The Effect of Lifestyle Interventions on the Progression towards Type 2 Diabetes Mellitus in Prediabetic Patients: A Systematic Review

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ABSTRACT

Background: The incidence of Diabetes Mellitus (DM) type II is increasing quickly worldwide. Important factors driving it include overweight and obesity. Long-term complications include heart attack, stroke, blindness, kidney failure and lower limb amputation. A healthy lifestyle consisting of diet and physical activity can possibly prevent or delay DM type II in at-risk patients.

Objective: To assess the effects of diet, physical activity or both on the progression towards DM type II in prediabetic patients.

Search method: Trials with a publication date limited to the last five years were identified through MEDLINE and EMBASE. The date of the last search of all databases was December 2019.

Selection criteria: We included randomized controlled trials (RCT's) comparing diet, physical activity or both as lifestyle intervention with no intervention in prediabetic patients with a duration of two years or more.

Results: We included six randomized controlled trials randomizing 2126 people. Trials ranged from 24 months to 36 months duration. Three studies compared a single type of physical activity with no intervention and did not find a significant reduction in risk of progression towards DM type II. One study investigated aerobic training, resistance training or both as intervention compared with no intervention. Combining resistance training with aerobic training was most beneficial in reducing the risk of DM type II (HR: 0.26 [95% CI: 0.11-0.62]) compared with only aerobic (HR: 0.35 [95% CI: 0.15-0.79]) or resistance training (HR: 0.28 [95% CI: 0.13-0.64]). Four studies compared a diet-only intervention with no intervention on the risk of progression towards DM type II. Dietary intervention consisting a decreased portion size (OR: 0.39 [95% CI: 0.25–0.60]), decreased oil intake (OR: 0.46 [95% CI: 0.30–0.69]), decreased consumption of carbohydrates (OR: 0.52 [95% CI: 0.34-0.78]), and decreased sugar consumption (HR: 0.44 [95% CI: 0.2-0.99]) significantly decreased the risk of developing DM type II. One RCT combined nutrition, physical activity and weight loss interventions as lifestyle intervention. The decrease in risk of developing DM type II in prediabetic patients was not significant. An ancillary finding showed that body weight reduction as an independent, conservative treatment had a significant effect on the progression towards DM type II. This in comparison with no treatment (OR: 0.15 [95% CI: 0.01–0.47]).

Conclusion: Diet, physical activity and body weight reduction as lifestyle interventions can possibly be important in the prevention or delay of the progression towards DM type II in prediabetic patients. Further research should be performed on the different intervention types to implement these conservative treatments into daily practice.

INTRODUCTION

Diabetes Mellitus (DM) type II is a worldwide epidemic affecting 422 million adults (>18 years) globally in 2014. The number of adults aged 20–79 years with diabetes in the European region is estimated to be 59.3 million, representing 8.9% of the population in this age group.[1,2] In the long term, people with DM type II are at risk for complications in the microvascular (retinopathy, nephropathy and neuropathy) and macrovascular (cardiovascular disease) system [3] Beside health issues, DM type II has important economic consequences on a global scale with the US medical expenditures being two to three times higher in patients diagnosed with diabetes[4]. Although known as an aging-associated disease, the average age of onset of diabetes is 42.5 years which can partially be explained by the consumption of high sugar and high-calorie diets, sedentary lifestyle and genetic susceptibility[5].

DM type II can be diagnosed based on four criteria : 1/ Fasting Plasma Glucose (FGP) ≥ 126 mg/dL (7.0 mmol/L), 2/ 2-h PG ≥ 200 mg/dL (11.1 mmol/L) during oral glucose tolerance tests (OGTT), 3/ haemoglobin A1C (HbA1C) ≥ 6.5% (48 mmol/mol), 4/ or in a patient with classic symptoms of hyperglycaemia or hyperglycaemic crisis and random plasma glucose ≥ 200 mg/dL (11.1 mmol/L). An elevated blood glucose level (but below the diagnostic threshold for DM type II) is diagnosed as prediabetes and is defined by the presence of impaired fasting glucose (IFG) and/or impaired glucose tolerance (IGT) and/or HbA1C 5,7-6,4% (39-47 mmol/mol)[6].

