Effect of oats and oat β-glucan on glycemic control in diabetes: a systematic review and meta-analysis of randomized controlled trials

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ABSTRACT

Introduction Current health claims recognize the ability of oat β-glucan to lower blood cholesterol; however, its ability to improve glycemic control is less certain. We undertook a systematic review and meta-analysis of randomized controlled trials (RCTs) to update the evidence on the effect of oats and oat β-glucan on glycemic control in individuals with diabetes.

Research design and methods MEDLINE, EMBASE and Cochrane were searched (June 2021) for RCTs of ≥2 weeks investigating the effect of oat β-glucan on glycemic control in diabetes. The outcomes were hemoglobin A1c (HbA1c), fasting glucose, 2-hour postprandial glucose (2h-PG) from a 75g oral glucose tolerance test, homeostatic model assessment of insulin resistance (HOMA-IR) and fasting insulin. Independent reviewers extracted the data and assessed the risk of bias. Data were pooled using the generic inverse variance method. Heterogeneity was assessed (Cochran Q) and quantified (I²). Pooled estimates were expressed as mean difference (MD) with 95% CI. The certainty of evidence was assessed using the Grading of Recommendations, Assessment, Development and Evaluations approach.

Results Eight trial comparisons (n=407) met the eligibility criteria. All trials were in adults with type 2 diabetes who were predominantly middle-aged, overweight and treated by antihyperglycemic medications or insulin. A median dose of 3.25g of oat β-glucan for a median duration of 4.5 weeks improved HbA1c (MD, −0.47% [95% CI −0.84 to −0.10], p=0.001), fasting glucose (−0.75 mmol/L [−1.00 to −0.50], p<0.001), 2h-PG (−0.39 mmol/L [−0.70 to −0.09], p=0.003) and HOMA-IR (−0.20 [−0.36 to −0.04], p=0.001). There was a non-significant reduction in fasting insulin (−4.30 pmol/L [−11.96 to 3.35], p=0.27). The certainty of evidence was high for fasting glucose, moderate for HOMA-IR and fasting insulin (downgraded for imprecision), and low for HbA1c and 2h-PG (downgraded for imprecision and inconsistency).

Conclusions Consumption of oats and oat β-glucan results in generally small improvements in established markers of fasting and postprandial glycemic control beyond concurrent therapy in adults with type 2 diabetes. The current evidence provides a very good indication for reductions in fasting glucose and less of an indication for reductions in HbA1c, 2h-PG, fasting insulin and HOMA-IR in this population.

Trial registration number NCT04631913.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Oat β-glucan has been recognized for its ability to lower cholesterol and reduce postprandial glycemic response, with approved health claims in Canada, USA and/or Europe.

⇒ Systematic reviews and meta-analyses of randomized controlled trials have shown beneficial effects of oats and oat β-glucan on glycemic control in diabetes, but are out of date, limited in their measures of glycemic control, and lack dose response analyses and assessments of certainty of evidence.

WHAT THIS STUDY ADDS

⇒ Our synthesis of eight randomized controlled trial comparisons in 407 adults with type 2 diabetes who were predominantly middle-aged, overweight or obese and with moderately controlled diabetes treated by antihyperglycemic medications or insulin showed that oats or oat β-glucan at a median β-glucan dose of 3.25g over a median study duration of 4.5 weeks resulted in small important improvements in hemoglobin A1c (HbA1c) and fasting glucose and more trivial improvements in 2-hour postprandial glucose (2h-PG), fasting insulin and homeostatic model assessment of insulin resistance (HOMA-IR) beyond concurrent therapy.

⇒ The certainty of evidence was high for fasting glucose, moderate for HOMA-IR and fasting insulin, and low for HbA1c and 2h-PG, owing to downgrades for imprecision and/or inconsistency.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Current evidence suggests that oats and oat β-glucan improve fasting and postprandial glycemic profiles beyond concurrent therapy, suggesting that oats and oat β-glucan may be a useful add-on therapy for diabetes management, supporting current diabetes recommendations and providing a basis for the development of new health claims.

INTRODUCTION

Sustained glycemic control in order to reduce the risk of long-term complications remains a diabetes management challenge but can be
supported by dietary therapies.\(^1\)\(^2\) Viscous dietary fibers have been recognized as an important component of lifestyle management strategies for diabetes owing to their health benefits in improving glycemic control and reducing cardiovascular disease risk.\(^3\) The viscosity of fiber is also an important factor contributing to reducing postprandial glycemia.\(^4\) β-glucan found in oats is a viscous fiber that has been particularly recognized for its ability to lower low-density lipoprotein cholesterol, with approved health claims from Health Canada, the US Food and Drug Administration and the European Food Safety Authority (EFSA).\(^5\)\(^6\)\(^7\) Recently, EFSA has also recognized oat β-glucan for its ability to reduce postprandial glycemic response.\(^8\) Whether these postprandial reductions are sustainable and translate into longer term improvements in glycemic control is unclear.

