An eBook on Type2 Diabetes

Chapter 2

Lifestyle Intervention and Type 2 Diabetes

Carlos Vasconcelos

Polytechnic Institute of Viseu, Superior School of Education of Viseu, Portugal.

Email: cvasconcelos@esev.ipv.pt

Abstract

This review aimed to evaluate, through randomized controlled trials, the effects of lifestyle interventions on the evolution of cardiovascular risk factors in adult patients with type 2 diabetes. An electronic search was performed in PubMed and list of references from 2016 until May 2021 was made. Studies were eligible if 1) participants had type 2 diabetes; 2) mean age < 65 years old; 3) at least 3 cardiovascular risk factors measured before and after lifestyle intervention; 4) the study design was a randomized controlled trial. This review demonstrates that lifestyle interventions were effective in high-scale (more than 50% of interventions success) on the significant reduction of body mass index, waist circumference and glycated hemoglobin and in low-scale (less than 50% of interventions success) on the significant reduction of systolic blood pressure and diastolic blood pressure and on significant increase of high density lipoprotein. No lifestyle interventions effects were found regarding the decrease of low density lipoprotein mean values.

Keywords: Randomized controlled trials; lifestyle interventions; cardiovascular risk factors; adults; type 2 diabetes.

1. Introduction

Type 2 diabetes (T2D) is a chronic metabolic disorder characterized by long term high blood glucose levels due to deficiency in insulin production by pancreas and insulin resistance from body cells [1].

Its prevalence is increasing worldwide, with 462 million individuals with T2D in the year of 2017 [2] being a major concern in public health due to the macrovascular and microvascular

complications associated with this disease. The main cause of death of individuals with T2D is cardiovascular disease. According to Lorber et al. [3], it is urgent to minimize the risk of cardiovascular disease, with the control of its risk factors: hyperglicemia, obesity, hypertension and dyslipidemia. However, it remains a though task for these patients [4], which is directly associated with the lack of health promotion programs that increase their self-management abilities [5].

The adoption of lifestyle interventions with the purpose of modify physical activity and eating behaviors are considered the cornerstone of T2D management [3]. There is a meta-analysis conducted by Chen et al. [6] that concluded that lifestyle interventions showed significant benefit in cardiovascular risk factors in patients with type 2 diabetes, with mean age of participants ranging between 51.3 and 67.3 years old. There is a positive association between age and glycemic control in patients with type 2 diabetes with individuals with < 65 years old had worse glycemic control when compared to individuals with ≥ 65 years old [7].

Thus, the aim of this review is to evaluate, through randomized controlled trials (RCTs), the effects of lifestyle interventions on the evolution of cardiovascular risk factor in adult patients with type 2 diabetes

2. Methods

2.1. Search strategy

A search was carried out by one author [CV] in the electronic database "PubMed", from the year of 2016 until May 2021, to identify articles assessing the effects of a lifestyle interventions on the evolution of cardiovascular risk factors in adults with type 2 diabetes. For database search, the following keywords were used: (lifestyle intervention [Title]) AND (type 2 diabetes [Title]).

2.2. Selection of the studies

One author [CV] reviewed the search results and screened publications provided by database (Pubmed), according to the following steps: 1) articles were selected by the information from title and abstract; 2) full text analysis of potentially relevant articles was made to check their eligibility for this review.

Studies were considered eligible if: 1) participants were individuals with type 2 diabetes; 2) mean age < 65 years old; 3) at least 3 cardiovascular risk factors measured before and after lifestyle intervention; and 4) the study design was a randomized controlled trial.

Studies were excluded according to the following criteria: 1) participants at risk of type 2 diabetes; 2) mean age ≥ 65 years old; 3) studies that do not evaluate the evolution of at least 3 cardiovascular risk factors; 4) the study design was not a randomized controlled trial; 4)

studies with no access to full text.

2.3. Data extraction

Each selected article was evaluated by author to extract information regarding: (1) study characteristics (first author, year of publication, country); (2) study participants (including sample size, mean age ± standard deviation and gender information of intervention and control group); (3) time of intervention; (4) intervention and control groups (description of interventions); and (4) main results regarding the evolution of cardiovascular risk factors.

2.4. Data analysis

For each study, the differences in the evolution of cardiovascular risk factors between intervention and control group were analyzed. Body mass index (BMI); waist circumference (WC); systolic blood pressure (SBP), diastolic blood pressure (DBP); low density lipoprotein (LDL), high density lipoprotein (HDL) and glycated hemoglobin (HbA1c) were considered as cardiovascular risk factors.

3. Results

3.1. Study selection

A total of 90 references were identified in the initial search. After screening for title and abstract, 70 papers were excluded because of: 1) not assessing at least 3 cardiovascular risk factors; 2) non-randomized controlled trials studies and 3) patients at risk of type 2 diabetes. After full-text reading, 13 more papers were removed due to: 1) no access to full text and 2) non-randomized controlled trials. Thus, in final analysis 7 studies were included in this review.

3.2. Study characteristics

The characteristics of the studies included in this review are presented in **Table 1**.

Table 1: Main characteristics of each study that met the inclusion criteria.

