

Title	The separate effects of whole oats and isolated beta-glucan on lipid profile: a systematic review and meta-analysis of randomized controlled trials						
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Publication date	2022-12-19						
Original Citation	de Morais Junior, A. C., Schincaglia, R. M., Viana, R. B., Armet, A. M., Prado, C. M., Walter, J., Mota, J. F. (2022) 'The separate effects of whole oats and isolated beta-glucan on lipid profile: a systematic review and meta-analysis of randomized controlled trials', Clinical Nutrition ESPEN. doi: 10.1016/j.clnesp.2022.12.019						
Type of publication	Article (peer-reviewed)						
Link to publisher's version	10.1016/j.clnesp.2022.12.019						
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Download date	2025-09-13 22:48:57						
Item downloaded from	https://hdl.handle.net/10468/14083						



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PII: S2405-4577(22)01429-2

DOI: https://doi.org/10.1016/j.clnesp.2022.12.019

Reference: CLNESP 1589

To appear in: Clinical Nutrition ESPEN

Received Date: 12 December 2022

Accepted Date: 15 December 2022

Please cite this article as: de Morais Junior AC, Schincaglia RM, Viana RB, Armet AM, Prado CM, Walter J, Mota JF, The separate effects of whole oats and isolated beta-glucan on lipid profile: a systematic review and meta-analysis of randomized controlled trials, *Clinical Nutrition ESPEN*, https://doi.org/10.1016/j.clnesp.2022.12.019.

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The separate effects of whole oats and isolated beta-glucan on lipid profile: a systematic review and meta-analysis of randomized controlled trials

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Running title: Oat or isolated β-glucan on lipid profile

Abbreviations list:

TC, total cholesterol;

LDL, low density lipoprotein;

HDL, high density lipoprotein;

TG, triglycerides;

SMD, standardized mean difference;

CI, confidence interval;

PRISMA, preferred reporting items for systematic review and meta-analysis protocols;

PROSPERO, international prospective register of systematic reviews;

MESH, medical subject heading;

RCT, randomized clinical trial;

BMI, body mass index;

RoB2, cochrane risk-of-bias tool 2;

SD, standard deviation;

Registration: This review was registered at PROSPERO under the identification number CRD42021249983.

Abstract

Background & Aims: It is well known that dietary fiber positively impacts the microbiome and health as a whole. However, the health effects of β -glucan, a dietary fiber extracted from oats, have been questioned when administered alone or incorporated into other foods. The purpose of this systematic review and meta-analysis was to evaluate the impact of oats or β glucan supplements on the lipid profile. Methods: Randomized controlled trials with parallelarm or crossover blinded interventions at least two weeks in duration, for hyperlipidemic or non-hyperlipidemic men and women ≥ 18 years of age were selected. Only single (participants blinded) or double-blinded studies that compared oat or isolated β -glucan with a placebo/control group were considered for this review. The databases EMBASE, PubMed, Web of science and CINHAL were searched, from the earliest indexed year available online to the end of January 2022. Random-effects models were used to combine the estimated effects extracted from individual studies, and data were summarized as standardized mean difference (SMD) and 95% confidence interval (95%CI). Results: A total of 811 articles were screened for eligibility, and relevant data were extracted from 28 studies, totaling 1494 subjects. Oat interventions TC (-0.61, 95%CI: -0.84;-0.39, p<0.00001, and -0.70, 95%CI: -1.07;-0.34, p=0.0002, respectively) and LDL (-0.51, 95%CI: -0.71;-0.31, p<0.00001, and -0.38, 95% CI: -0.60; -0.15, p=0.001, respectively). Moreover, isolated β -glucan interventions from parallel-arm studies decreased TC (-0.73, 95%CI: -1.01;-0.45, p<0.00001), LDL (-0.58, 95%CI: -0.85;-0.32, p<0.0001) and triglycerides (-0.30, 95%CI: -0.49;-0.12, p=0.001). HDL was not altered by either oat or isolated β -glucan (p>0.05). Conclusion: Overall, this review showed that both oat and isolated β -glucan interventions improved lipid profiles. Furthermore, the ingestion of oats or isolated β -glucan supplements are effective tools to combat dyslipidemia and should be considered in cardiovascular disease prevention.

Keywords: Avena sativa; oats; beta-glucan; dietary fiber; blood cholesterol; meta-analysis

Introduction

Nutraceuticals have been used as lipid-lowering agents and have safely and successfully improved plasma lipid levels [1]. Among the nutraceuticals applied for improvement of the lipid profile is found dietary fiber, particularly a type of fiber called β -glucan. The term dietary fiber is believed to have been coined by Hipsley in 1953 [2] and it is usually related to the non-digestible carbohydrates found in plants. It is well documented that the ingestion of dietary fiber has drastically dropped as a result of major changes in human eating habits related to industrialization [3,4]. Dietary fiber intake has been inversely linked with inflammation [5,6], insulin resistance [7], risk for cardiovascular disease [8,9], certain cancers [10,11], and overall mortality [12]. High fiber intake has also been associated with increased satiety [13] and improved body weight management [14].

Viscous fibers, such as β -glucan found in oats and barley, have been specifically linked with improved markers of cardiovascular disease [15]. Mechanisms of action as to how these fibers help reduce total cholesterol (TC) and low-density lipoprotein cholesterol (LDL) [16] include reducing the reabsorption of intestinal bile acids [17,18], and changing the colonic bacterial metabolism [19]. Furthermore, these fibers promote a reduced absorption of cholesterol by thickening the contents of the intestinal tract and delaying migration of nutrients to the intestinal walls [20]; where viscosity of the fiber determines its effectiveness in reducing absorption [15]. Oats, as a source of β -glucan, have been studied extensively and have consistently shown promising results related to improved lipid profiles [21,22].

Although the benefits of intrinsic or endogenous dietary fiber present in whole plant foods are well established, the health effects of dietary fibers extracted from whole foods (so called isolated or purified fibers) when used as supplements or in foods that do not naturally contain such fibers have been questioned [23,24]. For example, the three-dimensional (3D)

matrix of the plant cell wall in which the fiber is organized in whole foods confers additional benefits such as affecting the digestibility of other nutrients contained within the cells. In contrast, purified fibers may have a reduction in the micronutrients and phytochemicals present in whole plant foods. Isolated β -glucan supplements could potentially fill the gap regarding the lack of dietary fiber in modern society's eating habits [25]. Important reviews and meta-analysis have been done along the last three decades but, without exception they have pooled oats and isolated β -glucan together in their analysis [21,22,26–29]. Recently, a review had the intention to conduct sub-analyses based on intervention type (oat or O β GREs [oat beta-glucan-rich extracts]), but due to the limited number of studies included, this was not possible [30]. To fulfill this role, it is necessary to validate and understand whether isolated β -glucan also provides benefits to health. Oats, instead of other β -glucan sources, have been chosen in this review due to its worldwide consumption when compared to other β -glucan sources like barley and shiitake and reishi mushrooms [31]. The aim of this systematic review and meta-analysis was, therefore, to evaluate the impact of oat ingestion and isolated β -glucan on lipidaemia.

Materials & Methods

The Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) [32] was used in this review as a reporting guideline. This review was registered with the International Prospective Register of Systematic Reviews (PROSPERO) under the identification number CRD42021249983.

Search strategy

The databases EMBASE, PubMed, Web of science and CINHAL were searched, from the earliest indexed year available online to January 2022. A combination of Medical Subject

Heading (MeSH) terms and keywords were used for the searches in the databases. The search strategy used was as follows: ("lipid profile" OR "dyslipidaemia" OR "cholesterol") AND ("oat meal", OR "oatmeal" OR "oats" OR "*Avena sativa*" OR "beta-glucan" OR "β-glucan") Titles and abstracts of the studies identified through the computerized searches were sent to the online application Rayyan [33] for further screening. Reference lists from the original articles were also screened for additional articles that potentially could be included.

Study selection criteria

Human intervention trials published in English were included. Specifically, randomized controlled trials (RCTs), including both parallel-arm and crossover designs, were eligible if carried out in men and/or women (\geq 18 years of age), who either had normal or high total cholesterol levels, defined as <5.18 mmol/L or \geq 5.18 mmol/L, respectively. Studies were required to have evaluated at least three of the four parameters of the lipid profile: TC, LDL, high-density lipoprotein cholesterol (HDL), and triglycerides (TG). Studies performed in populations with genetic syndromes (e.g., Down syndrome) or infectious diseases were excluded, as well as those with subjects on medications usually prescribed for hypercholesterolemia, such as statins.

Only single (participants blinded) or double-blinded studies that compared oat or isolated β -glucan with a placebo/control group were considered for this review. Intervention duration was required to be ≥ 2 weeks and, in the case of crossover designs, washout periods were required to be ≥ 2 weeks. Studies that had multiple-component interventions or that incorporated other active products that could not be separated from oats or isolated β -glucan were excluded. In studies with more than two intervention arms, of which two or more arms were eligible for inclusion, only the eligible arms were included. For studies with more than

two intervention arms, the results were taken for each arm and computed individually, comparing each intervention with the placebo/control group.

Through the initial search, titles and abstracts were evaluated independently by two of the reviewers (ACMJ and RMS) using the eligibility criteria regarding study design, population, type of intervention, and outcome. Full texts of the selected articles were examined independently by the same reviewers and disagreements were settled by consensus or by a third party (JFM). Authors of the reviewed publications were contacted by email when studies did not provide enough information. Unfortunately, several data requests were not responded to and, thus, these articles were not included in this review and meta-analysis.

Data extraction

All of the selected studies were independently reviewed and tabulated in a spreadsheet by ACMJ and RMS and later compared to eliminate discrepancies. Data was extracted on study design, population characteristics [sex, age (years), body mass index (BMI)], duration, type of blinding, washout period (for crossover studies), sample size, product used in the intervention (oats or isolated β -glucan), product used as control/placebo (corn starch, rice or wheat flour, corn flakes, etc.), intervention and control product presentation (noodles, porridge, powder, drink, bread, snacks etc.), consumed intervention and control amounts (grams per day), consumed fiber amount in the study, gastrointestinal side effects, and lipid profile data (TC, HDL, LDL and TG).

Risk of bias and study quality assessment

The Cochrane risk-of-bias tool (RoB 2) [34] was used to assess each study in the following aspects: a) randomization process; b) deviations from the intended interventions; c) missing outcome data; d) measurement of the outcome; e) selection of the reported results for RCTs

with parallel-arm groups and crossovers. For crossover RCTs, period and carryover effects were also included. Articles were classified as low risk, some concerns, or high risk of bias according to the tool's algorithms. Study quality assessment was done through the PEDro scale [35]. The studies were scored zero to ten according to the scale's criteria, with higher scores indicating better quality studies. Studies scoring nine or ten on the PEDro scale were considered methodologically to be of "excellent" quality, studies scoring from six to eight were of "good" quality, studies scoring four or five were of "fair" quality, and studies scoring below four were of "poor" quality [36]. All of the selected studies were evaluated jointly by ACMJ and RMS.

Statistical analysis

The available data from the included studies allowed us to conduct between-group metaanalyses using continuous data and random-effects models [37] to compare the effects of (i) oat interventions versus control groups from the parallel-arm included studies; (ii) Isolated β glucan supplements included in food interventions versus control groups from the parallelarm included studies; (iii) oat interventions versus control groups from the crossover included studies; and (iv) isolated β -glucan interventions versus control groups from the crossover included studies on lipid profile (TC, HDL, LDL, and TG). Parallel-arm and crossover studies were not combined in the meta-analyses since crossover studies may present carryover effects depending on the washout period, potentially interfering with the treatment effect [38,39].

Standardized mean differences (SMD) with 95% confidence intervals (95%CIs) were used to measure the effects of oat and isolated β -glucan as the included studies presented a considerable methodological heterogeneity (e.g., different interventions characteristics). The random-effects model analysis was performed considering the expectation that different interventions effects are not truly identical between studies [40]. The assessment of clinical relevance was made using three categories: small effect (SMD < 0.5); medium effect (SMD from 0.5 to 0.8); large effect (SMD > 0.8) [41].

Mean difference and its standard deviation of TC, HDL, LDL, and TG for oat interventions and control groups, as well as for isolated β -glucan interventions and control groups, were imputed into the Review Manager software (RevMan, version 5.4) [40]. As most of the included studies did not report the mean difference for lipid profile variables, we calculated the value as post-intervention mean value minus baseline mean value. Furthermore, as most of the included studies (n = 15) [42–56] did not report the standard deviation of mean difference of the lipid profile outcomes (TC, HDL, LDL, and TG), the following equation (1) was used to estimate the standard deviation of mean difference [57]:

$$SD_{meandifference} = \sqrt{(SD|pre - test|2 + SD_{post-test}^{2}) - (2r \times SD_{pre-test} \times SD_{post-test})}$$
(1)

For this equation, we estimated the within-participant pre-post correlation coefficients (r) for each outcome in each one of 11 included studies [58–68], which reported pre, post and change variability. After that, we averaged the r values for each outcome separated by each intervention group (oat/isolated β -glucan or control group). Thus, it was obtained the following r values: (i) for TC, r = 0.83 (oat/isolated β -glucan) and r = 0.80 (control group) [58–60,62–68]; (ii) for HDL, r = 0.88 (oat/isolated β -glucan) and r = 0.91 (control group) [59,60,62–68]; (iii) for LDL, r = 0.77 (oat/isolated β -glucan) and r = 0.78 (control group) [58,59,68,60–67]; and (iv) for TG, r = 0.82 (oat/isolated β -glucan) and r = 0.76 (control group) [58–60,63,64,66–68]. These calculations are recommended when continuous data are missing to perform meta-analysis of change scores [41].

The statistical heterogeneity of the treatment effect among studies was assessed using Tau squared (τ^2), Q statistic (the significance level was set p < 0.10) [40], and the

inconsistency I^2 test. The I^2 statistic estimates the degree of heterogeneity in effects among a set of studies between 0 and 100%, in which values above 30%, 50%, and 75% were considered indicative of moderate, substantial, and high heterogeneity, respectively [40]. Publication bias was visually assessed using funnel plots by plotting the SMD of each trial against its standard error. As recommended by Higgins and Thomas [40], "Egger's regression test" was not performed to assess asymmetry of the funnel plot because all between-groups meta-analyses involved less than 10 original studies. To improve our results, we conducted several sensitivity analyses (the one study removed method) to consider the influence of each study on the overall results, as well as to consider the influence of each study applying two or more oat or isolated β -glucan interventions. Moreover, a pre-planned subgroup analysis was conducted to test whether the participant's health status (non-hypercholesterolaemic or hypercholesterolaemic participants) influenced the outcomes. However, the included studies did not allow for pre-planned subgroup analyses to test whether participants' age (adults or older adults), sex (male or female), menopausal status (yes or no), and if equivalent or different amounts of total fiber intake in the intervention and control groups would influence the outcomes. All statistical analyses were performed in the Review Manager software (RevMan, version 5.4) [40]. A 2-tailed significance level was set at p < 0.05 for all analyses.

Results

Included studies

Our initial search retrieved 1643 records: 527 through CINAHL, 617 through EMBASE, 389 through PUBMED, and 110 through Web of Science. Two extra additional records were added through reviewing the reference lists of the retrieved articles, bringing the total to 1645 articles. After the removal of duplicates, 811 records were screened based on their title and/or abstract. A total of 49 full-text articles were assessed for eligibility. In our first assessment, 16 articles were excluded due to the following reasons: (i) insufficient data (n = 8); (ii)

combination of active products (n = 2); (iii) no control groups (n = 2); (iv) no washout period (n = 2); (v) no randomization (n = 1); and (vi) lack of blinding (n = 1). Another seven studies were excluded as they did not report information on change overtime (mean difference and its standard deviation) or pre- and post-intervention data (mean values and standard deviations) on lipid profile outcomes (TC, LDL, HDL, and TG) for intervention and control groups, and missing data could not be obtained from the authors [69–75]. In total, 28 studies were included in this systematic review and meta-analysis (Figure 1).

Nine parallel-arm/oat studies were included in the analysis for TC, HDL, LDL and TG [45,47,51–56,61], seven crossover/oat studies were included in the analysis for TC, HDL, LDL and TG [42,43,46,50,66–68], nine parallel-arm/isolated β -glucan studies were included in the analysis for TC, HDL and LDL [48,58–60,62–64,76,77], eight parallel-arm/isolated β -glucan studies were included in the analysis for TG [48,58–60,63,64,76,77], three crossover/isolated β -glucan studies were included in the analysis for TC, HDL and LDL [44,49,65], and two crossover/isolated β -glucan studies were included in the analysis for TG [44,49].