Previous systematic reviews and meta-analyses have shown that viscous fiber supplements that include oat β-glucan can improve glycemic control outcomes in type 2 diabetes. These syntheses, however, are now out of date, with the most recent census over 3 years old\(^9\) and have either not isolated the effect of oat β-glucan\(^9\) or have been limited in the measures used to assess glycemic control.\(^10\)\(^11\) Important dose response meta-regression analyses and assessment of the certainty of evidence have also been lacking.\(^10\)\(^11\)

To address these gaps, our aim was to conduct a systematic review and meta-analysis to synthesize the currently available evidence from randomized controlled trials (RCTs) on the effects of oats and oat β-glucan fiber on measures of glycemic control, hepatic insulin sensitivity, whole body insulin sensitivity and beta-cell function, and assess the certainty of evidence using the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach.

### METHODS

We followed the Cochrane Handbook for Systematic Reviews of Interventions\(^12\) to conduct this systematic review and meta-analysis and reported our results in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines\(^13\) (online supplemental table 1). The protocol is registered at ClinicalTrials.gov (NCT04631913).

**Data sources and searches**

We searched MEDLINE, EMBASE and Cochrane Central Register of Controlled Trials databases through June 6, 2021. Online supplemental table 2 outlines the detailed search strategy. Validated filters from the McMaster University Health Information Research Unit were applied to limit the database search to controlled studies only.\(^14\) Manual searches of the reference lists of included studies supplemented the systematic search.

**Study selection**

We included RCTs in human adults with diabetes, with a study duration of ≥2 weeks, that investigated the effects of oats or oat β-glucan compared with a suitable non-oat control (ie, non-viscous fiber, placebo or standard background diet without added oats or oat β-glucan) on markers of glycemic control, insulin sensitivity and beta-cell function. No restrictions were placed on language.

**Data extraction and quality assessment**

Two reviewers (VC and AA) independently extracted relevant data from eligible studies. Extracted data included study design, randomization, blinding, setting, funding sources, study duration, number of participants, participant characteristics (age, body mass index (BMI), sex and health status), oat β-glucan dose, oat β-glucan molecular weight, intervention form (whole grain oat or oat β-glucan), intervention food matrix, intervention and comparator energy comparison (isocaloric, hypocaloric or hypercaloric), available carbohydrate, food form, macronutrient profile, and outcome data. In the absence of numerical data, we extracted values from figures using a PlotDigitizer tool.\(^15\) If multiple control arms were reported with negative (usual care or no treatment) and positive (guideline-based treatment) controls, we selected the negative control arm as the comparator. If outcome data in a single trial were reported for multiple intervention study durations, we extracted data from the study duration that contained data for the most outcomes of interest; if this was the same, we used the longer study duration. When the β-glucan content was not provided, we estimated β-glucan dose from oats and oat bran at 5.0% and 6.9%, respectively.\(^16\)\(^17\) We extracted mean differences (MDs) and standard errors (SEs) between the intervention and comparator arms from each applicable trial comparison. When these were not provided, they were calculated from the available data using published formulas.\(^12\) MDs for change from baseline were preferred over change in end values. Authors were contacted if relevant data were missing from publications.

The same two investigators (VC and AA) assessed all included studies for risk of bias using the Cochrane Risk of Bias V2.0 tool.\(^18\) We assessed risk of bias from five domains, namely randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome and selection of the reported results. The tool provides a judgment of ‘low risk of bias’, ‘some concerns’ or ‘high risk of bias’ for each domain based on responses to signaling questions. An overall risk of bias was determined based on judgments from each domain. We resolved discrepancies in data extraction and risk of bias by consensus and review with a third investigator (JLS).

**Outcomes**

Outcomes included established markers of glycemic control (hemoglobin A1c (HbA1c), fasting glucose, fasting insulin, 2-hour postprandial glucose (2h-PG) from a 75g oral glucose tolerance test (OGTT)), and measures of hepatic insulin sensitivity (homeostatic model assessment of insulin resistance (HOMA-IR), hyperinsulinemic-euglycemic
Data synthesis and analysis

STATA 16.1 was used for all analyses. We expressed the pooled effect estimates for all outcomes as MD with 95% CI. Data were pooled using the generic inverse variance method with DerSimonian and Laird random effect models. Fixed effects were used when less than five trial comparisons were available for an outcome. A paired analysis was applied for crossover designs and for within-arm mean differences in parallel designs with an assumed correlation coefficient of 0.5. To mitigate a unit-of-analysis error, when arms of trials with multiple intervention or control arms were used more than once, the corresponding sample size was divided accordingly.

