has a beneficial effect on total cholesterol and LDL-cholesterol, particularly in hypercholesterolaemic subjects. The intervention trials described in the present review can generally be divided into three groups depending on the product used in the intervention: oat bran; whole-grain oat cereals; oatmeal. For the studies that showed a significant reduction in total cholesterol and/or LDL-cholesterol, the range of doses used was 25–135 g/d for oat bran, 45–90 g/d for whole-grain oat cereals and 60–150 g/d for oatmeal. So it appears that the form of oats does not really affect the outcome. The doses required to reach a significant effect were also similar. However, studies using amounts below 50 g/d are scarce, and more well-designed dose–response studies are needed to confirm the minimum amount required to have a clinical beneficial effect. The 3–6 % cholesterol reduction described in the larger studies would translate to a 6–18 % decrease in CHD risk. Some studies reported significant effects on blood cholesterol only 2 weeks after beginning the intervention, so it is likely that the benefits of increasing oats intake start very shortly after changing the diet. How long these effects on blood cholesterol remain if subjects revert to their original diet remains to be determined. However, there is no indication that it would significantly modulate insulin sensitivity. It is still unclear whether increased oat consumption would significantly affect other risk markers for CVD risk. More comprehensive, properly controlled intervention trials with adequate sample sizes are required to answer this question. The present review also highlighted the heterogeneity of treatments used as a control and notes the importance of carefully defining appropriately controlled interventions.

Supplementary material

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