Authors / Country	Objective	Participants (N); mean age (years ± SD); females (%)	Length of lifestyle program	Intervention group	Control group	Outcomes measured
Chee et al. (2017) (8) / Malaysia	Evaluate the effectiveness of a diabetes lifestyle program on the evolution of glycated hemoglobina in individuals with type 2 diabetes	INT 1: N = 58; 55±8 years old; 67.2% INT 2: N = 57; 55±8 years old; 87.4% CON: N =115; 54±8 years old; 48.7%	6 months	1) Physical activity prescription of at least 150 min. of physical activity per week 2) Structured low-calorie meal plan (1200 or 1500 kcal/day) plus 14-day meal plans 3) Nutrition and physical activity education through flip-charts The difference between the two intervention groups was the type of counseling (INT1: motivational interviewing principles vs. INT2: conventional counseling techniques)	Advice to follow a conventional low-calorie diet plan (1200 or 1500 kcal/ day).	At baseline and 6 months, BMI, WC, SBP; DBP; LDL; HDL and HbA1c were evaluated
Johansen et al. (2017) (9) / Denmark	Test whether a 12-month intensive lifestyle intervention results in equivalent glycemic control compared with usual care in type 2 diabetes patients	INT: N = 64; 53.6 ± 9.1 years old; 48% CON: N = 34; 56.6 ± 8.1 years old; 47%	12 months	5 to 6 weekly aerobic training sessions (duration 30-60 minutes), of which 2 to 3 sessions were combined with resistance training. Participants were also encouraged to be physically active in their leisure time ≥ 10000 steps per day). Besides, they received dietary plans with the purpose of attaining a body mass index of 25 or less.	Usual care at baseline and every 3months for 12 months. .	At baseline and 12 months, BMI, SBP; DBP; LDL; HDL and HbA1c were evaluated
Kempf et al. (2017) (10) / Germany	Evaluate the efficacy of a Telemedical Lifestyle Intervention Program in the improvement of metabolic control in type 2 diabetes patients	INT: N = 93 59.0 ± 9.0 years old; 45% CON: N = 74; 60.0 ± 8.0 years old; 47%	3 months	Intervention group received a self-management guide, weighing scales and step counters and received telemedical coaching including dietary intervention and target agreements about diet and physical activity for 3 months.	The control group got weighing scales and step counters and remained in routine care for 3 months.	At baseline and 3 months, BMI, SBP; DBP; LDL; HDL and HbA1c were evaluated
Larsen et al. (2019) (11) / Denmark	Averiguate whether a 12-month lifestyle intervention induces partial or complete type 2 diabetes remission type 2 diabetes patients.	INT: N = 62 53.5 ± 9.2 years old; 47% CON: N = 31; 56.7 ± 8.3 years old; 45%	12 months	During 12 months, supervised resistance and aerobic exercise for 30 to 60 minutes, on 5 or 6 days per week and individual dietary plans aiming for body mass index ≤ 25 kg/ m^2. No interventions were addressed at the follow-up period (between month 12 and month 24)	Standard care	At baseline and 24 months, BMI, SBP; DBP; LDL; HDL and HbA1c were evaluated
Lynch et al. (2019) (12) / USA	Determine whether a lifestyle intervention would result in sustained improvements in glycemic control in low-income African-American type 2 diabetes patients	INT: N = 106 55.1 ± 11.5 years old; 70.8% CON: N = 105; 54.8 ± 9.0 years old; 69.5%	12 months	The intervention was delivered in 28 group sessions over 12 months. The intervention had four main components: (1) culturally tailored diabetes nutrition education; (2) physical activity advice; (3) self-monitoring of blood glucose, and (4) social support.	Diabetes self-management education in two group sessions in the first 6 months of the study period	At baseline, 12 and 18 months, BMI, SBP; DBP and HbA1c were evaluated

Matushita et al. (2020) (13) / Japan	Determine the effectiveness of a lifestyle program on glucose metabolismo in type 2 diabetes patients	INT: N = 792 53.9 ± 0.4 years old; 29.4% CON: N = 3645; 51.6 ± 0.1 years old; 8.5%	12 months	1) Lectures about Nutritional aspects based on Dietary Guidelines for the Japanese and Physical Activity (adequate exercise intensity, methods for walking safely and self-training at home) 2) Experience-oriented diet and Exercise program (combination of aerobic and resistance exercise based on the Exercise and Physical Activity Guide for the Health Promotion)	Continued with usual care	At baseline and 24 months, BMI, WC, SBP; DBP; LDL; HDL and HbA1c were evaluated
Taheri et al. (2020) (14) / Qatar	Assess whether an intensive lifestyle intervention would lead to significant improvement on glycaemia in young individuals with early type 2 diabetes.	INT: N = 70 41.9 ± 5.4 years old; 30% CON: N = 77; 42.3 ± 5.8 years old; 25%	12 months	1) Nutritional intervention: a 12-week total diet replacement phase, in which it was given to participants a low-energy formula (800–820 kcal/day) diet meal replacement products (57% carbohydrate, 14% fat, 26% protein, and 3% fibre). In the following 12-weeks, structured food reintroduction phase was made. Thereafter, participants managed their own energy restricted food intake and lifestyle changes for 6 months. 2) Physical activity intervention: Physical activity support initially focused on walking (with an aim of at least 10 000 steps per day), followed by the recommendation of increasing unsupervised activity to at least 150 min/week. Participants were provided with an accelerometer and were directed to smartphone apps to monitor food intake and activity.	Usual diabetes medical care	At baseline and 12 months WC, SBP; DBP; LDL; HDL and HbA1c were evaluated