Heterogeneity was assessed using the Cochran Q statistic and quantified using the $I^2$ statistic, where $I^2 \geq 50\%$ and $p < 0.10$ were used as evidence of significant substantial heterogeneity. Potential sources of heterogeneity were explored using sensitivity analysis. Sensitivity analyses were done via two methods. We conducted an influence analysis by systematically removing one trial comparison at a time and recalculating the overall effect estimate and heterogeneity. We conducted a second sensitivity analysis by changing the assumed correlation coefficients used for pairwise analysis from 0.5 to 0.25 and 0.75. Linear dose response analyses were assessed by random effects with restricted maximum likelihood methods. Non-linear dose response was modeled with restricted cubic spline with three knots at Harrell’s recommended percentiles.

If $\geq 10$ trial comparisons were available, subgroup analyses were conducted using meta-regression (significance at $p<0.05$). A priori subgroup analyses were conducted by dose, comparator, intervention form, study duration, baseline level, design, body weight change, saturated fat intake, carbohydrate intake, protein intake, intervention food matrix, oat $\beta$-glucan molecular weight and risk of bias. If $\geq 10$ studies were available, publication bias was assessed by inspection of contour-enhanced funnel plot and formal testing with Egger’s and Begg’s tests (significance at $p<0.10$). If evidence of publication bias was suspected, the Duval and Tweedie trim-and-fill method was performed to adjust for funnel plot asymmetry by imputing missing study data and assess for small-study effects.

Grading of evidence

We employed the GRADE system to assess the certainty of evidence. The GRADE Handbook and GRADEpro V.3.2 software were used. The overall certainty in the evidence was graded as either high, moderate, low or very low. Two investigators (VC and AZ) independently performed GRADE assessments for each outcome. RCTs are initially graded as high. Reasons to downgrade include study limitations (risk of bias), inconsistency of results (substantial unexplained intersubject heterogeneity, $I^2 > 50\%$ and $p < 0.10$), indirectness of evidence, imprecision and publication bias. The results were considered imprecise if the 95% CI overlapped with the minimally important difference (MID) for each outcome, which was 0.3% for HbA1c, 0.5 mmol/L for fasting glucose, 5 pmol/L for fasting insulin, 0.5 mmol/L for 2h-PG from a 75 g OGTT and 1 for HOMA-IR. The evidence may be upgraded if a significant dose response gradient is detected.

RESULTS

Search results

Figure 1 shows the flow of the literature. We identified 3993 reports through database and manual searches. A total of seven reports met the inclusion criteria and contained data for eight trial comparisons involving 407 participants. These included eight trial comparisons for HbA1c and fasting glucose, three for 2h-PG, four for fasting insulin and five for HOMA-IR. No trials were available for other measures of hepatic insulin sensitivity, whole body insulin sensitivity or beta-cell function. All trials included were in individuals with type 2 diabetes as no trials were identified in populations with type 1 diabetes.

Trial characteristics

Table 1 shows the characteristics of the included trials. The trials were conducted in a variety of locations, with most conducted in China and France (n=2 trial comparisons each), followed by Sweden, Greece, Scotland, Mexico and USA (n=1 each). One trial was conducted in both France and Sweden. The median study size was 35 participants (range 13–140). The median age of the participants was 59 years (range 53–67) and majority of the participants were overweight or obese, with a median BMI of 28.5 kg/m$^2$ (range 25.2–31.5). Participants had a median baseline HbA1c of 7.4% (range 6.8–8.4), based on seven of eight trial comparisons that reported baseline HbA1c. Antihyperglycemic medications were reported in seven of eight trial comparisons, in which 88% of the participants were receiving pharmacotherapy with antihyperglycemic agents (59.9%), insulin (17.6%) or both (10.5%). The median duration of diabetes was 7.3 years (range 3.2–10.1), based on five of eight trial comparisons that reported diabetes duration. Five trial comparisons were parallel design and three were crossover design. Three studies were double-blinded, three were single-blinded and two were open-label. The median study duration was 4.5 weeks (range 3–8). The median oat $\beta$-glucan dose was 3.25 g (range 2–5.5). The intervention was delivered as either whole oats (n=4), oat $\beta$-glucan concentrate (n=3) or oat bran (n=1) and through various food matrices, most commonly porridge and cereal (n=3 each), followed by bread (n=2) and then soup, muffins, cereal bars and cake (n=1 each). The comparators included wheat cereal and/or bread (n=2), soup without added oat $\beta$-glucan clamp), whole body insulin sensitivity (Matsuda OGTT-Insulin Sensitivity Index, frequently sampled intravenous glucose tolerance test, hyperinsulinemic-euglycemic clamp) and beta-cell function (Insulin Secretion-Sensitivity Index 2).
(n=1), egg (n=1), no dietary intervention (n=2) or standard dietary advice (n=1). Seven of the eight trials reported on total dietary fiber intake. Five trials were matched for total dietary fiber between the control and intervention groups. Li et al had a difference in fiber between the control and intervention groups attributed to the addition of the oat intervention (36.1±4.2 g in the intervention vs 22.1±4.0 g in the control and 39.0±4.8 g in the intervention vs 22.1±4.0 g in the control).