Participant characteristics

Most of the studies were conducted with hypercholesterolaemic individuals [42,43,52,54– 56,58–63,44,67,76,77,45–51] except for four studies that included non-hypercholesterolaemic individuals [64–66,68] and one that had both non-hypercholesterolaemic and hypercholesterolaemic individuals [53]. The non-hypercholesterolaemic subjects were younger than those with hypercholesterolaemia, as seen in Table 1. The mean age and BMI of the participants were 49.73 (\pm 9.68) years and 26.17 (\pm 2.15) kg/m², respectively (Table 1).

Intervention characteristics

The interventions ranged from 14 [46,66] to 84 [76] days in length (Table 1). The number of participants ranged from 12 [43] to 191 [77] individuals. Half of the crossover studies had a 14-day washout period [43,44,46,65,68], the other half had washout periods >14 days [42,49,50,66,67]. The quantity of β -glucan ingested for all of the studies (oats and isolated β -glucan) ranged from 1.2 g/day [51] to 11.2 g/day [45]. Only 15 of the 28 studies included in this review reported the total amount of fiber ingested by the intervention and control groups and, of these 15 studies, nine reported no difference between groups regarding total fiber ingestion [43,44,47,50,55,58,59,62,76].

Lipid profile assessment

Almost half of the included studies did not mention or report precisely the information regarding the method used for the lipid profile assessment [46,49,63,67,53–56,58,60–62]. Of the remaining studies, 14 of them reported having used enzymatic methods of analysis [42,43,64,68,76,77,44,45,47,48,50–52,59] and two studies reported a combination of enzymatic and colorimetric methods [65,66]. For the majority of the studies that properly reported the methods used for lipid assessment, LDL was calculated using Friedewald's formula. Nevertheless, a few of them simply mentioned that LDL was determined by "calculation" or "subtraction" [43,45] and others did not specify how LDL was calculated [48,50,65,66,68].

Study quality and risk of bias assessment

All the included studies were rated at least "good" regarding their quality, as shown in Table 2. According to the tool used to evaluate Risk of Bias, 19 studies were classified as "high-risk" and nine studies as "some concern". Among different areas evaluated, randomization

procedures or lack of information about it were the most concerning area. The results for the assessment of study quality and risk of bias are presented in Table 2.

Oat interventions versus control groups

Parallel-arm studies

The meta-analysis on the effects of oat interventions versus control groups in the parallel-arm studies found a significant difference for changes in TC (SMD: -0.61, 95% CI: -0.84; -0.39, p < 0.00001) and LDL (SMD: -0.51, 95% CI: -0.71; -0.31, p < 0.00001), favoring oat interventions, with evidence of significant heterogeneity for TC ($\tau^2 = 0.09$, $l^2 = 46\%$, p = 0.03) and LDL ($\tau^2 = 0.06$, $l^2 = 36\%$, p = 0.08) (Figures 2A and C, respectively). However, there was no significant difference, between groups for changes in HDL (SMD: -0.06, 95% CI: -0.21; 0.10, p = 0.49) and TG (SMD: 0.02, 95% CI: -0.14; 0.17, p = 0.83), with no evidence of heterogeneity for HDL ($\tau^2 = 0.00$, $l^2 = 0\%$, p = 0.97) and TG ($\tau^2 = 0.00$, $l^2 = 0\%$, p = 0.84) (Figures 2B and D, respectively).

Crossover studies

Oat interventions with a crossover design showed positive effects on TC (SMD: -0.70, 95%CI: -1.07; -0.34, p = 0.0002) and LDL (SMD: -0.38, 95%CI: -0.60; -0.15, p = 0.001) compared to the control groups, with evidence of significant heterogeneity for TC ($\tau^2 = 0.15$, $I^2 = 61\%$, p = 0.02, Figure 3A) but not for LDL ($\tau^2 = 0.01$, $I^2 = 10\%$, p = 0.36) (Figure 3C). However, there was no difference between groups for changes on HDL (SMD: -0.09, 95%CI: -0.39; 0.21, p = 0.57) and TG (SMD: -0.21,95%CI: -0.46; 0.04, p = 0.11), with evidence of moderate heterogeneity for HDL ($\tau^2 = 0.08$, $I^2 = 47\%$, p = 0.08, Figure 3B) but not for TG ($\tau^2 = 0.00$, $I^2 = 0\%$, p = 0.71, Figure 3D).

β-glucan interventions versus control groups

Parallel-arm studies

In random-effects analyses of parallel-arm studies, significant differential effects of isolated β -glucan interventions versus control groups were observed for TC (SMD: -0.73; 95%CI: -1.01; -0.45, p < 0.0001), LDL (SMD: -0.58; 95%CI: -0.85; -0.32, p < 0.0001) and TG (SMD: -0.30, 95%CI: -0.49; -0.12, p < 0.0001), with evidence of significant heterogeneity for TC ($\tau^2 = 0.18$; $I^2 = 70\%$; p < 0.0001, Figure 4A) and LDL ($\tau^2 = 0.16$; $I^2 = 68\%$; p = 0.0002, Figure 4C) but not for TG ($\tau^2 = 0.03$; $I^2 = 31\%$; p = 0.14, Figure 4D). However, there were no significant differences between groups for changes in HDL (SMD: -0.04; 95%CI: -0.18; 0.10, p = 0.60), with no evidence of significant heterogeneity for HDL ($\tau^2 = 0.00$; $I^2 = 0\%$; p = 0.71, Figure 4B).

Crossover studies

The supplementation of isolated β -glucan in crossover studies lowered TC (SMD: -0.71; 95%CI: -1.39; -0.03, p = 0.04) and increased TG concentrations (SMD: 0.32; 95%CI: 0.07; 0.57, p = 0.01) compared to control group (Figure 5), with evidence of significant heterogeneity for the TC analysis ($\tau^2 = 0.29$; $I^2 = 83\%$; p = 0.003, Figure 5A) and no evidence of significant heterogeneity for the TG analysis (Figure 5D). There was no significant difference between groups for changes in HDL (SMD: -0.01; 95%CI: -0.25; 0.23, p = 0.94) and LDL (SMD: -0.74; 95%CI: -1.55; 0.07, p = 0.07), with no evidence of significant heterogeneity for the HDL analysis ($\tau^2 = 0.00$; $I^2 = 0\%$; p = 0.66, Figure 5B) and evidence of significant heterogeneity for the LDL analysis ($\tau^2 = 0.45$; $I^2 = 88\%$; p = 0.0002, Figure 5C).

Sensitivity analyses

Sensitivity analyses showed that the significant effect (p < 0.05) of the oat interventions on TC and LDL remained even after removing each one of the included studies, independently of the study design. The same occurred with isolated β -glucan interventions on TC, LDL and TG in parallel-arm studies. However, the positive effect of isolated β -glucan interventions on TC was not sustained after removing Cicero et al.[49] (SMD: -0.34, 95%CI: -0.72; 0.05, p = 0.09; heterogeneity: $\tau^2 = 0.00$, $I^2 = 0\%$, p = 0.39) or Ibrügger et al.[65], which were both crossover studies (SMD: -0.73, 95%CI: -1.67; 0.20, p = 0.13, heterogeneity: $\tau^2 = 0.42$, $I^2 = 91\%$, p = 0.130.0007). No sensitivity analysis was performed for the crossover studies assessing the effects of isolated β -glucan on TG since only two studies [44,49] were included in the meta-analysis. Additionally, a sensitivity analysis was performed removing all arms (≥ 2 interventions groups) of the parallel-arm studies composed by two or more arms [48,51,60,61], and a significant effect (p < 0.05) of oat and isolated β -glucan interventions remained for TC and LDL. However, a sensitivity analysis showed that a significant effect (p < 0.05) of isolated β glucan intervention on TG did not remain after removing all arms of the Keenan et al.[48] study (SMD: -0.24, 95% CI: -0.49; 0.01, p = 0.06, heterogeneity: $\tau^2 = 0.05$, $I^2 = 41\%$, p = 0.060.10).

Publication bias

Visual analyses of the funnel plots for all oat and isolated β -glucan interventions versus control groups from either parallel-arm or crossover studies determined no indication of publication bias (Figures S1, S2, and S3, respectively). However, it was not possible to perform a visual analysis involving isolated β -glucan interventions versus control groups in crossover studies since only three studies were included in this study (Figure S4). Furthermore, as reported in the methods, "Egger's regression test" was not performed to assess asymmetry of the funnel plot because all between-groups meta-analyses involved less than 10 original studies.

Subgroup meta-analysis

The available data allowed us to conduct only one of pre-planned subgroup analyses as the selected studies did not allow for further analysis (**Table 3**). Subgroup analysis from oat interventions in the crossover studies showed a significant effect on TC and LDL only in hypercholesterolaemic participants. However, a test for subgroups differences (non-hypercholesterolaemic vs. hypercholesterolaemic participants) found no significant subgroup differences (p > 0.05) for all outcomes (TC, LDL, HDL, and TG; see **Table 3**).

Discussion

The results of the current meta-analysis corroborate with other reviews regarding the benefits of oats and β -glucan on lipid profiles [21,22,26–28,78]. However, to our knowledge, this is the first meta-analysis that separately investigated the impact of oats and isolated β -glucan on lipid profiles. This approach was not conducted before, as previous reviews pooled oats and isolated β -glucan together in their analysis [21,22,26,28–30], preventing knowing whether both provide positive effects on lipid profile.

Our findings showed that isolated β -glucan improved lipid profiles, specifically TC and LDL concentrations, similarly to oats, suggesting that it is the main bioactive compound in oats. HDL cholesterol did not seem to be affected by oat or isolated β -glucan ingestion, suggesting that the mechanisms that reduce TC and LDL, mentioned previously, are different from the ones that would affect HDL. HDL can be reduced due to several factors, such as weight gain and excess saturated fat and calorie intake, while other factors can increase HDL levels, such as increased physical activity and unsaturated fat consumption [79,80]. These

changes occur due to adaptations in lipid metabolism, which increases the enzymatic activity of lipoprotein lipase, favors greater degradation of TG-rich lipoproteins, and thus causes less formation of atherogenic LDL and increases serum concentrations of the nascent HDL. Furthermore, an increase in lecithin-cholesterol-acyl-transferase and a decrease in the activity of hepatic lipase will increase the formation of HDL2-cholesterol subfractions [81]. It appears that oat and isolated β -glucan interventions are not involved with the above-mentioned mechanisms and consequently would not modify HDL levels.

The impact of oat or isolated β -glucan on TG is unclear. The parallel-arm and crossover oat groups in this meta-analysis showed no consistent improvements in TG. For the isolated β -glucan studies, TG was decreased in the parallel-arm studies, but the opposite was found in the crossover studies, as seen in Figures 4 and 5, respectively. Mechanisms of changes in the concentration of TG are linked to carbohydrates. The increase in the availability of glucose in serum, resulting from the absorption of carbohydrates, stimulates the secretion of insulin and, as a result, the synthesis of fatty acids in the liver is increased [82]. The mixed results found in this and other meta-analyses regarding TG [22,26,28,78] may be related to the fact that oats and isolated β -glucan were frequently administered through day-to-day processed foods which have sugar and other types of refined flour in their recipes. This also reinforces the fact that controlled feeding studies should be carried out to address this inconsistency regarding the effects on TG. Further, the contradictory results in the parallel-arm and crossover isolated β -glucan studies may be due to the fact that only two studies [44,49] were included in this analysis.

Considering that this review evaluated the impact of β -glucan (in oats and isolated), a viscous type of fiber, on the lipid profile, it could be judged appropriate to have other types of fiber (not β -glucan) ingested in similar amounts in the control groups of the included studies to verify if viscosity is the most important factor in cholesterol-lowering effect as seen in the

literature [15]. Nevertheless, we did not have enough studies that matched total fiber intake between intervention and control groups and, therefore, could not evaluate if the results were exclusively influenced by oat/isolated β -glucan supplementation or if other types of fiber in the background diet would have a similar impact on lipidemia. For the limited studies that did match total fiber intake between the intervention and control groups (n=9), five of them reported no significant difference in TC and LDL [43,55,59,62,76]. Therefore, future studies should match total fiber intake between groups so that the impact of β -glucan can be clearly distinguished from other types of dietary fibers.

Another aspect that also seems important to consider when analysing the impact of oat/isolated β -glucan on lipid profiles is the type and quantity of fat present in a person's diet. In this present review, none of the studies were rigorously controlled feeding trials and, therefore, did not consider background fat intake that may affect lipid profiles. Grajeta [83] found that rats fed diets containing polyunsaturated fat compared with diets containing saturated fat had different responses regarding the impact that amaranth and oat bran had on blood serum and liver lipids. Therefore, reducing saturated fat intake may be, in combination with increased viscous fiber intake from oats or isolated β -glucan, the most effective way to improve dyslipidaemia. In future studies, the amount and type of fat in the diet should be evaluated and considered accordingly.

Additionally, different oat cooking procedures, processing methods, and molecular weights would modify the viscosity and impact in cholesterol concentrations differently. Boiled oats, for instance, seem to impact the lipid profile in a greater way than brewed oats [84] and less processed oats appear to be more effective than processed oat products in improving lipidaemia [85]. Higher molecular weight is associated with increased viscosity and greater reduction in LDL [86]. It is also known that the process used to treat oats affects

its molecular weight, and the highest viscosities were observed as a consequence of dry processes in comparison to the ones that exhibit enzymatic activity [87].

It is important to mention that the intervention time for the crossover studies (30.10 [\pm 13.63] days) was significantly shorter (p < 0.001) than the intervention time for the parallelarm studies (46.67 [\pm 14.80] days). Therefore, that potentially could have interfered in the magnitude of the results found in the two distinct types of studies.

This review was able to evaluate separately the results obtained from oats and isolated β glucan regarding its impact on the lipid profile, which allowed us to discern the potential for use of purified β -glucan as supplements or to enrich food products with fiber in human nutrition and health. However, the clinical evidence for the health effects of fiber supplements remains inconsistent [88] differently of foods naturally rich in fiber. So, it has been questioned whether purified (isolated) forms of fiber maintain their physiological effects once removed from the three-dimensional plant cell wall matrix [23,24]. Our findings here support the notion that purified, isolated forms of β -glucan, if used as supplements or added to foods, maintain their physiological effects on the lipid profile.

This review is not without limitations. Some of the included studies did not mention the method by which the lipid concentrations were obtained, which also limits the proper evaluation of the obtained results. Additionally, there was no complete dietary and physical activity evaluation in most of the articles, and no studies directly compared oats and isolated β -glucan, which would have allowed for a more thorough evaluation of the two types of interventions. A number of studies included in this review were classified as "high risk of bias", which reinforces the need for more robust randomized controlled trials to advance human nutrition science [89]. Here 100% of the studies were classified as having some concerns or a high risk of bias, and the main reason can be attributed to the lack of details in the randomization process. This may be related to the RoB 2, which is relatively new, and

most studies predate the creation of the tool. Therefore, it is possible that there are good studies, but that did not follow the specific criteria proposed by RoB 2. Additionally, there are different tools that can be used to assess the risk of bias, and this would be related to discrepancies in the evaluations of the studies. Thus, a single instrument would be more adequate to avoid different risk of bias assessments. Finally, the tools used to assist in study design could differ from those that assess their quality when included in a systematic review or meta-analysis. This is a concern for researchers and should be rethought by guidelines.

Overall, the present systematic review and meta-analysis showed that oat interventions decreased TC and LDL concentrations. Moreover, isolated β -glucan interventions from parallel-arm studies decreased TC, LDL, and TG concentrations. Collectively, our findings show that both oat and isolated β -glucan interventions can improve lipid profiles and should be incorporated into one's regular eating habits. β -glucan supplements would be a potential tool to reduce the 'fiber gap' found in industrialized countries with low fiber intake, although the overall public health message should always focus on improving dietary quality as a whole. Future high quality and low risk of bias RCTs directly comparing oat versus isolated β -glucan interventions on lipid profiles would provide a more thorough evaluation of these two types of interventions and further inform clinical practice for cardiovascular disease prevention and treatment.

Acknowledgements

The authors would like to thank Dr Larissa Vaz for the consulting regarding the databases research used in this review. We also thank "*Coordenação de Aperfeiçoamento de Pessoal de Nível Superior*" (CAPES) for the scholarship provided to ACMJ, and "*Conselho Nacional de Desenvolvimento Científico e Tecnológico*" (CNPq) for the financial support given to JFM (305082/2019-1).

Sources of Support: None.

Conflict of interest

The authors report there are no competing interests to declare.

Author contributions

ACMJ, RMS, RBV, JW and JFM were responsible for the project conception and design research; ACMJ and RMS conduct research, extraction, and data recording. RBV performed statistical analysis; ACMJ, RMS, RBV and JFM analyzed the data and interpreted the results; ACMJ, RMS and RBV prepared figures and tables; ACMJ, RMS and RBV had primary responsibility for final content; AMA, CP, JW and JFM edited, revised, and approved the final version of manuscript.

Data availability statement

The data set associated to this paper is available upon request.

