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**Projet SPICES : sélection parmi 5 recommandations de bonne pratique pour la prévention des maladies cardiovasculaires via les procédures AGREE II et ADAPTE. Identification des références bibliographiques des recommandations internationales, “ 2013 AHA/ACC/TOS. Guideline for the Management of Overweight and Obesity in Adults ” et “ 2015 NICE guideline: Preventing excess weight gain ”, à intégrer dans la matrice de recherche de l’étude SPICES**

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FACULTÉ DE MÉDECINE

**THESE DE DOCTORAT EN MEDECINE**

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- **Sélection parmi 5 recommandations de bonne pratique pour la prévention des maladies cardiovasculaires via les procédures AGREE II et ADAPTE.**
- **Identification des références bibliographiques des recommandations internationales, « 2013 AHA/ACC/TOS : Guideline for the Management of Overweight and Obesity in Adults » et « 2015 NICE guideline : Preventing excess weight gain », à intégrer dans la matrice de recherche de l'étude SPICES.**

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A Clément.

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## **Abstract:**

### **Introduction:**

Cardiovascular diseases (CVD) are the first cause of mortality in the world. Despite health-care prevention policies, the global burden of CVD increases. The SPICES project was created to implement innovative interventions about CVD prevention in Europe and Sub-Saharan Africa. The first step was a systematic review of the international recommendations on the topic using the ADAPTE procedure.

### **Method:**

ADAPTE Step 11 assessed quality of 5 guidelines with the AGREE II Instrument. Inclusion was based on an overall assessment score  $\geq 5$ . ADAPTE Step 13 was extraction of recommendations from “2013 AHA/ACC/TOS: Guideline for the Management of Overweight and Obesity in Adults” and “2015 NICE guideline: Preventing excess weight gain”. Recommendations were included if they were A or B level of evidence, 1++, 1+, 2++, 2+, Strong or Class 1. Recommendations were excluded if they focused on secondary or tertiary CVD prevention, diagnostic procedures, pharmacological or surgical treatments. References of selected recommendations were gathered in a matrix. If no grading of recommendations, references were included if they were randomized controlled trials or cohort interventional surveys.

### **Results:**

2 guidelines were included and 3 excluded. Regarding ADAPTE step 13, 17 recommendations and 316 references were selected and extracted to the research matrix.

### **Conclusion:**

A great disparity in the quality of guidelines and references was found. Main limitation was lack of time. The research group had to stop at a draft matrix. The next step will be finalization of the matrix to extract interventions and implementation from references.

## **Résumé:**

### **Introduction :**

Les maladies cardiovasculaires (MCV) sont la première cause de mortalité dans le monde. Malgré les politiques de prévention des soins de santé, le fardeau mondial des MCV augmente. Le projet SPICES a été créé pour mettre en œuvre des interventions innovantes sur la prévention des MCV en Europe et en Afrique subsaharienne. La première étape consistait à réaliser une revue systématique des recommandations internationales sur le sujet en utilisant la procédure ADAPTE.

### **Méthode :**

L'étape 11 d'ADAPTE a évalué la qualité de 5 recommandations de bonne pratique (RBP) avec l'instrument AGREE II. L'inclusion était basée sur un score d'évaluation globale  $\geq 5$ . L'étape 13 d'ADAPTE a été l'extraction des recommandations de "2013 AHA/ACC/TOS: Guideline for the Management of Overweight and Obesity in Adults" et "2015 NICE guideline: Preventing excess weight gain". Les recommandations ont été incluses si le niveau de preuve était A ou B, 1 ++, 1 +, 2 ++, 2+, Fort ou Classe 1. Elles ont été exclues si elles portaient sur la prévention secondaire ou tertiaire des MCV, des procédures de diagnostic, des traitements pharmacologiques ou chirurgicaux. Les références des recommandations sélectionnées ont été rassemblées dans une matrice. Pour les recommandations sans système de gradation, les références ont été incluses en cas d'essais contrôlés randomisés ou d'enquêtes interventionnelles de cohorte.

### **Résultats :**

2 RBP ont été incluses et 3 ont été exclues. Pour l'étape 13 d'ADAPTE, 17 recommandations et 316 références ont été sélectionnées et extraites dans la matrice.

### **Conclusion :**

Une grande disparité dans la qualité des RBP et des références a été constatée. La principale limitation a été le manque de temps. Le groupe de recherche a dû s'arrêter à un projet de matrice. L'étape suivante sera de finaliser la matrice pour extraire des références les interventions et leurs mises en œuvre.

## **I) Introduction :**

In 2015, non-communicable diseases (NCD) were the leading cause of death in the world. According to the World Health Organization (WHO), 70% of the 56.4 million global deaths were attributable to NCD. Cardiovascular diseases, cancers, diabetes and chronic lung diseases were the four main NCD (1). Cardiovascular diseases (CVD) like heart attacks and strokes, caused annually 17,7 million deaths (about 31% of all deaths worldwide) (2). In Europe, nearly half of deaths were due to CVD and a third of them concerned people under the age of 75 (3). In France, CVD caused more than 900.000 hospitalizations in 2013 and around 150.000 deaths in 2014 (4) (5). The most disadvantaged socio-economic countries were the most affected. More than 75% of CVD deaths occurred in low-income and middle-income countries (2). The global burden of CVD still increases. The number of deaths from stroke increased from 5.4 million in 2000 to 6.2 million in 2015 worldwide (6). According to estimates, global cardiovascular deaths are expected to increase from 16.7 million in 2002 to 23.3 million in 2030 (7).

An unhealthy diet, physical inactivity, smoking and the harmful use of alcohol are the key behavioral risk factors for CVD. They can lead to increased blood pressure, increased blood sugar, dyslipidemia and obesity, which are metabolic risk factors that lead to CVD (2). Each year, more than 7 million deaths were attributable to tobacco use, 4,1 million deaths to excess salt/sodium intake and 1,6 million deaths to insufficient physical activity. These deaths were avoidable and these behavioral and metabolic risk factors were modifiable (8).

To reduce CVD deaths, large-scale cost effectiveness interventions are possible (tobacco control policy, tax policy for food products high in fat, sugar and salt, development of pedestrian and bicycle paths to increase the physical activity of the population...) (2). Interventions focused on individuals are also possible, both in primary prevention and in secondary prevention using drugs or non-pharmacological interventions that have proven their effectiveness (2).

Non-pharmacological cardiovascular primary prevention measures have shown their ability to reduce exposure to risk factors by adopting a healthy lifestyle and smoking cessation (6). To adopt a healthy lifestyle, WHO recommends eating lots of fruits and vegetables (5 serving a day), reducing fat, sugar, alcohol consumption, salt intake and regularly exercising (a

minimum of 150 minutes of moderate-intensity physical activity during the week for adults) (9).

French National Authority for Health (HAS) recommends lifestyle modifications for each individual, regardless of cardiovascular risk level. HAS recommends to stop smoking and not to be exposed to tobacco, to eat a Mediterranean diet, by eating fish 2-3 times a week, 400 grams of fruits and vegetables a day, reducing salt intake. HAS recommends fighting a sedentary lifestyle, doing sport (to accumulate at least 150 min per week of moderate intensity activities, or 75 min of aerobic activities of high intensity, or a combination of both). Alcohol consumption is strongly discouraged. (10).

Health model of rich countries cannot be transposed to low-income countries because of the limitations of the health system (lack of health personnel, infrastructure, equipment and medicines, insufficient funding) (11). Cost-effective and easy-to-implement interventions would reduce the inequalities between these countries in terms of cardiovascular morbidity and mortality (12).

The SPICES (Scaling-up Packages of Interventions for Cardiovascular disease prevention in selected sites in Europe and Sub-Saharan Africa (SSA)) study is an international project involving Belgium, France, United Kingdoms, South Africa and Uganda. It aims to implement strategies of non-pharmacological primary cardiovascular prevention, especially for people having a limited access to cardiovascular prevention. Implementation science is a new field of research. Implementation studies are testing methods to extend at a large scale the systematic uptake of proven clinical treatments, practices, organizational and management interventions into routine practice, and to improve health. It includes the exploration of multiple influences on patients, healthcare professionals, and involves organizational behavior science techniques in healthcare or population settings (13).

SPICES project builds on progress in HIV / AIDS control in SSA and chronic disease management through innovative care for chronic diseases (ICCC framework), plan for WHO. ICCC framework was introduced in 2002 to improve chronic disease management. Creation of a healthcare triad is the central point of this model which is organized on 3 levels: microlevel, mesolevel and macrolevel. At the microlevel, a partnership between patients and families, health care teams and community supporters form a triad. The integration of mesolevel and macrolevel components, represented by the larger health care organization, the

broader community and the policy environment, allows for active patient and family involvement, supported by the community and the health care teams, in the management of chronic diseases (14). About HIV / AIDS control, WHO based its plan on four main themes: simplification of monitoring and treatment protocols, facilitation of access to antiretroviral therapy (ART), task shifting and involvement of the population and patients in the organization of this new system of care (15). For example, nurses have been trained in setting up and monitoring ART. The interventions implemented under this new WHO plan have demonstrated their effectiveness and cost-effectiveness in many countries in SSA (16)(17)(18)(19).

The SPICES team chose to retain a dozen of the most effective interventions for non-pharmacological primary prevention. The selected interventions would be grouped in the SPICES basket. Then community leaders could choose in the basket the ones they would use during the project. To select interventions, the SPICES consortium chose a new approach. A systematic review of the international recommendations on the topic was conducted following the ADAPTE procedure.

This research was a piece of the creation of the SPICES basket. The overall question of the review procedure was:

*Which lifestyle interventions related to smoking cessation, physical activity, healthy diet and weight loss are proven effective in reducing cardiovascular risk (primary /secondary outcomes) in primary prevention of cardiovascular diseases on primary health care and/or community level?*

*Which strategies for implementation of these interventions are proven to be effective (outcome measures on implementation)?*

The ADAPTE and AGREE II procedures were chosen to construct a research matrix from the references of the guidelines.

The ADAPTE procedure is a systematic approach for guideline developers created to quarry existing guidelines, to product new ones, adapted to a specific cultural and organizational context. Its purpose is to take advantage of existing guidelines in order to enhance the efficient production and use of high-quality adapted guidelines (20).This procedure is

structured by the use of the ADAPTE Manual and Resource Toolkit. One step of the ADAPTE procedure is to assess the quality of guideline by using the AGREE instrument.

The original AGREE instrument was published in 2003. It has since been improved to make it easier to use and to increase its reliability and validity, leading to the AGREE II instrument. AGREE II is a quality assessment grid of recommendations for clinical practice. This tool was developed because the potential benefits provided by the guidelines depend on their quality of elaboration. The AGREE II instrument assesses the methodological rigor and transparency of the guideline development process and address the problem of variability in the quality of guidelines. It is composed of 23 questions organized into six domains, followed by two general elements of evaluation. Each domain deals with a particular dimension of the quality of the guidelines.

The systematic review of international (Netherlands, Europe, USA, Australia) and of national (each country participating in the SPICES project) guidelines has been conducted from July to October 2017 by SPICES Project team. The ADAPTE Process methodology was partly used for the guideline review. ADAPTE steps 7 to 13 were carried out. The search was conducted on the G-I-N database (Guidelines International Network) and TRIP Database (Turning Research Into Practice). This review followed the PRISMA Statement quality criteria. After the identification and selection process of the guidelines, 48 guidelines were eligible for a full text evaluation by AGREE II instrument. Guidelines were assigned within a research group, the following guidelines were attributed to our study:

- 2013 AHA/ACC/TOS: Guideline for the Management of Overweight and Obesity in Adults (21),
- 2014 BC Guidelines: Cardiovascular Disease - Primary Prevention: Resource Guide for Physicians (22),
- 2014 UMHS Lipid Therapy Guideline update, Screening and Management of Lipids (23),
- 2015 BC Guidelines: A Guide for Patients: Management of Hypertension (24),
- 2012 WHO: Prevention and control of non-communicable diseases: guidelines for primary health care in low resource settings (25).

Guidelines selected by the AGREE II procedure were then analyzed to describe effective interventions and their implementation strategies. Data, references and interventions will be

further gathered in a research matrix. The research matrix will allow several uses, synthesis of the data, comparison of the recommendations, identification of the high-level recommendations. It will provide a basis for a discussion within the consortium to select the dozen of most effective interventions for non-pharmacological primary prevention.

Guidelines assessed within this study were:

- 2013 AHA/ACC/TOS: Guideline for the Management of Overweight and Obesity in Adults (21),
- 2015 NICE guideline: Preventing excess weight gain (26).

The research questions of the current study were:

- *Among the 5 attributed guidelines identified in the SPICES study, which guidelines should be selected using the AGREE II and ADAPTE procedures?*
- *In the 2 subsequent attributed guidelines what are the bibliographical references for non-pharmacological interventions in primary cardiovascular prevention to be included in the research matrix of the SPICES study?*

## II) Method:

This study was developed within the Département Universitaire de Médecine générale (DUMG) of Brest in a thesis workgroup. The group comprised medical trainees, junior researchers and a senior research teacher. The group met monthly to discuss difficulties encountered, to exchange their views on the work progress and to ascertain the procedure was followed.

Among the 48 guidelines eligible for a full text evaluation by AGREE II instrument, 27 guidelines were assigned to the Brest research team. Then guidelines were assigned to 6 medical trainees of the thesis workgroup concurrently with the three researchers. The study was conducted from June 2017 to January 2018.

The following assigned guidelines to this work were evaluated with the AGREE II Instrument:

- 2013 AHA/ACC/TOS: Guideline for the Management of Overweight and Obesity in Adults (21);
- 2014 BCGuidelines: Cardiovascular Disease - Primary Prevention: Resource Guide for Physicians (22);
- 2014 UMHS Lipid Therapy Guideline update, Screening and Management of Lipids (23);
- 2015 BCGuidelines: A Guide for Patients: Management of Hypertension (24);
- 2012 WHO: Prevention and control of non-communicable diseases: guidelines for primary health care in low resource settings (25);

To answer the research question, step 11, step 12 and step 13 of the ADAPTE procedure were used.

### **a) Step 11. Assess guideline quality (Using AGREE II instrument):**

Step 11 of the ADAPTE procedure was used to assess guideline quality with the AGREE II Instrument. After full text reading, researchers rated the 23 items on a 7-point scale, 1 being the worst and 7 being the best possible quality. Domain scores were calculated by summing up all the scores of the individual items in a domain and by scaling the total as a percentage of the maximum possible score for that domain. An overall assessment (OA) was scored. This

was not the calculated average of the item scores but was estimated independently as expected by the tool's developers.

The 23 items were distributed in 6 domains:

- Domain 1. Scope and Purpose
- Domain 2. Stakeholder Involvement
- Domain 3. Rigor of Development
- Domain 4. Clarity of Presentation
- Domain 5. Applicability
- Domain 6. Editorial Independence

Regarding the domain Scope and Purpose (items 1-3), the researcher ensured that the objective of the guideline, the health question and the target population were clearly described.

Regarding the domain Stakeholder Involvement (items 4-6), the researcher ensured that the guideline development group included individuals from all appropriate professional groups, the views and preferences of the target population and the target users.

Regarding the domain Rigor of development (items 7-14), the researcher ensured that the process used to collect and synthesize the evidence was suitable, the methods to formulate the recommendations, and to update them were provided.

Regarding the domain Clarity of Presentation (items 15-18), the researcher ensured that the language, structure and presentation of the guideline were suitable: specific and unambiguous recommendations, easily identifiable key recommendations.

Regarding the domain Applicability (items 19-21), the researcher ensured that barriers and facilitators were considered as well as an approach to improve their adoption.

Regarding the domain Editorial Independence (items 22-23), the researcher ensured that identification of biases resulting from conflicts of interest was considered.

As recommended by the ADAPTE Manual and Resource Toolkit (20), the thesis workgroup experimented AGREE II on a first guideline, *the 2016 European Guidelines on Cardiovascular Disease Prevention in Clinical Practice* (27), as a common training exercise. The members individually scored the guideline. Then the group had a meeting to compare the scoring, to discuss any question or discrepancy, and to reach a consensus about in the evaluation of each domain.

Each screened guideline was assessed independently with the AGREE II instrument by at least two researchers. To conclude the evaluation, the researchers assessed the quality of the guidelines by assigning the OA score and answering three questions: “*I would recommend this guideline for use. Yes - Yes, with modifications – No*”.

The selection of the guidelines for subsequent research was based on OA scores:

- All appraisers OA scores superior or equal to 5 (over 7): inclusion
- All appraisers OA scores inferior to 5: exclusion
- OA score around cut-off: exclusion (One OA score of 4 and one OA score of 5)
- Discrepant OA scores, i.e. difference of more than 1 point with at least one OA score being superior or equal to 5: discussion between appraisers and consensual decision.

#### **b) Step 12. Assess guidelines currency:**

Selected guidelines were published after 2011, the team considered that their bibliography was current and did not require re-evaluation.