**Risk of bias**

Online supplemental tables 3–7 and online supplemental figures 1–5 show the risk of bias assessments of the individual trials by the Cochrane Risk of Bias V.2.0.
### Table 1  Trial characteristics

| Study, year | n | Design | Blinding | Study duration, weeks | Age, years | BMI, kg/m² | Baseline HbA1c, % | Antihyperglycemic therapy (n participants) | Diabetes duration, years | Background diet | Total fiber intake, g | Intervention dose, g | Description | Setting | Funding | Outcomes |
|-------------|---|--------|----------|-----------------------|------------|------------|------------------|--------------------------------------------|--------------------------|------------------|---------------------|-------------------|-------------|---------|---------|----------|
| Stevens et al, 1985<sup>16</sup> | 25 (M: 8, F: 17) | P | OL | 6 | I: 53±10.8 | NR | None | I: increased fiber diet | I: 7.7±9.7 | NR | I: 11.0 | 3.5 | I: 50 g oat bran as hot cereal or in muffins | OP, USA | A | HbA1c, FG |
| Kabir et al, 2002<sup>1</sup> | 13 (M: 13, F: 0) | CO | DB | 4 | 59±7.2 | 28±3.6 | I: 8.3±1.80 | Medication* (12); diet (1) | NR | Usual | NR† | 3 | I: cereal with muesli containing 3 g oat β-glucan | OP, France | A, IN | HbA1c, FG, Fi |
| Cugnet-Anceau et al, 2010<sup>3</sup> | 53 (M: 32, F: 21) | P | DB | 8 | 62±9.1 | 30.5±4.1 | I: 7.3±0.92 | Insulin or medication (8); diet and/or medication (20) | NR | Usual | I: 19.7±5.3 | 3.5 | I: oat β-glucan-enriched soup | OP, Sweden | A and France | HbA1c, FG |
| Liatis et al, 2009<sup>26</sup> | 41 (M: 23, F: 18) | P | DB | 3 | 60±9.1 | 29.6±4.8 | I: 7.3±1.61 | Medication* (19); diet (4) | NR | General dietary instruction | NR | 3 | I: oat β-glucan-enriched bread | OP, Greece | NR | HbA1c, FG, Fi, HOMA-IR |
| McGeoch et al, 2013<sup>27</sup> | 27 (M: 18, F: 9) | CO | OL | 8 | 61±6.4 | 31.5±5.1 | 6.8±0.14 | NR | I: oat-enriched diet | I: 23.9 | 5.5 | I: carbohydrate content substituted for oat-based product | OP, Scotland | A | HbA1c, FG, Fi, 2h-PG, HOMA-IR |
| Ballesteros et al, 2015<sup>28</sup> | 29 (M: 10, F: 19) | CO | SB | 5 | 54±8.3 | 30.8±6.5 | 6.8±0.89 | Medication* (26); insulin (6) | NR | Usual | I: 27.5±9.2 | 2.0 | I: 40 g oatmeal | OP, Mexico | IN | HbA1c, FG, Fi, HOMA-IR |

Continued
Table 1 Continued

| Study, year n | Design | Blinding | Study duration, weeks | Age, years | BMI, kg/m² | Baseline HbA1C, % | Antihyperglycemic therapy (n participants) | Diabetes duration, years | Background diet | Total fiber intake, g | Intervention dose, g | Description | Setting | Funding | Outcomes |
|---------------|--------|----------|-----------------------|------------|------------|----------------|----------------------------------|-----------------------|-----------------|----------------|----------------|-------------|----------|---------|----------|
| Li et al., 2016 [31] | 140    | P        | SB 4                  | 59±6.1     | 8.4±1.44   | Medication* (43); insulin (16); combined (15) | l: low-fat and high-fiber | l: 8.3±6.3         | l: 36.1±4.2     | l: 50 g whole grain oats | 2.65         | IP, China  | HOMA-IR | HBA1c, FG, 2h-PG, HOMA-IR |
|                |        |          |                       |            |            | C: 6.6±3.0     | C: usual                             | C: 22.1±4             | C: no dietary intervention |
|                | 139    | P        | SB 4                  | 59±6.8     | 8.3±1.35   | Medication* (47); insulin (12); combined (14) | l: low-fat and high-fiber | l: 7.9±6.4         | l: 39.0±4.8     | l: 100 g whole grain oats | 5.30         | IP, China  | HOMA-IR | HBA1c, FG, 2h-PG, HOMA-IR |
|                |        |          |                       |            |            | C: 6.6±3.0     | C: usual                             | C: 22.1±4             | C: no dietary intervention |

*Specified oral agent.†Treatments matched for fiber.