Patients who meet the criteria of 'prediabetes' are often asymptomatic, what makes it a condition that is usually underdiagnosed but evidence shows already an increased cardiovascular risk in these patients[7] and approximately 5% to 10% of people with prediabetes become diabetic every year[8]. It is not clear if any specific intervention, especially glucose-lowering drugs, should be recommended for people with increased risk of diabetes[9]. Contrary, several major randomized controlled trials have demonstrated reductions in the risk of developing diabetes among prediabetic individuals after lifestyle interventions and prediabetes may even convert back to normoglycemia[10].

The WHO also pleads for strategies at community level and in national programs for the early detection of DM type II.[1] This will identify people who are at high risk for future development of type 2 diabetes and makes counselling on weight loss, diet, physical activity and smoking possible. WHO has developed recommendations on healthy diet and physical activity that can reduce an individual's risk of type 2 diabetes.[1]

This systematic review examines the effect of diet and physical activity on the progression towards DM type II in adult, prediabetic patients. In this systematic review we analysed randomised controlled studies (RCT's) from the last five years (December 2014 - December 2019).

METHODS

For this systematic review, we used the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) protocol which holds an evidence-based minimum set of items needed for reporting in systematic reviews and meta-analyses.

We searched for randomised controlled trials (RCTs) with a publication date from the last five years (September 2014 - September 2019). Patients enrolled in these studies are nondiabetic individuals that meet the diagnostic criteria for 'prediabetes'. To be consistent with the changing diagnostic criteria for 'prediabetes' over the years, the diagnosis had to be established using the standard criteria valid at the time of the trial commencing. To be included in the review, all trials had to have a minimum duration of intervention of two years No exclusion criteria were based on participants' race or sex. We excluded trials with participants diagnosed with metabolic syndrome or gestational diabetes as well as trials using pharmacological agents in the intervention and trials focussing on diets consisting of single-food or supplement dietary changes. We investigated the effect of lifestyle interventions consisting of diet and/or physical activity compared with standard care or no intervention. We want to investigate the effect of these lifestyle interventions on the progression of prediabetic patients towards DM type II with incidence of DM type II as a primary outcome. We excluded trials if our primary outcome was not reported.

A literature review was done through online medical databases (PubMed and EMBASE) and libraries, looking for literature that met our criteria as previously mentioned.. Our last search dates from December 2019. To result in a complete overview of literature about our topic, it was important that the MESH-terms would cover all the different appellations for Prediabetes ('Prediabetes', 'Impaired Fasting Glucose', 'Impaired Glucose Tolerance', 'Glucose Intolerance', 'Insulin Resistance', 'Prediabetic State') and for Lifestyle Interventions ('Exercise', 'Physical Activity', 'Physical Fitness', 'Diet', 'Lifestyle', 'Life-Style'). The used search terms can be found in **Figure 1**.

Figure 1. Search Terms

"Prediabetes" OR "Impaired Fasting Glucose" OR
"Impaired Glucose Tolerance" OR "Glucose Intolerance"
OR "Insulin Resistance" OR "Prediabetic State"