#### **c) Step 13. Asses guideline content:**

A part of step 13 of the ADAPTE procedure consisted in creating a research matrix of recommendations to be evaluated. The following guidelines were assigned to this study:

- 2013 AHA/ACC/TOS: Guideline for the Management of Overweight and Obesity in Adults (21),
- 2015 NICE guideline: Preventing excess weight gain (26),

Their recommendations were listed in structured research matrix with the references related to recommendations. The structure of the guidelines, recommendations and references and the link between recommendations and related references were described. Recommendations on

lifestyle interventions were retained. Pharmacological and surgical interventions recommendations were excluded. Inclusion criteria for recommendations were:

- Recommendations with A or B level of evidence or 1++, 1 +, 2++, 2+ for NICE grading system,
- Strong or Class 1 recommendations (regardless of the level of evidence).
- For guidelines without recommendation grades, references were included if they were randomized controlled trials (RCTs), cohort interventional surveys, or systematic reviews and meta-analysis of such surveys.

Recommendations were excluded if they treated exclusively of:

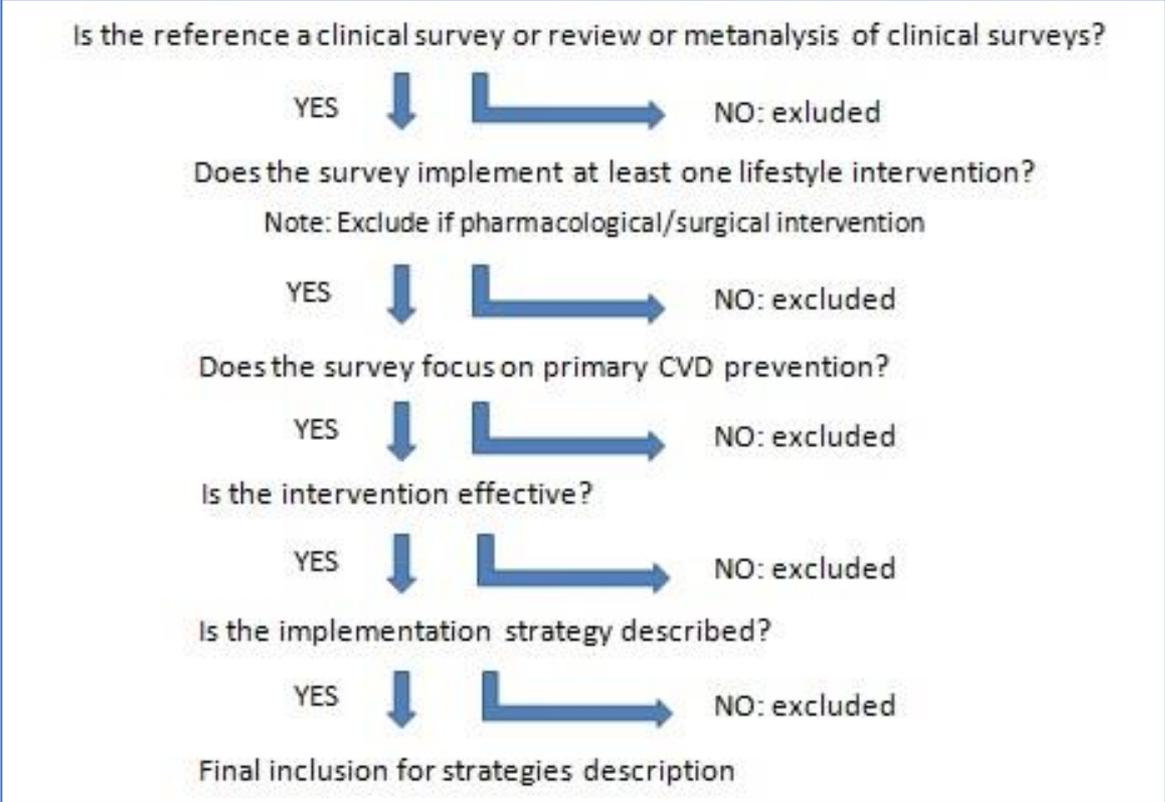
- Secondary or tertiary CVD prevention
- Diagnostic procedures
- Pharmacological or surgical treatments

Very-low calories diet were excluded as such interventions need a strict medical follow-up which is out of scope for SPICES project.

First references were defined as studies cited in the bibliography of the guidelines. Derived references were defined as studies included in meta-analysis and literature reviews cited by the guidelines. First and derived references of the recommendations were included into the research matrix. References were first included or excluded according to their title and abstract. Clinical surveys, review and meta-analysis of clinical surveys were included. Studies that did not focus on primary CVD prevention and did not include at least one lifestyle intervention were excluded. When a researcher was unsure about the inclusion of a study, the reference was included in the research matrix for later evaluation. Duplicates were searched for and removed.

The following protocol was used to select references from included recommendations:

Figure 1: Selection process for references inclusion



New members of the thesis workgroup worked later on the research matrix. Interventions and implementation strategies used in the included references were then described in details. They were ranked accordingly to their reliability and effectiveness.

### III) Results:

#### A) Step 11. Assess guideline quality (Using AGREE II instrument):

*Table 1: listbox of assigned guidelines.*

<u>Number of the guideline</u>	<u>Name of the guideline</u>	<u>Year of publication</u>
Guideline # 1	AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society.(21)	2013
Guideline # 2	BCGuidelines.ca: Cardiovascular Disease - Primary Prevention: Resource Guide for Physicians.(22)	2014
Guideline # 3	UMHS Lipid Therapy Guideline: Screening and Management of Lipids. (23)	2014
Guideline # 4	BCGuidelines.ca: Hypertension – Diagnosis and Management (24)	2015
Guideline # 5	Prevention and Control of Noncommunicable Diseases: Guidelines for primary health care in low-resource settings. WHO (25)	2012

Two guidelines were included and three guidelines were excluded after step 11 of the ADAPTE procedure.

OA scores of the guideline # 1 were 6 for the first appraiser, 5 for the second appraiser, the final decision was inclusion.

OA scores of the guideline # 2 were 3 for the first appraiser, 4 for the second appraiser, the final decision was exclusion.

OA scores of the guideline # 3 were 4 for the first appraiser, 3 for the second appraiser, the final decision was exclusion.

OA scores of the guideline # 4 were 2 for the first appraiser, 2 for the second appraiser, the final decision was exclusion.

OA scores of the guideline # 5 were 5 for the first appraiser, 5 for the second appraiser, the final decision was inclusion.

The AGREE scores are presented in Table 2 with the OA score for each evaluator, their comments and the final decision, inclusion or exclusion. Details of AGREE's score and all appraiser's comments for each item and for each domain were reported in appendix 1, 2, 3, 4 and 5.

Table 2: AGREE score results.

Guidelines	First appraiser evaluation	Second appraiser evaluation	Final decision
<b>Guideline # 1 : 2013 AHA/ACC/TOS</b>	<u>OA score:</u> 6 <u>Comment:</u> Insufficient info on implementation strategy + no formal cost analysis	<u>OA score:</u> 5 <u>Comment:</u> Assess global CV risk	Q1 – 1 Q2 – 1 Q3 – 0  <b>FD: INCLUSION</b>
<b>Guideline # 2 : 2014 BC Guidelines</b>	<u>OA score:</u> 3 <u>Comment:</u> NC	<u>OA score:</u> 4 <u>Comment:</u> Main limitation is research methodology	Q1 – 0 Q2 – 0 Q3 – 2  <b>FD: EXCLUSION</b>
<b>Guideline # 3 : 2014 UMHS</b>	<u>OA score:</u> 4 <u>Comment:</u> Yes with modifications. Lack of information concerning the methodology.	<u>OA score:</u> 3 <u>Comment:</u> Purely pharmacological no references to link recommendations to literature search methodology is not clear (no inclusion exclusion criteria)	Q1 – 0 Q2 – 1 Q3 – 1  <b>FD: EXCLUSION</b>
<b>Guideline # 4 : 2015 BC Guidelines</b>	<u>OA score:</u> 2 <u>Comment:</u> Insufficient (NO) info on overall development process!!!	<u>OA score:</u> 3 <u>Comment:</u> NC	Q1 – 0 Q2 – 0 Q3 – 2  <b>FD: EXCLUSION</b>
<b>Guideline # 5 : 2012 WHO</b>	<u>OA score:</u> 5 <u>Comment:</u> Good process description but could be more detailed. Not specifically about CVD but T2D	<u>OA score:</u> 5 <u>Comment:</u> Nothing about SMOKING CESSATION. positive points: not a lot of guideline for low income countries	Q1 – 1 Q2 – 1 Q3 – 0  <b>FD: INCLUSION</b>

NC: no comment, Q1: I would recommend this guideline for use: Yes, Q2: I would recommend this guideline for use: Yes, with modifications, Q3: I would recommend this guideline for use: No, FD: Final decision.

**B) Step 13. Assess guideline content:**

*Table 3: listbox of assigned guidelines.*

<u>Number of the guideline</u>	<u>Name of the guideline</u>	<u>Year of publication</u>
Guideline # 1	AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society.(21)	2013
Guideline # 6	NICE guideline : Preventing excess weight gain.(26)	2015

**I. Guideline # 1:**

Eleven recommendations of the guideline # 1 were included and six were excluded. The recommendations included are presented in Table 4. The excluded recommendations and the reason for the exclusion are presented in appendix 6.

This guideline was organized in critical question (CQ) connected to recommendations. Each recommendation was related to a CQ. References were not linked to the recommendations but to the CQs. Methodology had to be adapted. “Good” and “fair” references of the CQs were included in the research matrix. The “good and fair” rating was attributed by the guideline # 1 creators, after a structured assessment of the quality of the references. CQs retained if following the inclusion criteria were:

CQ1: Among overweight and obese adults, does weight loss produce CVD health benefits and what health benefits can be expected with different degrees of weight loss?

CQ2: What are the CVD-related health risks of overweight and obesity and are the current cutpoints for overweight (BMI 25–29.9kg/m<sup>2</sup>), obesity (BMI >30kg/m<sup>2</sup>), and waist circumference (>102 cm (M) and >88 cm (F)) appropriate for population subgroups?

CQ3: Which dietary strategies are effective for weight loss?

CQ4: What is the efficacy/effectiveness of a comprehensive lifestyle intervention program (i.e., diet, physical activity, and behavior therapy) in facilitating weight loss or maintaining weight loss?

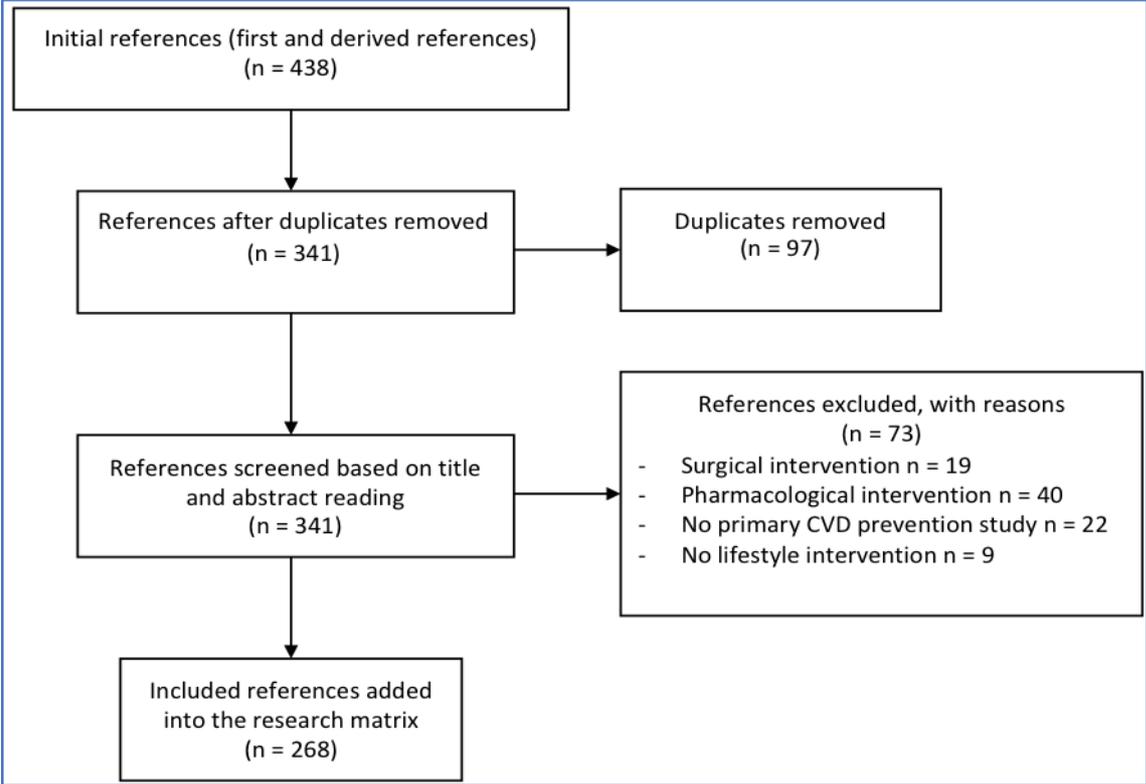
*Table 4: Included recommendations for 2013 AHA/ACC/TOS Guideline for the Management of Overweight and Obesity in Adult.*

Recommendation	Critical Question (CQ)	Grade of recommendations	
		CLASS	LEVEL
<p>Counsel overweight and obese adults with cardiovascular risk factors (high BP, hyperlipidemia, and hyperglycemia) that lifestyle changes that produce even modest, sustained weight loss of 3%–5% produce clinically meaningful health benefits, and greater weight losses produce greater benefits.</p> <p>a. Sustained weight loss of 3%–5% is likely to result in clinically meaningful reductions in triglycerides, blood glucose, hemoglobin A1c, and the risk of developing type 2 diabetes;</p> <p>b. Greater amounts of weight loss will reduce BP, improve LDL–C and HDL–C, and reduce the need for medications to control BP, blood glucose, and lipids as well as further reduce triglycerides and blood glucose.</p>	CQ1	A	I
<p>Advise overweight and obese adults that the greater the BMI, the greater the risk of CVD, type 2 diabetes, and all-cause mortality.</p>	CQ2	A	I
<p>Advise adults that the greater the waist circumference, the greater the risk of CVD, type 2 diabetes, and all-cause mortality. The cutpoints currently in common use (from either NIH/NHLBI or WHO/IDF) may continue to be used to identify patients who may be at increased risk until further evidence becomes available.</p>	CQ2	E/B	IIa
<p>Prescribe a diet to achieve reduced calorie intake for obese or overweight individuals who would benefit from weight loss, as part of a comprehensive lifestyle intervention. Any one of the following methods can be used to reduce food and calorie intake:</p> <p>a. Prescribe 1200–1500 kcal/d for women and 1500–1800 kcal/d for men (kilocalorie levels are usually adjusted for the individual’s body weight);</p> <p>b. Prescribe a 500-kcal/d or 750-kcal/d energy deficit;</p> <p>or</p> <p>c. Prescribe one of the evidence-based diets that restricts certain food types (such as high-carbohydrate foods, low-fiber foods, or high-fat foods) in order to create an energy deficit by reduced food intake.</p>	CQ3	A	I

Prescribe a calorie-restricted diet, for obese and overweight individuals who would benefit from weight loss, based on the patient's preferences and health status, and preferably refer to a nutrition professional for counseling.	CQ3	A	I
Advise overweight and obese individuals who would benefit from weight loss to participate for $\geq 6$ months in a comprehensive lifestyle program that assists participants in adhering to a lower-calorie diet and in increasing physical activity through the use of behavioral strategies.	CQ4	A	I
Prescribe on-site, high-intensity (ie, $\geq 14$ sessions in 6 mo) comprehensive weight loss interventions provided in individual or group sessions by a trained interventionist.†	CQ4	A	I
Advise overweight and obese individuals who have lost weight to participate long term ( $\geq 1$ year) in a comprehensive weight loss maintenance program.	CQ4	A	I
For weight loss maintenance, prescribe face-to-face or telephone-delivered weight loss maintenance programs that provide regular contact (monthly or more frequently) with a trained interventionist† who helps participants engage in high levels of physical activity (ie, 200–300 min/wk), monitor body weight regularly (ie, weekly or more frequently), and consume a reduced-calorie diet (needed to maintain lower body weight).	CQ4	A	I
Electronically delivered weight loss programs (including by telephone) that include personalized feedback from a trained interventionist† can be prescribed for weight loss but may result in smaller weight loss than face-to-face interventions.	CQ4	B/A	IIa
Some commercial-based programs that provide a comprehensive lifestyle intervention can be prescribed as an option for weight loss, provided there is peer-reviewed published evidence of their safety and efficacy	CQ4	B/A	IIa

The included recommendations of the *AHA/ACC/TOS Guideline* led to 438 initial references (first and derived references). 73 references were excluded (see Appendix 8), 97 duplicates were removed, and 268 references were added (see Table 6) to the research matrix. (Figure 2)

*Figure 2: Flow chart for 2013 AHA/ACC/TOS Guideline for the Management of Overweight and Obesity in Adult.*



## II. Guideline # 6:

Six recommendations of the guideline # 6 were included and four were excluded. The grade of the recommendations was not formulated in this guideline but the recommendations were based on high quality systematic reviews. The recommendations were formulated as a result of evidence statements based on the literature. The included recommendations are presented in Table 2. The excluded recommendations and the reason for the exclusion are presented in appendix 7.