A: agency; BMI, body mass index; C, control; CO, crossover; DB, double-blind; F, female; FG, fasting glucose; FI, fasting insulin; HbA1c, hemoglobin A1c; HOMA-IR, homeostatic model assessment of insulin resistance; 2h-PG, 2-hour postprandial glucose from a 75 g oral glucose tolerance test; I, intervention; IN, industry; IP, inpatient; M, male; NR, not reported; OL, open-label; OP, outpatient; P, parallel; SB, single-blind.

Figure 2 and online supplemental figure 2 show the effect of oats and oat ß-glucan on HbA1c. In eight trial comparisons involving 407 participants with a median study duration of 4.5 weeks, oats and oat ß-glucan reduced HbA1c (MD, −0.47% (95% CI −0.80 to −0.13), pMD = 0.006), with significant substantial heterogeneity (I² = 81.60%, pQ < 0.001). There was no evidence of a non-linear dose response relationship with a reduced HbA1c of −0.67% (95% CI −0.87 to −0.47, pMD = 0.006) for the highest compared to the lowest dose of oat ß-glucan (slope = −0.39 (95% CI −0.64 to −0.14), p < 0.001). Changing the correlation coefficient from 0.5 to 0.75 did not alter the magnitude, direction or significance of the effect estimate (range of MD, from −0.57% (95% CI −1.00 to −0.04) to −0.14% (95% CI −0.44 to −0.04)). Changing the correlation coefficient from 0.5 to 0.75 did not alter the magnitude, direction or significance of the effect estimate (range of MD, from −0.57% (95% CI −1.00 to −0.04) to −0.14% (95% CI −0.44 to −0.04)). Changing the correlation coefficient from 0.5 to 0.75 did not alter the magnitude, direction or significance of the effect estimate (range of MD, from −0.57% (95% CI −1.00 to −0.04) to −0.14% (95% CI −0.44 to −0.04)).

Online supplemental figure 7 and online supplemental figure 8 show the results of the sensitivity analysis for HbA1c. Removal of individual trials did not alter the magnitude, direction or significance of the effect estimate (range of MD, from −0.57% (95% CI −1.00 to −0.04) to −0.14% (95% CI −0.44 to −0.04)). Changing the correlation coefficient from 0.5 to 0.75 did not alter the magnitude, direction or significance of the effect estimate (range of MD, from −0.57% (95% CI −1.00 to −0.04) to −0.14% (95% CI −0.44 to −0.04)). Changing the correlation coefficient from 0.5 to 0.75 did not alter the magnitude, direction or significance of the effect estimate (range of MD, from −0.57% (95% CI −1.00 to −0.04) to −0.14% (95% CI −0.44 to −0.04)).

Online supplemental figure 10 and online supplemental figure 11 show the results of the sensitivity analysis for fasting glucose. Removal of individual trials did not alter the magnitude, direction or significance of the effect estimate (range of MD, from −0.57% (95% CI −1.00 to −0.04) to −0.14% (95% CI −0.44 to −0.04)). Changing the correlation coefficient from 0.5 to 0.75 did not alter the magnitude, direction or significance of the effect estimate (range of MD, from −0.57% (95% CI −1.00 to −0.04) to −0.14% (95% CI −0.44 to −0.04)). Changing the correlation coefficient from 0.5 to 0.75 did not alter the magnitude, direction or significance of the effect estimate (range of MD, from −0.57% (95% CI −1.00 to −0.04) to −0.14% (95% CI −0.44 to −0.04)).

Online supplemental figure 9 and online supplemental figure 12 show the results of the sensitivity analysis for fasting glucose. Removal of individual trials did not alter the magnitude, direction or significance of the effect estimate (range of MD, from −0.57% (95% CI −1.00 to −0.04) to −0.14% (95% CI −0.44 to −0.04)). Changing the correlation coefficient from 0.5 to 0.75 did not alter the magnitude, direction or significance of the effect estimate (range of MD, from −0.57% (95% CI −1.00 to −0.04) to −0.14% (95% CI −0.44 to −0.04)). Changing the correlation coefficient from 0.5 to 0.75 did not alter the magnitude, direction or significance of the effect estimate (range of MD, from −0.57% (95% CI −1.00 to −0.04) to −0.14% (95% CI −0.44 to −0.04)).

