The Saudi clinical practice guideline for the management of overweight and obesity in adults

Assim A. Alfadda, MD, FRCPC, *Madhawi M. Al-Dhwayan,* MSc, *Abdulhameed A. Alharbi,* JBCM, SBCM, *Basema K. Al Khudhair,* MD, ABFM, *Omar M. Al Nozha,* SSCIM, ArBIM, *Nawal M. Al-Qahtani,* MD, FFCM, *Saad H. Alzahrani,* SSC-IM, MD(UK), *Wedad M. Bardisi,* SBFCM, ABFCM, *Reem M. Sallam,* MBBCh, PhD, *John J. Riva,* DC, MSc, *Jan L. Brożek,* MD, PhD, *Holger J. Schünemann,* MD, PhD, *Ainsley Moore,* MD, MSc.

ABSTRACT

الأهداف: صياغة مجموعة من الأدلة الإرشادية السريرية لمساعدة مقدمي الرعاية الصحية في اتخاذ القرارات المبنية على الأدلة السريرية لعلاج البالغين المصابين بالسمنة في المملكة العربية السعودية.

الطريقة: بمبادرة من وزارة الصحة في المملكة العربية السعودية، فقد اجتمع فريق من الخبراء في علاج السمنة بالمملكة العربية السعودية بدعم من فريق الخبراء في الطب المبني على البراهين من جامعة ماكماستر و قاموا بصياغة هذه الأدلة الإرشادية عام 2015 في الرياض. وقد تمت دراسة 11 سؤالاً، ووضع التوصيات المناسبة لها حسب نهج GRADE (دراسة وتقييم التوصيات، وتحليلها، وصياغتها).

النتائج: اتخذ فريق الخبراء توصيات قوية بدعم التدخلات في نمط الحياة بدلاً من الرعاية المعتادة في علاج السمنة، وكذلك دعم النظام الغذائي والنشاط البدني. أما بالنسبة لاستخدام الأدوية في علاج السمنة، فقد تم اقتراح استخدام عقار الميتفورمين، وأورليستات كتوصيات مشروطة لعلاج السمنة لدى البالغين. كما تم اتخاذ توصية مشروطة لاستخدام جراحات السمنة في الأشخاص البالغين المصابين بالسمنة (مؤشر كتلة الجسم أعلى من أو يساوي 40، أو أعلى من أو يساوي 35 كلجم/م^2 مع وجود أمراض مصاحبة للسمنة).

الخاتمة: تحتوي هذه الأدلة الإرشادية على توصيات ترتبط بتغيير نمط الحياة، و توصيات تخص استخدام الأدوية، و الجراحة في علاج المصابين بالسمنة. ويوصي فريق الخبراء بإجراء مزيد من الأبحاث في جوانب تتعلق بعلاج السمنة في المجتمع السعودي.

Objective: To assist healthcare providers in evidence-based clinical decision-making for the management of overweight and obese adults in Saudi Arabia.

Methods: The Ministry of Health, Riyadh, Kingdom of Saudi Arabia assembled an expert Saudi panel to produce this clinical practice guideline in 2015. In collaboration with the methodological working group from McMaster University, Hamilton, Canada, using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach, which describes both the strength of recommendation and the quality of evidence

Results: After identifying 11 questions, corresponding recommendations were agreed upon as guidance for the management of overweight and obese adults. These included strong recommendations in support of lifestyle interventions rather than usual care alone, individualized counseling interventions rather than generic educational pamphlets, physical activity rather than no physical activity, and physical activity in addition to diet rather than diet alone. Metformin and orlistat were suggested as conditional recommendations for the management of overweight and obesity in adults. Bariatric surgery was recommended, conditionally, for the management of obese adults (body mass index of ≥40 or ≥35 kg/m^2 with comorbidities).

Conclusions: The current guideline includes recommendation for the non-pharmacological, pharmacological, and surgical management of overweight and obese adults. In addition, the panel recommends conducting research priorities regarding lifestyle interventions and economic analysis of drug therapy within the Saudi context, as well as long term benefits and harms of bariatric surgery.

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In the Kingdom of Saudi Arabia (KSA), obesity (defined as body mass index (BMI) of ≥30 kg/m^2) and overweight (defined as BMI of 25-29.9 kg/m^2) represent an alarming threat for population health based on their high prevalence.[1] Both genders are affected, with some differences existing, where obesity is more prevalent among females, while overweight is higher among males.[1] The high prevalence is a real concern; especially since obesity and overweight are well known risk factors for several life-threatening conditions including type 2 diabetes, coronary artery disease, hypertension, and certain cancers, in addition to impaired quality of life. Obesity and its comorbidities are multifactorial (including genetic, environmental, psychological, social, and cultural factors), requiring multiple approaches to population management in various settings with input from a range of stakeholders.