*Table 5: Included recommendations for Preventing excess weight gain NICE guideline.*

Included recommendations	Evidence Base Statement	Grade of recommendations
<b>Recommendation 1:</b> Encourage people to make changes in line with existing advice	Evidence Statement 1.17: Relationship between sugar sweetened beverage (SSB) consumption and weight related outcomes	None
	Evidence Statement 1.31: Relationship between adherence to population dietary guidelines and weight related outcomes in adults	
	Evidence Statement 1.33: Relationship between dietary pattern and weight related outcomes in children and young people	
	Evidence Statement 1.37: Relationship between total carbohydrate consumption and weight related outcomes	
	Evidence Statement 1.50: Relationship between snacking/snacks and weight related outcomes	
	Evidence Statement 2.7: Combining messages for diet and physical activity	
	Evidence Statement 2.8: Conflicting messages	
	Evidence Statement 2.10: General content	
<b>Recommendation 2:</b> Encourage physical activity habits to avoid low energy expenditure	Evidence Statement 1.3: Relationship between leisure and recreational activity and weight related outcomes in adults and children	None
	Evidence Statement 1.4: Relationship between sport and weight related outcomes	
	Evidence Statement 1.5: Relationship between active travel and weight related outcomes	
	Evidence Statement 1.6: Relationship between walking and weight related outcomes	
	Evidence Statement 1.7: Relationship between cycling and weight related outcomes	
	Evidence Statement 1.8: Relationship between activities of daily living and weight related outcomes	
	Evidence Statement 1.9: Relationship between incidental physical activity and weight related	
	Evidence Statement 1.11: Relationship between aerobic exercise and weight related outcomes	
	Evidence Statement 1.12: Relationship between physical activity (PA) intensity/frequency/duration and weight related outcomes in adults	
	Evidence Statement 1.15: Relationship between TV and other screen time and weight related outcomes	

<b>Recommendation 3:</b> Encourage dietary habits that reduce the risk of excess energy intake	Evidence Statement 1.17: Relationship between sugar sweetened beverage (SSB) consumption and weight related outcomes	None
	Evidence Statement 1.18: Relationship between fruit juice consumption and weight related outcomes	
	Evidence Statement 1.19: Relationship between water consumption and weight related outcomes	
	Evidence Statement 1.20: Relationship between tea and coffee consumption and weight related outcomes	
	Evidence Statement 1.22: Relationship between milk and dairy consumption and weight related outcomes	
	Evidence Statement 1.23: Relationship between whole grain consumption and weight related outcomes	
	Evidence Statement 1.24: Relationship between refined grain consumption and weight related outcomes	
	Evidence Statement 1.25: Relationship between fruit and vegetable consumption and weight related outcomes	
	Evidence Statement 1.26: Relationship between meat consumption and weight related outcomes	
	Evidence Statement 1.27: Relationship between fish consumption and weight related outcomes	
	Evidence Statement 1.28: Relationship between legume consumption and weight related outcomes	
	Evidence Statement 1.29: Relationship between nut consumption and weight related outcomes	
	Evidence Statement 1.30: Relationship between Mediterranean diet and weight related outcomes in adults	
	Evidence Statement 1.33: Relationship between dietary pattern and weight related outcomes in children and young people	
	Evidence Statement 1.34: Relationship between vegetarian or vegan diet and weight related outcomes	
	Evidence Statement 1.35: Relationship between total fat consumption and weight related outcomes	
	Evidence Statement 1.36: Relationship between total protein consumption and weight related outcomes	
	Evidence Statement 1.37: Relationship between total carbohydrate consumption and weight related outcomes	
	Evidence Statement 1.39: Relationship between dietary fibre consumption on healthy weight maintenance	
	Evidence Statement 1.40: Relationship between energy density (ED) and weight related outcomes	
	Evidence Statement 1.41: Relationship between non-nutritive sweeteners and weight related outcomes	
	Evidence Statement 1.42: Relationship between dietary sugar consumption (sucrose, glucose, fructose, high fructose corn syrup) and weight related outcomes	
	Evidence Statement 1.43: Relationship between catechin intake and weight related outcomes	
	Evidence Statement 1.44: Relationship between caffeine intake and weight related outcomes	
	Evidence Statement 1.45: Relationship between eating meals prepared outside of home (eating out/fast food/takeaway meals) and weight related outcomes	
	Evidence Statement 1.48: Relationship between family meals and weight related outcomes	
	Evidence Statement 1.49: Relationship between breakfast consumption or skipping and weight related outcomes	
	Evidence Statement 1.50: Relationship between snacking/snacks and weight related outcomes	

<b>Recommendation 4:</b> Further advice for parents and carers of children and young people	Evidence Statement 1.3: Relationship between leisure and recreational activity and weight related outcomes in adults and children	None
	Evidence Statement 1.4: Relationship between sport and weight related outcomes	
	Evidence Statement 1.11: Relationship between aerobic exercise and weight related outcomes	
	Evidence Statement 1.13: Relationship between physical activity intensity/frequency/duration and weight related outcomes in children and young people	
	Evidence Statement 1.15: Relationship between TV and other screen time and weight related outcomes	
	Evidence Statement 1.48: Relationship between family meals and weight related outcomes	
	Evidence Statement 1.51: Relationship between sleep and weight related outcomes	
<b>Recommendation 5:</b> Encourage adults to limit the amount of alcohol they drink	Evidence Statement 1.21: Relationship between alcohol consumption and weight related outcomes	None
<b>Recommendation 6:</b> Encourage self-monitoring	Evidence Statement 1.52: Relationship between physical activity monitoring and weight related outcomes	None
	Evidence Statement 2.8: Conflicting messages	

The included recommendations of the NICE guideline led to 134 initial references (first and derived references). 34 references were excluded (see Appendix 9), 52 duplicates were removed, and 48 references were added (see Table 7) to the research matrix. (Figure 3)

Figure 3: Flow chart: Included references for: Preventing excess weight gain NICE guideline.

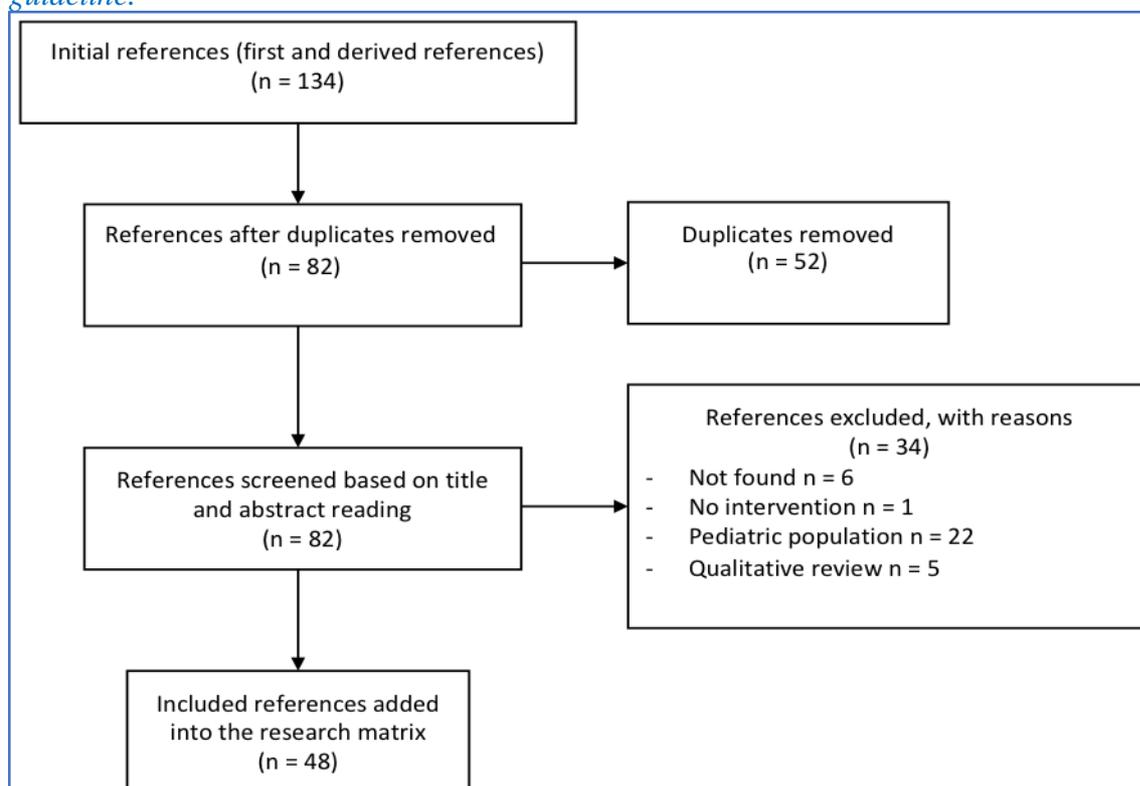


Table 6: 268 included references added into the research matrix for 2013 AHA/ACC/TOS guideline.

Guideline # 1 AHA/ACC/TOS	
Included references added into the research matrix	
Tuomilehto J, Lindstrom J, Eriksson J. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. <i>N Engl J Med</i> 2001; 344: 1343–1350.	Hartwell SL, Kaplan RM, Wallace JP. Comparison of behavioral interventions for control of type II diabetes mellitus. <i>Behavior Therapy</i> 1986;17:447–61.
Wing RR, Venditti E, Jakicic JM, Polley BA, Lang W. Lifestyle intervention in overweight individuals with a family history of diabetes. <i>Diabetes Care</i> 1998; 21: 350–359.	Heitzmann CA, Kaplan RM, Wilson DK, Sandler J. Sex differences in weight loss among adults with type II diabetes mellitus. <i>Journal of Behavioral Medicine</i> 1987;10:197–211.
Wing RR, Jeffery RW, Hellerstedt WL. A prospective study of effects of weight cycling on cardiovascular risk factors. <i>Arch Intern Med</i> . 1995; 155:1416 –1422.	Heller SR, Clarke P, Daly H, Davis I, McCulloch DK, Allison SP, et al. Group education for obese patients with type 2 diabetes: greater success at less cost. <i>Diabetic Medicine</i> 1988;5:552–6.
Kauffmann R, Bunout D, Hidalgo C, Aicardi V, Rodriguez R, Canas L, Roessler E. A 2-year follow-up of a program for the control of cardio-vascular risk factors among asymptomatic workers. <i>Rev Med Chil</i> . 1992; 120:822– 827.	Hockaday TD, Hockaday JM, Mann JI, Turner RC. Prospective comparison of modified fat-high-carbohydrate with standard low-carbohydrate dietary advice in the treatment of diabetes: one year follow-up study. <i>British Journal of Nutrition</i> 1978;39(2):357–62.
Sjostrom M, Karlsson AB, Kaati G, Gyngve A, Green LW, Bygren LO. A four week residential program for primary health care patients to control obesity and related heart risk factors: effective application of principles of learning and lifestyle change. <i>Eur J Clin Nutr</i> . 1999;53(suppl 2):S72–S77.	Julius U, Gross P, Hanefeld M. Work absenteeism in type 2 diabetes mellitus: results of the prospective diabetes intervention study. <i>Diabetes Metabolism</i> 1993;19:202–6.
Black DR, Lantz CE. Spouse involvement and a possible long-term follow-up trap in weight loss. <i>Behav Res Ther</i> 1984;22:557–62.	Kaplan RM, Wilson DK, Hartwell SL, Merino KL, Wallace JP. Prospective evaluation of HDL cholesterol changes after diet and physical conditioning programs for patients with type II diabetes mellitus. <i>Diabetes Care</i> 1985;8:343–8.
Blonk MC, Jacobs MAJM, Biesheuvel EHE, Weeda- Mannak WL, Heine RJ. Influence on weight loss in type 2 diabetic patients: little long-term benefit from group behaviour therapy and exercise training. <i>Diabet Med</i> 1994;11:449–57.	Korhonen T, Uusitupa M, Aro A, Kumpulainen T, Siitonen O, Voutilainen E, et al. Efficacy of dietary instructions in newly diagnosed non-insulin-dependent diabetic patients. <i>Acta Medica Scandinavica</i> 1987;222: 323–31.
Cohen MD, D'Amico FJ, Merenstein JH. Weight reduction in obese hypertensive patients. <i>Fam Med</i> 1991;23:25–8	Lindner J, Schmechel H, Hanefeld M, Schwanebeck U, Bauch K. Coronary heart disease and insulin concentration in type II diabetic patients—results of a diabetes intervention dy. [German]. <i>Zeitschrift für die Gesamte Innere Medizin und Ihre Grenzgebiete</i> 1992;47(6):246–50.
Cousins JH, Rubovits DS, Dunn JK, Reeves RS, Ramirez AG, Foreyt JP. Family versus individually oriented intervention for weight loss in Mexican American women. <i>Public Health Rep</i> 1992;107:549–55.	McCarron DA, Oparil S, Chait A, Haynes RB, Kris- Etherton P, Stern JS, et al. Nutritional management of cardiovascular risk factors. A randomized clinical trial. <i>Archives of Internal Medicine</i> 1997;157(2):169–77.
de Waard, 1993a (Netherlands cohort) de Waard, 1993b (Poland cohort) de Waard FD, Ramlau R, Mulders Y, Vries TD, Waveren SV. A feasibility study on weight reduction in obese postmenopausal breast cancer patients. <i>Eur J Cancer Prev</i> 1993;2:233–8.	McCarron DA, Reusser ME. Reducing cardiovascular disease risk with diet. <i>Obesity Research</i> 2001;9:335S–40S.
DISH, Langford HG, Blaufox MD, Oberman A, Hawkins CM, Curb JD, Cutter GR, et al. Dietary therapy slows the return of hypertension after stopping prolonged medication. <i>JAMA</i> 1985;253:657–64.	Metz JA, Kris-Etherton PM, Morris CD, Mustad VA, Stern JS, Oparil S, et al. Dietary compliance and cardiovascular risk reduction with a prepared meal plan compared with a self-selected diet. <i>American Journal of Clinical Nutrition</i> 1997;66:373–385.
Blaufox MD, Langford HG, Oberman A, Hawkins CM, Wassertheil-Smoller SW, Cutter GR. Effect of dietary change on the return of hypertension after withdrawal of prolonged antihypertensive therapy (DISH). <i>Dietary Intervention Study of Hypertension</i> . <i>J Hypertens</i> 1984; 2(Suppl 3):179–81.	Metz JA, Stern JS, Kris-Etherton P, Reusser RB, Morris CD, Hatton DC, et al. A randomized trial of improved weight loss with a prepared meal plan in overweight and obese patients—impact on cardiovascular risk reduction. <i>Archives of Internal Medicine</i> 2000;160(14):215–8.
Wassertheil-Smoller S, Langford HG, Blaufox MD, Oberman A, Hawkins M, Levine B, et al. Effective dietary intervention in hypertensives: sodium restriction and weight reduction. <i>J Am Diet Assoc</i> 1985;85:423–30.	Milne RM, Mann JI, Chisholm AW, Williams SM. Long-term comparison of three dietary prescriptions in the treatment of NIDDM. <i>Diabetes Care</i> 1994;17(1):74–80.
FDPS, Eriksson J, Lindstrom J, Valle T, Aunola S, Hamalainen H, Ilanne-Parikka P, et al. Prevention of type II diabetes in subjects with impaired glucose tolerance: the Diabetes Prevention Study (DPS) in Finland. Study design and 1-year interim report on the feasibility of the lifestyle intervention programme. <i>Diabetologia</i> 1999; 42:793–801.	Muchmore DB, Springer J, Miller M. Self-monitoring of blood glucose in overweight type 2 diabetic patients. <i>Acta Diabetologica</i> 1994;31:215–9.
Uusitupa M, Lindi V, Lindstrom J, Louheranta A, Laakso M, Tuomilehto J. Impact of Pro12Ala polymorphism of PPAR- gene on body weight and diabetes incidence in the Finnish Diabetes Prevention Study. <i>Int J Obes</i> 2001;25(Suppl 2):S5.	Pascale RW, Wing RR, Blair EH, Harvey JR, Guare JC. The effect of weight-loss on change in waist-to-hip ratio in patients with type 2 diabetes. <i>International Journal of Obesity</i> 1992;16(1):59–65.
Lindstrom J, Tuomilehto J, Louheranta A, Mannelini M, Rastas M, Salminen V, et al. Prevention of type 2 diabetes by lifestyle intervention – the Finnish Diabetes Prevention Study. <i>Int J Obes</i> 2001;25(Suppl 2):S21.	Pascale R, Wing RR, Butler B, Mullen M, Bononi P. Effects of a behavioral weight loss program stressing calorie restriction versus calorie plus fat restriction in obese individuals with NIDDM or a family history of diabetes. <i>Diabetes Care</i> 1995;18:1241–8.
Foreyt JP, Goodrick GK, Reeves RS, Raynaud AS, Darnell L, Brown AH, et al. Response of free-living adults to behavioral treatment of obesity: attrition and compliance to exercise. <i>Behav Ther</i> 1993;24:659–69.	Smith DE, Wing RR. Diminished weight loss and behavioral compliance during repeated diets in obese patients with type II diabetes. <i>Health Psychology</i> 1991;10 (6):378–83.
Skender ML, Goodrick GK, Del Junco DJ, Reeves RS, Darnell L, Gotto AM, et al. Comparison of 2-year weight loss trends in behavioral treatments of obesity: diet, exercise, and combination interventions. <i>J Am Diet Assoc</i> 1996;96:342–6.	Sone H, Katagiri A, Ishibashi S, Abe R, Saito Y, Murase T, Yamashita H, et al. Effects of lifestyle modifications on patients with type 2 diabetes: the Japan Diabetes Complications Study (JDCS) study design, baseline analysis and three year-interim report. <i>Hormone and Metabolic Research</i> 2002;34(9):509.
Frey-Hewitt B, Vranizan KM, Dreon DM, Wood PD. The effect of weight loss by dieting or exercise on resting metabolic rate in overweight men. <i>Int J Obes</i> 1990; 14:327–34.	Trento M, Passera P, Bajardi M, Tomalino M, Grassi G, Borgo E, et al. Lifestyle intervention by group care prevents deterioration of Type II diabetes: a 4-year randomized controlled clinical trial. <i>Diabetologia</i> 2002;45(9):1231–9.
Hakala P, Karvetti RL. Weight reduction on lactovegetarian and mixed diets. Changes in weight, nutrient intake, skinfold thicknesses and blood pressure. <i>Eur J Clin Nutr</i> 1989;43:421–30.	Trento M, Passera P, Tomalino M, Pagnozzi F, Pomero F, Vaccari P, et al. Therapeutic group education in the follow-up of patients with non-insulin treated, non-insulin dependent diabetes mellitus. <i>Diabetes, Nutrition and Metabolism</i> 1998;11:212–6.
Hakala P. Weight reduction programme based on dietary and behavioural counselling – a 2-year follow-up study. <i>Int J Obes</i> 1993;17:49.	Vanninen E, Laitinen J, Uusitupa M. Physical activity and fibrinogen concentration in newly diagnosed NIDDM. <i>Diabetes Care</i> 1994;17(9):1031–8.
Marniemi J, Seppanen A, Hakala P. Long-term effects on lipid metabolism of weight reduction on lactovegetarian and mixed diet. <i>Int J Obes</i> 1990; 14:113–25.	Wing R, Koeske R, Epstein L, Nowalk M, Gooding W, Becker D. Long-term effects of modest weight loss in type II diabetic patients. <i>Archives of Internal Medicine</i> 1987;147: 1749–53.
Hakala P, Karvetti R-L, Ronnema T. Groups vs. individual weight reduction programmes in the treatment of severe obesity – a five year follow-up study. <i>Int J Obes</i> 1993;17:97–102.	Wing RR, Epstein LH, Nowalk MP, Scott N. Self-regulation in the treatment of Type II diabetes. <i>Behavior Therapy</i> 1988;19:11–23.
HOT, Jones DW, Miller ME, Wofford MR, Anderson DC, Cameron ME, Willoughby DL, et al. The effect of weight loss intervention on antihypertensive medication requirements in the Hypertension Optimal Treatment (HOT) study. <i>Am J Hypertens</i> 1999;12:1175–80.	Wing RR, Epstein LH, Nowalk MP, Scott N, Koeske R, Hagg S. Does self-monitoring of blood glucose levels improve dietary compliance for obese patients with type II diabetes?. <i>American Journal of Medicine</i> 1986;81(5):830–6.
HPT, Hypertension Prevention Trial Research Group. The Hypertension Prevention Trial: three-year effects of dietary changes on blood pressure. <i>Arch Intern Med</i> 1990;150:153–62	Zapotoczky H, Semlitsch B, Herzog G, Bahadori B, Siebenhofer A, Pieber TR, Zapotoczky HG. A controlled study of weight reduction in type 2 diabetics treated by two reinforcers. <i>International Journal of Behavioral Medicine</i> 2001;8(1):42–9.
Forster JL, Jeffery RW, Van Natta M, Pirie P. Hypertension prevention trial: do 24-h food records capture usual eating behavior in a dietary change study? <i>Am J Clin Nutr</i> 1990;51:253–7.	Norris, S, L; Zhang, X; Avenell, A; Gregg, E; Schmid, C, H; Lau, J Long-term non-pharmacological weight loss interventions for adults with prediabetes. <i>Cochrane database of systematic reviews (Online)</i> Jan 2005. (2) : CD005270
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Table 7: 48 included references added into the research matrix for 2015 NICE guideline.