Online supplemental figure 11 and online supplemental figure 12 show the results of the sensitivity analysis for fasting glucose. Removal of individual trials did not alter the magnitude, direction or significance of the effect estimate (range of MD, from −0.57% (95% CI −1.00 to −0.04) to −0.14% (95% CI −0.44 to −0.04)). Changing the correlation coefficient from 0.5 to 0.75 did not alter the magnitude, direction or significance of the effect estimate (range of MD, from −0.57% (95% CI −1.00 to −0.04) to −0.14% (95% CI −0.44 to −0.04)). Changing the correlation coefficient from 0.5 to 0.75 did not alter the magnitude, direction or significance of the effect estimate (range of MD, from −0.57% (95% CI −1.00 to −0.04) to −0.14% (95% CI −0.44 to −0.04)).
study duration of 4 weeks, oats and oat β-glucan reduced 2h-PG (MD, −0.42 mmol/L (95% CI −0.70 to −0.14), $p_{MD}=0.003$), with significant substantial heterogeneity ($I^2=94.68\%$, $p_Q<0.001$).

Online supplemental figure 13 and online supplemental table 8 show the sensitivity analysis for 2h-PG. Removal of McGeoch et al.43 did not alter the direction or significance of the effect, but did increase the magnitude (MD, −2.87 mmol/L (95% CI −3.70 to −2.04), $p<0.001$) and explained the heterogeneity ($I^2<0.01\%$, $p_Q=0.605$). Changing the correlation coefficient from 0.25 to 0.75 did not alter the magnitude, direction or significance of the effect estimate or the evidence for heterogeneity.

Online supplemental figure 14 shows the dose response analysis for 2h-PG. No significant linear dose response was observed. A non-linear dose response was not modeled due to an insufficient number of trial comparisons.

**Fasting insulin**

Figure 2 and online supplemental figure 15 show the effect of oats and oat β-glucan on fasting insulin. In four trial comparisons involving 110 participants with a median study duration of 4.5 weeks, oats and oat β-glucan reduced fasting insulin (MD, −4.30 pmol/L (95% CI −11.96 to 3.35), $p_{MD}=0.271$), with significant substantial heterogeneity ($I^2=94.68\%$, $p_Q<0.001$).

Online supplemental figure 16 and online supplemental table 8 show the results of the sensitivity analysis for fasting insulin. Removal of individual trials did not alter the magnitude, direction or significance of the effect estimate (range of MD, from −9.07 pmol/L (95% CI −23.39 to 5.26) to −2.23 pmol/L (95% CI −10.09 to 5.63)). Removal of Liatis et al.41 explained the substantial heterogeneity (MD, −2.23 (95% CI −10.09 to 5.63), $p_{MD}=0.579$, $I^2=39.42\%$, $p_Q=0.192$). Changing the correlation coefficient from 0.5 to 0.25 or 0.75 did not alter the magnitude, direction or significance of the effect estimate or the evidence for heterogeneity.

Online supplemental figure 17 shows the dose response analysis for fasting insulin. No significant linear dose response was observed. A non-linear dose response was not modeled due to an insufficient number of trial comparisons.

**Homeostatic model assessment of insulin resistance**

Figure 2 and online supplemental figure 18 show the effect of oats and oat β-glucan on HOMA-IR. In five trial comparisons involving 316 participants with a median study duration of 4 weeks, oats and oat β-glucan reduced HOMA-IR (MD, −0.88 (95% CI −1.55 to −0.20), $p_{MD}=0.011$), with significant substantial heterogeneity ($I^2=56.42\%$, $p_Q=0.057$).

Online supplemental figure 19 and online supplemental table 8 show the results of the sensitivity analysis for HOMA-IR. Removal of individual trials did not alter the magnitude of the effect estimate or the direction or significance of the effect (range of MD, from −1.56 (95% CI −2.80 to −0.31) to −0.65 (95% CI −1.17 to −0.12)). Removal of Liatis et al.41 explained the substantial heterogeneity (MD, −0.65 (95% CI −1.17 to −0.12), $p_{MD}=0.016$, $I^2=41.82\%$, $p_Q=0.161$). Changing the correlation coefficient to 0.25 or 0.75 did not alter the magnitude, direction or significance of the effect estimate or the heterogeneity.

Online supplemental figure 20 shows the dose response analysis for HOMA-IR. No significant linear dose response was observed. A non-linear dose response was observed.

**Table 8** POOLED EFFECT ESTIMATES and HETEROGENEITY. *Values are mean difference (MD) or standardized mean difference (SMD), with 95% confidence intervals (CI). 10 trials.*
was not modeled due to an insufficient number of trial comparisons.

**Subgroup analyses and publication bias**
As <10 trial comparisons were available for each outcome, sources of heterogeneity were not explored in subgroup analyses and publication bias was not assessed.