AND

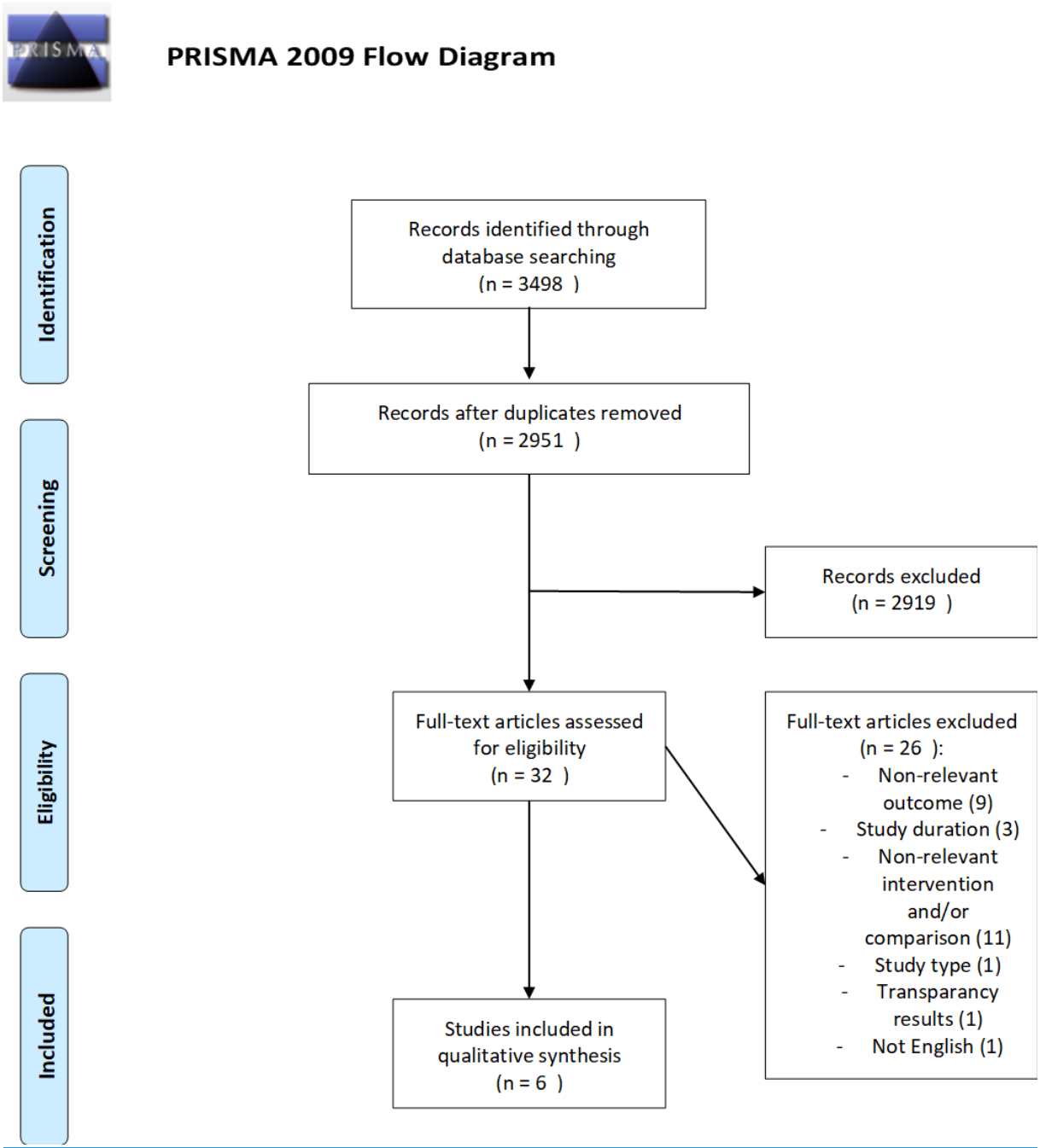
"Exercise" OR "Physical Activity" OR "Physical Fitness"
OR "Diet" OR "Lifestyle" OR "Life-style"

Our selection process is presented in a flow chart (**Figure 2**). With our search terms, we found a total of 3498 items in the databases. These were first filtered on duplicates, ending with 2951 articles.

A first screening was performed based on the title and abstract to match the articles with our PICO (Population, Intervention, Comparison, Outcome). We maintained a total of 32 full papers with some relevance for this systematic review. After we assessed the full-text articles and abstracts for eligibility, we excluded 26 articles. In total we incorporated a total of 6 items in this systematic review.