Guideline # 6 NICE: Included references added into the research matrix		
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Kaiser et al. 2013 (++) Kaiser KA, Shikany JM, Keating KD et al. Will reducing sugar-sweetened beverage consumption reduce obesity? Evidence supporting conjecture is strong, but evidence when testing effect is weak. Obesity Reviews. 2013 23742715 [Epub ahead of print];14(8):SP-620.	Costigan et al. 2013 (++) Costigan SA, Barnett L, Plotnikoff RC et al. The health indicators associated with screen-based sedentary behavior among adolescent girls: a systematic review. Journal of Adolescent Health. 2013;52(4):382-92.	Wanders et al. 2011 (+) Wanders AJ, van den Borne JJ, de GC et al. Effects of dietary fibre on subjective appetite, energy intake and body weight: a systematic review of randomized controlled trials. Obesity Reviews. 2011 20110616 [Epub ahead of print];12(9):724-39.
Te Morenga et al. 2012 (++) Te Morenga L, Mallard S, Mann J. Dietary sugars and body weight: systematic review and meta-analyses of randomised controlled trials and cohort studies. BMJ. 2013 20120115 [Epub ahead of print];346:e7492.	Malik et al. 2013 (++) Malik VS, Pan A, Willett WC et al. Sugar-sweetened beverages and weight gain in children and adults: a systematic review and meta-analysis. American Journal of Clinical Nutrition. 2013 20130821 [Epub ahead of print];98(4):1084-102.	USDA 2010c (+) U.S. Department of Agriculture. How are non-caloric sweeteners related to energy intake and body weight? (DGAC 2010). Washington (DC): U.S. Department of Agriculture; 2010c. Available from: <a href="http://www.nel.gov/conclusion.cfm?conclusion_statement_id=250279">http://www.nel.gov/conclusion.cfm?conclusion_statement_id=250279</a> .
Fogelholm et al. 2012 (+) Fogelholm M, Andersson S, Gunnarsdottir I et al. Dietary macronutrients and food consumption as determinants of long-term weight change in adult populations: a systematic literature review. Food & Nutrition Research. 2012;56.	Kaiser et al. 2013 (++) Kaiser KA, Shikany JM, Keating KD et al. Will reducing sugar-sweetened beverage consumption reduce obesity? Evidence supporting conjecture is strong, but evidence when testing effect is weak. Obesity Reviews. 2013 23742715 [Epub ahead of print];14(8):SP-620.	Wiebe et al. 2011 (++) Wiebe N, Padwal R, Field C et al. A systematic review on the effect of sweeteners on glycemic response and clinically relevant outcomes. BMC Medicine. 2011 20111117 [Epub ahead of print];9:123.
Vadiveloo et al. 2013 (+) Vadiveloo M, Dixon LB, Parekh N. Associations between dietary variety and measures of body adiposity: a systematic review of epidemiological studies. British Journal of Nutrition. 2013 20130227 [Epub ahead of print];109(9):1557-72.	Te Morenga et al. 2012 (++) Te Morenga L, Mallard S, Mann J. Dietary sugars and body weight: systematic review and meta-analyses of randomised controlled trials and cohort studies. BMJ. 2013 20120115 [Epub ahead of print];346:e7492.	Te Morenga et al. 2013 (++) Te Morenga L, Mallard S, Mann J. Dietary sugars and body weight: systematic review and meta-analyses of randomised controlled trials and cohort studies. BMJ. 2013 20120115 [Epub ahead of print];346:e7492.
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Mesas et al. 2012 (+) Mesas AE, Munoz-Pareja M, Lopez-Garcia E et al. Selected eating behaviours and excess body weight: a systematic review. Obesity Reviews. 2012 20110928 [Epub ahead of print];13(2):106-35.	Louie et al. 2011 (++) Louie JC, Flood VM, Hector DJ et al. Dairy consumption and overweight and obesity: a systematic review of prospective cohort studies. Obesity Reviews. 2011 20110427 [Epub ahead of print];12(7):e582-e592.	Phung et al. 2010 (++) Phung OJ, Baker WL, Matthews LJ et al. Effect of green tea catechins with or without caffeine on anthropometric measures: a systematic review and meta-analysis. American Journal of Clinical Nutrition. 2010 20091111 [Epub ahead of print];91(1):73-81.
USDA 2010m (+) U.S. Department of Agriculture. What is the relationship between snacking and body weight? (DGAC 2010). Washington (DC): U.S. Department of Agriculture; 2010m. Available from: <a href="http://www.nel.gov/conclusion.cfm?conclusion_statement_id=250319&amp;highlight=snacking&amp;home=1">http://www.nel.gov/conclusion.cfm?conclusion_statement_id=250319&amp;highlight=snacking&amp;home=1</a> .	Bautista-Castano and Serra-Majem 2012 (++) Bautista-Castano I, Serra-Majem L. Relationship between bread consumption, body weight, and abdominal fat distribution: evidence from epidemiological studies. Nutrition Reviews. 2012;70(4):218-33.	Bezerra et al. 2012 (++) Bezerra IN, Curioni C, Sichieri R. Association between eating out of home and body weight. Nutrition Reviews. 2012;70(2):65-79.
Saunders et al. 2013 (+) Saunders LE, Green JM, Petticrew MP et al. What are the health benefits of active travel? A systematic review of trials and cohort studies. PLoS ONE [Electronic Resource]. 2013 20130815 [Epub ahead of print];8(8):e69912.	Pol et al. 2013 (++) Pol K, Christensen R, Bartels EM et al. Whole grain and body weight changes in apparently healthy adults: a systematic review and meta-analysis of randomized controlled studies. American Journal of Clinical Nutrition. 2013 20130814 [Epub ahead of print];98(4):872-84.	USDA 2010i (+) U.S. Department of Agriculture. What is the relationship between eating out and body weight? (DGAC 2010). Washington (DC): U.S. Department of Agriculture; 2010i. Available from: <a href="http://www.nel.gov/conclusion.cfm?conclusion_statement_id=250315&amp;highlight=eating%20out&amp;home=1">http://www.nel.gov/conclusion.cfm?conclusion_statement_id=250315&amp;highlight=eating%20out&amp;home=1</a> .
Murphy et al. 2007 (++) Murphy MH, Nevill AM, Murtagh EM et al. The effect of walking on fitness, fatness and resting blood pressure: a meta-analysis of randomised, controlled trials. Preventive Medicine. 2007 20061224 [Epub ahead of print];44(5):377-85.	USDA 2010e (+) U.S. Department of Agriculture. In adults, what is the relationship between the intake of vegetables and fruits, not including juice, and body weight? (DGAC 2010). Washington (DC): U.S. Department of Agriculture; 2010e. Available from: <a href="http://www.nel.gov/conclusion.cfm?conclusion_statement_id=250343&amp;highlight=vegetables&amp;home=1">http://www.nel.gov/conclusion.cfm?conclusion_statement_id=250343&amp;highlight=vegetables&amp;home=1</a> .	Magee and Hale 2012 (+) Magee L, Hale L. Longitudinal associations between sleep duration and subsequent weight gain: a systematic review. Sleep Medicine Reviews. 2012 20110723 [Epub ahead of print];16(3):231-41.
Oja et al. 2011 (+) Oja P, Titze S, Bauman A et al. Health benefits of cycling: A systematic review. Scandinavian Journal of Medicine and Science in Sports. 2011 21496106 [Epub ahead of print];21(4):SP-496	USDA 2010o (+) U.S. Department of Agriculture. What is the relationship between the intake of cooked dry beans and peas and body weight? (DGAC 2010). Washington (DC): U.S. Department of Agriculture; 2010o. Available from: <a href="http://www.nel.gov/conclusion.cfm?conclusion_statement_id=250357&amp;highlight=cooked%20dry%20beans&amp;home=1">http://www.nel.gov/conclusion.cfm?conclusion_statement_id=250357&amp;highlight=cooked%20dry%20beans&amp;home=1</a> .	USDA 2010x (++) U.S. Department of Agriculture. What is the relationship between alcohol intake and weight gain? (DGAC 2010). Washington (DC): U.S. Department of Agriculture; 2010x. Available from: <a href="http://www.nel.gov/conclusion.cfm?conclusion_statement_id=250128&amp;highlight=alcohol&amp;home=1">http://www.nel.gov/conclusion.cfm?conclusion_statement_id=250128&amp;highlight=alcohol&amp;home=1</a> .
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Kelley and Kelley 2006 (++) Kelley GA, Kelley KS. Effects of aerobic exercise on C-reactive protein, body composition, and maximum oxygen consumption in adults: a meta-analysis of randomized controlled trials. Metabolism: Clinical & Experimental. 2006;55(11):1500-7.	Hooper et al. 2012 (++) Hooper L, Abdelhamid A, Moore HJ et al. Effect of reducing total fat intake on body weight: systematic review and meta-analysis of randomised controlled trials and cohort studies. BMJ. 2012 20121206 [Epub ahead of print];345:e7666.	Bravata et al. 2007 (+) Bravata DM, Smith-Spangler C, Sundaram V et al. Using pedometers to increase physical activity and improve health: a systematic review. JAMA. 2007;298(19):2296-304.
Murphy et al. 2009 (-) Murphy MH, Blair SN, Murtagh EM. Accumulated versus continuous exercise for health benefit: a review of empirical studies. Sports Medicine. 2009;39(1):29-43.	Santesso et al. 2012 (++) Santesso N, Akl EA, Bianchi M et al. Effects of higher- versus lower-protein diets on health outcomes: a systematic review and meta-analysis. European Journal of Clinical Nutrition. 2012 20120418 [Epub ahead of print];66(7):780-8.	USDA 2010j (+) U.S. Department of Agriculture. What is the relationship between glycemic index or glycemic load and body weight? (DGAC 2010). Washington (DC): U.S. Department of Agriculture; 2010j. Available from: <a href="http://www.nel.gov/conclusion.cfm?conclusion_statement_id=250355">http://www.nel.gov/conclusion.cfm?conclusion_statement_id=250355</a> .

#### IV) **Discussion:**

##### a) **Main results:**

During step 11 of the ADAPTE procedure, the AGREE II instrument was used to assess the methodological quality of the 5 guidelines assigned. Based on OA score, two guidelines were included, the 2013 AHA/ACC/TOS: Guideline for the Management of Overweight and Obesity in Adults (21) and the 2012 WHO: Prevention and control of non-communicable diseases: guidelines for primary health care in low resource settings (25).

During step 13 of the ADAPTE procedure, the recommendations of the 2 assigned guidelines were selected:

- For the 2013 AHA/ACC/TOS: Guideline for the Management of Overweight and Obesity in Adults (21): 11 recommendations were retained and 268 references related to these recommendations were included into the research matrix.
- For the 2015 NICE guideline (26): Preventing excess weight gain: 6 recommendations were retained and 48 references related to these recommendations were included into the research matrix.

##### b) **Limits and biases:**

Some limits and biases in the method may have occurred. Some **information biases** could occur as studies could be not listed by guidelines. This was managed as the research team focused on effective interventions and recent guidelines. A **confusion bias** was also possible when assessing the guidelines with the AGREE II tool because of the subjectivity between appraisers' evaluation. This was controlled by a double-blind evaluation and a consensus meeting. **Information bias** was also possible because there was no standardized format for guidelines. We had trouble analyzing and retrieving the data. Some **confusion biases** may have occurred. The choice of OA score as an inclusion criteria could be discussed as some items seemed more influential or relevant for implementation research. Major limitation of this study was the lack of time. To complete this work, it will be necessary to finalize the draft matrix.

## **Limits and biases related to studied material:**

### Guidelines:

Considering the time needed to publish a guideline, an **information bias** was possible as studies published after the publication of the guideline could not be considered. To limit this bias, we selected recent guidelines.

Another **information bias** was possible. We considered that existing recommendations on the subject were based on the best available level of evidence and that irrelevant studies had been eliminated (28)(29). There may have been a "positive" selection of the studies used to establish the recommendations by the authors of the guidelines assigned for the ADAPTE step 13. Similarly, when we created our research matrix, the studies that were selected and then included were those with "positive" results. Thus, it is possible that some studies whose results do not support the effectiveness of the intervention in terms of morbi-mortality in primary cardiovascular prevention have been forgotten due to this double "positive" selection.

### Recommendations and references:

**Information bias** was also possible. Among the 2 assigned guidelines, each had a specific structure. In this study, the lack of formalization of the structure of the guidelines was a problem for two reasons. First, in the selection of the recommendations because the gradation of the recommendations was not consistent between the 2 guidelines and it was sometimes difficult to define which recommendation was of sufficient quality to be included. For the guideline # 6 NICE (26), the recommendations were presented without grading system, for the guideline # 1 AHA / ACC / TOS (21), the strength of the recommendations was presented according to the NHLBI grading of recommendation methodology by Class and level. Then, it was difficult to track the references related to the recommendations. There was no direct link between the recommendations and the related references for the 2 assigned guidelines. The reading of several appendix was necessary to associate the references and recommendations.

In this study, the number of references included in the research matrix and the reference difference included between guideline # 1 AHA/ACC/TOS (21) (268 references retained) and

guideline # 6 NICE (26) (48 references retained). This could raise an uncertainty about the exhaustiveness of the bibliography. In this study, guidelines analyzed were of very good quality but the number of references that have been retained in the research matrix was high as 316 references were retained. In H el ene Roux study (30), analyzed guidelines were of very good quality but 22 references only were retained in the research matrix.