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Study (year)	Type of study	n (M/W)	Health status	n	Age (years)	BMI (kg/m²)	B-	Total fiber intake (g/day)		#days	Products used
							glucan (g/day)				
								EXP	Control	-	
Oat						.0					
Charlton <i>et</i>	Parallel-	87	HCh	EXP-OH:	52.43	26.74 (2.95)	3.24	NR	NR	42	Porridge and
al. (2012)	arm	(41/46)		30	(10.46)	27.28 (5.33)	1.45	NR	NR	42	cereal bars with
				EXP-OL:	51.93 (9.87)	27.74 (3.88)					oats or corn and
				26	49.75						rice flakes and
				Control: 31	(10.42)						wheat
Davidson <i>et</i>	Parallel-	140	HCh	EXP-OB28:	51.6 (NR)	24.6 (NR)	2.0	17.8	14.0	42	Powder to be
al. (1991)	arm	(80/60)		23	52.6 (NR)	24.8 (NR)	4.0	(NR)	(NR)	42	used as hot
				EXP-OB56:	54.8 (NR)	25.0 (NR)	6.0	22.6	14.0	42	cereal, muffins
				20	51.1 (NR)	26.2 (NR)	1.2	(NR)	(NR)	42	shake with oats
				EXP-OB84:	55.0 (NR)	26.1 (NR)	2.4	25.9	14.0	42	or wheat flour

Table 1. Characteristics of the participants and interventions of the included studies.

				21	51.0 (NR)	25.2 (NR)	3.6	(NR)	(NR)	42	
				EXP-	53.1 (NR)	25.8 (NR)		17.2	14.0		
				OM28: 20				(NR)	(NR)		
				EXP-				15.3	14.0		
				OM56: 21				(NR)	(NR)		
				EXP-				20.4	14.0		
				OM84: 20				(NR)	(NR)		
				Control: 15							
Gerhardt and	l Parallel-	44	HCh	EXP-OB:	51.7 (1.5)	W: 25.82	6.72^{*}	NR	NR	42	Powder to be
Gallo (1998)	arm	(23/21)		13		(NR)					mixed with food
				Control-RB:		M: 23.05					using oats or rice
				14		(NR)					starch and rice
											bran
Liao <i>et al</i> .	Parallel-	74 (NR)	HCh	EXP: 37	38 to 76	23.38 (0.62)	3.12	NR	NR	70	Noodles made
(2019)	arm		and	Control: 37		23.66 (0.69)					with oats or
			Non-								wheat

Lovegrove	Parallel-	62	HCh	EXP: 31	56.3 (9.4)	26.0 (3.2)	3.0	NR	NR	56	Cereal with oats
et al. (2000)	arm	(31/31)		Control: 31	56.8 (9.2)	25.8 (3.7)					or wheat bran
Martensson	Parallel-	56	HCh	EXP: 20	55 (9)	25.3 (3.3)	3.0	No differ	rence	35	Fermented
<i>et al.</i> (2005)	arm	(24/32)		Control: 18				between	groups but		beverage made
								values N	R		with oats or dairy
Reynolds et	Parallel-	43	HCh	EXP: 22	51.6 (NR)	23.8(0.7)	2.7	25.5	16.8	28	Cereal with oats
al. (2000)	arm	(21/22)		Control: 21		25.0(0.5)		(1.5)	(1.1)		or corn flakes
Torronen et	Parallel-	28 (28/0)	HCh	EXP: 13	40 (NR)	NR	11.2	39.7	23.1	56	Bread made with
al. (1992)	arm			Control: 15	42 (NR)			(7.2)	(6.8)		oats or
											wheat flour
Uusitupa <i>et</i>	Parallel-	36	HCh	EXP: 20	50 (6)	26.3 (3.3)	10.3	20.9	19.0	56	Powder to be
al. (1992)	arm	(20/16)		Control: 16	45 (9)	26.7 (2.5)		(7.6)	(6.4)		added to juices,

HCh

yogurt, porridge

or desserts, from

oats or wheat

	$\mathbf{n}\mathbf{r}$	

											bran
Amundsen	Crossover	16 (9/7)	HCh	EXP: 16	57.09 (7.9)	25.49 (1.9)	5.1	28.0	24.3	21	Cereal, cake,
et al. (2003)				Control: 16				(NR)	(NR)		bread, muffin,
											pasta, and apple
											juice with oats or
											wheat and rye
Bremer et al.	Crossover	12 (5/7)	HCh	EXP: 12	53 (10)	NR	3.6*	32.2	34.1	28	Bread with oats
(1991)				Control: 12				(10.3)	(11.1)		or wheat bran
Connolly et	Crossover	30	HCh	EXP: 30	42 (NR)	26.4 (5.7)	1.3	18.8	18.2	42	Granola cereal
al. (2016)		(11/19)		Control: 30				(4.41)	(5.39)		with oats or
											without oats
Kristensen	Crossover	24 (NR)	Non-	EXP: 24	25.2 (2.7)	24.9 (2.9)	8.2^{*}	26	16	14	Bread with oats
and Bügel			HCh	Control: 24							or without oats
(2011)											
Önning <i>et al</i> .	Crossover	52 (52/0)	HCh	EXP: 52	62.9 (5.9)	27 (NR)	3.8	NR	NR	35	Vegetable
(1999)				Control: 52	62.2 (5.1)						milk from oats or

											rice
Swain <i>et al</i> .	Crossover	20 (4/16)	Non-	EXP: 20	30 (NR)	NR	8.0^{*}	38.9	18.4	42	Ready to eat
(1990)			HCh	Control: 20				(8.5)	(10.4)		entrees and
											muffins with oats
											or wheat flour
Trinidad et	Crossover	21 (4/17)	HCh	EXP: 21	M: 50 (3)	M: 25 (2)	4.7^{*}	NR	NR	14	Cereal with oats
al. (2004)				Control: 21	W: 48 (1)	W: 25 (1)					or corn flakes
β-glucan											
Biörklund et	Parallel-	89	HCh	EXP-Oat-5:	56 (10)	25.2 (3.3)	5.0	NR	NR	35	Beverage with β-
al. (2005)	arm	(44/45)		19			10.0	NR	NR	35	glucan or rice
				EXP-Oat-							starch
				10: 15							
				Control: 20							
Biörklund et	Parallel-	43	HCh	Control: 20 EXP: 22	58.8 (8.2)	25.0 (3.1)	4.0	18.7	17.4	35	Soup with β-

β-glucan

Cugnet-	Parallel-	53	HCh	EXP: 19	61.9 (9.1)	30,48 (4.08)	3.5	19.7	22.3	56	Soup with β -
Anceau et	arm	(32/21)		Control: 24	61.8 (7.5)	29.02 (4.05)		(5.3)	(12.0)		glucan or without
al. (2010)											β-glucan
Ferguson et	Parallel-	36	HCh	EXP: 18	56.39 (2.88)	27.81 (0.67)	3.0	30.35	27.24	42	Biscuits with β -
al. (2019)	arm	(16/20)		Control: 18	54.78 (2.81)	28.49 (1.04)		(NR)	(NR)		glucan or without
											β-glucan
Keenan et	Parallel-	155	HCh	EXP-	53.9 (10.2)	29.6 (5.9)	3.0	NR	NR	42	Beverage and
al. (2007)	arm	(75/80)		3HMW: 32	55 (10.1)	28.1 (4.3)	3.0	NR	NR	42	cereal with β -
				EXP-	58.6 (10.6)	28.9 (6.7)	5.0	NR	NR	42	glucan or without
				3LMW: 31	52.8 (11.9)	28.9 (5.3)	5.0	NR	NR	42	β-glucan
				EXP-	52.8 (11.9)	30.8 (4.0)					
				5HMW: 32							
				EXP-							
				5LMW: 30							
				Control: 30							
Morales et	Parallel-	52	HCh	EXP: 28	50.8 (10)	26.01 (3)	3.5	25.2	16.3	56	Soup with β -

al. (2021)	arm	(14/38)		Control: 24		24.54 (3.09)		(7.0)	(4.8)		glucan or without
											β-glucan
Naumann et	Parallel-	47	Non-	EXP: 25	M: 56 (9)	M: 26 (2)	5.0	NR	NR	35	Fruit beverage
al. (2006)	arm	(18/29)	HCh	Control: 12	W: 49 (16)	W: 23 (3)					with β -glucan or
											rice starch
Pino <i>et al</i> .	Parallel-	37 (9/28)	HCh	EXP: 20	EXP: 49.3	EXP: 33.2	5.0	22.1	21.4	84	Powder to be
(2021)	arm			Control: 17	(6.75)	(5.16)		(11.8)	(6.9)		mixed with water
					Control:	Control: 34.2					or milk with β -
					52.8 (3.45)	(7.04)					glucan or
											microcrystalline
											cellulose
Wolever et	Parallel-	191	HCh	EXP: 96	47.6 (11.4)	27.9 (4.6)	3.0	26.1	21.1	28	Powder to be
al. (2021)	arm	(72/119)		Control: 95				(0.9)	(1.0)		mixed with water
											containing β-
											glucan or rice
Cicero et al.	Crossover	83	HCh	EXP: 83	52.3 (4.4)	NR	3.0	NR	NR	56	Cereal with β -

(2020)		(35/48)		Control: 83							glucan or without
											β-glucan
Ibrugger et	Crossover	13 (6/7)	Non-	EXP: 13	22.9 (2.1)	22.8 (2.3)	3.3	23.2	26.6	21	Yogurt and
al. (2013)			HCh	Control: 13				(2.7)	(2.8)		beverage with β -
											glucan or without
											β-glucan
Theuwissen	Crossover	42	HCh	EXP: 40	M: 54 (10)	M: 26 (2)	5.0	22.41	22.68	28	Muesli with β -
and Mensink		(20/22)		Control: 40	W: 51 (12)	W: 24 (3)		(5.81)	(6.48)		glucan or wheat
(2007)											bran
Doto proconto	d ag magn (g	tondond day	vistion)	DML b a day mag	aa in daw. Can	<u> </u>		D. ann anima		· M	NIA . mot

Data presented as mean (standard deviation). BMI: body mass index; Control: control group; EXP: experimental group; M: men; NA: not applicable; NR: not reported; HCh: hypercholesterolemic (total cholesterol > 5.18 mmol/L); W: women; *0.08 g of B-glucan per gram of oat bran.

Articles	Intervention	Study	Study	Risk of bias ²
Arucies	Intervention	type	quality1	RISK OF DIAS-
Charlton et al. (2012)	Oat	Parallel-	Good	High Risk
		arm		
Davidson et al. (1991)	Oat	Parallel-	Good	High Risk
		arm		
Gerhardt and Gallo (1998)	Oat	Parallel-	Good	High Risk
		arm		
Liao et al. (2019)	Oat	Parallel-	Good	High Risk
		arm		
Lovegrove et al. (2000)	Oat	Parallel-	Good	High Risk
		arm		
Martensson et al. (2005)	Oat	Parallel-	Good	Some concerns
		arm		
Reynolds et al. (2000)	Oat	Parallel-	Good	High Risk
		arm		
Torronen <i>et al.</i> (1992)	Oat	Parallel-	Good	Some concerns
		arm		
Uusitupa <i>et al.</i> (1992)	Oat	Parallel-	Good	Some concerns
		arm		
Amundsen et al. (2003)	Oat	Crossover	Good	High Risk
Bremer <i>et al.</i> (1991)	Oat	Crossover	Good	High Risk
Connolly et al. (2016)	Oat	Crossover	Good	Some concerns
Kristensen and Bügel	Oat	Crossover	Excellent	Some concerns

Table 2. Study quality and risk of bias of the included studies.

(2011)				
Önning et al. (1999)	Oat	Crossover	Good	High Risk
Swain et al. (1990)	Oat	Crossover	Good	High Risk
Trinidad et al. (2004)	Oat	Crossover	Good	High Risk
Biörklund et al. (2005)	β-glucan	Parallel- arm	Good	Some concerns
Biörklund et al. (2008)	β-glucan	Parallel- arm	Good	Some concerns
Cugnet-Anceau <i>et al.</i> (2010)	β-glucan	Parallel- arm	Good	High Risk
Ferguson et al. (2019)	β-glucan	Parallel- arm	Excellent	High Risk
Keenan <i>et al.</i> (2007)	β-glucan	Parallel- arm	Good	High Risk
Morales <i>et al.</i> (2021)	β-glucan	Parallel- arm	Good	High Risk
Naumann <i>et al</i> . (2006)	β-glucan	Parallel- arm	Excellent	Some concerns
Pino et al. (2021)	β-glucan	Parallel- arm	Good	High Risk
Wolever et al. (2021)	β-glucan	Parallel- arm	Excellent	High Risk
Cicero et al. (2020)	β-glucan	Crossover	Excellent	High Risk
Ibrugger et al. (2013)	β-glucan	Crossover	Good	High Risk
Theuwissen and Mensink	β-glucan	Crossover	Good	Some concerns

(2007)

Assessed by PEDro Scale; ²Assessed by The Cochrane risk-of-bias tool (RoB 2).

oumateror

Table 3. Summary of subgroup analyses.

Outco	omes	Non-HCh (n=2)	р	HCh (n=5)	р	<i>p</i> [¥]
TC	SMD (95%CI)	-0.41 (-1.09; 0.28)	0.25	-0.82 (-1.26; -0.38)	0.0002	
	Heterogeneity	$\tau^2 = 0.15, I^2 = 61\%$	0.11	$\tau^2 = 0.15, I^2 = 62\%$	0.03	0.32
HDL	SMD (95%CI)	0.09 (-1.12; 1.30)	0.88	-0.17 (-0.41; 0.08)	0.18	
	Heterogeneity	$\tau^2=0.66,I^2=87\%$	0.005	$\tau^2 = 0.00, I^2 = 0\%$	0.58	0.68
LDL	SMD (95%CI)	-0.19 (-0.60; 0.23)	0.39	-0.45 (-0.75; -0.15)	0.004	
	Heterogeneity	$\tau^2 = 0.00, I^2 = 0\%$	0.74	$\tau^2 = 0.03, I^2 = 26\%$	0.25	0.32
TG	SMD (CI95%)	-0.29 (-0.72; 0.13)	0.17	-0.22 (-0.46; 0.02)	0.08	
	Heterogeneity	$\tau^2 = 0.00, I^2 = 0\%$	0.57	$\tau^2 = 0.00, I^2 = 0\%$	0.61	0.76

SMD: standardized mean difference; CI: confidence interval; TC: total cholesterol; HDL: high density lipoprotein cholesterol; LDL: low density lipoprotein cholesterol; TG: triglycerides; HCh: hypercholesterolemic participants; non-HCh: non-hypercholesterolemic participants; τ^2 : absolute heterogeneity; *P*: heterogeneity in percentual; [¥]Test for subgroups differences.

Figure legends

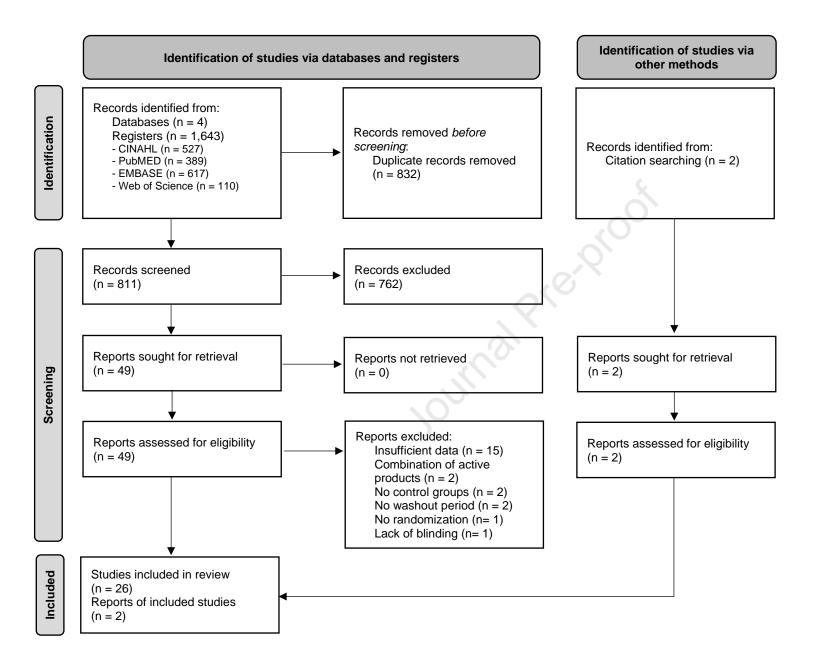
Figure 1. Diagram flow of outcomes of review.

Figure 2. Main effects of oat interventions versus control groups from parallel-arm on the lipid profile (A) total cholesterol, (B) high density lipoprotein cholesterol, (C) low density lipoprotein cholesterol, and (D) triglycerides.