The Cochrane risk-of-bias tool for randomized trials (RoB 2.0) was used to examine six different domains of bias (selection bias, performance bias, detection bias, attrition bias, reporting bias, and other bias.) (**Appendix**)

Figure 2: Prisma 2009 Flow Diagram



RESULTS

Study characteristics

The study characteristics are presented in **Table 1**. Six randomized controlled trials (RCTs) met the inclusion criteria of which five studied the effect of physical exercise[11,12,14-16], five the effect of dietary regimens[11-14,16] and two also studied other lifestyle intervention[11,16] (e.g. BMI[11]). IGT patients were included in all studies. Patients who met the IFG criteria were included in four studies.[12-15] Only one study included the patients who solely met the HbA1c criterium.[15] The study populations consisted of adult (≥18 years), prediabetic patients). Three of these studies only included population with an Asian ethnicity.[11,13,15] All studies had more than 100 participants with a maximum of 673 participants[12] of whom complete data have been assessed. All patients were followed for a minimum of 24 months. All included studies described progression to DM type II as a primary or secondary outcome. The outcome measures however where diverse (Hazard Ratio (HR), Odds Ratio (OR), and Risk Ratio (RR)). Due to a lack of raw data and a different setup of the analysed RCTs, we were not able to form a unique outcome measure over all studies.

Primary Analysis

Physical activity

Five studies investigated the effect of physical exercise as intervention type on progression to DM type II but every study had a different study design setup (aerobic exercise 30 min. per day or daily, strenuous work[11]) (**Table 2**). Davies M. et al.[12] investigated the combined effect of physical activity and diet with a single outcome. This study will therefore be discussed separately. Three out of four studies, with a physical activity-only intervention arm, investigated only one type of physical exercise (either aerobic training, DE-PLAN or moderate-intensity training) and did not find a significant reduction in risk of progression towards DM type II.[11,14,16] In the study of Dai et al[15], the authors investigated aerobic training and resistance training, separately or combined and found a reduced risk for DM type II in all intervention groups. Combining resistance training with aerobic training was most beneficial in reducing the risk of DM type II (HR: 0.26 [95% CI: 0.11-0.62]) compared with only aerobic (HR: 0.35 [95% CI: 0.15-0.79]) or resistance training (HR: 0.28 [95% CI: 0.13-0.64]) (**Table 2**). The aerobic training-only intervention arm consisted of aerobic dancing for one hour. Fifty minutes of this exercise the subjects trained at 60-70% of their HR_{max} (Maximal heart rate). In the Resistance training-only intervention arm the major muscle groups were trained for one hour at 60-80% of the one repetition maximum (measured monthly). Within the intervention group that combined aerobic and resistance training each of the components were carried out for 30 minutes. Each of these three intervention groups trained three non-consecutive days per week for 24 months. This within a research centre.[15]

Diet

Four studies examined the effect of diet-alone as intervention type on the progression towards DM type II [11,13,14,16] (**Table 3**). All cited studies investigated a different dietary modality with most studies having more than 100 participants[11,13,14] in the intervention group. The risk of developing DM type II was significantly decreased in prediabetic patients who had a regimen of decreased portion size[11] (OR: 0.39 [95% CI: 0.25–0.60]), decreased oil intake[11] (OR: 0.46 [95% CI: 0.30–0.69]), decreased consumption of carbohydrates[11] (OR: 0.52 [95% CI: 0.34-0.78]), decreased sugar consumption[16] (HR: 0.44 [95% CI: 0.2-0.99]) and a diet consisting of a high mono-unsaturated fats (HMF) (RR: 0.43 [95% CI:

0.1-0.9]), While a decreased portion and HMF were the dietary regimens that showed the most prominent results, no significant effects were observed in participants with an intervention consisting of a normal fat diet, combined diet, increased fruit/vegetables consumption, or increased dairy product consumption. The intervention groups using only dietary regimens reduced the risk of developing DM type II less compared to these focussing on physical activity (estimates ranging from 0.39 to 0.52 for dietary regimens[11,16] vs. 0.26 to 0.35 for physical exercise[15]). However three of the four studies investigating diet-only proved statistical significant results.[11,13,16] This compared to only one of the four studies, who had a physical activity-only intervention arm.[15] We should keep in mind that there are differences in study design, sample population, ethnicity, etc. so directly comparing effect estimates might be biased.