### **Limits and biases related to our work:**

#### ADAPTE procedure:

One of the main limitations of this work was the time required to carry out a review of the literature with the ADAPTE procedure. We have assumed that using existing literature integrated within guidelines would save time by avoiding a new systematic review of the literature on the subject. In this study, we found that the use of the ADAPTE procedure was very time consuming. It was originally planned to do steps 14 and 15 of the ADAPTE procedure to obtain the SPICES basket of cost-effective interventions with morbidity and mortality efficacy for non-pharmacological primary cardiovascular prevention but this could not be done in this study due to workload. The time required for the evaluation of the guidelines was evaluated as reasonable in the 2003 study "development and validation of international appraisal instrument for assessing the quality of clinical practice guideline: the AGREE project" (31). The estimated average time for evaluating a guideline with the AGREE II tool was 1H30. Then, a pan-Canadian study had concluded that « Guideline adaptation is a positive initial step toward evidence-informed care, but adaptation (vs. "de novo" development) did not meet expectations for reducing time or resource commitments » (32). It was a too broad work compared to the usual time allocated for a medical thesis. The trainees had to stop before creating the final matrix. To complete the literature review on the subject, it will be necessary for new members of the thesis working group to work on the research matrix and to rank the interventions and implementation strategies according to their reliability and effectiveness. The division of tasks between SPICES teams and between medical trainees and senior researchers facilitated the control of time and resources needed to complete the project.

## AGREE:

Some **confusion biases** may have occurred. The choice of the OA as a selection criterion can be discussed. Despite the organization of AGREE II instrument in 23 items, the OA score was not calculated on average of item scores but had to be estimated independently. To bypass the subjective nature of the OA score, we could have based our selection on a specific domain. The AGREE II tool was used with the aim of solving the problem of variability in the methodological quality of the guidelines. A specific domain score among the six domains scores could have led the selection of guidelines. Domain 3 "Rigor of Development" as well as domain 6 "Editorial Independence" seemed suitable to select methodologically rigorous guidelines whose authors' conflicts of interest do not influence the results. In a recent study, it has been suggested that the domain « Rigour of development » and « Editorial independence » seem to have the strongest influence on the two global assessments (33). In this study, the third domain obtained a score > 50% for the 2 included guidelines and a score < 35% for the 3 excluded guidelines. The score of the sixth domain was not correlated with the inclusion of the guidelines. Domain 5 "Applicability" could also have been a selection criterion because an implementation study such as the SPICES project needs an adaptation of the guidelines recommendations to the local context (34)(35). However, the number of selected guidelines could have been limited because the science of implementation is recent and was still poorly developed in the guidelines which were scored (36). Another domain that could encounter implementation objectives was the views of the target population. In the scored guidelines, the experiences and expectations of the target population was not considered enough. The score obtained for the item 5 " The views and preferences of the target population " was only 1 for all the guidelines assigned except for guideline # 5 developed by the WHO which was scored 4.

Despite the potential biases related to the choice of the overall assessment, AGREE II instrument has been validated and tested internationally on a large number of guidelines. It has become a reference for assessing the quality of the guidelines (37). AGREE II has been used successfully on many guidelines and more and more learned society of the medical community uses this tool. In 2012, the WHO evaluated the quality of four of its guidelines in maternal health (38) and in 2013 a team from the United Kingdoms evaluated the quality of 101 guidelines in cardiac clinical practice using AGREE II instrument (39).

**Information biases** were possible with regard to OA score and item rating due to the difference of experience in the evaluation of the guidelines between medical trainees and senior researcher. There could have been a significant difference in the OA score and item rating by each of the appraisers. On another hand, depending on the order and quality of the evaluated guidelines, the item rating could be different. Starting the evaluation with a guideline with a poor methodology could have influenced upwards the rating of the next guidelines to score for the same appraiser. To limit these biases, the research team trained on a first guideline and the guidelines were evaluated by at least 2 appraisers including a medical trainee and a more experienced senior researcher. A discussion between medical trainees and senior researchers was sometimes necessary to clarify the rating of an item. An opportunity was given to change the scores after discussion between the appraisers and the OA final score was given after a consensus between the 2 appraisers. In this study, the OA score of the 2 appraisers were close together and did not show more than 1-point difference.

c) **Strengths and originality:**

A new and original methodological approach using AGREE II and ADAPTE procedures were chosen to do a systematic review on primary CVD prevention compared to a more conventional methodology using the PRISMA criteria (40). The advantage of the PRISMA criteria was to seek for quantified data from meta-analyses, but its weakness was to obtain an unprecise and broad description of the interventions and run the risk of an inability to implement chosen strategies. Compared to other literature reviews, ADAPTE is related to the implementation objective to apply recommendations at the local level.

In comparison with a literature review carried out following the PRISMA criteria, additional time was needed for the multiplicity of steps:

- Selection of the guidelines with a different search base,
- Familiarization ourselves with a new tool,
- Solving of the divergent evaluations of the guidelines by consensus,
- Extraction of the recommendations and their related references,
- Elimination of duplicates,
- Creation of a search matrix.

This multiplicity was a difficulty as a strength as it conducted to an in-depth sight of guidelines via the AGREE tool. This allowed the research team to better understand the structure of a guideline, to characterize the quality of a guideline.

One of the strengths of this study and the SPICES project is that we were the first to have carried out an overview of the literature of guidelines on the subject. This created a global vision of what nonpharmacological primary cardiovascular prevention should be and underlines choices of each guidelines developer for guidance (as physical activity to promote or dietary improvement to promote).

ADAPTE and AGREE II open up prospects in terms of teaching and clinical practice. In the teaching objectives of the medical studies second cycle, recommendations from French guidelines serve as an inescapable basis for learning. However, when we evaluated the quality of the guidelines and references related to the recommendations, we discovered a great disparity. Training in handling tools like AGREE II and ADAPTE could be useful for medical learning to develop the critical thinking of medical students. Before applying guideline-based recommendations in clinical practice, it seems important to understand how these guidelines were developed, to assess their quality and limits, to know how to check levels of evidence underlying their recommendations and identify their applicability criteria. From the clinical practice perspective, this review highlights gaps between guidelines and practice. The application of many recommendations even from good quality guidelines into routine practice in primary care seem difficult without an adaptation of these to the local context (41).

## V) **Conclusion:**

This study, was part of the SPICES Project, participated to the overview of the literature on the non-pharmacological primary cardiovascular prevention using an original approach using AGREE II and ADAPTE procedures.

The final objective was to select the most effective primary care prevention interventions to reduce the occurrence of CVD in a target population.

Implementation of interventions were not described in the recommendations and references related to the selected recommendations had to be analyzed. 17 recommendations on the subject were included and a total of 316 references related to these recommendations were added into a research matrix.

This study showed a disparity in the quality of the guidelines and references as well a lack of standardization of the guidelines structures. This disparity could question our teaching practices particularly the use of guidelines as an inescapable basis for medical learning. Progress on the development of the guidelines seems necessary. AGREE II would help improving harmonization and quality of guidelines.

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## **Appendix:**

### *APPENDIX 1: AGREE score for guideline # 1:*

<b>AGREE items</b>	<b>Appraiser 1</b>	<b>Appraiser 3</b>	<b>Calculates SCORE</b>
<b><i>Domain 1. Scope and Purpose</i></b>			<b>58%</b>
1. Overall Objective(s)	<b>Score: 4</b> develop clinical practice guidelines for management of overweight and obesity in adults	<b>Score: 4</b>	
2. The health question(s)	<b>Score: 2</b>	<b>Score: 7</b>	
3. The population	<b>Score: 4</b> overweight and obese adult patients	<b>Score: 6</b>	
<b><i>Domain 2. Stakeholder Involvement</i></b>			<b>44%</b>
4. all relevant professional groups	<b>Score: 4</b>	<b>Score: 4</b>	
5. The views and preferences of the target population	<b>Score: 1</b> ??	<b>Score: 2</b>	
6. The target users	<b>Score: 6</b> Intended Users Advanced Practice Nurses Allied Health Personnel Dietitians Health Care Providers Nurses Pharmacists Physician Assistants Physicians Psychologists/Non-physician Behavioral Health Clinicians	<b>Score: 5</b>	
<b><i>Domain 3. Rigour of Development</i></b>			<b>68%</b>
7. Systematic methods were used to search for evidence.	<b>Score: 7</b>	<b>Score: 6</b>	
8. The criteria for selecting the evidence	<b>Score: 6</b>	<b>Score: 6</b>	
9. The strengths and limitations of the body of evidence	<b>Score: 6</b> Rating Schema for the Strength of the Evidence Applying Classification of Recommendations and Level of Evidence	<b>Score: 6</b>	
10. The methods for formulating the recommendations	<b>Score: 6</b> Process for the Development of Evidence Statements, Recommendations, and Panel Voting	<b>Score: 6</b>	
11. The health benefits, side effects, and risks	<b>Score: 6</b>	<b>Score: 3</b>	
12. Explicit link between the recommendations and the supporting evidence.	<b>Score: 6</b>	<b>Score: 5</b>	

13. Externally reviewed by experts prior to publication	<b>Score: 4</b>	<b>Score: 5</b>	
14. procedure for updating	<b>Score: 1</b> ??	<b>Score: 2</b>	
<b>Domain 4. Clarity of Presentation</b>			<b>81%</b>
15. The recommendations are specific and unambiguous	<b>Score: 6</b>	<b>Score: 5</b>	
16. Options for management of the condition or health issue	<b>Score: 6</b> Interventions and Practices Considered:  1. Identifying patients who need to lose weight by body mass index (BMI), waist circumference, and cardiometabolic risk factors  2. Identifying risk of cardiovascular disease (CVD) and other comorbidities  3. Advising patients about risk of CVD, type 2 diabetes, and all-cause mortality  4. Matching treatment benefits with risk profiles  5. Counseling overweight and obese patients with CVD risk factors on the benefits of lifestyle changes to lose weight  6. Diets for weight loss (calorie restriction, restriction of certain food types)  7. Lifestyle intervention and counseling (comprehensive lifestyle interventions that include lower-calorie diets and increasing physical activity) Face-to-face programs Electronically delivered programs Commercial-based programs Very-low-calorie diets (in limited circumstances) Maintenance programs  8. Selecting and referring patients for bariatric surgical treatment	<b>Score: 6</b>	
17. Key recommendations	<b>Score: 6</b> 'major recommendations'	<b>Score: 6</b>	
<b>Domain 5. Applicability</b>			<b>29%</b>
18. facilitators and barriers	<b>Score: 1</b> Description of Implementation Strategy An implementation strategy was not provided	<b>Score: 2</b>	

19. advice and/or tools	<b>Score: 4</b> Implementation Tools Clinical Algorithm Patient Resources Pocket Guide/Reference Cards Resources Slide Presentation Staff Training/Competency Material	<b>Score: 2</b>	
20. Potential resource implications of applying	<b>Score: 2</b> Cost Analysis A formal cost analysis was not performed and published cost analyses were not reviewed	<b>Score: 1</b>	
21. The guideline presents monitoring and/or auditing criteria	<b>Score: 6</b> Major Outcomes Considered Reduction in body weight as measured by: Weight (kg, lb, %) Body fat measures (body mass index [BMI] and BMI change) Waist circumference Weight loss maintenance Cardiovascular disease (CVD) events Myocardial infarction Heart failure Hospitalization for heart failure or stroke CVD risk factors Systolic blood pressure or diastolic blood pressure Total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), non-HDL-C, triglycerides Fasting insulin, fasting glucose, glycosylated hemoglobin, diagnosis of diabetes C-reactive protein (CRP) Morbidity Coronary heart disease/CVD Type 2 diabetes Mortality (CVD-related, all-cause, overall)	<b>Score: 4</b>	
<b>Domain 6. Editorial Independence</b>			<b>54%</b>
22. Views of the funding body have not influenced the content	<b>Score: 5</b>	<b>Score: 2</b>	
23. Competing interests	<b>Score: 4</b>	<b>Score: 6</b>	

*APPENDIX 2: AGREE score for guideline # 2:*

<b>AGREE items</b>	<b>Appraiser 5</b>	<b>Appraiser 4</b>	<b>Calculates SCORE</b>
<b>Domain 1. Scope and Purpose</b>			<b>61%</b>
1. Overall Objective(s)	<b>Score: 5</b>	<b>Score: 3</b>	
2. The health question(s)	<b>Score: 4</b>	<b>Score: 4</b> not clearly described, but globally defined by chapter titles (which tool, who to assess..)	

3. The population	<b>Score: 5</b>	<b>Score: 7</b>	
<b>Domain 2. Stakeholder Involvement</b>			<b>22%</b>
4. all relevant professional groups	<b>Score: 4</b> Not specify, authors?	<b>Score: 1</b> Name of people in the committee are not available	
5. The views and preferences of the target population	<b>Score: 1</b>	<b>Score: 2</b> tools to help discuss with patients	
6. The target users	<b>Score: 3</b>	<b>Score: 3</b> guess it is physician (GPs) but it is not said	
<b>Domain 3. Rigour of Development</b>			<b>24%</b>
7. Systematic methods were used to search for evidence.	<b>Score: 2</b>	<b>Score: 1</b> nothing on research and inclusion exclusion methodology	
8. The criteria for selecting the evidence	<b>Score: 1</b>	<b>Score: 1</b> nothing on research and inclusion exclusion methodology	
9. The strengths and limitations of the body of evidence	<b>Score: 3</b>	<b>Score: 1</b> not even a discussion on the most used risk calculator tools	
10. The methods for formulating the recommendations	<b>Score: 3</b>	<b>Score: 2</b> pdf doc for all guidelines development. poor info <a href="https://www2.gov.bc.ca/assets/gov/health/practitioner-pro/bc-guidelines/gpac-handbook/gpachandbook2017.pdf">https://www2.gov.bc.ca/assets/gov/health/practitioner-pro/bc-guidelines/gpac-handbook/gpachandbook2017.pdf</a>	
11. The health benefits, side effects, and risks	<b>Score: 5</b>	<b>Score: 2</b>	
12. Explicit link between the recommendations and the supporting evidence.	<b>Score: 3</b>	<b>Score: 4</b> not always. framingham risk tool is recommended though it is not consensual on evidence and on international guidelines	
13. Externally reviewed by experts prior to publication	<b>Score: 3</b> imprecise	<b>Score: 3</b> external review by peer (no more info)	
14. procedure for updating	<b>Score: 4</b>	<b>Score: 1</b>	
<b>Domain 4. Clarity of Presentation</b>			<b>64%</b>
15. The recommendations are specific and unambiguous	<b>Score: 5</b>	<b>Score: 5</b>	
16. Options for management of the condition or health issue	<b>Score: 4</b> not enough developed	<b>Score: 4</b>	
17. Key recommendations	<b>Score: 5</b>	<b>Score: 6</b> yes, but no reference for most of them	
<b>Domain 5. Applicability</b>			<b>29%</b>
18. facilitators and barriers	<b>Score: 1</b>	<b>Score: 2</b>	

19. advice and/or tools	<b>Score: 4</b>	<b>Score: 4</b> tools	
20. Potential resource implications of applying	<b>Score: 4</b>	<b>Score: 1</b>	
21. The guideline presents monitoring and/or auditing criteria	<b>Score: 4</b>	<b>Score: 2</b>	
<b>Domain 6. Editorial Independence</b>			<b>21%</b>
22. Views of the funding body have not influenced the content	<b>Score: 2</b>	<b>Score: 4</b> not clear: Funding for GPAC and its projects is made available through the 2014 Physician Master Agreement.	
23. Competing interests	<b>Score: 2</b>	<b>Score: 1</b> Not available	

*APPENDIX 3: AGREE score for guideline # 3:*

<b>AGREE items</b>	<b>Appraiser 5</b>	<b>Appraiser 4</b>	<b>Calculates SCORE</b>
<b>Domain 1. Scope and Purpose</b>			<b>69%</b>
1. Overall Objective(s)	<b>Score: 6</b>	<b>Score: 6</b>	
2. The health question(s)	<b>Score: 5</b>	<b>Score: 3</b>	
3. The population	<b>Score: 6</b>	<b>Score: 5</b> what is \"severe\" dyslipidemia?	
<b>Domain 2. Stakeholder Involvement</b>			<b>39%</b>
4. all relevant professional groups	<b>Score: 5</b>	<b>Score: 5</b> no patients no paramed	
5. The views and preferences of the target population	<b>Score: 1</b>	<b>Score: 1</b>	
6. The target users	<b>Score: 5</b>	<b>Score: 3</b>	
<b>Domain 3. Rigour of Development</b>			<b>33%</b>
7. Systematic methods were used to search for evidence.	<b>Score: 5</b>	<b>Score: 3</b> up to 2011 they use the literature search done by others (the college of endocrinologist)	
8. The criteria for selecting the evidence	<b>Score: 4</b>	<b>Score: 1</b> nothing	
9. The strengths and limitations of the body of evidence	<b>Score: 2</b>	<b>Score: 2</b>	
10. The methods for formulating the recommendations	<b>Score: 2</b>	<b>Score: 5</b>	
11. The health benefits, side effects, and risks	<b>Score: 5</b>	<b>Score: 2</b>	