Figure 3. Main effects of oat interventions versus control groups from crossover studies on the lipid profile (A) total cholesterol, (B) high density lipoprotein cholesterol, (C) low density lipoprotein cholesterol, and (D) triglycerides.

Figure 4. Main effects of isolated β -glucan interventions versus control groups from parallelarm on the lipid profile (A) total cholesterol, (B) high density lipoprotein cholesterol, (C) low density lipoprotein cholesterol, and (D) triglycerides.

Figure 5. Main effects of isolated β -glucan interventions versus control groups from crossover studies on the lipid profile (A) total cholesterol, (B) high density lipoprotein cholesterol, (C) low density lipoprotein cholesterol, and (D) triglycerides.



		•	Tatal	March 1	interio Gal		mar	int. Mean Etherence NJ, Randers, 1975 Cl	Shit. Minam Ofference M, Randors, 95% CI
charbm et al. (2012) 041	1.4	1412	26	-0.16	0.627	21	115	0221038 E152	in named, \$75 C
	-142	3.442	- 29	-0.36	0.487	- 21	0.1%	-0141-036, 6.001	
	-8.55	3.564	- 22		0.526	- 15	5.8%		
Davidson et al. (1987) DR 56 Davidson et al. (1987) DR 56	-0.24	2.475	22		0.526	15	1.45	-0.51 (117, 8.15)	
Davidson et al. (1997) DE M.	-149	2.491	- 22		0.338	- 22	1.14	-137 5112 -6.82 -0.04 5148, -6.23	
Danishin et al. (1997) Dil 55	1.11	3,000	- 53		0.01	- 3	1.12	-0.883128, 8.001	
	.821	3.645	- 24	0.82	0.08	- 66	6.7%		
	-8.95	8.325	- 22	0.82	0.495	- 95	5.45		
Liso et el. (29110)	-0.800	3.864	- 27	-0114	0333	17	175	-0:0011.45,-6.538	
Lovegrow et al. (2003) Mattension et al. (2005)	-61	3.851	- 22	071	0.583	21	1/6	-0.343-0.34, 8.158 -0.133-0.78, 8.523	
Martinesson et al. (2000) Prevention et al. (2000)			- 77	0.11	0,835	- 77	125	-0331-078,8.02	
Tonores et al. (1992)	- 311	1.01	- 55		0.181	- 61		-0121087.8421	
Available and all of \$121	-0.14	6.6	20	0.13	0.828	- 16	1.05	-0.3310.38 8.328	
hand didn. rm.			-				-	ASSIAM ATE	
noral (ron-cl) Heteropeneity Tau*= 3.88, Ch Teathr overall effect Z = 5.45	P=21.70 P=1.00	Leri sa Ilito		83).P**	455	30	186.0%	031[404C-038]	S Farmer Out Farmer Owned
в									
Stady or Subgrap	New	**	Tetal	Moon	inted 50		with	int. Mean Etherence NJ, Randers, 1975 Cl	Skd. Minae Ofference M, Randers, 95% CI
Charlen at al. (2012) (M	-111	1151	-30	-0.11	0151	21	315	0111031E2D	10, 60 molt, 80% (J
Charlten et al. (2012) On Charlten et al. (2012) OL	-4.11	1,152	- 8		0150	- 11	115		
	1.89	8.225	- 22	0.33	0122	- 15	5.7%		
Davidson et al. (1991)-DR 56	8.00	8,205	- 22		0733	- 15	5.4%	0171-058, 8.541	
M BO (THE) IS M ACCESSING	1.00	\$ 299	21		0122	15	5.5%	0141033,880	
Danabaco el al (1987) De 28 Danabaco el al (1987) De 66	1.11	3.160	20		0122	- 10	1.05	0.3010.87, 0.411	
Danisson et al. (1997) Dil 68. Danisson et al. (1997) Dil 68.	1.00	2.164	- 21		0111	- 22	1.04	0381037,833	
	- 114	1,205	- 15	0.12	0141	- 6	125		
	-0122	3.162	- 16	-0141	0186	17	11.76	0181-025.8.558	
Longtow et al. (2003	-6.1	1342	- 91	1	0.2%	- 21	9.7%	-0.251035,615	
Martinesson et al. (2005)	8.00	8.14	- 22		0132	- 19	5.2%	-0.141-0.7%, 8.428	
President et al. (2000) Torroren et al. (2000)	-0.301	8.182	22		8.12	21	1.2%	-0.351-0.85, 8.551 -0.871-0.82, 8.411	
Solonie d. a. († 192) Ovskeja d. a. († 192)		8.12	13		0141	- 22	1.06	-0.35(-0.32, 8.81) -0.36(-1.01, 8.31)	
Total (05h-CB)			337			284	186.0%	4.81(4.11,0.91)	+
Helengeneitr Tauf = 3.80, Ch	r=5.89.	d=141	2+02	61.7=0	×				44 2 63
Teet for overall affect Z × 0.38	P+143								Fareurs Cell Favours Control
С		0.0							
	line	30	Telai	Mage:	83		WHIM.		Mill. Minar Officerace NJ, Random, NYS CI
Kely of Kelgroup Charter et al. (2012) (M	-0.30	122	22	Mean -0.242	0.483	21	West LTh	N, Randers, MVs Cl -0181038, 8311	
Charter et al. (2012) OH Charter et al. (2012) OH Charter et al. (2012) OL	-8.30	1.72 1.92	22	0240 0240	9.482 0.482	11	175	N, Randers, WYLCI -0181038, 8311 -0211076, 8311	
Riedy of Ridgroup Charlter et al. (2012) CH Charlter et al. (2012) CL Danieson et al. (2012) CL Danieson et al. (2017) CB 20	-8.30 -0.385 -0.1	80 1.72 1.811 1.95	20 28 22	0240 0240 0240	9.83 0.483 0.883 0.884	11 11 16	17% 17% 17%	N, Banders, MYs C 018 [038, 8317] 021 [076, 8317] 038 [127, 807]	
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Nitely of Noteman Chardine et al. (2012) CH Chardine et al. (2012) CH Chardine et al. (2012) CL Davidson H al. (1917) CB 20 Davidson H al. (1917) CB 20 Davidson H al. (1917) CB 24 Davidson H al. (1917) CB 25 Davidson H al. (1917) CB 55 Davidson H al. (19	-4.36 -0.301 -4.31 -4.31 -4.35 -4.35 -4.34 -4.34 -4.34	82 1.72 1.811 1.86 1.405 1.405 1.405 1.722 1.334	2812222222	0240 0240 0310 0310 0310 0310 0310 0310 0310 03	ND 0.482 0.484 0.484 0.484 0.484 0.484 0.484 0.484 0.484	111111111111111111111111111111111111111	274 175 175 175 175 175 175 175 175 175	N, Randen, WY CI 0.753 (0.88, 0.11) 0.221 (0.74, 0.11) 0.383 (1.27, 0.07) 1.683 (2.48, 400) 1.235 (1.68, 4.50) 4.775 (1.47, 4.67) 0.483 (1.5, 0.78) 4.775 (1.47, 4.67) 0.483 (1.5, 0.78) 4.099 (1.00, 4.19) 0.209 (1.55, 0.78)	
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Thinky on Multiprese Charther et al. (2012) CH Charther et al. (2012) Charthere et al. (2012)	4.00 4.00 4.01 4.02 4.01 4.02 4.02 4.04 4.04 4.02 4.02 4.02 4.02	\$20 1,72 1,811 1,805 1,805 1,700 1,720 1,720 1,720 1,721 1,800 1,872 1,301 1,800 1,872 1,301 1,800 1,872	22222222221122222	Block 0.240 0.240 0.30 0.32 0.32 0.32 0.32 0.32 0.33 0.34 0.35 0.3	N3 0.482 0.484	11110000000000000000000000000000000000	175 175 175 175 175 175 175 175 175 175	N, Banders, RW, CT 0.21 (0.28, E.21) 0.21 (0.28, E.21) 0.21 (0.27, E.21) 0.21 (0.27, E.21) 0.21 (0.28, E.20) 1.23 (1.06, E.40) 0.123 (1.06, E.40) 0.23 (1.25, E.20) 0.24 (1.25,	
Milley of Milligname Charlins et al. (2017) CH Charlins et al. (2017) CH Charlins et al. (2017) CS Develope et al. (2017) DS De Develope et al. (2017) Develope et al	4.00 4.00 4.0 4.0 4.0 4.0 4.0 4.0 4.0 4.	820 8.72 1.811 8.86 8.45 8.450 1.450 1.450 1.722 1.334 1.834 1.834 1.837 1.344 1.837 1.344 1.522	22222222221122222	Block 0.240 0.240 0.30 0.32 0.32 0.32 0.32 0.32 0.33 0.34 0.35 0.3	N3 0.482 0.484	11110000000000000000000000000000000000	175 175 175 175 175 175 175 175 175 175	M.Randers, BYS G. -0.13 (-0.08, E.11) -0.21 (-0.74, E.12) -0.21 (-0.7	
Which at Multiple way Charlins and J. (2012) CM Charlins and J. (2012) CM Charlins and J. (2012) CM Charlins and J. (2012) CM Charlins and A. (2012) CM Charlins and A. (2012) CM Charlins and A. (2012) Charlins and A. (2012) Charlins and A. (2010) Maritemistics and A.	4.00 4.00 4.0 4.0 4.0 4.0 4.0 4.0 4.0 4.	320 1.72 1.811 1.815 1.405 1.405 1.400 1.722 1.334 1.834 1.834 1.837 1.344 1.837 1.344 1.522	22222222221122222	Block 0.240 0.240 0.30 0.32 0.33 0.33 0.33 0.34 0.35 0.3	N3 0.482 0.484	11110000000000000000000000000000000000	175 175 175 175 175 175 175 175 175 175	M.Randers, BYS G. -0.13 (-0.08, E.11) -0.21 (-0.74, E.12) -0.21 (-0.7	
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Titley to Markage use, Contrained all control (c) (1) Contrained all control (c)	4.38 4.38 4.31 4.31 4.32	100 102 102 102 102 102 102 102 102 102	7 = 0	Boai C 24C C	MI 0.002 0.002 0.00400000000	21 21 11 16 16 16 16 16 16 16 16 16 16 16 16	Maget 178 178 178 178 178 178 178 178	M. Readers, WY, CU - 0.111 (-0.01, 0.117) - 0.211 (-0.01, 0.117) - 0.211 (-0.01, 0.117) - 0.211 (-0.01, 0.117) - 0.211 (-0.01, 0.117) - 1.211 (-0.01, 0.117) - 1.211 (-0.01, 0.117) - 0.211 (-	
Titley & Mady use, College and a college and college an	4.86 4.86 4.87 4.77 4	100 172 184 184 184 184 184 184 184 184 184 184	22 11 22 22 22 22 22 22 22 22 22 22 22 2	Boai C 240 C	NO 0.002 0.002 0.004 0.004 0.004 0.005 0.0	21 21 21 21 21 21 21 21 21 21 21 21 21 2	Weight 12% 12% 12%	M. Names, WU C. 0.4710-018, EU1	
Titley to Margues Control of Control Contro	4.38 4.38 4.31 4.31 4.32	100 172 172 100 172 100 100 172 100 100 100 100 100 100 100 100 100 10	22 22 22 22 22 22 22 22 22 22 22 22 22	Boal C 190 C	NO 0.002 0.002 0.004 0.004 0.004 0.005 0.0	21 21 21 21 21 21 21 21 21 21 21 21 21 2	Weight 12% 12% <td>M. Ramon, WU C. Ortholis, WU C. -0019(018, U11) -0019(018, U11)</td> <td></td>	M. Ramon, WU C. Ortholis, WU C. -0019(018, U11)	
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Titley to Margues Control of the Cont	4.88 4.38 4.31	100 102 102 102 102 102 102 102	10000000000000000000000000000000000000	Head C 190 C	100 0.002 0.002 0.004 0.004 0.00540000000000	21 21 10 10 10 10 10 10 10 10 10 10 10 10 10	Weight 27% 12% 12% 12% <td>M. Ranker, WY C. O'Holman, WY C. - 0713 (10), E173 (10) - 0713 (10), E173 (10)</td> <td></td>	M. Ranker, WY C. O'Holman, WY C. - 0713 (10), E173 (10)	
Titley & Mady use, Control (1) Dealesch et al. (1117) (2) Dealesch et al. (2) De	4.38 4.38 4.31	ND ND 1.72 1.81 1.80 2.84 1.80 2.45 1.80 2.22 1.33 1.80 1.430 2.321 1.34 3.321 1.444 3.521 1.80 2.321 1.810 2.321 1.845 1.521 0.00 1.421 1.810 1.422 1.810 1.425 1.810 1.425 1.810 1.425 1.810 1.425 1.810 1.425 1.810 1.425 1.810 1.425 1.810 1.425 1.810 1.425 1.810 1.425 1.810 1.425 1.810 1.425 1.810 1.425 1.810 1.425 1.810 1.425 1.810 1.425 1.810 1.425 1.810 1.42	19 19 19 19 19 19 19 19 19 19 19 19 19 1	Base C 190 C	100 0.002 0.002 0.0040 0.00400000000	21 11 16 16 16 16 16 16 16 16 16 16 16 16	Weight Project 12% 12% 12% 12% 12% 52% 52% 52% 52% 52% 12% 12%	M. Names, WY C. 0.7112-018. EUT. 0.7112-018	
Titley to Margues Control of the Cont	4.88 4.88 4.11	100 102 102 102 102 102 102 102 102 102	19 18 19 19 19 19 19 19 19 19 19 19 19 19 19	Bana C 240 C 24	MB 0.0012 0.002 0.00400000000	21 21 14 14 14 14 14 14 14 14 14 14 14 14 14	Weight Weight 12% 12% 12% 12% 12% 55% 55%<	M. Raman, WU C. 0.2112018, USE C. 0.211218, USE C. 0.211214, USE C. 0.	
Thinky to Marguese Control Contelecce Control Control Control Control Contelecce Co	4.88 4.88 4.88 4.89 4.89 4.89 4.89 4.89 4.89 4.89 4.89 4.89 4.89 4.89 4.99 4	NB NB 0.72 0.72 0.81 0.81 0.81 0.81 0.80 0.81 0.80 0.81 0.80 0.81 0.81 0.81	19 18 18 18 18 18 18 18 18 18 18 18 18 18	Bital -0.200 -0.201 0.202 0.203 0.204 -0.204 -0.204 -0.204 -0.204 -0.204 0.204 0.204 0.204 0.204 0.204 0.204	0.002 0.002 0.002 0.00400000000	11111111111111111111111111111111111111	Weight Project 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 176 175 176 175 176 175 176 175 176 175 176 175 176 175 177 175 178 175 178 175 178 175 178 175 178 175 178 175 178 175 178 175 178 175 178 175 178 175 178	M. Ranker, WY C. O'Holman, WY C. C 1913 (31), E113 (21), C113 (21), C1	
Thinky on Multiprese Charther et al. (2012) CH Charther et al. (2012)	4.88 4.88 4.88 4.89 4.89 4.89 4.89 4.89 4.89 4.89 4.89 4.89 4.89 4.89 4.99 4	100 102 102 102 102 102 102 102 102 102	19 18 18 18 18 18 18 18 18 18 18 18 18 18	Bana C 240 C	0.002 0.002 0.002 0.00400000000	11111111111111111111111111111111111111	Weight Project 175 175 175	M. Raman, WU C. 0.2112018, USE C. 0.211218, USE C. 0.211214, USE C. 0.	