Table 1: Study characteristics

Author	Study population	Inclusion criteria	Exclusion criteria	Intervention type
Ram J. et al. (2014)	- United Kingdom - Asian ethnicity - 517 participants - Mean age: 46.0 ± 4.7 years - Mean BMI: 25.8 ± 3.1 kg/m^2 - 24 month follow-up	- IGT - Asian, Indian men - Age: 35-55 years - BMI: ≥ 23 kg/m^2 - Family history of DM type II - Ownership of a mobile phone - Ability to read and understand mobile phone messages in English	- Diabetes or major illness (e.g. cancer, chronic liver disease) - Physical disability - Recruitment in another trial - Severe mental Illness (e.g. depression)	- Diet - Physical exercise - BMI reduction
Davies M. et al. (2015)	- United Kingdom - European and Asian ethnicity - 673 participants - Mean age at baseline: 63.9 years* - 36 month follow-up	- IGT and/or IFG - Age: a) 40-75 years (white Europeans); - b) 25-75 years (South Asians)	- Unable to give informed consent - Pregnant or lactating - Diabetes or a terminal illness - Requirement of an interpreter	- Diet - Physical exercise -
Shahbazi S. et al. (2018)	- Iran - Asian ethnicity - 322 participants - Mean age: 43.6 years† - 24 months follow-up	- IGT and/or IFG - BMI: 27-40 kg/m^2	- Severe physical activity - Already on a diet therapy - Accompanying diseases which reduce - life expectancy (e.g. cancer) - Several medications - (e.g. thiazide diuretics, beta-blockers)	- Diet
Barengo N.C. et al. (2019)	- Colombia - No information on ethnicity - 390 participants - 24 month follow-up - Mean age: 52.8 years†	- IGT and/or IFG - Age: 34-69 years	- Pharmacologically treated diabetes and/or hypertriglyceridemia - History of life-limiting diseases or events - Unwillingness to sign an informed consent	- Diet - Physical exercise

Table 1: Study characteristics (cont.)

Author	- Study population	- Inclusion criteria	- Exclusion criteria	- Intervention type
Dai X. et al. (2019)	- China - Asian ethnicity - 137 participants - Mean age: 59 years‡ - 24 month follow-up	- IGT and/or IFG and/or HbA1c (≥5.7 and <6.4 mmol/L) - Age: 55-75 years	- DM type II - Severe medical comorbidities (e.g. cardiopulmonary, musculoskeletal) that restricted exercise training - Pregnant or nursing women	- Physical exercise
Khalangot M.D. et al. (2019)	- Ukraine - European ethnicity - 123 participants - Mean age: 62.0 years - Follow-up average 2.8 years	- IGT - Age: 18-79 years	- DM type II - Absence of a signed, informed consent	- Diet - Physical exercise - Other lifestyle interventions

* Only age at baseline, no information on age at follow-up.

† Mean age calculated from different subpopulations described in article.

‡ No standard deviation given in original article of Dai X. et al. 2019.

Table 2: Studies describing the effect of different physical activity modalities on the progression towards Diabetes Mellitus type II

Author	Follow-up	Population (Intervention group)	Physical activity	Estimate (95% CI)*
Ram J. et al. (2014)	24 months	IGT; n = 136	Aerobic exercise and/or strenuous work	OR: 1.14 (0.70-1.89)
Barengo N.C. et al. (2019)	24 months	IGT and/or IFG; n = 132	Moderate Intensity Training	RR: 1.43 (0.70-2.93)
Dai X. et al. (2019)	24 months	IGT and/or IFG and/or HbA1c n = 34	Aerobic training	HR: 0.35 (0.15-0.79)
		IGT and/or IFG and/or HbA1c n = 31	Resistance training	HR: 0.28 (0.13-0.64)
		IGT and/or IFG and/or HbA1c n = 37	Aerobic training + Resistance training	HR: 0.26 (0.11-0.62)
Khalangot et al. (2019)	2.8 years average	IGT; n = not reported	Increase physical activity (DE-PLAN)*	HR: 0.71 (0.37-1.38)

* DE-PLAN: The intervention set-up within this program differs in different studies (references). In the study of Khalangot et al. (2019) no specific set-up is reported. Mainly this type of intervention focusses on group education of diabetes, diet and physical exercise. Within physical activity, subjects can take part in two exercise sessions per week.