12. Explicit link between the recommendations and the supporting evidence.	<b>Score: 2</b>	<b>Score: 4</b>	
13. Externally reviewed by experts prior to publication	<b>Score: 3</b>	<b>Score: 4</b> but no experts name, just experts from university	
14. procedure for updating	<b>Score: 3</b>	<b>Score: 1</b>	
<b>Domain 4. Clarity of Presentation</b>			<b>61%</b>
15. The recommendations are specific and unambiguous	<b>Score: 5</b>	<b>Score: 5</b>	
16. Options for management of the condition or health issue	<b>Score: 5</b>	<b>Score: 4</b> very little on non pharmacological therapy	
17. Key recommendations	<b>Score: 4</b>	<b>Score: 5</b>	
<b>Domain 5. Applicability</b>			<b>33%</b>
18. facilitators and barriers	<b>Score: 2</b>	<b>Score: 2</b>	
19. advice and/or tools	<b>Score: 3</b>	<b>Score: 1</b>	
20. Potential resource implications of applying	<b>Score: 4</b>	<b>Score: 3</b> only statin prices	
21. The guideline presents monitoring and/or auditing criteria	<b>Score: 5</b>	<b>Score: 5</b> treat to target vs risk based treatment	
<b>Domain 6. Editorial Independence</b>			<b>54%</b>
22. Views of the funding body have not influenced the content	<b>Score: 4</b>	<b>Score: 2</b> don't know who fund it	
23. Competing interests	<b>Score: 6</b>	<b>Score: 5</b>	

*APPENDIX 4: AGREE score for guideline # 4:*

<b>AGREE items</b>	<b>Appraiser 1</b>	<b>Appraiser 3</b>	<b>Calculates SCORE</b>
<b>Domain 1. Scope and Purpose</b>			<b>50%</b>
1. Overall Objective(s)	<b>Score: 4</b> This guideline provides recommendations on how to diagnose and manage hypertension (HTN) in adults aged ≥ 19 years.	<b>Score: 4</b>	
2. The health question(s)	<b>Score: 2</b>	<b>Score: 4</b>	

3. The population	<p><b>Score: 4</b> This guideline provides recommendations on how to diagnose and manage hypertension (HTN) in adults aged <math>\geq 19</math> years.</p> <p>Outside the scope of this guideline is the management of secondary causes of HTN,* accelerated HTN, acute HTN in emergency settings, and in pregnant adults. The amount of randomized controlled trials informing care of the elderly with raised blood pressure is limited.</p>	<b>Score: 6</b>	
<b>Domain 2. Stakeholder Involvement</b>			<b>14%</b>
4. all relevant professional groups	<p><b>Score: 1</b> ?? no where mentioned</p>	<b>Score: 4</b>	
5. The views and preferences of the target population	<p><b>Score: 1</b> no</p>	<b>Score: 2</b>	
6. The target users	<p><b>Score: 1</b> no</p>	<b>Score: 2</b>	
<b>Domain 3. Rigour of Development</b>			<b>15%</b>
7. Systematic methods were used to search for evidence.	<p><b>Score: 1</b> not mentioned, also couldn't find it on the website or in appendix</p>	<b>Score: 2</b>	
8. The criteria for selecting the evidence	<p><b>Score: 1</b></p>	<b>Score: 1</b>	
9. The strengths and limitations of the body of evidence	<p><b>Score: 2</b> only in top recommendations??</p>	<b>Score: 2</b>	
10. The methods for formulating the recommendations	<p><b>Score: 1</b> no</p>	<b>Score: 2</b>	
11. The health benefits, side effects, and risks	<p><b>Score: 1</b></p>	<b>Score: 2</b>	
12. Explicit link between the recommendations and the supporting evidence.	<p><b>Score: 4</b> yes: see references</p>	<b>Score: 3</b>	
13. Externally reviewed by experts prior to publication	<p><b>Score: 1</b> process not mentioned</p>	<b>Score: 3</b>	
14. procedure for updating	<p><b>Score: 1</b> none found</p>	<b>Score: 3</b>	

<b>Domain 4. Clarity of Presentation</b>			<b>56%</b>
15. The recommendations are specific and unambiguous	<b>Score: 4</b>	<b>Score: 4</b>	
16. Options for management of the condition or health issue	<b>Score: 5</b>	<b>Score: 4</b>	
17. Key recommendations	<b>Score: 4</b>	<b>Score: 5</b>	
<b>Domain 5. Applicability</b>			<b>38%</b>
18. facilitators and barriers	<b>Score: 1</b>	<b>Score: 2</b>	
19. advice and/or tools	<b>Score: 4</b> practical guide for physicians + for patients	<b>Score: 3</b>	
20. Potential resource implications of applying	<b>Score: 5</b> annual cost, cost for the patient,..	<b>Score: 4</b>	
21. The guideline presents monitoring and/or auditing criteria	<b>Score: 3</b>	<b>Score: 4</b>	
<b>Domain 6. Editorial Independence</b>			<b>13%</b>
22. Views of the funding body have not influenced the content	<b>Score: 1</b> ??	<b>Score: 3</b>	
23. Competing interests	<b>Score: 1</b> ??	<b>Score: 2</b>	

*APPENDIX 5: AGREE score for guideline # 5:*

<b>AGREE items</b>	<b>Appraiser 1</b>	<b>Appraiser 3</b>	<b>Calculates SCORE</b>
<b>Domain 1. Scope and Purpose</b>			<b>69%</b>
1. Overall Objective(s)	<b>Score: 6</b> provide technical guidance to countries in integrating costeffective interventions against major NCDs into their health systems The primary goal of the guideline is to improve the quality of care and the outcome in people with type 2 diabetes in low-resource settings.	<b>Score: 6</b>	
2. The health question(s)	<b>Score: 4</b> Guideline provides a basis for development of simple algorithms for management of diabetes with essential medicines and technology available in fist-contact health services in low-resource settings. It recommends a set of basic interventions to integrate management of diabetes into primary health care.	<b>Score: 6</b>	

3. The population	<b>Score: 4</b> The recommendations are limited to patients with type 2 diabetes, as the more complex management of type 1 diabetes requires more specialized care.	<b>Score: 5</b>	
<b>Domain 2. Stakeholder Involvement</b>			<b>58%</b>
4. all relevant professional groups	<b>Score: 5</b>	<b>Score: 5</b> absence of the WONCA (World Organization of National Colleges, Academic and Academic Associations of General Practitioners / Family Physicians)	
5. The views and preferences of the target population	<b>Score: 4</b> There are no data on individual diabetic patient values and preferences in low resource settings, and they could vary between populations.	<b>Score: 3</b> No point of view of the target population, no formal consultation of patients and the public in the development of CPR, but consideration of low resource countries	
6. The target users	<b>Score: 5</b> The target users are health care professionals responsible for developing diabetes treatment protocols which will be used by health care staff in primary care units in low-resource settings.	<b>Score: 5</b>	
<b>Domain 3. Rigour of Development</b>			<b>69%</b>
7. Systematic methods were used to search for evidence.	<b>Score: 6</b>	<b>Score: 4</b> Research protocol explained but not sufficiently detailed, not reproducible with the data provided in the guideline	
8. The criteria for selecting the evidence	<b>Score: 5</b>	<b>Score: 5</b>	
9. The strengths and limitations of the body of evidence	<b>Score: 6</b>	<b>Score: 6</b>	
10. The methods for formulating the recommendations	<b>Score: 6</b>	<b>Score: 6</b>	

11. The health benefits, side effects, and risks	<b>Score: 5</b> The alternative for most of the recommendations in low-resource settings in primary care is usually no intervention. The consequences of untreated type 2 diabetes have been inferred from trials data on patients that did not achieve improvement in established risk factors for complications, and there is no doubt that diabetes substantially increases the risk of premature mortality, limb amputation, blindness and kidney failure	<b>Score: 5</b>	
12. Explicit link between the recommendations and the supporting evidence.	<b>Score: 6</b>	<b>Score: 5</b>	
13. Externally reviewed by experts prior to publication	<b>Score: 4</b>	<b>Score: 5</b> methods used for external review not described, no reviewers designated as methodologist	
14. procedure for updating	<b>Score: 4</b> The guideline will be updated in 2016, unless made seriously obsolete earlier by breakthrough research.	<b>Score: 4</b>	
<b>Domain 4. Clarity of Presentation</b>			<b>78%</b>
15. The recommendations are specific and unambiguous	<b>Score: 6</b>	<b>Score: 5</b>	
16. Options for management of the condition or health issue	<b>Score: 6</b>	<b>Score: 5</b>	
17. Key recommendations	<b>Score: 6</b>	<b>Score: 6</b> Table 5	
<b>Domain 5. Applicability</b>			<b>56%</b>
18. facilitators and barriers	<b>Score: 3</b>	<b>Score: 3</b> Not detailed in the guideline, more informations but not specifically to diabetes but to NCDs in: Package of Essential Noncommunicable (PEN) Disease Interventions for Primary Health Care in Low-Resource Settings	
19. advice and/or tools	<b>Score: 3</b>	<b>Score: 4</b>	

20. Potential resource implications of applying	<b>Score: 6</b>	<b>Score: 5</b>	
21. The guideline presents monitoring and/or auditing criteria	<b>Score: 5</b>	<b>Score: 6</b>	
<b>Domain 6. Editorial Independence</b>			<b>75%</b>
22. Views of the funding body have not influenced the content	<b>Score: 5</b> This work was funded by WHO funds	<b>Score: 6</b>	
23. Competing interests	<b>Score: 5</b> This work was funded by WHO funds. Every member of the guideline development group and the peer reviewers (See CD for list of peer reviewers), completed a standard WHO declaration of interest forms (see CD).	<b>Score: 6</b>	

*APPENDIX 6: Excluded recommendations for 2013 AHA/ACC/TOS: Guideline for the Management of Overweight and Obesity in Adult:*

<b>Excluded recommendations</b>	<b>Reason for exclusion</b>
Measure height and weight and calculate BMI at annual visits or more frequently.	Diagnostic procedures
Use the current cutpoints for overweight (BMI 25.0–29.9 kg/m <sup>2</sup> ) and obesity (BMI ≥30 kg/m <sup>2</sup> ) to identify adults who may be at elevated risk of CVD and the current cutpoints for obesity (BMI ≥30 kg/m <sup>2</sup> ) to identify adults who may be at elevated risk of mortality from all causes.	Diagnostic procedures
Use a very-low-calorie diet (defined as <800 kcal/d) only in limited circumstances and only when provided by trained practitioners in a medical care setting where medical monitoring and high-intensity lifestyle intervention can be provided. Medical supervision is required because of the rapid rate of weight loss and potential for health complications.	Very-low calories diet
Advise adults with a BMI ≥40 kg/m <sup>2</sup> or BMI ≥35 kg/m <sup>2</sup> with obesity-related comorbid conditions who are motivated to lose weight and who have not responded to behavioral treatment with or without pharmacotherapy with sufficient weight loss to achieve targeted health outcome goals that bariatric surgery may be an appropriate option to improve health and offer referral to an experienced bariatric surgeon for consultation and evaluation.	Bariatric Surgical Treatment for Obesity
For individuals with a BMI <35 kg/m <sup>2</sup> , there is insufficient evidence to recommend for or against undergoing bariatric surgical procedures.	Bariatric Surgical Treatment for Obesity
Advise patients that choice of a specific bariatric surgical procedure may be affected by patient factors, including age, severity of obesity/BMI, obesity-related comorbid conditions, other operative risk factors, risk of short- and long-term complications, behavioral and psychosocial factors, and patient tolerance for risk, as well as provider factors (surgeon and facility).	Bariatric Surgical Treatment for Obesity

*APPENDIX 7: Excluded recommendations for 2015 NICE guideline: Preventing excess weight gain:*

<b>Excluded Recommendations</b>	<b>Reasons for exclusion</b>
<b>Recommendation 7:</b> Clearly communicate the benefits of maintaining a healthy weight	Qualitative evidence review
<b>Recommendation 8:</b> Clearly communicate the benefits of gradual improvements to physical activity and dietary habit	Qualitative evidence review
<b>Recommendation 9:</b> Tailor messages for specific group	Qualitative evidence review
<b>Recommendation 10:</b> Ensure activities are integrated with the local strategic approach to obesity	Qualitative evidence review

*APPENDIX 8 : 73 excluded references for 2013 AHA/ACC/TOS: Guideline for the Management of Overweight and Obesity in Adult:*

<b>Excluded references for 2013 AHA/ACC/TOS</b>	<b>Reason for exclusion</b>
Williamson DF, Flanders D, Thompson TJ, Pamuk E, Thun M, Byers T. Intentional weight loss and mortality among overweight individuals with diabetes. <i>Diabetes Care</i> 2000; 23: 1499–1504	No intervention
Chaturvedi N, Fuller JH. Mortality risk by body weight and weight change in people with NIDDM. The WHO Multinational Study of Vascular Disease in Diabetes. <i>Diabetes Care</i> 1995; 18: 766–774.	No intervention
Ford ES, Williamson DF, Liu S. Weight change and diabetes incidence: findings from a national cohort of US adults. <i>Am J Epidemiol</i> 1997; 146: 214–222.	No intervention
Moore LL, Visioni AJ, Wilson PW, D’Agostino RB, Finkle WD, Ellison RC. Can sustained weight loss in overweight individuals reduce the risk of diabetes mellitus? <i>Epidemiology</i> 2000; 11: 269–273.	No intervention
Wannamethee SG, Shaper AG. Weight change and duration of overweight and obesity in the incidence of type 2 diabetes. <i>Diabetes Care</i> 1999; 22: 1266–1272.	No intervention
Long SD, O’Brien K, MacDonald KG Jr et al. Weight loss in severely obese subjects prevents the progression of impaired glucose tolerance to type II diabetes. A longitudinal interventional study. <i>Diabetes Care</i> 1994; 17: 372–375.	Surgical intervention
Sjostrom CD, Peltonen M, Wedel H, Sjostrom L. Differentiated long-term effects of intentional weight loss on diabetes and hypertension. <i>Hypertension</i> 2000; 36: 20–25.	Surgical intervention
Pories WJ, MacDonald KG Jr, Flickinger EG et al. Is type II diabetes mellitus (NIDDM) a surgical disease? <i>Ann Surg</i> 1992; 215: 633–643	Surgical intervention
O’Leary JP. Overview: Jejunoileal bypass in the treatment of morbid obesity. <i>Am J Clin Nutr</i> 1980; 33: 389–394.	Surgical intervention
Hauptman J, Lucas C, Boldrin MN, Collins H, Segal KR. Orlistat in the long-term treatment of obesity in primary care settings. <i>Arch Fam Med</i> . 2000;9:160–167.	Pharmacological intervention
Rosner S, Sjostrom L, Noack R, Meinders AE, Nosedá G. Weight loss, weight maintenance, and improved cardiovascular risk factors after 2 years treatment with orlistat for obesity. European Orlistat Obesity Study Group. <i>Obes Res</i> . 2000;8:49–61.	Pharmacological intervention
Teupe B, Bergis K. Prospective randomized two-years clinical study comparing additional metformin treatment with reducing diet in type 2 diabetes. <i>Diabetes Metab</i> . 1991;17:213–217.	Pharmacological intervention
Karason K, Wikstrand J, Sjostrom L, Wendelhag I. Weight loss and progression of early atherosclerosis in the carotid artery: a four-year controlled study of obese subjects. <i>Int J Obes Relat Metab Disord</i> . 1999;23:948–956.	Surgical intervention
Carson JL, Ruddy ME, Duff AE, Holmes NJ, Cody RP, Brolin RE. The effect of gastric bypass surgery on hypertension in morbidly obese patients. <i>Arch Intern Med</i> . 1994;154:193–200.	Surgical intervention
Kunesova M, Hainer V, Parizkova J, Stich V, Fried M. Long-term treatment of obesity in the obesity unit. <i>Sb Lek</i> . 1998;99:279–286.	Surgical intervention
Foley EF, Benotti PN, Borlase BC, Hollingshead J, Blackburn GL. Impact of gastric restrictive surgery on hypertension in the morbidly obese. <i>Am J Surg</i> . 1992;163:294–297.	Surgical intervention
Broom I, Wilding J, Stott P, Myers N, on behalf of the UK Multimorbidity Study Group. Randomised trial of the effect of orlistat on body weight and cardiovascular disease risk profile in obese patients: UK Multimorbidity Study. <i>Int J Clin Pract</i> 2002;56:494–9. Broom I. Randomised trial of the effect of orlistat on body weight and CVD risk profile in overweight and obese patients with co-morbidities. <i>Int J Obes</i> 2001; 25(Suppl 1):S106. Wilding J. Early response to orlistat treatment predicts long-term success in overweight and obese patients with co-morbidities. <i>Int J Obes</i> 2001;25(Suppl 1):S108.	Pharmacological intervention
Broom I, Hughes E, Dodson P, Reckless J, on behalf of the Orlistat UK Study Group. The role of orlistat in the treatment of obese patients with mild to moderate hypercholesterolaemia: consequences for coronary risk. <i>Br J Cardiol</i> 2001;9:460–8.	Pharmacological intervention
Davidson MH, Hauptman J, DiGirolamo M, Foreyt JP, Halsted CH, Heber D, et al. Weight control and risk factor reduction in obese subjects treated for 2 years with orlistat: a randomized controlled trial [published erratum in <i>JAMA</i> 1999;281:1174]. <i>JAMA</i> 1999; 281:235–42.	Pharmacological intervention
Finer N, James WPT, Kopelman PG, Lean MEJ, Williams G. One-year treatment of obesity: a randomized, double-blind, placebo-controlled, multicentre study of orlistat, a gastrointestinal lipase inhibitor. <i>Int J Obes</i> 2000;24:306–13.	Pharmacological intervention
Farrell J. Long-term management of obesity in primary care: the role of orlistat (Xenical). <i>Obes Res</i> 1997; 5(Suppl 1):10S.	Pharmacological intervention
Hauptman J, Lucas C, Boldrin M, Segal KR. Long-term weight loss with orlistat: impact of selection algorithm on outcomes. <i>Obes Res</i> 1999;7(Suppl 1):50S.	Pharmacological intervention