**GRADE assessment**
Online supplemental table 9 shows the certainty of evidence for each outcome assessed by GRADE. The certainty of evidence was rated as low for HbA1c and 2h-PG due to inconsistency and imprecision of the pooled effect estimates, moderate for fasting insulin and HOMA-IR due to imprecision of the pooled effect estimates, and high for fasting glucose owing to a downgrade for imprecision of the pooled effect estimate and upgrade for a linear dose response gradient. We did not downgrade the evidence for serious inconsistency for either fasting insulin or HOMA-IR, as the evidence of substantial heterogeneity was explained through influence analysis with the removal of Liatis et al. Although we were able to explain the evidence of substantial heterogeneity by influence analysis for 2h-PG, there were insufficient trial comparisons to warrant not downgrading.

**DISCUSSION**
We conducted a systematic review and meta-analysis of seven RCTs involving eight trial comparisons of the effect of oats and oat 2β-glucan at a median oat 2β-glucan dose of 3.25 g on markers of glycemic control and insulin sensitivity over a median study duration of 4.5 weeks in 407 adults with type 2 diabetes who were predominantly middle-aged, overweight or obese and with moderately controlled diabetes treated by antihyperglycemic medications or insulin. No data were available in type 1 diabetes. We showed that oat 2β-glucan intake resulted in small important reductions in HbA1c and fasting glucose and more trivial reductions in 2h-PG, fasting insulin (not statistically significant) and HOMA-IR beyond concurrent therapy. There was a significant linear dose response gradient in fasting glucose indicating a 0.39 mmol/L reduction in fasting glucose per 1 g oat 2β-glucan.

**Results in the context of the literature**
Three previous systematic reviews and meta-analyses assessed the role of viscous fiber from oats on glycemic markers in individuals with diabetes. The first two syntheses by Shen et al. and Hou et al. focused exclusively on oat 2β-glucan, showed reductions in HbA1c and fasting glucose and non-significant reductions in fasting insulin and HOMA-IR. The magnitude of the reductions in HbA1c (MD, −0.42% and MD, −0.21% vs MD, −0.47%) and fasting glucose (MD, −0.39 mmol/L and MD, −0.52 mmol/L vs MD, −0.75 mmol/L) became greater and the reduction in HOMA-IR became significant in our updated synthesis which captured four more eligible trials than Shen et al. and up to three more eligible trials in some glycemic control outcomes than Hou et al. The third synthesis by Jovanovski et al. investigated the effects of total viscous fiber sources (2β-glucan from oats or barley, guar gum, konjac, psyllium, pectin, xanthan gum, locust bean gum, and alginate and agar) on glycemic control in individuals with diabetes. It showed no effect modification by viscous fiber type, suggesting a ‘class-effect’ such that the reductions seen in HbA1c, fasting glucose and HOMA-IR held across the different fiber types including 2β-glucan. There was no effect of viscous fiber or effect modification by viscous fiber type on insulin. Three fewer trial comparisons in HbA1c and fasting glucose and two fewer trial comparisons in HOMA-IR were included in their pooled effect estimate as they explored only supplemental sources of 2β-glucan.

Several other systematic reviews and meta-analyses have assessed the effects of oats and oat products on measurements of glycemic control in mixed populations with and without diabetes. These syntheses, some of which missed several eligible trials in individuals with diabetes showed significant reductions in fasting insulin but failed to show consistent significant reductions in HbA1c, fasting glucose or HOMA-IR, suggesting the effects may be more evident in individuals with diabetes.

None of the previous systematic reviews and meta-analyses assessed the effect of oat 2β-glucan on 2h-PG. As an important contributor to HbA1c and risk of diabetes complications, the reduction seen in 2h-PG in the present synthesis supports the reductions seen in other established markers of glycemic control in individuals with diabetes.

One of the eight included trials (Ballesteros et al.) used a comparator of eggs rather than a similar food without oat 2β-glucan, no dietary intervention or standard dietary advice; sensitivity analyses demonstrated that the magnitude, direction and significance of the effect for all outcomes were not altered by the removal of Ballesteros et al (online supplemental figures 7, 10, 13, 19).

Total fiber interventions, including a combination of insoluble fiber and viscous soluble fiber, have been shown to improve markers of glycemic control. A systematic review and meta-analysis of RCTs demonstrated that increased dietary fiber significantly improved HbA1c by −0.66%, fasting glucose by −0.80 mmol/L, insulin by −11.67 pmol/L and HOMA-IR by −1.27 in individuals living with diabetes. Synthesis of RCTs has also shown that viscous soluble fiber supplementation significantly improved HbA1c by −0.58%, fasting glucose by −0.82 mmol/L and HOMA-IR by −1.89 in individuals living with diabetes. Our results for oat 2β-glucan support the benefits provided by viscous soluble fibers.