Table 3: Studies describing the effect of different dietary modalities on the progression towards Diabetes Mellitus type II

Author	Follow-up	Population (Intervention group)	Dietary modality	Estimate (95% CI)*
Ram. et al. (2014)	24 months	IGT; n = 137	Decreased portion size	OR: 0.39 (0.25–0.60)
		IGT; n = 162	Decreased oil consumption	OR: 0.46 (0.30–0.69)
		IGT; n = 149	Decreased consumption of carbohydrates	OR: 0.52 (0.34–0.78)
Shahbazi. et al. (2018)	24 months	IGT and/or IFG; n = 107	High mono-unsaturated fat diet	RR: 0.43 (0.1-0.9)†
		IGT and/or IFG; n = 106	Normal fat diet	RR: 0.60 (0.2–1.2)
Barengo et al. (2019)	24 months	IGT; n = 136	Combined diet[1]	RR: 1.38 (0.67–2.84)
Khalangot et al. (2019)	2.8 years average	IGT; n = not reported	Increase vegetables/fruits consumption	HR: 1.012(0.54–1.89)
		IGT; n = not reported	Increase dairy products consumption	HR: 1.115(0.62–1.99)
		IGT; n = 99	Decreased sugar consumption	HR: 0.44 (0.2-0.99)

1These goals were (i) **reduction in weight of >5%** (ii) total fat intake less than 30% of energy consumed, (iii) saturated fat intake less than 10 % of energy consumed, and (iv) fruit or vegetable intake of at least 500 g per day.

* OR: Odds ratio ; HR: Hazard Ratio; RR: Risk Ratio

† Result derived from article. Not reported directly.

Combination

Only one of the included studies in this systematic review examined the effect of dietary regimens, physical exercise and other lifestyle measures in their intervention group.[12] The impact of the different treatment aspects were not analysed separately, but the different subgroups of the prediabetic population were compared. A total of 673 patients between 25 and 75 years were examined. The Let's Prevent programme[17] was used for patient education in group sessions. The focus of this program was to increase knowledge of prediabetes, promote healthy behaviour and to provide patient empowerment. The dietary regimens followed the Diabetes Prevention Program[18] and the Finnish Prevention Study.[19] Their key goals were a total fat intake of less than 30%, a low saturated fat intake of less than 10% and a higher fiber intake. Within these protocols[18,19] also a reduction in body weight of more than 5% was promoted The physical exercise aspect followed the PREPARE-program[20,21], which used a pedometer to improve the amount of steps-per-day. Combining nutrition, physical activity and weight loss interventions did not significantly lower the risk of developing DM type II in patients with IGT (HR: 0.79 [95% CI: 0.45-1.38], IFG (HR: 0.52 [95% CI: 0.15-1.83], or both IGT and IFG (HR: 0.51 [95%CI: 0.22-1.16] .

Ancillary Analysis

Besides dietary regimens and physical activity, reduction in body weight showed to be an interesting intervention strategy to reduce the risk of developing DM type II.[11] Reducing the BMI with at least one BMI point has a protective effect in the development of diabetes among prediabetic Asian Indian men (OR: 0.15 [95% CI: 0.01–0.47]).[11] However, it needs to be noted that the sample size was relatively small (intervention = 27 vs. control n = 34) and the reduction in BMI is coherent with dietary regimens and physical activity.