Hill JO, Hauptman J, Anderson JW, Fujioka K, O'Neil PM, Smith DK, et al. Orlistat, a lipase inhibitor, for weight maintenance after conventional dieting: a 1-y study. <i>Am J Clin Nutr</i> 1999;69:1108-16. Anderson JW, on behalf of the Orlistat Weight Maintenance Study Group. Prevention of weight regain after conventional dieting: a 1-year study with orlistat (Xenical), a new gastrointestinal lipase inhibitor. <i>Obes Res</i> 1997;5(Suppl 1):S2.	Pharmacological intervention
Hollander PA, Elbein SC, Hirsch IB, Kelley D, McGill J, Taylor T, et al. Role of orlistat in the treatment of obese patients with type 2 diabetes. A 1-year randomized double-blind study. <i>Diabetes Care</i> 1998; 21:1288-94.	Pharmacological intervention
Lindgarde F, on behalf of the Orlistat Swedish Multimorbidity Study Group. The effect of orlistat on body weight and coronary heart disease risk profile in obese patients: the Swedish Multimorbidity Study. <i>J Intern Med</i> 2000;248:245-54. Lindgarde F. Orlistat improves coronary heart disease in high-risk obese population: the Swedish Multimorbidity Study. <i>Obes Res</i> 1999;7:70.	Pharmacological intervention
Toornvliet AC, Pijl H, Frolich M, Westendorp RGJ, Meinders AE. Insulin and leptin concentrations in obese humans during long-term weight loss. <i>Neth J Med</i> 1997; 51:96-102.	Pharmacological intervention
Sjostrom L, Rissanen A, Andersen T, Boldrin M, Golay A, Koppeschaar HP, et al. Randomised placebo-controlled trial of orlistat for weight loss and prevention of weight regain in obese patients. European Multicentre Orlistat Study Group. <i>Lancet</i> 1998;352:167-72. Franson K, Rossner S. Fat intake and food choices during weight reduction with diet, behavioural modification and a lipase inhibitor. <i>J Intern Med</i> 2000;247:607-14. Karhunen L, Franssila-Kallunki A, Rissanen P, Valve R, Kolehmainen M, Rissanen A, et al. Effect of orlistat treatment on body composition and resting energy expenditure during a two-year weight-reduction programme in obese Finns. <i>Int J Obes</i> 2000;24:1567-72. Rissanen P, Vahtera E, Krusius T, Uusitupa M, Rissanen A. Weight change and blood coagulability and fibrinolysis in healthy obese women. <i>Int J Obes</i> 2001; 25:212-18. Vidgren HM, Agren JJ, Valve RS, Karhunen LJ, Rissanen AM, Uusitupa MI. The effect of orlistat on the fatty acid composition of serum lipid fractions in obese subjects. <i>Clin Pharmacol Ther</i> 1999;66:315-22.	Pharmacological intervention
Apfelbaum M, Vague P, Ziegler O, Hanotin C, Thomas F, Leutenegger E. Long-term maintenance of weight loss after a very-low-calorie diet: a randomized blinded trial of the efficacy and tolerability of sibutramine. <i>Am J Med</i> 1999;106:179-84.	Pharmacological intervention
McMahon FG, Fujioka K, Singh BN, Mendel CM, Rowe E, Rolston K, et al. Efficacy and safety of sibutramine in obese white and African patients with hypertension. A 1-year, double-blind, placebo-controlled, multicenter trial. <i>Arch Intern Med</i> 2000; 160:2185-91. Fujioka K, McMahon FG, Mendel CM, Rowe E, Mooradian AD. Efficacy and safety of sibutramine in promoting and maintaining weight loss in obese African-Americans and caucasians with hypertension controlled by calcium channel blockers. <i>Obes Res</i> 1999; 7(Suppl 1):69S.	Pharmacological intervention
Smith IG, on behalf of the members of the Sibutramine Clinical Study 1047 Team, Goulder MA. Randomized placebo-controlled trial of long-term treatment with sibutramine in mild to moderate obesity. <i>J Fam Pract</i> 2001;50:505-12. Jones SP, Smith IG, Kelly F, Gray JA. Long term weight loss with sibutramine. <i>Int J Obes</i> 1995;19:41. Smith IG. Long-term weight loss with sibutramine, a once-daily serotonin and norepinephrine reuptake inhibitor. <i>Obes Res</i> 1997;5(Suppl 1):80S.	Pharmacological intervention
James WPT, Astrup A, Finer N, Hilsted J, Kopelman P, Rossner S, et al. Effect of sibutramine on weight maintenance after weight loss: a randomised trial. <i>Lancet</i> 2000;356:2119-25. Astrup A, Finer N, Hansen DL, Toubro S, Goulder M, Kopelman P, et al. Initial weight loss response to sibutramine predicts 2 yrs outcome in STORM. <i>Int J Obes</i> 2001;25(Suppl 2):S104. Hansen D, Astrup A, Toubro S, Finer N, Kopelman P, Hilsted J, et al., for the STORM Study Group. Predictors of weight loss and maintenance during 2 years of treatment by sibutramine in obesity. Results from the European multi-centre STORM trial. <i>Int J Obes</i> 2001; 25:496-501. James P, Astrup A, Finer N, Hilsted J, Kopelman P, Rossner S, et al. Sibutramine Trial in Obesity Reduction and Maintenance (STORM). <i>Obes Res</i> 1999;7:50. Mertens I, Wauters M, Peiffer F, Van de Sompel M, Van der Planken B, Corhouts B, et al. A 2 year combined weight loss program with a hypocaloric diet, sibutramine and physical activity increases antithrombin III levels in obese subjects. <i>Obes Res</i> 1999;7:125. Toubro S, Hansen DL, Hilsted JC, Porsborg PA, Astrup AV, for the STORM Study Group. Effekt af sibutramin til vaegttaabsvedligeholdelse. En randomiseret klinisk kontrolleret undersogelse. <i>Ugeskr Laeger</i> 2001;163:2935-40.	Pharmacological intervention
Bitsch M, Skrummsager BK. Femoxetine in the treatment of obese patients in general practice. <i>Int J Obes</i> 1987; 11:183-90.	Pharmacological intervention
Breum L, Bjerre U, Bak JF, Jacobsen S, Astrup A. Long-term effects of fluoxetine on glycemic control in obese patients with non-insulin-dependent diabetes mellitus or glucose intolerance: influence on muscle glycogen synthase and insulin receptor kinase activity. <i>Metabolism</i> 1995;44:1570-6.	Pharmacological intervention
Goldstein DJ, Ramppe AH, Enas GG, Potvin JH, Fludzinski LA, Levine LR. Fluoxetine: a randomized clinical trial in the treatment of obesity. <i>Int J Obes</i> 1994; 18:129-35. Darga LL, Lucas CP, Carrol-Michels L. The effect of fluoxetine, a serotonin-uptake inhibitor, on weight loss in obese subjects. <i>Am J Clin Nutr</i> 1988;47:764. Darga LL, Carroll-Michals L, Botsford SJ, Lucas CP. Fluoxetine's effect on weight loss in obese subjects. <i>Am J Clin Nutr</i> 1991;54:321-5. Marcus MD, Wing RR, Ewing L, Kern E, McDermott M, Gooding W. A double-blind, placebo-controlled trial of fluoxetine plus behavior modification in the treatment of obese binge-eaters and non-binge-eaters. <i>Am J Psychiatry</i> 1990;147:876-81.	Pharmacological intervention
O'Kane M, Wiles PG, Wales JK. Fluoxetine in the treatment of obese type 2 diabetic patients. <i>Diabet Med</i> 1994;11:105-10.	Pharmacological intervention
Wadden TA, Bartlett SJ, Foster GD, Greenstein RA, Wingate BJ, Stunkard AJ, et al. Sertraline and relapse prevention training following treatment by very-low-calorie diet: a controlled clinical trial. <i>Obes Res</i> 1995; 3:549-57. Foster GD, Wadden TA, Peterson FJ, Leitizia KA, Bartlett SJ, Conill AM. A controlled comparison of three very-low-calorie diets: effects on weight, body composition, and symptoms. <i>Am J Clin Nutr</i> 1992;55:811-17.	Pharmacological intervention
Fontbonne A, Andre P, Eschwege E. BIGPRO (Biguanides and the Prevention of the Risk of Obesity): study design. A randomized trial of metformin versus placebo in the correction of the metabolic abnormalities associated with insulin resistance. <i>Diabete Metabolisme</i> 1991;17:249-54. Bard JM, Charles MA, Juhan-Vague I, Vague P, Andre P, Safar M, et al. Accumulation of triglyceride-rich lipoprotein in subjects with abdominal obesity: the biguanides and the prevention of the risk of obesity (BIGPRO) I study. <i>Arterioscler Thromb Vasc Biol</i> 2001; 21:407-14. Charles MA, Morange P, Eschwege E, Andre P, Vague P, Juhan-Vague I. Effect of weight change and metformin on fibrinolysis and the von Willebrand factor in obese nondiabetic subjects: the BIGPRO1 Study. Biguanides and the Prevention of the Risk of Obesity. <i>Diabetes Care</i> 1998;21:1967-72. Fontbonne A, Charles MA, Juhan-Vague I, Bard JM, Andre P, Isnard F, et al. The effect of metformin on the metabolic abnormalities associated with upper-body fat distribution. BIGPRO Study Group. <i>Diabetes Care</i> 1996; 19:920-6.	Pharmacological intervention

<p>UK Prospective Diabetes Study (UKPDS) Group. Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34) [published erratum in Lancet 1998;352:1557]. Lancet 1998;352:854-65.</p> <p>Clarke P, Gray A, Adler A, Stevens R, Raikou M, Cull C, et al. Cost-effectiveness analysis of intensive blood-glucose control with metformin in overweight patients with type II diabetes (UKPDS no. 51). Diabetologia 2001; 44:298-304.</p> <p>Turner RC, Mann JI, Keeton G. UK prospective study of therapies of maturity-onset diabetes. I. Effect of diet, sulphonylurea, insulin or biguanide therapy on fasting plasma glucose and body weight over one year. Diabetologia 1983;24:404-11.</p> <p>Turner RC, Holman RR, Mathews DR, Oakes SF, Bassett PA, Stratton IM, et al. UK Prospective Diabetes Study (UKPDS). VIII. Study design, progress and performance. Diabetologia 1991;34:877-90.</p> <p>Turner R, Murchison L, Wright AD, Oakley N, Kohner E, Hayes R, et al. United Kingdom prospective diabetes study 24: A 6-year, randomized, controlled trial comparing sulphonylurea, insulin, and metformin therapy in patients with newly diagnosed type 2 diabetes that could not be controlled with diet therapy. Ann Intern Med 1998;128:165-75.</p> <p>Turner RC, Cull CA, Frighi V, Holman RR. Glycemic control with diet, sulphonylurea, metformin, or insulin in patients with type 2 diabetes mellitus: progressive requirement for multiple therapies (UKPDS 49). UK Prospective Diabetes Study (UKPDS) Group. JAMA 1999;281:2005-12.</p> <p>UK Prospective Diabetes Study Group. UK prospective diabetes study 16. Overview of 6 years' therapy of type II diabetes: a progressive disease. [published erratum in Diabetes 1996;45:1655]. Diabetes 1995;44:1249-58.</p> <p>United Kingdom Prospective Diabetes Study (UKPDS). 13: Relative efficacy of randomly allocated diet, sulphonylurea, insulin, or metformin in patients with newly diagnosed non-insulin dependent diabetes followed for three years. BMI 1995;310:83-8.</p> <p>Wright AD, Cull CA, Holman RR, Turner RC. UKPDS 28: a randomized trial of efficacy of early addition of metformin in sulphonylurea-treated type 2 diabetes. Diabetes Care 1998;21:87-92.</p>	Pharmacological intervention
<p>Chiasson JL, Josse RG, Hunt JA, Palmason C, Rodger NW, Ross SA, et al. The efficacy of acarbose in the treatment of patients with non-insulin-dependent diabetes mellitus. Ann Intern Med 1994;121:928-35.</p> <p>Rodger NW, Chiasson J-L, Josse RG, Hunt JA, Palmason C, Ross SA, et al. Clinical experience with acarbose: results of a Canadian multicentre study. Clin J Invest Med 1995;18:318-24.</p> <p>Wolever TM, Chiasson JL, Josse RG, Hunt JA, Palmason C, Rodger NW, et al. Small weight loss on long-term acarbose therapy with no change in dietary pattern or nutrient intake of individuals with non-insulin-dependent diabetes. Int J Obes Relat Metab Disord 1997;21:756-63.</p> <p>Wolever TMS, Chiasson J-L, Josse RG, Hunt JA, Palmason C, Rodger NW, et al. No relationship between carbohydrate intake and effect of acarbose on HbA1c or gastrointestinal symptoms in type 2 diabetic subjects consuming 30-60% of energy from carbohydrate. Diabetes Care 1998;21:1612-18.</p> <p>Wolever TMS, Radmard R, Chiasson J-L, Hunt JA, Josse RG, Palmason C, et al. One-year acarbose treatment raises fasting serum acetate in diabetic patients. Diabet Med 1995;12:164-72.</p>	Pharmacological intervention
Ho GY, Blaufox MD, Wassertheil-Smoller S, Oberman A, Langford H. Plasma renin predicts success of antihypertensive drug withdrawal. Am J Hypertens 1994; 7:679-84.	no CVD primary prevention
Thaler L, Wassertheil-Smoller S, Blaufox MD, Oberman A, Langford HG. Effect of withdrawal of antihypertensive drug on depressive mood. Am J Hypertens 1993;6:1055-62.	no CVD primary prevention
Hankey CR, Leslie WS, Currall JE, Matthews D, Lean ME. Weight change after myocardial infarction: statistical perspectives for future study. J Hum Nutr Dietet 2002;15:439-44.	no CVD primary prevention
Hankey CR, Leslie WS, Lean MEJ. An energy deficit approach to weight management during nutritional counselling post myocardial infarction. Proc Nutr Soc 2001;60:33A.	no CVD primary prevention
Leslie WS, Hankey CR, Currall JE, Matthews D, Lean ME. The impact of a transferable programme of intensified nutritional counselling in cardiac rehabilitation following myocardial infarction. Proc Nutr Soc 2000;59: 69A.	no CVD primary prevention
Canter PL, Borhani NO, Oberman A, Cutler J, Prineas RJ, Langford H, et al. The Hypertension Prevention Trial: assessment of the quality of blood pressure measurements. Am J Epidemiol 1991; 134:379-92.	No intervention
Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 2002; 346: 393-403.	Pharmacological intervention
Sjöström L, Rissanen A, Andersen T, Boldrin M, Golay A, Koppeschaar HP, Krempf M. Randomised placebo-controlled trial of orlistat for weight loss and prevention of weight regain in obese patients. Lancet 1998; 352: 167-173.	Pharmacological intervention
Davidson MH, Hauptman J, DiGirolamo M, Foreyt JP, Halsted CH, Heber D, Heimburger DC, Lucas CP, Robbins DC, Chung J, Heymsfield SB. Weight controlled and risk factor reduction in obese subjects treated for 2 years with orlistat. A randomized controlled trial. JAMA 1999; 281: 235-242.	Pharmacological intervention
Kelley DE, Bray GA, Pi-Sunyer FX, Klein S, Hill J, Miles J, Hollander P. Clinical efficacy of orlistat therapy in overweight and obese patients with insulin-treated type 2 diabetes. Diabetes Care 2002; 25: 1033-1041.	Pharmacological intervention
Miles JM, Leiter L, Hollander P, Wadden T, Anderson JW, Doyle M, Foreyt J, Aronne L, Klein S. Effect of orlistat in overweight and obese patients with type 2 diabetes treated with metformin. Diabetes Care 2002; 25: 1123-1128.	Pharmacological intervention
Bakris G, Calhoun D, Hellman C, Dolker, Kingma I, on behalf of the orlistat and resistant hypertension investigators. Orlistat improves blood pressure control in obese subjects with treated but inadequately controlled hypertension. J Hypertens 2002; 20: 2257-2267.	Pharmacological intervention
Hanefeld M, Sache G. The effects of orlistat on body weight and glycaemic control in overweight patients with type 2 diabetes: a randomized placebo-controlled trial. Diabetes Obes Metabol 2002; 4: 415-423.	Pharmacological intervention
McMahon FG, Weinstein SP, Rowe E, Ernst KR, Johnson F, Fujioka K, the Sibutramine in Hypertension Clinical Study Group. Sibutramine is safe and effective for weight loss in obese patients whose hypertension is well controlled with angiotensin-converting enzyme inhibitors. J Hum Hypertens 2002; 16: 5-11.	Pharmacological intervention
McNulty SJ, Ur E, Williams G, for the Multicenter Sibutramine Study Group. A randomized trial of sibutramine in the management of obese type 2 diabetic patients treated with metformin. Diabetes Care 2003; 26: 125-131.	Pharmacological intervention
Lechner GW, Elliot DW. Comparison of weight loss after gastric exclusion and partitioning. Arch Surg 1983; 118: 685-692.	Surgical Intervention
Capella JF, Capella RF. The weight reduction operation of choice: vertical banded gastroplasty or gastric bypass? Am J Surg 1996; 171: 74-79.	Surgical Intervention
Sapala JA, Wood MH, Sapala MA, Flake Jr TM. Marginal ulcer after gastric bypass: a prospective 3-year study of 173 patients. Obes Surg 1998; 8: 505-516.	Surgical Intervention
Sjöström CD, Lissner L, Wedel H, Sjöström M. Reduction in incidence of diabetes, hypertension and lipid disturbances after intentional weight loss induced by bariatric surgery: the SOS Intervention Study. Obes Res 1999; 7: 477-484.	Surgical Intervention