The number of patients per study ranged widely from 31 to 3645 patients. The mean age is associated with adulthood, ranging from 41.9 to 60.0 years. The proportion of patients that were female had a wide range (from 8.5% and 87.4%). The length of studies ranged from 3 to 12 months, with 5 studies with 12-month duration. The time of post-intervention evaluations ranged from 3 to 24 months. Related to diet intervention, in 5 studies it was applied diet prescription [8, 9, 11, 13, 14] and in 4 studies diet education [8, 10, 12, 13]. Regarding physical activity interventions, in 6 studies it was applied physical activity advice [8-10, 12-14] and in 4 studies participants integrated an exercise program (supervised exercise) [8, 9, 11, 13].

3.3. Comparison of cardiovascular risk factos between groups

In the study of Chee et al. (2017) [8], authors found that at 6 months:

1) BMI decreased significantly in IG1 (-2.3 ± 0.4 kg/m^2, $p < 0.001$) and IG2 (-2.0 ± 0.4 kg/m^2; $p < 0.001$) but not in CG (-0.1 ± 0.2 kg/m^2; $p = 0.702$);

2) WC decrease significantly in IG1 (-4.0 ± 1.1 cm, $p=0.002$) but not in IG2(-2.7 ± 1.0 cm,

p=0.062) and CG (−0.5±0.5 cm, p=0.960);

3) SBP decreased significantly in IG1 (−9 ± 2 mm Hg, p<0.001) and IG2 (−9 ± 2 mmHg, p=0.001), but not in CG (−1 ± 2 mm Hg, p=1.000);

4) DBP significantly lowered in IG2 (−6 ± 2 mm Hg, p=0.008), but not in the IG1 (−3 ± 1 mm Hg, p=0.442) and CG (−1 ± 1 mm Hg, p=0.980);

5) LDL did not reach significant differences in IG1 (−0.08 ± 0.08 mmol/L, p=0.980) and in IG2 (−0.18 ± 0.09 mmol/L, p=0.386). On the opposite way, LDL reach a significant decrease on CG (−0.26 ± 0.07 mmol/L, p=0.005);

6) HDL did not reach significant differences in IG1 (0.01 ± 0.03 mmol/L, p=1.000), IG2 (0.05 ± 0.04 mmol/L, p=0.888) and CG (0.002 ± 0.03 mmol/L, p = 1.000);

7) HbA1c decreased significantly in IG1 (−1.1 ± 0.1%, p < 0.001) and IG2 (−0.5 ± 0.1%; p = 0.001) but not in CG (−0.2 ± 0.1%; p = 0.231)

In the study of Johansen et al. (2017) [9], results at 12 months were:

1) the mean values of BMI decreased in both groups (-2.01 kg/m^2 in IG and -0.69 kg/m^2 in CG; between group difference of -1.32 kg/m^2). Intervention group significantly decrease mean values of BMI when compared to CG (p = 0.001).

2) the mean values of SBP decreased in both groups (-1.5 mmHg in IG and -3.7 mmHg in CG; between group difference of 2.2 mmHg), but non statistical significance was found between groups (p = 0.37).

3) the mean values of DBP decreased in both groups (-1.4 mmHg in IG and -3.4 mmHg in CG; between group difference of 2.0 mmHg), but non statistical significance was found between groups (p = 0.28).

4) the mean values of LDL decreased in both groups (12.8 mg/dl in IG and 11.2 mg/dl in CG; between group difference of 1.6 mg/dl), but non statistical significance was found between groups (p = 0.79).

5) the mean values of HDL decreased in both groups (8.3 mg/dl in IG and 5.4 mg/dl in CG; between group difference of 2.9 mg/dl), but non statistical significance was found between groups (p = 0.13).

6) the mean values of HbA1c decreased in both groups (-0.31% in IG and -0.04% in CG; between group difference of -0.26%), but non statistical significance was found between groups (p = 0.15).

In the study of Kempf et al. (2017) [10], differences on cardiovascular risk factos between intervention and control group at 3 months was:

1) BMI reduction at 3 months was significantly higher in the Intervention group (-2.0 kg/m^2 vs. -0.3 kg/m^2; $p < 0.0001$).

2) SBP reduction at 3 months was significantly higher in the Intervention group (-6.0 mmHg vs. 1 mmHg; $p < 0.05$).

3) DBP reduction at 3 months was not significantly higher in the Intervention group (-13.0 mmHg vs. -1 mmHg; *p* value not presented).

4) LDL change during the 3 months 3 months was not significantly higher in the Intervention group (-3.0 mg/dl vs. -1.0 mg/dl; *p* value not presented).

5) HDL change during the 3 months 3 months was not significantly higher in the Intervention group (1.0 mg/dl vs. 1.0 mg/dl; *p* value not presented).

6) HbA1c reduction at 3 months was significantly higher in the Intervention group (-1.1% vs. -0.2%; $p < 0.001$).

In the study of Larsen et al. (2019) [11], the evolution of cardiovascular risk factos at 24 months was:

1) in BMI, decrease of 0.45 kg/m^2 on intervention group and 0.31 kg/m^2 on control group, with no statistically differences between groups (p=0.74).