DISCUSSION

Main Findings

Conservative interventions including physical activity and dietary regimens show promising results in treating prediabetic patients and reducing the incidence of DM Type II.[22-24] The vast majority of our findings showed an outcome measure promoting the intervention[11-13,15,16], though some RCT's failed to provide statistical significant results probably due to small samples sizes.[12,14] The assessed modalities in physical exercise showing the most prominent results were resistance training and aerobic training.[15] In the dietary interventions, significant effects were observed in reducing the risk of DM type II by decreasing the portion size[11], oil intake[11], consumption of carbohydrates[11], sugar consumption[16]. Also a diet consisting of high doses of mono-unsaturated fats showed to be effective and significant. The intervention groups focussing on physical activity alone[11,14-16] were more effective in reducing the risk of developing DM type II compared to the dietary regimens[11,13,14,16]. Although it was not part of our primary research, we found that BMI reduction as an independent therapy proved to reduce the risk of DM type II.[11] This finding shows that different lifestyle interventions, having an impact on body weight, can be effective in reducing the DM type II incidence. Thus being an interesting choice of therapy for prediabetic patients because weight loss also has beneficial results on other comorbidities that are associated with this subgroup (e.g. essential hypertension).[25-28] Depending on the patient's profile, the main focus can be targeted on diet, physical exercise or other lifestyle measures.

Comparison with other systematic reviews

The last decades, there have been several larger and prominent studies examining the effects of conservative treatments and lifestyle interventions in prediabetic patients. A recent publication by Hemmingsen B. et al.(2017)[22] analysed 12 of these RCTs. Each of these studies looked at the effect on the progression towards DM type II. However this review[22] did not focus solely on the effect of dietary regimens. For this reason, we added the results from a systematic review and meta-analysis by Pang B. et al. (2017)[23] A total of 63 RCT's were incorporated in this analysis, where 11 different treatments were investigated.

Physical exercise vs control

Two RCT's included by Hemmingsen et al.[22] examined the effect of physical exercise as a stand-alone treatment. The Risk Ratios were 0.61 [95% CI 0.48, 0.76] (Da Qing 1997; After 6 years of follow-up) and 0.66 [95% CI 0.27, 1.61] (Hellgren 2016; after 3 years of follow-up). Only the Da Qing study proved statistical significance. Within the study of Pang B et al.[23] physical exercise-only showed a Risk Ratio of 0.32 [95% CI 0.20, 0.51].

Diet vs control

Pang B. et al.[23] proved a significant RR of 0.43 [95% CI 0.31, 0.61]. This however within a wide variety of dietary regimens.

Physical exercise AND diet vs control

11 studies incorporated by Hemmingsen et al.[22] were relevant in this analysis. 10 studies only included IGT-patients and a total of 4511 patients were assessed. The RR was 0.57 [95% CI 0.50, 0.64] When the intervention and control group were divided using a BMI cut-off (BMI ≥30 kg/m2 or BMI <30kg/m2), we saw that obese patients have a higher overall risk of developing DM type II but have a higher Risk Reduction Ratio (RRR) with these treatments than lean patients. (0.50 [95% CI 0.43, 0.58] for a BMI ≥ 30; 0.66 [95% CI 0.55, 0.80] for a BMI <30). The obese group thus having a relatively higher benefit with these treatments. This result correlates with our research[11], showing that a reduction of BMI as an independent intervention could reduce the risk of developing DM type II. In the Chinese meta-analysis[23] we saw that combining diet and physical exercise had a RR of 0.39 [95% CI 0.28, 0.53] . Both studies used RCT's with a wide variety of dietary and physical activity regimens.

Strengths and limitations

A major strength of this systematic review is the strict selection procedure of specific RCTs that met our research question on the progression of DM type II in prediabetic patients. We used a large set of MESH terms to potentially increase the number of relevant articles that met our criteria. Secondly, we provide a detailed description of study characteristics and results in a uniform way. Thirdly, this systematics review contains the most recent RCTs as it included only studies from the past five years.