The mechanism by which 2β-glucan improves blood glucose control is thought to relate to its effect on post-prandial absorption and metabolism of carbohydrates. Its ability to increase intestinal viscosity and consequently
slow the rate of gastric emptying and the absorption of carbohydrate has the effect of decreasing the postprandial glycemic response to the carbohydrate contained in a meal. Systematic reviews and meta-analyses of acute RCTs have shown a strong linear relationship between reductions in postprandial glucose following a carbohydrate meal and an increase in the dose and molecular weight of β-glucan. The alpha-glucosidase inhibitor acarbose provides important biological analogy as an oral prandial agent that effectively converts the diet to a low glycemic index (GI) diet by decreasing the absorption of the carbohydrate contained in a meal, thereby decreasing the acute postprandial glycemic response.

Large RCTs and systematic reviews and meta-analyses of RCTs of acarbose have shown similar reductions in HbA1c and fasting glucose in individuals at risk of and with type 2 diabetes, which have translated into reductions in incident diabetes, hypertension, cardiovascular disease (CVD), myocardial infarction and stroke in individuals at risk of type 2 diabetes (although the data are only suggestive for cardiovascular benefit, as a recent trial failed to confirm the reduction in cardiovascular events with a lower dose of acarbose in Chinese adults who were at risk of diabetes and had pre-existing coronary disease). Like low GI foods or acarbose, high β-glucan foods which may also have lower GI can be expected to reduce diabetes incidence in individuals at risk of diabetes and improve management of HbA1c, and decrease CVD risk in individuals with established type 2 diabetes.

Strengths and limitations

Our systematic review and meta-analysis has several strengths. First, we completed a comprehensive systematic search of the available literature. Second, we included only RCTs, a study design which provides the greatest protection against systematic error. Third, there was a significant linear dose response gradient for fasting glucose, which increased our certainty of evidence for fasting glucose. Finally, we included a GRADE assessment to explore the certainty of available evidence.

Our analysis also revealed several limitations. There was evidence of inconsistency between the available trials for HbA1c and 2h-PG. We were not able to conduct subgroup analyses to further explore sources of inconsistency as <10 trial comparisons were available for each outcome. The evidence for HbA1c and 2h-PG was therefore downgraded for inconsistency. Another limitation was the serious imprecision in the pooled estimates across all outcomes with the 95% CIs overlapping the MID in each case, leading to further downgrades for imprecision. Finally, although publication bias was not suspected, we were unable to assess publication bias as <10 trial comparisons were available for each outcome.

Weighing these strengths and limitations, the certainty of evidence was assessed as high for fasting glucose due to a downgrade for imprecision and an upgrade for a significant dose relationship, moderate for fasting insulin and HOMA-IR due to a downgrade for imprecision, and low for HbA1c and 2h-PG due to downgrades for both inconsistency and imprecision.

Implications

Maintaining glycemic control is essential in the prevention of diabetes-related microvascular and, to a lesser extent, macrovascular complications. Nutrition therapy is the cornerstone of diabetes management which when optimized can have significant improvements in diabetes control. Dietary fibers, particularly viscous fibers, are highlighted as an important part of medical nutrition therapy. The average intake of dietary fiber, however, continues to fall more than 30% short of recommendations. The failure to achieve the recommended intake for health benefits extends to oats. Although oats have seen a 3.5-fold increase in production (as rolled oats) in the 9 years since the approval of the health claim for oats and cholesterol reduction, those who consume oatmeal on average consume one cup or 2 g of oat β-glucan per day, which is well below both the dose required by the health claim (3 g) for cholesterol reduction and the median dose of intake identified in our synthesis (3.25 g) for an improvement in glycemic control. These low intakes suggest that most individuals have an important opportunity to realize the benefits of oats through an increase in intake of oats and oat β-glucan. Our findings strengthen the indication for the use of whole oats and oat β-glucan as add-on therapy in the management of people with type 2 diabetes, supporting current clinical practice guidelines and providing a basis for the future development of health claims for oat β-glucan and glucose regulation.

CONCLUSION

Oats and oat β-glucan consumption over the short-term to moderate-term results in improvements in established markers of fasting and postprandial glycemic control beyond concurrent therapy in adults with type 2 diabetes who were predominantly middle-aged, overweight or obese and with moderately controlled diabetes treated by antihyperglycemic medications or insulin. The available evidence provides a very good indication for small important reductions in fasting glucose and less of an indication for small important reductions in HbA1c and more trivial reductions in 2h-PG, fasting insulin and HOMA-IR in this population. The main sources of uncertainty in the evidence were imprecision and inconsistency. More large, high-quality RCTs are required to improve the precision of the pooled effect estimates and to allow for better exploration and understanding of the sources of inconsistency (heterogeneity) in the estimates between trials.

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