A	Favours Oat		ıt	0	control		5	Std. Mean Difference		Std. Mean Di	ference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl		IV, Random,	95% CI	
Amundsen et al. (2003)	-0.71	0.426	16	-0.3	0.575	16	12.4%	-0.79 [-1.51, -0.07]				
Bremer et al. (1991)	-0.3	0.703	12	-0.3	0.717	12	11.2%	0.00 [-0.80, 0.80]				
Connolly et al. (2016)	-0.52	0.592	30	0.49	0.752	30	15.1%	-1.47 [-2.05, -0.90]		_		
Kristensen and Bügel (2011)	-0.59	0.54	24	-0.16	0.59	24	14.8%	-0.75 [-1.33, -0.16]				
Önning et al. (1999)	-0.17	0.59	52	0.19	0.54	52	18.7%	-0.63 [-1.03, -0.24]				
Swain et al. (1990)	-0.36	0.406	20	-0.34	0.406	20	14.2%	-0.05 [-0.67, 0.57]				
Trinidad et al. (2004)	-0.647	0.667	21	0.104	0.714	21	13.6%	-1.07 [-1.72, -0.42]	8 <u>.</u>			
Total (95% CI)			175			175	100.0%	-0.70 [-1.07, -0.34]		•		
Heterogeneity: Tau ² = 0.15; Ch	i ² = 15.54	, df = 6	(P = 0.0)	(2); I ² = 1	61%				+	<u> </u>		-+
Test for overall effect: Z = 3.76	(P = 0.00))2)							-2	-1 U Favours Oat F	1 avours Control	2

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		Oat		(Control		5	Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% CI
Amundsen et al. (2003)	-0.21	0.249	16	-0.15	0.213	16	11.7%	-0.25 [-0.95, 0.44]	
Bremer et al. (1991)	0.1	0.087	12	0.09	0.115	12	9.8%	0.09 [-0.71, 0.90]	
Connolly et al. (2016)	0.02	0.216	30	-0.01	0.181	30	16.6%	0.15 [-0.36, 0.66]	· · · · · · · · · · · · · · · · · · ·
Kristensen and Bügel (2011)	-0.15	0.1	24	-0.08	0.16	24	14.6%	-0.52 [-1.09, 0.06]	
Önning et al. (1999)	-0.07	0.46	52	0.05	0.17	52	20.6%	-0.34 [-0.73, 0.04]	
Swain et al. (1990)	0.01	0.118	20	-0.08	0.1282	20	12.9%	0.72 [0.07, 1.36]	· · · · · ·
Trinidad et al. (2004)	-0.129	0.286	21	-0.054	0.249	21	13.8%	-0.27 [-0.88, 0.33]	
Total (95% CI)			175			175	100.0%	-0.09 [-0.39, 0.21]	-
Heterogeneity: Tau ² = 0.08; Ch	i ^z = 11.36	, df = 6 ((P = 0.0)	18); I ^z = 4	7%				
Test for overall effect: Z = 0.56	(P = 0.57)		-1-12-22-22-22-22-22-22-22-22-22-22-22-2						-1 -0.5 0 0.5 1 Favours Oat Favours Control

<u>^</u>									
C		Oat		(Control			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% CI
Amundsen et al. (2003)	-0.4	0.364	15	-0.01	0.478	15	8.6%	-0.89 [-1.65, -0.14]	· · · · · · · · · · · · · · · · · · ·
Bremer et al. (1991)	-0.3	0.741	12	-0.4	0.789	12	7.7%	0.13 [-0.67, 0.93]	
Connolly et al. (2016)	-0.3	3.966	30	0.31	0.55	30	17.7%	-0.21 [-0.72, 0.29]	
Kristensen and Bügel (2011)	-0.35	0.52	24	-0.29	0.45	24	14.6%	-0.12 [-0.69, 0.44]	
Önning et al. (1999)	-0.21	0.45	51	0.04	0.62	51	27.3%	-0.46 [-0.85, -0.06]	
Swain et al. (1990)	-0.27	0.299	20	-0.19	0.299	20	12.3%	-0.26 [-0.88, 0.36]	
Trinidad et al. (2004)	-0.351	0.368	21	0.033	0.539	21	11.9%	-0.82 [-1.45, -0.18]	
Total (95% CI)			173			173	100.0%	-0.38 [-0.60, -0.15]	•
Heterogeneity: Tau ² = 0.01; Ch	i ² = 6.64.	df = 6 (F	P = 0.38	i); l² = 1	0%				
Test for overall effect: Z = 3.24									-1 -0.5 0 0.5 1 Favours Oat Favours Control

		Oat		Co	ontrol			Std. Mean Difference		Std. Mean Dif	ference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl		IV, Random,	95% CI	
Amundsen et al. (2003)	-0.2	0.574	16	-0.47	1.006	16	13.0%	0.32 [-0.38, 1.02]			•	
Bremer et al. (1991)	-0.2	0.541	12	0	0.462	12	9.7%	-0.38 [-1.19, 0.43]	8 <u>0</u>			
Connolly et al. (2016)	-0.08	0.362	30	0.08	0.762	30	24.5%	-0.26 [-0.77, 0.24]				
(ristensen and Bügel (2011)	-0.19	0.34	24	-0.08	0.16	24	19.3%	-0.41 [-0.98, 0.16]		-	28	
Ónning et al. (1999)	0.1	0.58	52	0.29	0.63	52		Not estimable				
Swain et al. (1990)	-0.5	0.908	20	-0.35	0.908	20	16.4%	-0.16 [-0.78, 0.46]				
rinidad et al. (2004)	-0.599	0.476	21	-0.4629	0.611	21	17.1%	-0.24 [-0.85, 0.36]	8	•		
otal (95% CI)			123			123	100.0%	-0.21 [-0.46, 0.04]				
Heterogeneity: Tau² = 0.00; Ch Test for overall effect: Z = 1.61		•	P = 0.71); I ^z = 0%				and the second sec	-1	-0.5 0	0.5	1