Torgerson JS, Sjöström L. The Swedish Obese Subjects (SOS) Study: Rationale and results. <i>Int J Obes Relat Metab Disord</i> 2001; 25 (Suppl 1): S2–S4.	Surgical Intervention
Sjöström CD, Peltonen M, Wedel H, Sjöström L. Differential long-term effects of intentional weight loss on diabetes and hypertension. <i>Hypertension</i> 2000; 36: 20–25.	Surgical Intervention
Løvig T, Haffner JFW, Kaarsen R, Nygaard K, Stadaas JO. Gastric banding for morbid obesity: five years follow-up. <i>Int J Obes Relat Metab Disord</i> 1993; 17: 453–457.	Surgical Intervention
Sugerman HJ, Londrey GL, Kellum JM, Wolf L, Liszka T, Engle KM, Birkenhauer R, Starkey JV. Weight loss with vertical banded gastroplasty and Roux-Y gastric bypass for morbid obesity with selective versus random assignment. <i>Am J Surg</i> 1989; 157: 93–102.	Surgical Intervention
Hall JC, Watts JM, O'Brien PE, Dunstan RE, Walsh JF, Slavotinek AH, Elmslie RG. Gastric surgery for morbid obesity. The Adelaide Study. <i>Ann Surg</i> 1990; 4: 419–427.	Surgical Intervention
Brolin RE, Bradley LJ, Wilson AC, Cody RP. Lipid risk profile and weight stability after gastric restrictive operations for morbid obesity. <i>J Gastrointest Surg</i> 2000; 4: 464–469.	Surgical Intervention
Pontiroli AE, Pizzocci P, Librenti MC, Vedani P, Marchi M, Cucchi E, Orena C, Paganelli M, Giacomelli M, Ferla G, Folli F. Laparoscopic adjustable banding for the treatment of morbid (grade 3) obesity and its metabolic complications: a three-year study. <i>J Clin Endocrinol Metab</i> 2002; 87: 3361–3355.	Surgical Intervention
Ruvolo G, Greco E, Speziale G, Di N. M. Marino B. Effects of amlodipine and hypocaloric diet on the left ventricular mass in hypertensive obese patients [in Italian]. <i>Minerva Cardioangi</i> 1994; 42 (6): 289–292.	Pharmacological intervention
Norris, S, L; Zhang, X; Avenell, A; Gregg, E; Schmid, C, H; Lau, J. Pharmacotherapy for weight loss in adults with type 2 diabetes mellitus. <i>Cochrane database of systematic reviews</i> (Online) Jan 2005, (1) : CD004096-	Pharmacological intervention
Padwal, R; Li, S, K; Lau, D, C, W. Long-term pharmacotherapy for obesity and overweight. <i>Cochrane database of systematic reviews</i> (Online) Jan 2004, (3) : CD004094-	Pharmacological intervention
Padwal, R; Li, S, K; Lau, D, C, W. Long-term pharmacotherapy for overweight and obesity: a systematic review and meta-analysis of randomized controlled trials. <i>International journal of obesity and related metabolic disorders : journal of the International Association for the Study of Obesity</i> Dec 2003, 27 (12) : 1437-46	Pharmacological intervention
Rucker, Diana; Padwal, Raj; Li, Stephanie, K; Curioni, Cintia; Lau, David, C, W. Long term pharmacotherapy for obesity and overweight: updated meta-analysis. <i>BMJ (Clinical research ed.)</i> Dec 2007, 335 (7631) : 1194-9	Pharmacological intervention
Emerging Risk Factors Collaboration; Wormser, David; Kaptoge, Stephen; Di Angelantonio, Emanuele; Wood, Angela, M; Pennells, Lisa; Thompson, Alex; Sarwar, Nadeem; Kizer, Jorge, R; Lawlor, Debbie, A; Nordestgaard, Børge, G; Ridker, Paul; Salomaa, Veikko; Stevens, June; Woodward, Mark; Sattar, Naveed; Collins, Rory; Thompson, Simon, G; Whitlock, Gary; Danesh, John. Separate and combined associations of body-mass index and abdominal adiposity with cardiovascular disease: collaborative analysis of 58 prospective studies. <i>Lancet</i> Mar 2011, 377 (9771) : 1085-95	No intervention
Lenz, Matthias; Richter, Tanja; Mühlhauser, Ingrid. The morbidity and mortality associated with overweight and obesity in adulthood: a systematic review. <i>Deutsches Arzteblatt international</i> Oct 2009, 106 (40) : 641-8	No intervention
Prospective Studies Collaboration; Whitlock, Gary; Lewington, Sarah; Sherliker, Paul; Clarke, Robert; Emberson, Jonathan; Halsey, Jim; Qizilbash, Nawab; Collins, Rory; Peto, Richard. Body-mass index and cause-specific mortality in 900 000 adults: collaborative analyses of 57 prospective studies. <i>Lancet</i> Mar 2009, 373 (9669) : 1083-96	No intervention

*APPENDIX 9 : 34 excluded references for 2015 NICE guideline: Preventing excess weight gain:*

<b>Excluded references for 2015 NICE</b>	<b>Reason for exclusion</b>
USDA 2010u (++) U.S. Department of Agriculture. Is intake of sugar-sweetened beverages associated with adiposity in children? (DGAC 2010). Washington (DC): U.S. Department of Agriculture; 2010u. Available from: <a href="http://www.nel.gov/conclusion.cfm?conclusion_statement_id=250242&amp;highlight=sugar&amp;home=1">http://www.nel.gov/conclusion.cfm?conclusion_statement_id=250242&amp;highlight=sugar&amp;home=1</a> .	Pediatric population
Smithers et al. 2011 (+) Smithers LG, Golley RK, Brazionis L et al. Characterizing whole diets of young children from developed countries and the association between diet and health: a systematic review. <i>Nutrition Reviews</i> . 2011;69(8):449-67.	Pediatric population
Kuhl et al. 2012 (-) Kuhl ES, Clifford LM, Stark LJ. Obesity in preschoolers: behavioral correlates and directions for treatment. <i>Obesity</i> . 2012 20110714 [Epub ahead of print];20(1):3-29.	Pediatric population
Larson and Story 2013 (+) Larson N, Story M. A review of snacking patterns among children and adolescents: what are the implications of snacking for weight status? <i>Childhood Obesity</i> . 2013 20130307 [Epub ahead of print];9(2):104-15	Pediatric population
Department of Health 2008 (+)	Not Found/qualitative review
Boylan et al. 2012 (+)	Not Found/qualitative review
NHS Somerset 2011 (+)	Not Found/qualitative review
Marno 2011 (+)	Not Found/qualitative review
Croker et al. 2009 (++)	Not Found/qualitative review
te Velde et al. 2009 (+)	Not Found
Nelson et al. 2011 (+) Nelson TF, Stovitz SD, Thomas M et al. Do youth sports prevent pediatric obesity? A systematic review and commentary. <i>Current Sports Medicine Reports</i> . 2011;10(6):360-70.	No intervention
Schoeppe et al. 2013 (++) Schoeppe S, Duncan MJ, Badland H et al. Associations of children's independent mobility and active travel with physical activity, sedentary behaviour and weight status: a systematic review. <i>Journal of Science &amp; Medicine in Sport</i> . 2013;16(4):312-9.	Pediatric population
Laframboise and Degraauw 2011 (+) Laframboise MA, Degraauw C. The effects of aerobic physical activity on adiposity in school-aged children and youth: a systematic review of randomized controlled trials. <i>Journal of the Canadian Chiropractic Association</i> . 2011;55(4):256-68.	Pediatric population
te Velde et al. 2012 (+) te Velde SJ, van Nassau F, Uijtdevilligen L et al. Energy balance-related behaviours associated with overweight and obesity in preschool children: a systematic review of prospective studies. <i>Obesity Reviews</i> . 2012;13 Suppl 1:56-74.	Pediatric population
Leblanc et al. 2012 (++) Leblanc AG, Spence JC, Carson V et al. Systematic review of sedentary behaviour and health indicators in the early years (aged 0-4 years). <i>Applied Physiology, Nutrition, &amp; Metabolism = Physiologie Appliquee, Nutrition et Metabolisme</i> . 2012;37(4):753-72.	Pediatric population
Tremblay et al. 2011 (++) Tremblay MS, Leblanc AG, Kho ME et al. Systematic review of sedentary behaviour and health indicators in school-aged children and youth. <i>International Journal of Behavioral Nutrition &amp; Physical Activity</i> . 2011 20110921 [Epub ahead of print];8:98.	Pediatric population
Wahi et al. 2011 (++) Wahi G, Parkin PC, Beyene J et al. Effectiveness of interventions aimed at reducing screen time in children: a systematic review and meta-analysis of randomized controlled trials. <i>Archives of Pediatrics &amp; Adolescent Medicine</i> . 2011 20110704 [Epub ahead of print];165(11):979-86.	Pediatric population
USDA 2010u (++) U.S. Department of Agriculture. Is intake of sugar-sweetened beverages associated with adiposity in children? (DGAC 2010). Washington (DC): U.S. Department of Agriculture; 2010u. Available from: <a href="http://www.nel.gov/conclusion.cfm?conclusion_statement_id=250242&amp;highlight=sugar&amp;home=1">http://www.nel.gov/conclusion.cfm?conclusion_statement_id=250242&amp;highlight=sugar&amp;home=1</a> .	Pediatric population
USDA 2010s (++) U.S. Department of Agriculture. Is intake of 100% fruit juice associated with adiposity in children? (DGAC 2010). Washington (DC): U.S. Department of Agriculture; 2010s. Available from:	Pediatric population
USDA 2010r (+) U.S. Department of Agriculture. Is intake of calcium and/or dairy (milk and milk products) related to adiposity in children? (DGAC 2010). Washington (DC): U.S. Department of Agriculture; 2010r	Pediatric population
USDA 2010t (++) U.S. Department of Agriculture. Is intake of fruits and vegetables associated with adiposity in children? (DGAC 2010). Washington (DC): U.S. Department of Agriculture; 2010t. Available from: <a href="http://www.nel.gov/conclusion.cfm?conclusion_statement_id=250239&amp;highlight=fruits&amp;home=1">http://www.nel.gov/conclusion.cfm?conclusion_statement_id=250239&amp;highlight=fruits&amp;home=1</a> .	Pediatric population
USDA 2010n (+)	Not Found
Kastorini et al. 2011 (+)	Not Found
USDA 2010y (++) U.S. Department of Agriculture. Is intake of dietary fat associated with adiposity in children? (DGAC 2010). Washington (DC): U.S. Department of Agriculture; 2010y. Available from: <a href="http://www.nel.gov/conclusion.cfm?conclusion_statement_id=250240&amp;highlight=dietary%20fat&amp;home=1">http://www.nel.gov/conclusion.cfm?conclusion_statement_id=250240&amp;highlight=dietary%20fat&amp;home=1</a> .	Pediatric population
Schwingshackl and Hoffmann 2013 (++)	Not Found
USDA 2010w (++) U.S. Department of Agriculture. Is intake of dietary fiber related to adiposity in children? (DGAC 2010). Washington (DC): U.S. Department of Agriculture; 2010w. Available from: <a href="http://www.nel.gov/conclusion.cfm?conclusion_statement_id=250245">http://www.nel.gov/conclusion.cfm?conclusion_statement_id=250245</a> .	Pediatric population
Brown et al. 2010 (-) Brown RJ, de Banate MA, Rother KL. Artificial sweeteners: a systematic review of metabolic effects in youth. <i>International Journal of Pediatric Obesity</i> . 2010;5(4):305-12.	Pediatric population
Rosenheck et al. 2008 (+)	Not Found
Hammons and Fiese 2011 (+) Hammons AJ, Fiese BH. Is frequency of shared family meals related to the nutritional health of children and adolescents? <i>Pediatrics</i> . 2011 20110502 [Epub ahead of print];127(6):e1565-e1574.	Pediatric population
USDA 2010f (+)	Not Found
Larson and Story 2013 (+) Larson N, Story M. A review of snacking patterns among children and adolescents: what are the implications of snacking for weight status? <i>Childhood Obesity</i> . 2013 20130307 [Epub ahead of print];9(2):104-15	Pediatric population
Ekelund et al. 2012 (+) Ekelund U, Luan J, Sherar LB et al. Moderate to vigorous physical activity and sedentary time and cardiometabolic risk factors in children and adolescents. <i>JAMA</i> . 2012;307(7):704-12.	Pediatric population
Janssen and Leblanc 2010 (+) Janssen I, Leblanc AG. Systematic review of the health benefits of physical activity and fitness in school-aged children and youth. <i>International Journal of Behavioral Nutrition &amp; Physical Activity</i> . 2010 [Epub ahead of print];7:40.	Pediatric population
Chen et al. 2008 (+) Chen X, Beydoun MA, Wang Y. Is sleep duration associated with childhood obesity? A systematic review and meta-analysis. <i>Obesity</i> . 2008;16(2):265-74.	Pediatric population



**IMPRIME 3 – AUTORISATION D'IMPRIMER**

**THESE DE DOCTORAT EN MEDECINE**

**INTERNE**

Madame / Monsieur VIMFLES Nicolas  
Inscrit-e en DES de Médecine Générale

Titre définitif de la thèse soutenue :

Projet SPICES :

- **Sélection parmi 5 recommandations de bonne pratique pour la prévention des maladies cardiovasculaires via les procédures AGREE II et ADAPTE.**
- **Identification des références bibliographiques des recommandations internationales, « 2013 AHA/ACC/TOS : Guideline for the Management of Overweight and Obesity in Adults » et « 2015 NICE guideline : Preventing excess weight gain », à intégrer dans la matrice de recherche de l'étude SPICES.**

**ACCORD DU PRESIDENT DU JURY DE THESE SUR L'IMPRESSION DE LA THESE**

OUI :

La présente autorisation d'imprimer sa thèse est délivrée à l'interne susmentionné.

A Podgorica (Montenegro) le 10 octobre 2018.

**Le directeur de l'UFR de médecine et des  
sciences de la santé de Brest**

  
C. BERTHOU

**Le président du jury de thèse**

  
Dr. Jean-François Riou  
MONTENEGRO 2018/10/10  
18 10 2018

VIMFLES (Nicolas) – Projet SPICES :

- Sélection parmi 5 recommandations de bonne pratique pour la prévention des maladies cardiovasculaires via les procédures AGREE II et ADAPTE.
- Identification des références bibliographiques des recommandations internationales, « 2013 AHA/ACC/TOS : Guideline for the Management of Overweight and Obesity in Adults » et « 2015 NICE guideline : Preventing excess weight gain », à intégrer dans la matrice de recherche de l'étude SPICES.

Th. : Méd. : Brest 2018

**ABSTRACT:**

**Introduction:**

Cardiovascular diseases (CVD) are the first cause of mortality in the world. Despite health-care prevention policies, the global burden of CVD increases. The SPICES project was created to implement innovative interventions about CVD prevention in Europe and Sub-Saharan Africa. The first step was a systematic review of the international recommendations on the topic using the ADAPTE procedure.

**Method:**

ADAPTE Step 11 assessed quality of 5 guidelines with the AGREE II Instrument. Inclusion was based on an overall assessment score  $\geq 5$ . ADAPTE Step 13 was extraction of recommendations from “2013 AHA/ACC/TOS: Guideline for the Management of Overweight and Obesity in Adults” and “2015 NICE guideline: Preventing excess weight gain”. Recommendations were included if they were A or B level of evidence, 1++, 1+, 2++, 2+, Strong or Class 1. Recommendations were excluded if they focused on secondary or tertiary CVD prevention, diagnostic procedures, pharmacological or surgical treatments. References of selected recommendations were gathered in a matrix. If no grading of recommendations, references were included if they were randomized controlled trials or cohort interventional surveys.

**Results:**

2 guidelines were included and 3 excluded. Regarding ADAPTE step 13, 17 recommendations and 316 references were selected and extracted to the research matrix.

**Conclusion:**

A great disparity in the quality of guidelines and references was found. Main limitation was lack of time. The research group had to stop at a draft matrix. The next step will be finalization of the matrix to extract interventions and implementation from references.

**MOTS CLES :**

FAMILY MEDICINE; CARDIOVASCULAR DISEASES; PRIMARY PREVENTION; CLINICAL PRACTICE GUIDELINE

**JURY :**

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