2) in SBP, no differences in its evolution on intervention group and an increase of 1.3 mmHg on control group, with no statistically differences between groups (p=0.59).

3) in DBP, decrease of 0.45 mmHg on intervention group and na increase of 1.0 mmHg on control group, with no statistically differences between groups (p=0.57).

4) in LDl, increase of 0.5 mmol/L on intervention group and 0.4 mmol/L on control group, with no statistically differences between groups (p=0.71).

5) in HDL, increase of 0.1 mmol/L on intervention group and no differences in its evolution on control group, with no statistically differences between groups (p=0.19).

6) in HbA1c, increase of 2.7 mmol/mol on intervention group and 3.2 mmol/mol on control group, with no statistically differences between groups (p=0.80).

In the study of Lynch (2019) [12], cardiovascular risk factos were evaluated at 12 and 18 months and the findings were:

At 12 months:

1) BMI decreased 0.7 kg/m^2 on intervention group and 0.2 kg/m^2 on control group, with no statistically differences between groups (*p* value non stated).

2) SBP decreased 0.9 mmHg on intervention group and 0.1 mmHg on control group, with no statistically differences between groups (*p* value non stated).

3) DBP decreased 0.3 mmHg on intervention group and increased 0.6 mmHg on control group, with no statistically differences between groups (*p* value non stated.).

4) HbA1c decreased 0.58% on intervention group and 0.33% on control group, with no statistically differences between groups (*p* value non stated).

At 18 months:

1) BMI decreased 0.5 kg/m^2 on intervention group and 0.8 kg/m^2 on control group, with no statistically differences between groups (*p* value non stated).

2) SBP increased 1.7 mmHg on intervention group and decreased 3.9 mmHg on control group. Statistical differences were noticed in favour of control group ($p < 0.05$).

3) DBP mantained with equal mean values on intervention group and decreased 0.7 mmHg on control group, with no statistically differences between groups (*p* value non stated).

4) HbA1c decreased 0.58% on intervention group and 0.33% on control group, with no statistically differences between groups (*p* value non stated).

In the study of Matushita et al. (2020) [13], the main results of cardiovascular risk factos in both groups in the 24-mont follow-up period were:

1) BMI decrease 0.6 kg/m^2 on intervention group and increase of 0.1 kg/m^2 on control group, with statistically differences between groups ($p < 0.001$).

2) WC decrease 1.5 cm on intervention group and increase of 0.4 cm on control group, with statistically differences between groups ($p < 0.001$).

3) SBP increase 0.1mmHg on intervention group and 0.7 mmHg on control group, with no statistically differences between groups ($p=0.643$).

4) DBP decrease 0.5 mmHg on intervention group and increase of 0.5 mmHg on control group, with no statistically differences between groups ($p=0.658$).

5) LDL, decrease 5.5 mg/dl on intervention group and 1.6 mg/dl on control group, with no statistically differences between groups ($p=0.084$).

6) HDL increase 1.7 mg/dl on intervention group and 1.0 mg/dl on control group, with statistically differences between groups ($p < 0.001$)

7) HbA1c decrease 0.04% on intervention group and increase 1.02% on control group, with statistically differences between groups ($p < 0.001$).

In the study of Taheri et al. (2020) (14), results were:

1) WC decrease 11.4 cm on intervention group and 4.0 cm on control group, with statistically differences between groups ($p < 0.0001$).

2) SBP decrease 5.6 mmHg on intervention group and 2.2 mmHg on control group, with no statistically differences between groups (p=0.827).

3) DBP decrease 0.5 mmHg on intervention group and increase of 0.5 mmHg on control group, with no statistically differences between groups (p=0.177).

4) LDL increase 0.30 mmol/L on intervention group and decrease 0.366 mmol/L on control group, with statistically differences between groups ($p < 0.0001$).

5) HDL increase 0.05 mmol/L on intervention group and 0.03 mmol/L on control group, with statistically differences between groups ($p = 0.033$)

6) HbA1c decrease 0.89% on intervention group and 0.35% on control group, with statistically differences between groups ($p = 0.020$).

The main results of this review were that lifestyle interventions addressed to T2D patients were effective in the significative reduction of 1) BMI mean values in 66.6% of RCTs (4 out of 6); 2) WC mean values in 100% of RCTs (3 out of 3); 3) SBP mean values in 28.6% of RCTs (2 out of 7); 4) DBP mean values in 14.3% of RCTs (1 out of 7); 5) HbA1c mean values in 57.1% of RCTs (4 out of 7) and in the significant increase of 6) HDL mean values in 33.3% of RCTs (2 out of 6). Lifestyle interventions was not effective in the significative reduction of LDL mean values.

4.4. Data of cardiovascular risk factors on intervention groups

Table 2 described the detailed data regarding cardiovascular risk factors on intervention groups.

Table 2. Detailed data regarding the evolution of cardiovascular risk factors on intervention group(s).