Favours Oat Favours Control

Study or Subgroup	Mean	glucan SD	Total	Mean	ontrol SD	Total	Weight	Std. Mean Difference IV, Random, 95% Cl	Std. Mean Difference IV, Random, 95% Cl
Biörklund et al. (2005) Oat-10	-0.32	0.39	19	0.17	0.49	20	6.8%	-1.08 [-1.76, -0.40]	
Biörklund et al. (2005) Oat-5	-0.12	0.54	15	0.17	0.49	20	6.8%	-0.55 [-1.24, 0.13]	
Biörklund et al. (2008)	-0.18	0.38	22	-0.09	0.34	21	7.5%	-0.24 [-0.85, 0.36]	
Cugnet-Anceau et al. (2010)	-0.06	0.52	29	0.01	0.52	24	8.0%	-0.13 [-0.67, 0.41]	
Ferguson et al. (2019)	-0.41	0.51	18	0.02	0.55	18	6.8%	-0.79 [-1.47, -0.11]	
Keenan et al. (2007) 3HMW	-0.494		32	-0.02	0.55	30	8.0%	-1.11 [-1.65, -0.57]	
Keenan et al. (2007) 3LMW	-0.462		31	-0.07	0.416	30	8.0%	-1.03 [-1.56, -0.49]	
Keenan et al. (2007) 5HMW	-0.402		32		0.416	30	7.6%	-1.70 [-2.28, -1.11]	
Keenan et al. (2007) 5HMW	-0.683		30	-0.07	0.416	30	7.7%	-1.47 [-2.05, -0.90]	
	-0.003	0.406	28	-0.07	0.410	24	8.0%		
Morales et al. (2021)								0.00 [-0.55, 0.55]	
Naumann et al. (2006)	-0.19	0.39	25	0.11	0.37	22	7.5%	-0.77 [-1.37, -0.18]	
Pino et al. (2021)	-0.248		20		1.673	17	7.1%	-0.16 [-0.80, 0.49]	
Wolever et al. (2021)	-0.22	0.441	96	0.04	0.529	90	10.2%	-0.53 [-0.82, -0.24]	
Total (95% CI)			397			381	100.0%	-0.73 [-1.01, -0.45]	•
Heterogeneity: Tau ² = 0.18; Ch	ni² = 39.98	. df = 12	(P < 0.	0001): P	= 70%				-2 -1 -1 -1 -2
Test for overall effect: Z = 5.13	(P < 0.000	001)							Favours B-glucan Favours Control
в									
-		glucan	.		ontrol			Std. Mean Difference	Std. Mean Difference
tudy or Subgroup	Mean		Total	Mean			Weight	IV, Random, 95% CI	IV, Random, 95% Cl
liörklund et al. (2005) Oat-10	-0.01	0.15	19	0.07	0.14	20	4.9%	-0.54 [-1.18, 0.10]	
liörklund et al. (2005) Oat-5	0.06	0.1	15	0.07	0.14	20	4.4%	-0.08 [-0.75, 0.59]	
liörklund et al. (2008)	-0.03		22	-0.07	0.26	21	5.6%	0.16 [-0.43, 0.76]	
Cugnet-Anceau et al. (2010)	0.05	0.1	29	0.03	0.14	24	6.8%	0.16 [-0.38, 0.71]	
erguson et al. (2019)	-0.03	0.13	18	0.04	0.17	18	4.5%	-0.45 [-1.11, 0.21]	
(eenan et al. (2007) 3HMW	-0.013	0.14			0.151	30	8.0%	0.02 [-0.48, 0.52]	
(eenan et al. (2007) 3LMW		0.197			0.151	30	7.8%	0.26 [-0.24, 0.77]	
(eenan et al. (2007) 5HMW	0.028	0.176		-0.016	0.151	30	8.0%	0.26 [-0.24, 0.76]	
(eenan et al. (2007) 5LMW	-0.018	0.171	30	-0.016	0.151	30	7.8%	-0.01 [-0.52, 0.49]	
torales et al. (2021)	-0.03	0.2	28	-0.03	0.2	24	6.7%	0.00 [-0.55, 0.55]	
laumann et al. (2006)	0.03	0.08	25	0.06	0.1	22	6.0%	-0.33 [-0.91, 0.25]	
'ino et al. (2021)		0.234	20	0.059	0.266	17	4.8%	-0.05 [-0.70, 0.59]	
Volever et al. (2021)	-0.01	0.194	96	0.01	0.161	95	24.7%	-0.11 [-0.40, 0.17]	
otal (95% CI)			397			204	100.0%	0.041.0.40.0.103	
leterogeneity: Tau² = 0.00; Chi	R = 0.05 a	K- 10/		N 18 - 01	v	381	100.0%	-0.04 [-0.18, 0.10]	
est for overall effect: Z = 0.52 ((P = 0.85, 0	1 - 12 (- 0.7	0,1 = 0	<i>1</i> 0				-1 -0.5 0 0.5 1
	(1 = 0.00)								Favours B-glucan Favours Control
С		-						Chil Marco Difference	Favours B-glucan Favours Control
С		glucan SD	Total	C Mean	ontrol SD	Total	Weight	Std. Mean Difference	Favours B-glucan Favours Control Std. Mean Difference
C Study or Subgroup	B- Mean	SD		Mean	SD		Weight 6.9%	IV, Random, 95% Cl	Favours B-glucan Favours Control
C Study or Subgroup Blörklund et al. (2005) Oat-10	B- Mean -0.24	SD 0.35	19	Mean 0.05	SD 0.38	20	6.9%	IV, Random, 95% Cl -0.78 [-1.43, -0.12]	Favours B-glucan Favours Control Std. Mean Difference
C Study or Subgroup Biörklund et al. (2005) Oat-10 Biörklund et al. (2005) Oat-5	B- Mean -0.24 -0.11	SD 0.35 0.54	19 15	Mean 0.05 0.05	SD 0.38 0.38	20 20	6.9% 6.7%	V, Random, 95% CI -0.78 [-1.43, -0.12] -0.34 [-1.02, 0.33]	Favours B-glucan Favours Control Std. Mean Difference
C Study or Subgroup Blörklund et al. (2005) Oat-10 Blörklund et al. (2005) Oat-5 Blörklund et al. (2008)	B- Mean -0.24 -0.11 -0.16	SD 0.35 0.54 0.36	19 15 22	Mean 0.05 0.05 -0.05	SD 0.38 0.38 0.27	20 20 21	6.9% 6.7% 7.4%	IV, Random, 95% CI -0.78 [-1.43, -0.12] -0.34 [-1.02, 0.33] -0.34 [-0.94, 0.26]	Favours B-glucan Favours Control Std. Mean Difference
C Study or Subgroup Blörklund et al. (2005) Oat-10 Blörklund et al. (2008) Slörklund et al. (2008) Ugnet-Anceau et al. (2010)	B- Mean -0.24 -0.11 -0.16 -0.05	SD 0.35 0.54 0.36 0.38	19 15 22 29	Mean 0.05 0.05 -0.05 -0.1	SD 0.38 0.38 0.27 0.51	20 20 21 24	6.9% 6.7% 7.4% 7.9%	V, Random, 95% Cl -0.78 [-1.43, -0.12] -0.34 [-1.02, 0.33] -0.34 [-0.94, 0.26] 0.11 [-0.43, 0.65]	Favours B-glucan Favours Control Std. Mean Difference
C Study or Subgroup Biörklund et al. (2005) Oat-10 Biörklund et al. (2008) Ougnet-Anceau et al. (2010) Erguson et al. (2019)	B- -0.24 -0.11 -0.16 -0.05 -0.42	SD 0.35 0.54 0.36 0.38 0.47	19 15 22 29 18	Mean 0.05 0.05 -0.05 -0.1 -0.05	SD 0.38 0.38 0.27 0.51 0.51	20 20 21 24 18	6.9% 6.7% 7.4% 7.9% 6.7%	IV, Random, 95% CI -0.78 [-1.43, -0.12] -0.34 [-1.02, 0.33] -0.34 [-0.94, 0.26] 0.11 [-0.43, 0.65] -0.74 [-1.42, -0.06]	Favours B-glucan Favours Control Std. Mean Difference
C Study or Stubgroup Biorklund et al. (2005) Oat-10 Biorklund et al. (2005) Oat-5 Biörklund et al. (2010) Cugnet-Anceau et al. (2010) Ferguson et al. (2017) 3HMW	B- -0.24 -0.11 -0.16 -0.05 -0.42 -0.362	SD 0.35 0.54 0.36 0.38 0.47 0.516	19 15 22 29 18 32	Mean 0.05 0.05 -0.05 -0.1 -0.05 -0.047	SD 0.38 0.27 0.51 0.51 0.412	20 20 21 24 18 30	6.9% 6.7% 7.4% 7.9% 6.7% 8.2%	V, Random, 95% CI -0.78 [-1.43, -0.12] -0.34 [-1.02, 0.33] -0.34 [-0.94, 0.26] 0.11 [-0.43, 0.66] -0.74 [-1.42, -0.06] -0.66 [-1.18, -0.15]	Favours B-glucan Favours Control Std. Mean Difference
C Study or Subgroup Biorklund et al. (2005) Oat-10 Biorklund et al. (2006) Oat-5 Biorklund et al. (2008) Ugnet-Anceau et al. (2010) Forguson et al. (2017) Genan et al. (2007) 3LMW	B- Mean -0.24 -0.11 -0.16 -0.05 -0.42 -0.362 -0.347	SD 0.35 0.54 0.36 0.38 0.47 0.516 0.263	19 15 22 29 18 32 31	Mean 0.05 0.05 -0.05 -0.1 -0.05 -0.047 -0.047	SD 0.38 0.27 0.51 0.51 0.412 0.412	20 20 21 24 18 30 30	6.9% 6.7% 7.4% 7.9% 6.7% 8.2% 8.1%	V, Random, 95% Cl -0.78 [-1.43, -0.12] -0.34 [-1.02, 0.33] -0.34 [-0.94, 0.26] 0.11 [-0.43, 0.66] -0.74 [-1.42, -0.06] -0.66 [-1.18, -0.15] -0.86 [-1.39, -0.33]	Favours B-glucan Favours Control Std. Mean Difference
C Study or Subgroup Storklund et al. (2005) Oat-10 Biorklund et al. (2005) Oat-5 Biorklund et al. (2007) Sugnet-Anceau et al. (2010) Segnas et al. (2017) Super-S	B- Mean -0.24 -0.11 -0.16 -0.05 -0.42 -0.362 -0.347 -0.582	SD 0.35 0.54 0.36 0.38 0.47 0.516 0.263 0.273	19 15 22 29 18 32 31 32	Mean 0.05 0.05 -0.05 -0.1 -0.05 -0.047 -0.047 -0.047	SD 0.38 0.38 0.27 0.51 0.51 0.412 0.412 0.412	20 20 21 24 18 30 30 30	6.9% 6.7% 7.4% 7.9% 6.7% 8.2% 8.1% 7.7%	V, Random, 95% Cl -0.78 [-1.43, -0.12] -0.34 [-1.02, 0.33] -0.34 [-0.94, 0.26] 0.11 [-0.43, 0.66] -0.74 [-1.42, -0.06] -0.66 [-1.18, -0.15] -0.86 [-1.39, -0.33] -1.52 [-2.09, -0.95]	Favours B-glucan Favours Control Std. Mean Difference
C Study or Subgroup Biorklund et al. (2005) Oat-10 Biorklund et al. (2005) Oat-5 Biorklund et al. (2006) Sugnet-Anceau et al. (2010) Ferguson et al. (2007) 3LMWV Geenan et al. (2007) 3LMWV Geenan et al. (2007) 3LMWV Geenan et al. (2007) 5LMWV	B- Mean -0.24 -0.11 -0.16 -0.05 -0.42 -0.362 -0.362 -0.347 -0.582 -0.525	SD 0.35 0.54 0.36 0.38 0.47 0.516 0.263 0.273 0.333	19 15 22 29 18 32 31 32 30	Mean 0.05 0.05 -0.05 -0.1 -0.05 -0.047 -0.047 -0.047 -0.047	SD 0.38 0.38 0.27 0.51 0.51 0.412 0.412 0.412 0.412	20 20 21 24 18 30 30 30 30	6.9% 6.7% 7.4% 7.9% 6.7% 8.2% 8.1% 7.7% 7.8%	V, Random, 95% CI -0.78 [-1.43, -0.12] -0.34 [-0.94, 0.26] 0.11 [-0.43, 0.65] -0.74 [-1.42, -0.06] -0.66 [-1.38, -0.15] -0.86 [-1.39, -0.33] -1.52 [-2.09, -0.95] -1.52 [-1.82, -0.70]	Favours B-glucan Favours Control Std. Mean Difference
C Study or Subgroup 3idrklund et al. (2005) Oat-10 3idrklund et al. (2005) Oat-5 3idrklund et al. (2007) Sugnet-Anceau et al. (2010) Firguson et al. (2007) 3HMWV Geenan et al. (2007) 5HMWV Geenan et al. (2007) 5HMW Geenan et al. (2007) 5HMW Granate et al. (2007) 5HMW	B- 0.24 -0.11 -0.16 -0.05 -0.362 -0.362 -0.347 -0.582 -0.525 0.08	SD 0.35 0.54 0.36 0.38 0.47 0.516 0.263 0.273 0.273 0.333 0.65	19 16 22 29 18 32 31 32 30 28	Mean 0.05 0.05 -0.05 -0.05 -0.047 -0.047 -0.047 -0.047 0.01	SD 0.38 0.38 0.27 0.51 0.51 0.412 0.412 0.412 0.412 0.412 0.412 0.73	20 20 21 24 18 30 30 30 30 24	6.9% 6.7% 7.4% 7.9% 6.7% 8.2% 8.1% 7.7% 7.8% 7.9%	V, Random, 95% Cl -0.78 [-1.43, -0.12] -0.34 [-1.02, 0.33] -0.34 [-0.94, 0.26] 0.11 [-0.43, 0.65] -0.74 [-1.42, -0.06] -0.66 [-1.18, -0.15] -0.86 [-1.39, -0.33] -1.52 [-2.09, -0.95] -1.26 [-1.82, -0.70] 0.10 [-0.45, 0.65]	Favours B-glucan Favours Control Std. Mean Difference
C Study of Stubgroup Biofklund et al. (2005) Oat-5 Diofklund et al. (2005) Oat-5 Diofklund et al. (2006) Ugupel-Anceau et al. (2010) Vegenan et al. (2020) Seenan et al. (2020) Seenan et al. (2020) Morales et al. (2021) Morales et al. (2020)	B- Mean -0.24 -0.11 -0.16 -0.05 -0.42 -0.362 -0.347 -0.582 -0.525 0.08 -0.21	SD 0.35 0.54 0.38 0.47 0.516 0.263 0.273 0.333 0.65 0.37	19 15 22 29 18 32 31 32 30 28 25	Mean 0.05 0.05 -0.05 -0.047 -0.047 -0.047 -0.047 -0.047 0.01 0.1	SD 0.38 0.38 0.27 0.51 0.412 0.412 0.412 0.412 0.412 0.412 0.73 0.34	20 20 21 24 18 30 30 30 24 22	6.9% 6.7% 7.9% 6.7% 8.2% 8.1% 7.7% 7.8% 7.8% 7.9% 7.4%	V, Random, 95% CI -0.78 [-1.43, -0.12] -0.34 [-0.20, 0.33] -0.34 [-0.94, 0.26] -0.74 [-1.42, -0.06] -0.66 [-1.18, -0.15] -0.86 [-1.18, -0.15] -1.26 [-1.82, -0.70] -0.10 [-0.45, 0.65] -0.86 [-1.46, -0.25]	Favours B-glucan Favours Control Std. Mean Difference
C Study or Subgroup 310/kHund et al. (2005) 0-at-10 310/kHund et al. (2005) 0-at- 310/kHund et al. (2005) 2009-2000 et al. (2017) 2009-2000 et al. (2017) 2007) 540W Ceenan et al. (2007) 540W Ceenan et al. (2007) 540W Ceenan et al. (2007) 540W Corales et al. (2021) 4uamann et al. (2002)	B- Mean -0.24 -0.11 -0.16 -0.05 -0.42 -0.362 -0.347 -0.582 -0.525 0.08 -0.21 0.141	SD 0.35 0.54 0.38 0.47 0.516 0.263 0.273 0.333 0.65 0.37 0.967	19 15 22 29 18 32 31 32 30 28 25 20	Mean 0.05 0.05 -0.05 -0.047 -0.047 -0.047 -0.047 0.01 0.1 -0.03	SD 0.38 0.27 0.51 0.412 0.412 0.412 0.412 0.412 0.412 0.73 0.34 0.613	20 20 21 24 18 30 30 30 24 22 17	6.9% 6.7% 7.4% 6.7% 8.2% 8.1% 7.7% 7.8% 7.9% 7.9% 7.4% 7.0%	V, Random, 95% CI -0.78 [-1.43, 0.12] -0.34 [-0.24, 0.33] -0.34 [-0.24, 0.65] -0.74 [-1.42, -0.06] -0.66 [-1.18, -0.15] -0.86 [-1.39, -0.33] -1.52 [-2.09, -0.95] -1.26 [-1.42, -0.70] 0.10 [-0.45, 0.65] -0.86 [-1.46, -0.25] 0.20 [-0.45, 0.85]	Favours B-glucan Favours Control Std. Mean Difference
C Study or Subgroup 310/kHund et al. (2005) 0-at-10 310/kHund et al. (2005) 0-at- 310/kHund et al. (2005) 2009-2000 et al. (2017) 2009-2000 et al. (2017) 2007) 540W Ceenan et al. (2007) 540W Ceenan et al. (2007) 540W Ceenan et al. (2007) 540W Corales et al. (2021) 4uamann et al. (2002)	B- Mean -0.24 -0.11 -0.16 -0.05 -0.42 -0.362 -0.347 -0.582 -0.525 0.08 -0.21 0.141	SD 0.35 0.54 0.38 0.47 0.516 0.263 0.273 0.333 0.65 0.37	19 15 22 29 18 32 31 32 30 28 25	Mean 0.05 0.05 -0.05 -0.047 -0.047 -0.047 -0.047 0.01 0.1 -0.03	SD 0.38 0.38 0.27 0.51 0.412 0.412 0.412 0.412 0.412 0.412 0.73 0.34	20 20 21 24 18 30 30 30 24 22	6.9% 6.7% 7.9% 6.7% 8.2% 8.1% 7.7% 7.8% 7.8% 7.9% 7.4%	V, Random, 95% CI -0.78 [-1.43, -0.12] -0.34 [-0.20, 0.33] -0.34 [-0.94, 0.26] -0.74 [-1.42, -0.06] -0.66 [-1.18, -0.15] -0.86 [-1.18, -0.15] -1.26 [-1.82, -0.70] -0.10 [-0.45, 0.65] -0.86 [-1.46, -0.25]	Favours B-glucan Favours Control Std. Mean Difference
C Study or Subgroup Biofklund et al. (2005) Gat-10 Biofklund et al. (2006) Giofklund et al. (2008) Uugnet-Anceau et al. (2010) Gregueson et al. (2007) Seenan et al. (2007) SHAW doraines et al. (2007) Murrane et al. (2007) Shaw doraines et al. (2001) Whorelas et al. (2001) Whorever et al. (2021) Voiever et al. (2021) Voiever et al. (2021)	B- Mean -0.24 -0.11 -0.16 -0.42 -0.362 -0.362 -0.525 0.08 -0.21 0.141 -0.22	SD 0.35 0.54 0.36 0.47 0.516 0.263 0.273 0.333 0.657 0.37 0.967 0.439	19 15 22 29 18 32 31 32 30 28 25 20 96 397	Mean 0.05 0.05 -0.05 -0.047 -0.047 -0.047 -0.047 -0.047 0.01 0.1 -0.03 0.03	SD 0.38 0.38 0.27 0.51 0.412 0.412 0.412 0.412 0.412 0.412 0.73 0.34 0.613 0.384	20 20 21 24 30 30 30 24 22 17 95	6.9% 6.7% 7.4% 6.7% 8.2% 8.1% 7.7% 7.8% 7.9% 7.9% 7.4% 7.0%	V, Random, 95% CI -0.78 [-1.43, 0.12] -0.34 [-0.24, 0.33] -0.34 [-0.24, 0.65] -0.74 [-1.42, -0.06] -0.66 [-1.18, -0.15] -0.86 [-1.39, -0.33] -1.52 [-2.09, -0.95] -1.26 [-1.42, -0.70] 0.10 [-0.45, 0.65] -0.86 [-1.46, -0.25] 0.20 [-0.45, 0.85]	Favours B-glucan Favours Control Std. Mean Difference
C Study of Subgroup Biokkund et al. (2005) Oat-10 Biokkund et al. (2005) Oat-10 Biokkund et al. (2005) Groupen-Anceau et al. (2011) Groupen-Anceau et al. (2007) Biokkund et al. (2007) Subwrown et al. (2007) Shuwy Genane et al. (2007) Shuwy Genane et al. (2007) Shuwy Gorales et al. (2021) Wolewer et al. (2021) Wolewer et al. (2021) Volaver et al. (2	B- Mean -0.24 -0.11 -0.16 -0.05 -0.42 -0.362 -0.362 -0.525 0.08 -0.21 0.141 -0.22 i ^p = 37.68,	SD 0.35 0.54 0.36 0.47 0.516 0.263 0.273 0.65 0.333 0.65 0.37 0.967 0.439 df = 12	19 15 22 29 18 32 31 32 30 28 25 20 96 397	Mean 0.05 0.05 -0.05 -0.047 -0.047 -0.047 -0.047 -0.047 0.01 0.1 -0.03 0.03	SD 0.38 0.38 0.27 0.51 0.412 0.412 0.412 0.412 0.412 0.412 0.73 0.34 0.613 0.384	20 20 21 24 30 30 30 24 22 17 95	6.9% 6.7% 7.4% 6.7% 8.2% 8.1% 7.7% 7.8% 7.8% 7.9% 7.4% 7.0%	$\begin{array}{c} \textbf{V}, \textbf{Random}, 95\% CI \\ -0.78 \left[+ .43, 0.12 \right] \\ -0.34 \left[+ .02, 0.33 \right] \\ -0.34 \left[+ .02, 0.33 \right] \\ -0.34 \left[+ .043, 0.65 \right] \\ -0.74 \left[+ .42, -0.06 \right] \\ -0.66 \left[+ .18, 0.15 \right] \\ -0.86 \left[+ .139, -0.33 \right] \\ -1.52 \left[+ .209, -0.95 \right] \\ -1.26 \left[+ .129, -0.70 \right] \\ -0.16 \left[45, 0.65 \right] \\ -0.66 \left[- 1.46, 0.25 \right] \\ -0.60 \left[- 0.48, 0.31 \right] \\ \end{array}$	Favours B-glucan Favours Control Std. Mean Difference
C Study or Subgroup Biofklund et al. (2005) Gat-10 Biofklund et al. (2008) Ougnet-Anceau et al. (2010) Uugnet-Anceau et al. (2010) Genann et al. (2007) 3HAW decannal et al. (2007) 3HAW decannal et al. (2007) 5HAW dorelas et al. (2021) Whorelas et al. (2021) Whoever et al. (2021) total (2055) CL	B- Mean -0.24 -0.11 -0.16 -0.05 -0.42 -0.362 -0.362 -0.525 0.08 -0.21 0.141 -0.22 i ^p = 37.68,	SD 0.35 0.54 0.36 0.47 0.516 0.263 0.273 0.65 0.333 0.65 0.37 0.967 0.439 df = 12	19 15 22 29 18 32 31 32 30 28 25 20 96 397	Mean 0.05 0.05 -0.05 -0.047 -0.047 -0.047 -0.047 -0.047 0.01 0.1 -0.03 0.03	SD 0.38 0.38 0.27 0.51 0.412 0.412 0.412 0.412 0.412 0.412 0.73 0.34 0.613 0.384	20 20 21 24 30 30 30 24 22 17 95	6.9% 6.7% 7.4% 6.7% 8.2% 8.1% 7.7% 7.8% 7.8% 7.9% 7.4% 7.0%	$\begin{array}{c} \textbf{V}, \textbf{Random}, 95\% CI \\ -0.78 \left[+ .43, 0.12 \right] \\ -0.34 \left[+ .02, 0.33 \right] \\ -0.34 \left[+ .02, 0.33 \right] \\ -0.34 \left[+ .043, 0.65 \right] \\ -0.74 \left[+ .42, -0.06 \right] \\ -0.66 \left[+ .18, 0.15 \right] \\ -0.86 \left[+ .139, -0.33 \right] \\ -1.52 \left[+ .209, -0.95 \right] \\ -1.26 \left[+ .129, -0.70 \right] \\ -0.16 \left[45, 0.65 \right] \\ -0.66 \left[- 1.46, 0.25 \right] \\ -0.60 \left[- 0.48, 0.31 \right] \\ \end{array}$	Favours B-glucan Favours Control
Study or Subgroup Biofklund et al. (2005) Oal-10 Biofklund et al. (2005) Oal-50 Diofklund et al. (2006) Ugnet-Anceau et al. (2010) Genenn et al. (2007) SHAW Genenn et al. (2007) SHAW Genenn et al. (2007) SHAW Morales et al. (2021) Jaurann et al. (2005) SLAW Veren et al. (2007) SHAW Hore et al. (2021) Vere et al. (2021) Volaver et al. (2021) Volaver et al. (2021) Volar (95% CL) Teal (95% CL)	B- Mean -0.24 -0.11 -0.16 -0.05 -0.42 -0.362 -0.362 -0.525 0.08 -0.21 0.141 -0.22 i ^p = 37.68,	SD 0.35 0.54 0.36 0.47 0.516 0.263 0.273 0.65 0.37 0.967 0.439 df = 12	19 15 22 29 18 32 31 32 30 28 25 20 96 397	Mean 0.05 0.05 -0.05 -0.047 -0.047 -0.047 -0.047 -0.047 0.01 0.1 -0.03 0.03 0002); I ²	SD 0.38 0.38 0.27 0.51 0.412 0.412 0.412 0.412 0.412 0.412 0.413 0.384 0.613 0.384 = 68%	20 20 21 24 30 30 30 24 22 17 95	6.9% 6.7% 7.4% 6.7% 8.2% 8.1% 7.7% 7.8% 7.8% 7.9% 7.4% 7.0%	M. Random, 95% C. -0.78 (+ 14.3, -0.17) -0.78 (+ 14.3, -0.17) -0.78 (+ 14.3, -0.16) -0.34 (+ 10.2, 0.35) -0.34 (+ 10.2, 0.35) -0.36 (+ 1.42, -0.16) -0.36 (+ 1.39, -0.33) -1.52 (- 2.09, -0.56) -1.52 (- 2.09, -0.56) -0.66 (+ 1.49, -0.56) -0.66 (+ 0.89, -0.31) -0.58 (-0.85, -0.32)	Favours B-glucan Favours Control
Study of Subgroup Biofklund et al. (2005) 0.41-0 Biofklund et al. (2005) 0.41-0 Diofklund et al. (2005) 0.41-0 Diofklund et al. (2006) 0.01-0 Ugnet-Anceau et al. (2010) Seenan et al. (2007) 3.HAW Genann et al. (2007) 3.HAW Keenan et al. (2007) 3.HAW Keenan et al. (2007) 3.HAW Morales et al. (2021) Vauraman et al. (2005) 5.HAW Morales et al. (2021) Viewer et al. (2021) Viewere	B- Mean -0.24 -0.11 -0.16 -0.05 -0.42 -0.362 -0.347 -0.582 -0.525 0.08 -0.21 0.141 -0.22 i ^µ = 37.68, (P < 0.000	SD 0.35 0.54 0.36 0.38 0.47 0.516 0.263 0.273 0.33 0.65 0.37 0.967 0.439 df = 12 (1) glucan	19 15 22 29 18 32 30 28 25 20 96 397 (P = 0.1	Mean 0.05 0.05 -0.05 -0.047 -0.047 -0.047 -0.047 -0.047 0.01 0.01 0.03 0.03 0.002); I ²	SD 0.38 0.38 0.27 0.51 0.412 0.412 0.412 0.412 0.412 0.412 0.413 0.384 0.613 0.384 = 68% Control	20 20 21 24 30 30 30 24 22 17 95 381	6.9% 6.7% 7.4% 6.7% 8.2% 8.1% 7.8% 7.9% 7.4% 7.0% 10.3%	M. Random, 95% C. -0.78 [+1.43, -0.17] -0.78 [+1.43, -0.17] -0.47 [+0.20, 33] -0.34 [+0.20, 33] -0.34 [+0.20, 33] -0.34 [+0.20, 33] -0.34 [+0.20, 33] -0.35 [+0.85, 0.82] -0.36 [+0.80, 0.31] -0.35 [+0.85, 0.32] -0.35 [+0.85, 0.32] Std. Mean Difference	Favours B-glucan Favours Control
