Physical activity advice only or structured exercise training and association with HbA1c levels in type 2 diabetes: a systematic review and meta-analysis


CRD summary
This well-conducted review concluded that structured exercise training was associated with improved glycaemic control in patients with type 2 diabetes. Structured exercise training was more effective than physical activity advice combined with dietary advice. Whilst the authors' conclusions reflected the evidence presented, the significant variation between included trials plus low trial quality reduce the reliability of the conclusions.

Authors' objectives
To assess the associations of structured exercise training and physical activity advice on changes in glycated haemoglobin (HbA1c) levels in patients with type 2 diabetes.

Searching
MEDLINE, EMBASE, LILACS, the Cochrane Central Register of Controlled Trials (CENTRAL), SPORTDiscus and ClinicalTrials.gov were searched from January 1980 to February 2011; search terms were reported. Reference lists of selected studies were checked for additional relevant studies. Only full-text studies written in English, Portuguese or Spanish were included in the review.

Study selection
Randomised controlled trials (RCTs) that assessed structured exercise training (aerobic or resistance or a combination of both) or physical activity advice (with or without dietary advice) compared with a control group, in adult patients with type 2 diabetes, were eligible for inclusion. Eligible trials had to be of at least 12 weeks' duration, assess glycated haemoglobin (HbA1c) level as an outcome, include only patients who were able to exercise, and report means or differences between means at baseline and after the intervention.

Structured exercise training was defined as an intervention in which patients were engaged in planned, individualised, supervised exercise programmes. Physical activity advice was defined as an intervention in which patients were partially or not engaged in supervised exercise training, but received formal instructions to exercise regularly with or without an individualised exercise prescription.

The average age of participants in the included trials was between 52 and 69 years. In some trials participants had chronic co-morbidities including hypertension, obesity and cardiovascular diseases. The frequency of structured exercise sessions was usually three sessions per week, with programmes lasting from 12 weeks to one year. The frequency of physical activity advice interventions was usually three or five sessions per week, with programmes lasting from 12 weeks to two years. Control groups included dietary/nutrition advice with no exercise, weekly stretching classes, usual care, or sedentary habitual lifestyle.

Two reviewers independently assessed studies for inclusion in the review, disagreements were resolved by consensus or by a third reviewer (where necessary).

Assessment of study quality
Two reviewers independently assessed trial quality for adequacy of sequence generation, allocation concealment, blinding of outcome assessors, use of intention-to-treat analysis, and description of losses to follow-up and exclusions. Disagreements were resolved by consensus, or by a third reviewer, where necessary.

Data extraction
Two reviewers independently extracted mean differences in HbA1c levels before and after the interventions for treatment and control groups. Adherence to protocols, drop-out rates and adverse events were also extracted. Imputation and/or transformation methods were used where data were only reported as confidence intervals or interquartile ranges.
Data were extracted on an intention-to-treat basis, where possible. Authors of included trials were contacted for additional data, where required. Disagreements were resolved by consensus, or by a third reviewer (where necessary).

**Methods of synthesis**

Mean differences were pooled using a random-effects model; results were presented as weighted mean differences (WMDs) with 95% confidence intervals (CIs). Statistical heterogeneity was assessed using Cochran Q test and the $I^2$ statistic. Statistical heterogeneity was assessed by removing one trial at a time from the analyses, by conducting stepwise meta-regression analyses, and using univariate meta-regression models to assess clinical and methodological variables that influenced the association of exercise with HbA$_{1c}$ levels.

Sensitivity analyses were performed to evaluate subgroups of trials most likely to yield valid estimates of the intervention based on pre-specified relevant clinical information and on meta-regression analyses. A cut-off of 150 minutes per week was used to stratify trials according to their weekly amounts of exercise. Trials that evaluated physical activity advice were grouped according to the presence or absence of simultaneous dietary advice.

Publication bias was assessed using funnel plots and funnel plot asymmetry was evaluated by Begg and Egger tests. The trim-and-fill method was used to estimate the effect of publication bias on the interpretation of results.