RCT /Country	Body mass index (kg/m^2)	Waist Circumference (cm)	Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)	LDL- C (mmol/L)	HDL- C (mmol/L)	HbA1c %)
Chee et al. (2017) (8) / Malaysia	INT 1 Baseline: 31.8 ± 0.9 6 months: 29.5 ± 0.9 INT 2 Baseline: 30.5 ± 0.6 6 months: 28.5 ± 0.7	INT 1 Baseline: 102.9 ± 1.9 6 months: 98.9 ± 1.8 INT 2 Baseline: 101.8 ± 1.4 6 months: 99.1 ± 1.6	INT 1 Baseline: 134.0 ± 2.0 6 months: 124.0 ± 2.0 INT 2 Baseline: 136.0 ± 2.0 6 months: 127.0 ± 2.0	INT 1 Baseline: 77.0 ± 1.0 6 months: 74.0 ± 1.0 INT 2 Baseline: 79.0 ± 1.0 6 months: 73.0 ± 2.0	INT 1 Baseline: 2.72 ± 0.1 6 months: 2.63 ± 0.1 INT 2 Baseline: 2.94 ± 0.1 6 months: 2.76 ± 0.1	INT 1 Baseline: 1.31 ± 0.04 6 months: 1.32 ± 0.04 INT 2 Baseline: 1.23 ± 0.04 6 months: 1.28 ± 0.05	INT 1 Baseline: 8.0 ± 0.1 6 months: 6.9 ± 0.1 INT 2 Baseline: 8.1 ± 0.1 6 months: 7.6 ± 0.2
Johansen et al. (2017) (9) / Denmark	Baseline: 31.4 ± 3.9 12 months: -2.0 (change)	Not evaluated	Baseline: 127± 14 12 months: -1.5 (change)	Baseline: 79.0 ± 8.0 12 months: -1.4 (change)	* Baseline: 92.7 12 months: +12.8 (change)	* Baseline: 47.3 ± 13.2 12 months: +8.3 (change)	Baseline: 6.7 ± 0.8 12 months: -0.3 (change)
Kempf et al. (2017) (10) / Germany	Baseline: 35.3 ± 5.9 3 months: 33.3 ± 6.0	Not evaluated	Baseline: 139 ± 16 3 months: 133 ± 15	Baseline: 93 ± 10 3 months: 80 ± 9	* Baseline: 115 ± 40 3 months: 112 ± 36	* Baseline: 46 ± 12 3 months: 47 ± 13	Baseline: 8.4 ± 1.3 3 months: 7.3 ± 1.1
Larsen et al. (2019) (11) / Denmark	Baseline: 31.5 ± 3.9 24 months: -0.45 (change)	Not evaluated	Baseline: 127.0 ± 14.0 24 months: 0.0 (change)	Baseline: 79.0 ± 9.0 24 months: -0.1 (change)	Baseline: 2.4 ± 3.9 24 months: +0.5 (change)	Baseline: 1.2 ± 0.3 24 months: +0.1 (change)	** Baseline: 49.1 ± 9.1 24 months: +2.7 (change)
Lynch et al. (2019) (12) / USA	Baseline: 34.6* 12 months: -0.7 (change) 18 months: -0.5 (change)	Not evaluated	Baseline: 130.5* 12 months: -0.9 (change) 18 months: 1.7 (change)	Baseline: 79.3* 12 months: -0.3 (change) 18 months: 0.0(change)	Not evaluated	Not evaluated	Baseline: 8.6 12 months: -0.63 (change) 18 months: -0.58 (change)
Matushita et al. (2020) (13) / Japan	Baseline: 25.8 ± 0.1 24 months: 25.2 ± 0.2	Baseline: 89.5 ± 0.4 24 months: 88.0 ± 0.4	Baseline: 126.2 ± 0.6 24 months: 126.3 ± 0.6	Baseline: 78.7 ± 0.4 24 months: 78.2 ± 0.5	* Baseline: 131.6 ± 1.2 24 months: 126.1 ± 1.2	* Baseline: 57.3 ± 0.6 24 months: 59.0 ± 0.6	Baseline: 6.09 ± 0.03 24 months: 6.05 ± 0.03
Taheri et al. (2020) (14) / Qatar	Not evaluated	Baseline: 113.2 ± 12.5 12 months: 102.9 ± 14.0	Baseline: 131.1 ± 14.6 12 months: 124.7 ± 11.9	Baseline: 83.7 ± 8.9 12 months: 79.5 ± 8.4	Baseline: 3.01 ± 0.9 12 months: 3.29 ± 0.9	Baseline: 1.10 ± 0.4 12 months: 1.15 ± 0.3	Baseline: 6.95 ± 1.4 12 months: 5.96 ± 0.8

*Results presented in mg/dl; ** Results presented in mmol/mol

4. Discussion

This review summarizes the effects of lifestyle interventions on cardiovascular risk factors in adults with type 2 diabetes. In general, these studies indicated a benefit of lifestyle interventions on risk factors of cardiovascular disease in T2D patients. However not all findings were consistent across all studies. Lifestyle interventions were effective in high-scale (more than 50% of interventions success) on the significant reduction of BMI, WC and HbA1c and in low-scale (less than 50% of interventions success) on the significant reduction of SBP, DBP and significant increase of HDL. No lifestyle interventions effects were noticed regarding the decrease of LDL mean values.

4.1. Body Mass Index

World Health Organization (2021) [15] classifies individuals with BMI ≥ 30 kg/m^2 as obese. According to Ortega et al. (2016) [16], obesity has a positive association with higher risk of cardiovascular disease incidence and mortality. In almost all studies from this review that evaluated BMI mean values (5 out of 6), intervention group had baseline values ≥ 30 kg/m^2.