C Study of Subgroup Binklund et al. (2005) 0a1-10 Binklund et al. (2005) 0a1-0 Binklund et al. (2005) 0a1-0 Superk-Ancau et al. (2011) 'arguson et al. (2007) 3LMW Genann et al. (2007) 3LMW Genann et al. (2007) 3LMW Genann et al. (2007) 5LMW Ancalise stal. (2021) 'Molever et al. (202	B- Mean -0.24 -0.11 -0.16 -0.052 -0.362 -0.347 -0.525 0.08 -0.211 0.141 -0.22 ² = 37.68 (P < 0.000	SD 0.35 0.54 0.36 0.38 0.47 0.516 0.263 0.273 0.33 0.65 0.37 0.967 0.439 df = 12 (1)	19 15 22 29 18 32 31 32 30 28 25 20 96 397	Mean 0.05 0.05 -0.05 -0.047 -0.047 -0.047 -0.047 -0.047 0.01 0.1 -0.03 0.03 0002); I ²	SD 0.38 0.38 0.27 0.51 0.412 0.412 0.412 0.412 0.412 0.412 0.413 0.384 0.613 0.384 = 68% Control	20 20 21 24 30 30 30 24 22 17 95 381	6.9% 6.7% 7.4% 7.9% 6.7% 8.2% 8.1% 7.9% 7.9% 7.9% 10.3% 100.0%	M. Random, 95% C. -0.78 (+ 4.3, -0.17) -0.78 (+ 4.3, -0.17) -0.78 (+ 4.3, -0.17) -0.4 (+ 102, 0.33) -0.4 (+ 102, 0.36) -0.78 (+ 1.8, -0.15) -0.66 (+ 1.8, -0.15) -0.86 (+ 1.8, -0.15) -0.86 (+ 1.8, -0.15) -0.86 (+ 1.8, -0.15) -0.86 (+ 0.86, -0.86) -0.86 (+ 0.86, -0.31) -0.58 (+ 0.85, -0.32) Sitd. Mean Difference M. Random, 95% C	Favours B-glucan Favours Control Std. Mean Difference N, Random, 95% Cl
Study of Subgroup Biofklund et al. (2005) 0.41-0 Biofklund et al. (2005) 0.41-0 Diofklund et al. (2005) 0.41-0 Diofklund et al. (2006) 0.01-0 Ugnet-Anceau et al. (2010) Seenan et al. (2007) 3.HAW Genann et al. (2007) 3.HAW Keenan et al. (2007) 3.HAW Keenan et al. (2007) 3.HAW Morales et al. (2021) Vauraman et al. (2005) 5.HAW Morales et al. (2021) Viewer et al. (2021) Viewere	B- Mean -0.24 -0.11 -0.16 -0.05 -0.42 -0.362 -0.347 -0.582 -0.525 0.08 -0.21 0.141 -0.22 i ^µ = 37.68, (P < 0.000	SD 0.35 0.54 0.36 0.38 0.47 0.516 0.263 0.273 0.33 0.65 0.37 0.967 0.439 df = 12 (1) glucan	19 15 22 29 18 32 30 28 25 20 96 397 (P = 0.1	Mean 0.05 0.05 -0.05 -0.047 -0.047 -0.047 -0.047 -0.047 0.01 0.01 0.03 0.03 0.002); I ²	SD 0.38 0.38 0.27 0.51 0.412 0.412 0.412 0.412 0.412 0.412 0.413 0.384 0.613 0.384 = 68% Control	20 20 21 24 30 30 30 24 22 17 95 381	6.9% 6.7% 7.4% 6.7% 8.2% 8.1% 7.8% 7.9% 7.4% 7.0% 10.3%	M. Random, 95% C. -0.78 (+ 4.3, -0.17) -0.78 (+ 4.3, -0.17) -0.78 (+ 4.3, -0.17) -0.4 (+ 102, 0.33) -0.4 (+ 102, 0.36) -0.78 (+ 1.8, -0.15) -0.66 (+ 1.8, -0.15) -0.86 (+ 1.8, -0.15) -0.86 (+ 1.8, -0.15) -0.86 (+ 1.8, -0.15) -0.86 (+ 0.86, -0.86) -0.86 (+ 0.86, -0.31) -0.58 (+ 0.85, -0.32) Sitd. Mean Difference M. Random, 95% C	Favours B-glucan Favours Control Std. Mean Difference N, Random, 95% Cl
C Study of Subgroup Binklund et al. (2005) 0a1-10 Binklund et al. (2005) 0a1-0 Binklund et al. (2005) 0a1-0 Superk-Ancau et al. (2011) 'arguson et al. (2007) 3LMW Genann et al. (2007) 3LMW Genann et al. (2007) 3LMW Genann et al. (2007) 5LMW Ancalise stal. (2021) 'Molever et al. (202	B- Mean -0.24 -0.11 -0.16 -0.05 -0.362 -0.362 -0.525 -0.525 -0.525 -0.525 -0.525 -0.22 -0.525 -0.44 -0.141 -0.22 ² = 37.68, (P < 0.000) B- Mean	SD 0.35 0.54 0.38 0.47 0.516 0.273 0.333 0.65 0.37 0.967 0.439 df = 12 (1) glucan SD	19 15 22 29 18 32 31 32 30 28 25 20 96 96 397 (P = 0.	Mean 0.05 0.05 -0.05 -0.047 -0.047 -0.047 -0.047 0.01 0.1 -0.03 0.03 0.03 0.002); I ² (Mean	SD 0.38 0.38 0.38 0.27 0.51 0.51 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.414 0.414	20 20 21 24 18 30 30 30 30 24 22 17 95 381	6.9% 6.7% 7.4% 7.9% 6.7% 8.2% 8.1% 7.9% 7.9% 7.9% 10.3% 100.0%	W, Random, 95% C. -0.78 [+1.3, -0.12] -0.78 [+1.4, 3, -0.12] -0.78 [+1.4, 3, -0.12] -0.45 [+0.2, 0.33] -0.24 [-0.04] -0.14 [+0.4, 0.66] -0.74 [+1.4, 2, -0.06] -0.66 [+1.18, -0.15] -0.66 [+1.18, -0.15] -0.66 [+1.18, -0.15] -0.66 [+0.8, -0.31] -0.56 [+0.85, -0.52] -0.56 [+0.85, -0.32] Std. Mean Difference M, Random, 95% C. -0.61 [+1.25, 0.03]	Favours B-glucan Favours Control Std. Mean Difference N, Random, 95% CI Favours B-glucan Favours Control Std. Mean Difference N, Random, 95% CI
Study or Subgroup Binkfund et al. (2005) Gał-10 Binkfund et al. (2005) Gał-10 Binkfund et al. (2006) Gał-50 Binkfund et al. (2007) Julky Gregora et al. (2007) Julky Geanna et al. (2007) Julky Morales et al. (2021) Warman et al. (2007) Sluky Origen et al. (2021) Study or Subgroup Binkfund et al. (2025) Study or Subgroup Study or Subgroup	B- Mean -0.24 -0.11 -0.16 -0.05 -0.362 -0.362 -0.525 -0.382 -0.525 -0.382 -0.21 0.141 -0.22 ² = 37.68, (P < 0.000 B- Mean -0.14	SD 0.35 0.54 0.36 0.38 0.47 0.516 0.263 0.373 0.65 0.37 0.447 0.439 df = 12 11 glucan SD 0.37 0.37	19 15 22 29 18 32 31 32 30 20 20 96 397 (P = 0.) Total 19	Mean 0.05 0.05 -0.01 -0.047 -0.047 -0.047 -0.047 -0.047 0.01 0.01 0.03 0.03 00002); I ² (Mean 0.1	SD 0.38 0.38 0.38 0.27 0.51 0.51 0.51 0.51 0.412 0.412 0.412 0.413 0.384 0.384 50 Control 50 0.412 0.412 0.384 0.384	20 20 21 24 30 30 30 30 24 22 17 95 381 Total 20	6.9% 6.7% 7.9% 6.7% 8.2% 8.1% 7.7% 7.8% 7.8% 7.0% 10.3% 100.0% Weight 6.2%	M. Random, 95% C. -0.78 (+ 4.3, -0.17) -0.78 (+ 4.3, -0.17) -0.78 (+ 4.3, -0.17) -0.4 (+ 0.04, 0.28) -0.4 (+ 0.04, 0.28) -0.4 (+ 0.2, 0.08) -0.6 (+ 1.8), -0.51 -0.6 (+ 1.8), -0.51 -0.6 (+ 1.8), -0.51 -0.6 (+ 0.8), -0.64 -0.6 (+ 0.8), -0.31 -0.58 (-0.85, -0.32) Sidd. Mean Difference M. Random, 95% C -0.61 (+ 1.2, 0.03) -0.58 (-0.81 - 1.24, 0.13)	Favours B-glucan Favours Control
Study or Subgroup Biofklund et al. (2005) Gał-10 Biofklund et al. (2005) Gał-10 Biofklund et al. (2006) Gał-50 Diofklund et al. (2007) JHWV Genann et al. (2007) JHWV Keanna et al. (2007) JHWV Genann et al. (2007) JHWV Keanna et al. (2007) JHWV Koranna et al. (2007) JHWV Korann	B- Mean -0.24 -0.11 -0.16 -0.05 -0.42 -0.362 -0.362 -0.347 -0.582 -0.347 -0.582 -0.347 -0.141 -0.12 B- Mean -0.14 -0.14 -0.14	SD 0.35 0.54 0.36 0.36 0.38 0.47 0.516 0.263 0.273 0.665 0.38 0.373 0.656 0.37 0.967 0.439 df= 12 11 glucan SD 0.37 0.45 0.45 0.44	19 19 15 22 29 31 32 30 25 20 96 397 (P = 0.) Total 19 15	Mean 0.05 0.05 0.05 -0.05 -0.047 -0.047 -0.047 -0.047 0.01 0.03 0.03 0.03 0.03 0.03 0.03 0.03 0.03 0.05 0.05 0.05 0.05 -0.5 -0.5 -0.5 -0.5 -0.5 -0.5 -0.5 -0.5 -0.5 -0.	SD 0.38 0.38 0.38 0.27 0.51 0.412 0.412 0.412 0.412 0.73 0.384 0.384 = 68% SD 0.41 0.384	20 20 21 24 30 30 30 30 24 22 17 95 381 Total 20 20 20	6.9% 6.7% 7.9% 6.7% 8.2% 8.1% 7.7% 7.8% 7.9% 7.4% 7.0% 10.3% 10.3% 100.0%	W, Random, 95% C. -0.78 [+1.43, -0.12] -0.78 [+1.43, -0.12] -0.78 [+1.43, -0.12] -0.24 [+1.02, 0.33] -0.24 [-0.04, 0.26] -0.74 [+1.04, 0.06] -0.74 [+1.04, 0.06] -0.74 [+1.04, 0.06] -0.74 [+1.04, 0.06] -0.74 [+1.04, 0.06] -0.74 [+1.04, 0.06] -0.86 [+1.18, -0.13] -0.86 [+1.04, 0.07] -0.86 [+0.08], 0.31] -0.56 [-0.08, 0.32] -0.56 [-0.08, 0.32] Std. Mean Difference M, Random, 95% C. -0.56 [+1.25, 0.03] -0.56 [+1.25, 0.03] -0.56 [+1.25, 0.03] -0.56 [+1.25, 0.03] -0.56 [+1.25, 0.03]	Favours B-glucan Favours Control
Study of Subgroup Sinklund et al. (2005) 0a-10 Sinklund et al. (2005) 0a-10 Sinklund et al. (2005) 0a-10 Sinklund et al. (2016) Genan et al. (2007) 3LMW Jackson et al. (2008) 3LMW Jackson et al. (2005) 3LMW Jackson et al. (2007) 3L	B- 0.244 -0.11 -0.16 -0.052 -0.362 -0.362 -0.525 0.08 -0.21 0.141 -0.22 II = 37.68 (P ≤ 0.000 B- Mean -0.14 -0.14 -0.14 0.014 -0.14 0.000 -0.14 -0.14 -0.14 -0.14 0.000 -0.14 -0.14 -0.14 -0.14 -0.14 -0.14 -0.14 -0.14 -0.14 -0.15 -0.14 -0.15 -0.22 -0.24 -0.24 -0.24 -0.14 -0.14 -0.14 -0.24 -0.14 -0.24 -0.14 -0.24 -0.14 -0.24 -0.14 -0.24 -0.14 -0.24 -0.14 -0.24 -0.14 -0.24 -0.14 -0.24 -0.14 -0.24 -0.14 -0.24 -0.14 -0.24 -0	SD 0.35 0.54 0.36 0.36 0.38 0.47 0.516 0.273 0.273 0.363 0.3967 0.37 0.367 0.37 0.367 0.37 0.37 0.37 0.37 0.37 0.37 0.37 0.37 0.37 0.37 0.37 0.37 0.37 0.44 0.38	19 19 15 22 29 31 32 31 32 31 32 32 32 31 32 32 96 397 (P = 0. Total 19 15 22 29 20 96	Mean 0.05 0.05 0.05 -0.05 -0.05 -0.01 -0.05 -0.047 -0.047 -0.03 0.03 0.003 00002); P ((Mean 0.1 0.1 0.1 0.12	SD 0.38 0.38 0.38 0.27 0.51 0.51 0.412 0.412 0.412 0.412 0.38 0.384 0.384 0.384 0.613 0.384 0.394 0.613 0.394 0.613 0.394 0.613 0.412 0.613 0.394 0.613 0.394 0.613	20 20 21 24 30 30 30 24 22 17 95 381 20 20 20 20 21 24 24 22 20 20 20 21 24 24 22 20 20 20 20 20 21 24 24 24 24 24 24 24 24 24 24 24 24 24	6.9% 6.7% 7.4% 7.9% 6.7% 8.1% 7.7% 7.8% 7.9% 7.4% 7.0% 10.3% 100.0% Weight 6.2% 6.7% 7.0%	M. Random, 95% C -0.78 (+ 4.3, -0.17) -0.78 (+ 4.3, -0.17) -0.78 (+ 4.3, -0.17) -0.4 (+ 102, 0.38) -0.4 (+ 102, 0.08) -0.6 (+ 118, -0.15) -0.6 (+ 118, -0.15) -0.6 (+ 128, -0.38) -1.5 (+ 2.0, 0.08) -1.5 (+ 2.0, 0.08) -1.6 (+ 2.0, 0.08) -1.6 (+ 0.85, -0.32) -0.6 (+ 0.85, -0.32) Sid. Mean Difference M. Random, 95% C -0.6 (+ 128, 0.03) -0.6 (+ 128, 0.03) -0.6 (+ 128, 0.03) -0.6 (+ 128, 0.03) -0.6 (+ 128, 0.03) -0.6 (+ 128, 0.03) -0.6 (+ 128, 0.03) -0.6 (+ 128, 0.03) -0.6 (+ 128, 0.03) -0.6 (+ 128, 0.03) -0.6 (+ 128, 0.03) -0.6 (+ 128, 0.03) -0.6 (+ 128, 0.03) -0.6 (+ 128, 0.03) -0.6 (+ 138, 0.03) -0.6 (+ 138, 0.03) -0.6 (+ 128, 0.03) -0.6 (+ 138, 0.03) -0.6 (+ 138, 0.03) -0.6 (+ 138, 0.03) -0.6 (+ 138, 0.03) <td>Favours B-glucan Favours Control</td>	Favours B-glucan Favours Control
Study or Subgroup Binkfund et al. (2005) Gal-10 Binkfund et al. (2005) Gal-5 Binkfund et al. (2008) SugnetAnceau et al. (2010) SugnetAnceau et al. (2017) Seanna et al. (2007) SHMW Keenan et al. (2007) SHMW Keenan et al. (2007) SHMW Keenan et al. (2007) SHMW Kolever et al. (2007) SHMW Volever et al. (2021) Volever et al. (2020) Study or Subgroup BioRiving et al. (2025) Oak-10 BioRiving et al. (2025) Oak-10 BioRiving et al. (2015) Oak-10 BioRiving et al. (2016) CuperAnceau et al. (2017)	$\begin{array}{c} \textbf{B},\\ \hline \textbf{Mean}\\ -0.24\\ -0.5\\ -0.4\\ -0.5\\ -0.4\\ -0.5\\ -0.4\\ -0.5\\ -0.4\\ -0.5\\ -0.4\\ -0.5\\ -0.2\\ -0.5\\ -0.2\\ -0.5\\ -0.2\\ -0.5\\ -0.2\\ -0.5$	SD 0.35 0.54 0.36 0.38 0.47 0.516 0.263 0.273 0.308 0.655 0.37 0.665 0.37 0.439 df = 12 1) glucan SD 0.37 0.45 0.37 0.45 0.37 0.45 0.37 0.45 0.37 0.45 0.38 0.605	19 19 15 22 29 31 32 31 32 30 08 25 20 96 397 (P = 0. Total 19 15 22 29 39 39 39 39 32 30 30 30 30 30 30 30 30 30 30	Mean 0.05 0.05 0.05 -0.05 -0.05 -0.047 -0.047 -0.047 -0.043 0.043 0.043 0.043 0.03 00002); P (()) () <	SD 0.38 0.38 0.38 0.38 0.38 0.27 0.51 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.73 0.34 0.613 0.384 0.502 SD 0.4 0.412 0.412 0.412 0.412 0.412 0.412 0.384 0.502	20 20 21 24 30 30 30 24 22 17 95 381 20 20 20 20 21 24 30	6.9% 6.7% 7.4% 6.7% 8.1% 7.9% 7.8% 7.8% 7.4% 7.4% 7.0% 10.3% 100.0%	W, Random, 95% C. -0.78 [+14,3017] -0.78 [+14,3017] -0.74 [+102,033] -0.24 [+102,033] -0.24 [+02,033] -0.24 [+104,036] -0.74 [+122,-036] -0.76 [+142,-036] -0.86 [+148,-015] -0.86 [+148,-015] -0.86 [+148,-015] -0.86 [+148,-015] -0.86 [+148,-015] -0.86 [+0,031] -0.56 [-0,08,-0.32] -0.56 [-0,08,-0.32] -0.56 [-0,08,-0.32] -0.56 [-122,013 -0.56 [+122,013 -0.56 [+122,013 -0.56 [+124,013 -0.56 [+124,013 -0.56 [+124,013 -0.56 [+125,003 -0.56 [+125,003 -0.56 [+125,003 -0.56 [+125,003 -0.56 [+125,003 -0.56 [+126,013 -0.56 [+140,013 -0.56 [+140,013 -0.56 [+140,013 -0.56 [+140,013 -0.56 [+140,013 -0.56 [+140,013 -0.56 [+140,013 -0.58 [+130,0303 -0.58 [+13	Favours B-glucan Favours Control
Study of Subgroup Sinklund et al. (2005) 0a-1:0 Sinklund et al. (2005) 0a-1:0 Sinklund et al. (2005) 0a-1:0 Sinklund et al. (2017) 'argueson et al. (2007) 3.HWW Genann et al. (2007) 3.HWW Haeroganety Tau*= 0.16; Ch. Teatroganety Tau*= 0.16; Ch. Teatroganety Tau*= 0.16; Ch. Sitoky or Subgroup Biokkund et al. (2005) 0.45-10 Biokkund et al. (2005) 0.45-10 Biokkund et al. (2005) 0.45-10 Biokkund et al. (2007) 3.HWW Genann et al. (2007) 3.HWW	B- Mean -0.24 -0.11 -0.16 -0.362 -0.362 -0.347 -0.525 0.08 -0.21 0.141 -0.22 -0.21 0.141 -0.22 -0.21 0.141 -0.22 -0.21 -0.44 -0.22 -0.21 -0.21 -0.21 -0.21 -0.22 -0.21 -0.21 -0.22 -0.21 -0.22 -0.21 -0.22 -0.21 -0.22 -0.22 -0.21 -0.22 -0	SD 0.35 0.54 0.36 0.36 0.47 0.516 0.263 0.333 0.65 0.37 0.439 0.439 df=12 11) gluccan SD 0.37 0.444 0.38 0.605 0.37 0.444 0.38 0.605 0.605 0.444 0.38 0.605	19 19 15 22 29 18 32 31 32 30 28 25 20 0 28 25 20 96 397 (P = 0. Total 15 22 29 96 397 22 30 397 22 31 397 397 397 30 397 30 397 30 397 30 397 30 397 397 397 397 397 397 397 397 397 397	Mean 0.05 0.05 -0.05 -0.01 -0.05 -0.01 -0.05 -0.047 -0.047 -0.047 -0.047 -0.047 -0.047 -0.047 0.041 -0.03 0.03 0.03 0.002); P 0.002); P 0.011 0.021 0.022; P 0.033	SD 0.38 0.27 0.51 0.51 0.51 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.412 0.384 0.384 0.384 0.384 0.304 0.305 0.442 0.505 0.442 0.505 0.442 0.505 0.442 0.505 0.442 0.505	200 200 211 24 300 300 24 222 17 7 95 381 200 200 211 24 300 300 300 300 300 300 300 300 300 30	6.9% 6.7% 7.4% 7.9% 6.7% 8.2% 7.9% 7.9% 7.9% 7.9% 7.9% 7.0% 10.3% 100.0% Weight 6.2% 5.7% 7.0% 7.0% 8.8%	M. Random, 95% C -0.78 (+ 4.3, -0.17) -0.78 (+ 4.3, -0.17) -0.78 (+ 4.3, -0.17) -0.44 (- 0.06) -0.44 (- 0.06) -0.44 (- 0.07) -0.44 (- 0.08) -0.44 (- 0.08) -0.44 (- 0.08) -0.46 (- 1.80, -0.51) -0.66 (- 1.80, -0.51) -0.66 (- 1.80, -0.51) -0.66 (- 1.80, -0.51) -0.66 (- 1.80, -0.51) -0.66 (- 1.80, -0.51) -0.66 (- 1.80, -0.52) -0.66 (- 1.80, -0.52) -0.66 (- 1.40, -0.55) -0.66 (- 1.42, -0.13) -0.66 (- 1.42, -0.13) -0.66 (- 1.42, -0.13) -0.66 (- 1.42, -0.13) -0.68 (- 1.41, -1.30, -0.33) -0.38 (- 1.41, -1.30, -0.33) -0.38 (- 1.41, -0.33) -0.38 (- 1.41, -0.33) -0.38 (- 0.33)	Favours B-glucan Favours Control
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Study or Subgroup Sinkfund et al. (2005) 0a-16 Binkfund et al. (2001) Signer al. (2007) 5HWW Gerama et al. (2007) 5HWW	B. Hean -0.24 -0.116 -0.52 -0.347 -0.525 -0.347 -0.441 -0.44 -0.141 -0.141 -0.142 -0.141 -0.141 -0.142 -0.141 -0.142 -0.141 -0.142 -0.141 -0.142 -0.141 -0.122 -0.141 -0.122 -0.141 -0.122 -0.141 -0.122 -0.141 -0.122 -0.141 -0.122 -0.141 -0.22 -0.141 -0.22 -0.141 -0.22 -0.244 -0.22 -0.244 -0.22 -0.244 	SD 0.35 0.54 0.36 0.54 0.36 0.38 0.373 0.65 0.263 0.273 0.337 0.65 0.37 0.365 0.37 0.44 0.30 0.47 0.47 0.44 0.38 0.44 0.55 0.641 0.44 0.55 0.44 0.55 0.44 0.55 0.44 0.55 0.44 0.55 0.44 0.55 0.44 0.55 0.44 0.55 0.44 0.55 0.45 0.44 0.55 0.44 0.55 0.61 0.74 0.48 0.48 0.48	19 19 15 22 29 18 32 20 96 397 (P = 0. Total 19 16 22 20 96 397 307 307 307 307 307 307 307 30	Mean 0.05 0.05 -0.05 -0.05 -0.06 -0.07 -0.08 -0.09 -0.01 -0.02 -0.047 -0.047 -0.047 -0.047 -0.047 -0.03 0.03 0.03 0.002); P () ()	SD 0.38 0.38 0.38 0.27 0.51 0.412 0.412 0.73 0.412 0.73 0.412 0.73 0.412 0.73 0.412 0.73 0.412 0.73 0.412 0.73 0.34 0.613 0.384 0.384 0.505 0.444 0.505 0.562 0.562 0.562 0.452 0.562 0.452 0.562 0.452 0.562 0.477 1.558	20 20 21 24 18 30 30 30 30 24 22 17 95 381 20 20 20 20 21 24 30 30 30 30 30 22 21 24 22 17 7 95 381 20 20 21 24 21 24 20 24 24 24 24 24 24 24 24 24 24 24 24 24	6.9% 6.7% 7.4% 7.9% 6.7% 8.2% 8.2% 8.2% 7.7% 7.7% 7.0% 10.3% 100.0% Weight 6.2% 5.7% 7.0% 6.2% 8.8% 8.8% 8.9% 8.8% 8.9% 8.9% 8.9% 8.9	W. Random, 95% C. -0.78 [+14,3,-017] -0.78 [+14,3,-017] -0.74 [+102,038] -0.45 [+04,028] -0.45 [+04,028] -0.74 [+122,038] -0.74 [+122,038] -0.76 [+14,2,-038] -0.86 [+138,-013] -0.86 [+148,-015] -0.86 [+148,-017] -0.86 [+148,-017] -0.86 [+148,-017] -0.86 [+148,-017] -0.86 [+0,038] -0.86 [+0,038] -0.86 [+0,038] -0.86 [+148,-017] -0.86 [+148,-017] -0.86 [+148,-017] -0.86 [+148,-017] -0.86 [+148,-017] -0.86 [+148,-017] -0.86 [+148,-017] -0.86 [+148,-017] -0.86 [+148,-017] -0.86 [+128,-013] -0.86 [+128,-013] -0.86 [+128,-013] -0.86 [+148,-017] -0.86 [+148,-017] -0.86 [+128,-013] -0.86 [+128,-013] -0.86 [+138,-013] -0.86 [+118,-016] -0.86 [+118,-016] -0.86 [+118,-017] <	Favours B-glucan Favours Control
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Study or Subgroup Sinkfund et al. (2005) 0a-16 Binkfund et al. (2001) Signer al. (2007) 5HWW Gerama et al. (2007) 5HWW	B Mean -0.24 -0.16 -0.42 -0.347 -0.525 0.08 -0.21 0.141 -0.22 -0.21 0.141 -0.22 -0.21 0.441 -0.22 -0.21 -0.44 -0.44 -0.44 -0.44 -0.44 -0.44 -0.44 -0.44 -0.44 -0.44 -0.44 -0.44 -0.44 -0.44 -0.44 -0.42 -0.44	SD 0.35 0.54 0.54 0.54 0.36 0.38 0.47 0.516 0.33 0.263 0.273 0.263 0.37 0.967 0.439 df=12 11) glucan SD 0.439 0.439 0.439 0.444 0.38 0.655 0.81 0.444 0.555 0.81 0.74 0.452	Total 19 15 22 18 32 300 28 25 20 96 977 19 12 29 307 70 19 12 29 30 20 96 397 22 31 32 31 32 31 32 30 28 25 30 28 20 96 379	Mean 0.05 0.05 -0.05 -0.05 -0.047 -0.047 -0.047 -0.047 0.01 0.01 0.03 0.03 0.03 0.03 0.03 0.03 0.03 0.03 0.04 0.04 -0.05 0.05 0.05 0.05 0.047 -0.05 0.047 -0.047 -0.047 -0.047 -0.047 -0.05 -0.05 -0.05 -0.05 -0.05 -0.05 -0.05 -0.05 -0.05 -0.05 -0.05 -0.047 -0.047 -0.047 -0.047 -0.047 -0.047 -0.05 -0.05 -0.05 -0.047 -0.047 -0.047 -0.047 -0.047 -0.05 -0.05 -0.05 -0.047 -0.047 -0.047 -0.05 -0.05 -0.047 -0.047 -0.05 -0.05 -0.047 -0.047 -0.047 -0.05 -0.047 -0.047 -0.047 -0.05 -0.05 -0.047 -0.05 -0.047 -0.05 -0.055 -0	SD 0.38 0.37 0.38 0.27 0.51 0.51 0.412 0.43 0.43 0.34 0.613 0.384 0.38 0.384 0.34 0.384 0.30 0.384 0.30 0.412 0.505 0.44 0.40 0.505 0.505 0.562 0.562 0.562 0.562 0.48 0.47 1.558 0.48 0.47	200 200 211 24 300 300 24 222 381 381 200 200 211 200 200 211 200 200 211 200 200	6.9% 6.7% 7.4% 7.9% 6.7% 8.2% 8.2% 8.2% 7.7% 7.7% 7.0% 10.3% 100.0% Weight 6.2% 5.7% 7.0% 6.2% 8.8% 8.8% 8.9% 8.8% 8.9% 8.9% 8.9% 8.9	W. Random, 95% C. -0.78 [+1.43, -0.12] -0.78 [+1.43, -0.12] -0.78 [+1.43, -0.12] -0.74 [+1.43, -0.12] -0.24 [+1.02, 0.33] -0.24 [-0.04] -0.74 [+1.42, -0.06] -0.66 [+1.18, -0.13] -0.76 [+1.42, -0.06] -0.66 [+1.48, -0.15] -0.66 [+1.48, -0.15] -0.66 [+1.48, -0.27] -0.66 [+0.83, -0.32] -0.56 [-0.68, -0.32] -0.56 [-0.68, -0.32] -0.56 [-1.24, 0.13] -0.56 [-1.25, 0.13] -0.66 [+1.25, 0.03] -0.68 [+1.43, -0.12] -0.56 [+1.25, 0.03] -0.68 [+1.43, -0.12] -0.68 [+1.43, -0.13] -0.68 [+1.43, -0.13] -0.68 [+1.43, -0.13] -0.68 [+1.43, -0.13] -0.68 [+1.43, -0.13] -0.68 [+1.43, -0.13] -0.68 [+1.43, -0.13] -0.68 [+1.43, -0.13] -0.68 [+1.43, -0.13] -0.68 [+1.43, -0.13] -0.68 [+1.43, -0.13] -0.68 [+1.43, -0.13] -0.68 [+1.43, -0.13] -0.68 [+1.43, -0.13] <tr< td=""><td>Favours B-glucan Favours Control</td></tr<>	Favours B-glucan Favours Control