**Results of the review**

Forty-seven RCTs were included in the review (n=8,538 participants). Trial quality was low, with only 36% of trials reporting adequate sequence generation, 17% reporting allocation concealment, 17% with blinded assessment of outcomes, and 13% using an intention-to-treat analysis. Losses to follow-up and exclusions were described in 96% of trials. In structured exercise trials, adherence rates were above 75% in 14 of the 15 trials that reported adherence rates; drop-out rates were less than 20% in 19 of the 21 trials that reported drop-out rates. Adherence rates were not reported for physical activity advice trials; drop-out rates were less than 20% in 19 of the 24 physical activity advice trials.

**Structured exercise training**: Overall, structured exercise training was associated with a significant reduction in HbA$_{1c}$ levels (WMD -0.67%, 95% CI -0.84 to -0.49; 23 RCTs; $I^2$=91.3%) compared with control groups. Structured aerobic exercise (WMD -0.73%, 95% CI -1.06 to -0.40; 18 RCTs; $I^2$=92.8%), structured resistance training (WMD -0.57%, 95% CI -1.14 to -0.01; four RCTs; $I^2$=92.5) and both combined (WMD -0.51%, 95% CI -0.79 to -0.23; seven RCTs; $I^2$=67.5%) were all associated with a decline in HbA$_{1c}$ levels compared with control participants. A longer duration of structured exercise was associated with a larger reduction in HbA$_{1c}$ levels when durations of more than 150 minutes per week (WMD -0.89%, 95% CI -1.26 to -0.51; $I^2$=91.4%) were compared with durations of 150 minutes or less per week (WMD -0.36%, 95% CI -0.50 to -0.23; $I^2$=78.6%). Baseline HbA$_{1c}$ level, exercise frequency, total time spent in exercise during the study, and weekly exercise duration per week partially explained the heterogeneity.

**Physical activity advice**: Overall, physical activity advice interventions were associated with a significant reduction in HbA$_{1c}$ levels (WMD -0.43%, 95% CI -0.59 to -0.28; 24 RCTs; $I^2$=62.9%) compared with control groups. In a sensitivity analysis, combined physical activity and dietary advice was associated with a significant reduction in HbA$_{1c}$ levels (WMD -0.58%, 95% CI -0.74 to -0.43; 12 RCTs; $I^2$=57.5%) compared with control groups, but physical activity advice alone was not associated with significant changes in HbA$_{1c}$ levels.

There was significant statistical heterogeneity for all of these meta-analyses.

Only 17 of the included trials reported adverse events. No major adverse events were reported. Minor adverse events were reported in the review.

Funnel plots suggested publication bias in the analysis of structured exercise training. However, the trim-and-fill analysis suggested that publication bias did not interfere with the interpretation of results. There was no evidence of significant publication bias in the analysis of physical activity advice trials.

**Authors’ conclusions**

Structured exercise training for at least 12 weeks, consisting of aerobic training or resistance training, or a combination of both, was associated with improved glycaemic control in patients with type 2 diabetes. Structured exercise training...
for more than 150 minutes per week was associated with a greater reduction in HbA\textsubscript{1c} levels than training of 150 minutes or less per week. Structured exercise training reduced HbA\textsubscript{1c} levels more than physical activity advice. Physical activity advice was associated with a significant reduction in HbA\textsubscript{1c} levels, but only when combined with dietary advice.

**CRD commentary**

The review addressed a clear question supported by well defined inclusion criteria. Several databases were searched for relevant studies, including sources of unpublished data, which reduced the potential for publication bias. Publication bias was assessed and, although present for the analysis of structured exercise training, it was unlikely to interfere with the interpretation of results. Only studies written in English, Portuguese and Spanish were included in the review, which increased the potential for language bias. Appropriate methods were used to reduce the potential for reviewer bias and error.

Trial quality was assessed using appropriate criteria; the included trials were generally of poor quality. There was significant heterogeneity between trials, so it may not have been appropriate to pool the results.

Overall, this was a well-conducted systematic review and the authors’ conclusions reflected the evidence presented. However, the low quality of the included trials and significant heterogeneity between trials reduce the reliability of the conclusions.

**Implications of the review for practice and research**

**Practice:** The authors stated that patients with type 2 diabetes should receive dietary recommendations in combination with advice to increase physical activity.

**Research:** The authors did not state any implications for further research.

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