Interventions regarding the improvement of eating habits and physical activity behaviors are considered the cornerstone of obesity management [17].

Although it is not simple for T2D patients to lose weight (18), in 60% of those 5 RCTs [8-10], lifestyle interventions were effective in the significant reduction of BMI mean values, but in only 40% of RCTs [8, 9] that value reach values below 30 kg/m^2. The fact that these 2 studies used at least 3 strategies to improve diet and physical activity behaviors (diet prescription; physical activity advice and exercise program) may have contributed to these results.

4.2. Waist circumference

There is a direct association between abdominal obesity and risk of type 2 diabetes. Risk of type 2 diabetes duplicates with high values of abdominal obesity [19].

Abdominal obesity is considered an independent cardiovascular risk factor [20]. Waist circumference is the outcome most used to assess abdominal obesity as it provides a measure of both intra-abdominal and subcutaneous abdominal adipose tissue [21].

In all studies from this review that evaluated WC [8, 13, 14], lifestyle interventions were effective in the significative reduction of this outcome. As the optimal values for waist circumference differ by gender, it is difficult to discuss our results, as it were not separated by gender [22].

4.3. Blood pressure

Hypertension, classified as SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg, is an independent cardiovascular risk factor [23].

Hypertension and Diabetes are two diseases frequently related, as most patients with Hypertension exhibit insulin resistance. Prevalence of hypertension in patients with diabetes is two times higher when compared with patients without diabetes [24].

In this review, in neither study that evaluated SBP mean values (0 out of 7), intervention group had baseline values above 140 mmHg, which means a good hypertension management from participants that integrated theses studies. In 28.6% of RCTs [8, 10] , lifestyle interventions were effective in the significant reduction of SBP mean values.

In what concerns DBP, on only 14.3% of RCTs that evaluated DBP mean values (1 out of 7 studies) [8], intervention group had baseline values above 90 mmHg, which is a positive indicator of hypertension control. In this RCT [8], lifestyle intervention allowed a significative reduction of DBP mean values below 90 mmHg in one of the intervention groups when compared with control group. On the other 6 studies, where baseline values of DBP were already below 90 mmHg, it was found no significant decrease in this outcome in the group exposed to lifestyle intervention when compared to control group.

4.4. Cholesterol

Dyslipidemia is one of the main cardiovascular risk factors in T2D patients. High LDL and low HDL concentrations are two characteristic features of these patients [25].

According to the Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults [26], optimal LDL values are considered to be less than 100 mg/dl or 2.6 mmol/L and low HDL values under 40 mg/dl or 1.02 mmol/L.

In our review, in 66.7% of RCTs that evaluated LDL mean values (4 out of 6), participants from intervention group had baseline values above 100 mg/dl or 2.6 mmol/L. In neither of those RCTs, lifestyle intervention was effective on the significative reduction of LDL mean values. On the other 2 studies, where baseline values of LDL were already below 100 mg/dl or 2.6 mmol/L, in 1 study [14] there was a significant decrease in this outcome in favour of control group. This indicates a failure of the lifestyle intervention used in this study to reduce LDL mean values.

Regarding HDL mean values, in neither study (0 out of 6), participants from intervention group had baseline values below 40mg/d or 1.02 mmol/L, which is a positive indicator on patients that are customed to have low levels of this lipoprotein [27]. Only in 33.3% of RCTs (2

out of 6) that had baseline values of HDL above 40mg/d or 1.02 mmol/L, lifestyle intervention was effective in the significative increase of this outcome [13, 14].

4.5. Glycated hemoglobin

HbA1c is the gold standard outcome of long-term glycemic control [28] and is used as the main diagnostic test for the detection of diabetes (HbA1c $\geq$ 6.5%).

In 85.7% of RCTs that evaluated HbA1c mean values (6 out of 7), participants from intervention group had baseline values above 6.5% or 47.5 mmol/mol, which indicates a poor long-term glycemic control. In only 33.3% of those RCTs (8, 14), lifestyle interventions were effective in the significant reduction of HbA1c mean values below 6.5% or 47.5 mmol/mol.

Studies presented in this review varied widely in what concerns the duration of interventions, ranging from 3 to 12 months, with 2 studies [11, 14] having a follow-up period. Steinsbeck et al. [29], in a systematic review of self-management education in T2D patients, concluded that interventions held between 6 and 10 months achieved the best results in cardiovascular risk factors. Loveman et al. [30] adds that longer-interventions (higher than 6 months) with a shorter duration between the end of the intervention and the follow-up evaluation had higher benefits.

Regarding exercise interventions, literature indicates higher benefits when supervised exercise was used instead of non-supervised exercise [31-33]. Thus whenever possible interventions should apply supervised exercise for the improvement of cardiovascular risk factors on type 2 diabetes patients. According to a narrative review by Mendes et al. [34] scientific organisations recommended: 1) a minimum of 150 min of moderate-to-vigorous intensity aerobic activity (walking and/or jogging), spread over a minimum of 3 days a week; 2) resistance exercise for major muscle groups at least 2 days a week; and 3) flexibility exercises. Thus future interventions should follow these recommendations regarding physical activity intervention.