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A	B-glucan			C	control			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% CI
Cicero et al. (2020)	-0.52	0.381	83	0	0.478	83	37.9%	-1.20 [-1.53, -0.87]	
lbrugger et al. (2013)	-0.29	0.288	13	-0.02	0.505	13	26.6%	-0.64 [-1.43, 0.16]	
Theuwissen and Mensink (2007)	-0.24	0.595	40	-0.09	0.627	40	35.5%	-0.24 [-0.68, 0.20]	
Total (95% CI)			136			136	100.0%	-0.71 [-1.39, -0.03]	
Heterogeneity: Tau ² = 0.29; Chi ² = 1	11.80, df	= 2 (P =	0.003); I ² = 83	1%				-1 -0.5 0 0.5 1
Test for overall effect: Z = 2.04 (P =	0.04)								Favours B-glucan Favours Control

в	B-	glucan			Control		9	Std. Mean Difference	Std. Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl		
Cicero et al. (2020)	0.01	0.158	83	0	0.12	83	61.1%	0.07 [-0.23, 0.38]			
lbrugger et al. (2013)	-0.05	0.108	13	-0.05	0.1082	13	9.6%	0.00 [-0.77, 0.77]			
Theuwissen and Mensink (2007)	-0.03	0.251	40	0.01	0.192	40	29.3%	-0.18 [-0.62, 0.26]			
Total (95% CI)			136			136	100.0%	-0.01 [-0.25, 0.23]			

Heterogeneity: Tau² = 0.00; Chi² = 0.83, df = 2 (P = 0.66); I² = 0% Test for overall effect: Z = 0.07 (P = 0.94)

	+		-		
-	0.5	-0.25	Ó	0.25	0.5
Fav	ours	B-glu	can F	avours (Contro

C	B-glue			(Control		1	Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl
Cicero et al. (2020)	-0.59	0.435	83	0.04	0.47	83	36.4%	-1.38 [-1.72, -1.05]	 6 PG
Ibrugger et al. (2013)	-0.24	0.325	13	-0.04	0.397	13	28.6%	-0.53 [-1.32, 0.25]	
Theuwissen and Mensink (2007)	-0.21	0.624	40	-0.05	0.619	40	34.9%	-0.25 [-0.70, 0.19]	

136

Total (95% CI)

-

Heterogeneity: Tau² = 0.45; Chi² = 16.90, df = 2 (P = 0.0002); l² = 88% Test for overall effect: Z = 1.79 (P = 0.07)

, Random, 95% Cl

-1 -0.5 0 0.5 1 Favours B-glucan Favours Control

D											
D	B-	glucan		Control				Std. Mean Difference	Std. Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% CI		
Cicero et al. (2020)	0.13	0.638	83	-0.08	0.52	83	67.3%	0.36 [0.05, 0.67]			
Theuwissen and Mensink (2007)	0.13	0.795	40	-0.04	0.646	40	32.7%	0.23 [-0.21, 0.67]			
Total (95% CI)			123			123	100.0%	0.32 [0.07, 0.57]			
Heterogeneity: Tau ² = 0.00; Chi ² = 0		1 (P = 1	0.64); P	²= 0%				-	-0.5 -0.25 0 0.25 0.5		
Test for overall effect: Z = 2.47 (P =	0.01)								Favours B-glucan Favours Control		

136 100.0%

-0.75 [-1.56, 0.07]