However, due to the fact that only studies were included this period also results in a limitation of our study. We do not have a clear overall view about which regimens of nutrition or physical exercise have the best outcome. Not only were some RCTs relatively poor in quality (e.g. population quantity, score on the Cochrane Risk of Bias Tool), also the analysed interventions were only a few of the possibilities (e.g. no Mediterranean diet[24]). A second limitation is the heterogeneity of the study designs of the six discussed articles. There were differences in outcome measures, ethnicity, treatment modality, disproportional inclusion of subpopulations (e.g. IFG, IGT, and Elevated HbA1c) which makes a direct comparison between studies difficult. Lastly, the selected RCTs scored relatively poor on the Revised Cochrane Risk of Bias tool for randomized controlled trials (ROB 2.0)(**Appendix**) This in comparison to the studies assessed by Hemmingsen et. al.[22]

Implications

Although physical exercise, nutrition and/or weight loss have been shown to reduce the risk of developing DM type II in some RCTs, some caution is warranted putting these treatment modalities into daily practice. Further research is needed to investigate the relative effect of physical exercise and nutrition as separate treatments as it could result in a standard conservative treatment, in group or individual programs. Also the effects of a wide variety of different regimens in each of these treatment types as there is not a unique protocol in our included RCT's or the meta-analysis and systematic reviews in the discussion.[12] A new RCT can be set up using the most promising results in this review.[1,5,6] This by combining aerobic and resistance training, a reduction of portion size/oil intake/sugar intake/carbohydrate intake, a highly mono-unsaturated fat diet and a reduction of body weight. Aside from the effects on progression towards DM type II, these therapies have shown to improve other disease entities associated with prediabetes (e.g. essential hypertension).[25-28]

CONCLUSION

DM type II is a worldwide epidemic and the progression of the disease should be treated with specific prevention strategies. In this systematics review - that entails RCTs of the last five years - we observed that within our research question physical activity consisting of aerobic training and/or resistance training showed the most effective results. Secondly, a reduction of portion size/oil intake/sugar intake/carbohydrate intake and a high mono-unsaturated fat diet were the dietary regimens having the most beneficial results. Alternatively, body weight reduction, using conservative treatments, has a significant reduction of DM type II incidence and this finding correlates with larger studies of the last decades. Future studies should focus to include all prediabetic entities (IFG, IGT, elevated HbA1C) and use a combination of conservative intervention types.

CONFLICT OF INTEREST

The authors declare that there was no conflict of interest. There has been no financial support, nor did we receive support from any organisation outside of the K.U. Leuven.

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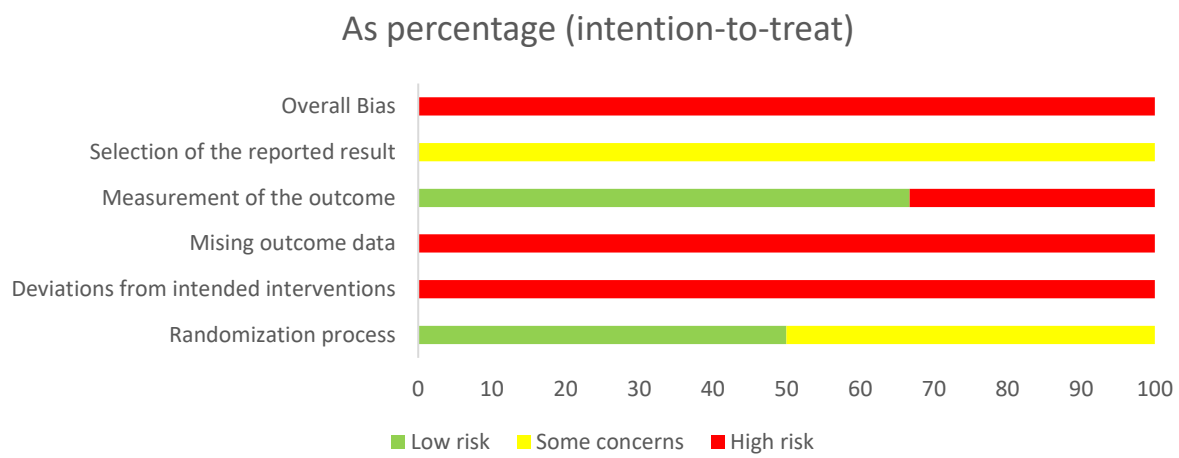
APPENDIX

Risk of bias graph: review author's judgement about each risk of bias item presented as percentages across all included studies



Risk of bias summary: review author's judgement about each risk of bias item for each included study