In what concerns diet interventions, there is not a “one size fits all” eating pattern, as different macronutrients distributions can improve cardiovascular risk factors in type 2 diabetes patients [35]. Thus it is extremelly difficult to prescribe the ideal diet for this population. Nutrition education for the improvement of disease self-management is also crucial. Aspects such as the decrease of total energy intake, preference for unsaturated fats, total fat intake below 30% of total energy intake, saturated fatty acids intake below 10% of total energy intake, fiber intake of 14g/1000kcal, eating at least three servings of vegetables and up to three servings of fruit every day should integrate the advices referred on nutrition education programs [35,36].

4.6. Strengths

As strengths of this review we can refer the compilation of only randomized controlled trials, the review of recent published studies (between 2016 and 2021); the focus on adulthood and the presence of at least 3 cardiovascular risk factors in each one of the studies.

4.7. Limitations

The main limitations of this review were: the search was made in only one Database, few number of studies that meet the inclusion criteria, heterogeneity of the characetristics of lifestyle interventions; little detail in some of the lifestyle interventions.

5. Conclusions

In general, these studies indicated a benefit of lifestyle interventions on risk factors of cardiovascular disease in T2D patients. However not all findings were consistent across all studies. Lifestyle interventions were effective in high-scale (more than 50% of interventions success) on the significant reduction of BMI, WC and HbA1c and in low-scale (less than 50% of interventions success) on the significant reduction of SBP, DBP and significant increase of HDL. No lifestyle interventions effects were noticed regarding the decrease of LDL mean values.

Future lifestyle interventions with the aim of improving cardiovascular risk factors in type 2 diabetes patients should have 6 to 10 months of duration with short pause between the end of the intervention and the follow-up evaluation, and be based on actual exercise and diet recommendations for this population.

6. References

1. Henning RJ. Type-2 diabetes mellitus and cardiovascular disease. Future Cardiol. 2018;14(6):491-509.

2. Khan MAB, Hashim MJ, King JK, Govender RD, Mustafa H, Al Kaabi J. Epidemiology of Type 2 Diabetes - Global Burden of Disease and Forecasted Trends. J Epidemiol Glob Health. 2020;10(1):107-11.

3. Lorber D. Importance of cardiovascular disease risk management in patients with type 2 diabetes mellitus. Diabetes Metab Syndr Obes. 2014;7:169-83.

4. Al Slail FY, Abid O, Assiri AM, Memish ZA, Ali MK. Cardiovascular risk profiles of adults with type-2 diabetes treated at urban hospitals in Riyadh, Saudi Arabia. J Epidemiol Glob Health. 2016;6(1):29-36.

5. Hashim MJ, Mustafa H, Ali H. Knowledge of diabetes among patients in the United Arab Emirates and trends since 2001: a study using the Michigan Diabetes Knowledge Test. East Mediterr Health J. 2017;22(10):742-8.

6. Chen L, Pei JH, Kuang J, Chen HM, Chen Z, Li ZW, et al. Effect of lifestyle intervention in patients with type 2 diabetes: a meta-analysis. Metabolism. 2015;64(2):338-47.

7. Berkowitz SA, Meigs JB, Wexler DJ. Age at type 2 diabetes onset and glycaemic control: results from the National Health and Nutrition Examination Survey (NHANES) 2005-2010. Diabetologia. 2013;56(12):2593-600.

8. Chee WSS, Gilcharan Singh HK, Hamdy O, Mechanick JI, Lee VKM, Barua A, et al. Structured lifestyle intervention based on a trans-cultural diabetes-specific nutrition algorithm (tDNA) in individuals with type 2 diabetes: a randomized controlled trial. BMJ Open Diabetes Res Care. 2017;5(1):e000384.

9. Johansen MY, MacDonald CS, Hansen KB, Karstoft K, Christensen R, Pedersen M, et al. Effect of an Intensive Lifestyle Intervention on Glycemic Control in Patients With Type 2 Diabetes: A Randomized Clinical Trial. Jama. 2017;318(7):637-46.

10. Kempf K, Altpeter B, Berger J, Reuß O, Fuchs M, Schneider M, et al. Efficacy of the Telemedical Lifestyle intervention Program TeLiPro in Advanced Stages of Type 2 Diabetes: A Randomized Controlled Trial. Diabetes Care. 2017;40(7):863-71.

11. Ried-Larsen M, Johansen MY, MacDonald CS, Hansen KB, Christensen R, Wedell-Neergaard AS, et al. Type 2 diabetes remission 1 year after an intensive lifestyle intervention: A secondary analysis of a randomized clinical trial. Diabetes Obes Metab. 2019;21(10):2257-66.

12. Lynch EB, Mack L, Avery E, Wang Y, Dawar R, Richardson D, et al. Randomized Trial of a Lifestyle Intervention for Urban Low-Income African Americans with Type 2 Diabetes. J Gen Intern Med. 2019;34(7):1174-83.

13. Matsushita M, Muramoto A, Nomura E, Eguchi Y, Kato A, Sano Y, et al. The Smart Life Stay (SLS) program: effects of a lifestyle intervention program in combination with health tourism and health guidance for type 2 diabetes. Nutr Diabetes. 2020;10(1):33.

14. Taheri S, Zaghloul H, Chagoury O, Elhadad S, Ahmed SH, El Khatib N, et al. Effect of intensive lifestyle intervention on bodyweight and glycaemia in early type 2 diabetes (DIADEM-I): an open-label, parallel-group, randomised controlled trial. Lancet Diabetes Endocrinol. 2020;8(6):477-89.

15. World Health Organization. Obesity and Overweight [Internet]. Geneve: WHO; 2021 [Available from: https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight.

16. Ortega FB, Lavie CJ, Blair SN. Obesity and Cardiovascular Disease. Circ Res. 2016;118(11):1752-70.

17. Kelley CP, Sbrocco G, Sbrocco T. Behavioral Modification for the Management of Obesity. Prim Care. 2016;43(1):159-75, x.

18. Norris SL, Zhang X, Avenell A, Gregg E, Bowman B, Serdula M, et al. Long-term effectiveness of lifestyle and behavioral weight loss interventions in adults with type 2 diabetes: a meta-analysis. Am J Med. 2004;117(10):762-74.

19. Freemantle N, Holmes J, Hockey A, Kumar S. How strong is the association between abdominal obesity and the incidence of type 2 diabetes? Int J Clin Pract. 2008;62(9):1391-6.

20. Dale CE, Fatemifar G, Palmer TM, White J, Prieto-Merino D, Zabaneh D, et al. Causal Associations of Adiposity and Body Fat Distribution With Coronary Heart Disease, Stroke Subtypes, and Type 2 Diabetes Mellitus: A Mendelian Randomization Analysis. Circulation. 2017;135(24):2373-88.

21. Klein S, Allison DB, Heymsfield SB, Kelley DE, Leibel RL, Nonas C, et al. Waist circumference and cardiometabolic risk: a consensus statement from Shaping America's Health: Association for Weight Management and Obesity Prevention; NAASO, The Obesity Society; the American Society for Nutrition; and the American Diabetes Association. Am J Clin Nutr. 2007;85(5):1197-202.

22. Lean ME, Han TS, Morrison CE. Waist circumference as a measure for indicating need for weight management. Bmj. 1995;311(6998):158-61.

23. Pescatello LS, MacDonald HV, Lamberti L, Johnson BT. Exercise for Hypertension: A Prescription Update Integrating Existing Recommendations with Emerging Research. Curr Hypertens Rep. 2015;17(11):87.

24. Petrie JR, Guzik TJ, Touyz RM. Diabetes, Hypertension, and Cardiovascular Disease: Clinical Insights and Vascular

Mechanisms. Can J Cardiol. 2018;34(5):575-84.

25. Mooradian AD. Dyslipidemia in type 2 diabetes mellitus. Nat Clin Pract Endocrinol Metab. 2009;5(3):150-9.

26. Expert Panel on Detection EaToHBCiA. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). Jama. 2001;285(19):2486-97.

27. Grant RW, Meigs JB. Prevalence and treatment of low HDL cholesterol among primary care patients with type 2 diabetes: an unmet challenge for cardiovascular risk reduction. Diabetes Care. 2007;30(3):479-84.

28. Peter A, Fritsche A, Stefan N, Heni M, Häring HU, Schleicher E. Diagnostic value of hemoglobin A1c for type 2 diabetes mellitus in a population at risk. Exp Clin Endocrinol Diabetes. 2011;119(4):234-7.

29. Steinsbekk A, Rygg L, Lisulo M, Rise MB, Fretheim A. Group based diabetes self-management education compared to routine treatment for people with type 2 diabetes mellitus. A systematic review with meta-analysis. BMC Health Serv Res. 2012;12:213.

30. Loveman E, Frampton GK, Clegg AJ. The clinical effectiveness of diabetes education models for Type 2 diabetes: a systematic review. Health Technol Assess. 2008;12(9):1-116, iii.

31. Nicolaï SP, Kruidenier LM, Leffers P, Hardeman R, Hidding A, Teijink JA. Supervised exercise versus non-supervised exercise for reducing weight in obese adults. J Sports Med Phys Fitness. 2009;49(1):85-90.

32. Gajanand T, Keating SE, Brown WJ, Hordern MD, Fassett RG, Coombes JS. Comparing the Efficacy of Supervised and Unsupervised Exercise Training on Glycaemic Control in Type 2 Diabetes: A Systematic Review. Curr Diabetes Rev. 2020;16(6):570-9.

33. Balducci S, Zanuso S, Nicolucci A, De Feo P, Cavallo S, Cardelli P, et al. Effect of an intensive exercise intervention strategy on modifiable cardiovascular risk factors in subjects with type 2 diabetes mellitus: a randomized controlled trial: the Italian Diabetes and Exercise Study (IDES). Arch Intern Med. 2010;170(20):1794-803.

34. Mendes R, Sousa N, Almeida A, Subtil P, Guedes-Marques F, Reis VM, et al. Exercise prescription for patients with type 2 diabetes-a synthesis of international recommendations: narrative review. Br J Sports Med. 2016;50(22):1379-81.

35. Evert AB, Boucher JL, Cypress M, Dunbar SA, Franz MJ, Mayer-Davis EJ, et al. Nutrition therapy recommendations for the management of adults with diabetes. Diabetes Care. 2014;37 Suppl 1:S120-43.

36. International Diabetes Federation. IDF Diabetes Atlas [Internet]. 8th ed.. Brussels: IDF; 2017. Available from: https://diabetesatlas.org/upload/resources/previous/files/8/IDF_DA_8e-EN-final.pdf.