The management of obesity is composed primarily of lifestyle interventions. These interventions are multi-component treatments that involve promoting healthy lifestyle habits, dietary interventions, dietary counseling, physical exercise training as well as psychological and behavioral interventions. Pharmacotherapies are often an adjunct to lifestyle interventions, especially in those who struggle to lose weight with lifestyle interventions alone. They can also help patients maintain weight loss. Surgical management of obesity is considered in patients who met certain criteria.[2]

Previous guideline statements available on this topic include: "Management of obesity: Saudi Clinical Guideline";[3] "Summary of updated National Institute for Health and Care Excellence (NICE) guidance";[4] "Canadian Task Force on Preventive Health Care, Obesity in Adults 2015;"[5] and "US Preventive Services Task Force (USPSTF), Obesity in Adults Screening, and recommendations 2012.[6]

Every population has its unique cultural, environmental, and lifestyle profiles, that are necessary to address within the current guideline of managing obese and overweight individuals in the KSA.

Rationale for KSA obesity guideline. Reduction in obesity is an important public health consideration for the KSA and this guideline considers the diversity of lifestyle, pharmacological, as well as surgical management strategies that contribute to the current development of a broad national strategy to combat obesity. The Ministry of Health (MOH) at KSA launched an evidence-based program to produce clinical practice guidelines (CPG) for the management of common diseases in KSA. Obesity was among the topics that were given a priority in this program, given its high negative impact on the health of individuals and the society as a whole. Compared with other guideline statements published for obesity; there is an agreement between Saudi Arabia, NICE, and USPSTF recommendations regarding lifestyle, exercise, medication, and surgical management, the Canadian guideline does not make management recommendations, but advises screening for obesity using BMI as does the USPSTF.

The Saudi Center for Evidence Based Health Care (EBHC) of the MOH coordinated the development of clinical practice guidelines between the methodological team from McMaster University and local clinical expert panel members in Saudi Arabia. Local clinical experts of multiple disciplines were recruited through Saudi specialist societies and also independent experts. Guidelines were based on pre-selected available evidence synthesis. Twelve topics for wave 2 were selected by the EBHC through consultation with local stakeholders and based on the selection criteria defined by the McMaster team. Guideline panel meetings took place in Riyadh on 15th-18th March 2015 and comprised 96 local experts from Saudi Arabia supported by 20 methodological experts from McMaster University, Hamilton, Canada.

From the Obesity Research Center (Alfadda, Al-Dhwayan, Sallam), Department of Medicine (Alfadda), Clinical Chemistry Unit, Pathology Department (Sallam), College of Medicine, Department of Community Health Sciences (Al-Dhwayan), College of Applied Medical Sciences, King Saud University, Post Graduate Program in Family Medicine (Al Khudhair), Ministry of Health, the Obesity, Endocrine, and Metabolism Center (Alzahrani), King Fahad Medical City Riyadh, Preventive Medicine Department (Alharbi), Ministry of Health, Yanbu General Hospital, Yanbu, Department of Medicine (Al Nozha), Taibah University, Madinah, the Family Medicine Post Graduate Centre (Al-Qahtani), Ministry of Health, Khobar, Directorate of Health Affairs, and the Directorate of Public Health (Bardisi), Prince Abdul Majeed Health Center, Kingdom of Saudi Arabia, Department of Family Medicine (Riva, Moore), and the Department of Clinical Epidemiology & Biostatistics and Medicine (Brożek, Schünemann), McMaster University, Hamilton, Canada.

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Address correspondence and reprint request to: Prof. Assim A. Alfadda, Obesity Research Center, College of Medicine, King Saud University, Riyadh, Kingdom of Saudi Arabia. E-mail: aalfadda@ksu.edu.sa

The Saudi Center for EBHC published full versions of all 12 guidelines in KSA, MOH Website in 2015. The full version of obesity management guideline (number 14) can be found at: http://www.moh.gov.sa/depts/Proofs/Pages/Guidelines.aspx.[7]

The obesity expert Saudi panel members formally prioritized questions addressed within this guideline. An existing systematic review on the management of obesity from 2013, published by the National Health and Medical Research Council of Australia was updated for all selected questions. Systematic searches were also conducted for information on patients' values and preferences, as well as costs and resource use specific to the Saudi context. These systematic reviews formed the basis of recommendations following the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach. Evidence profiles were developed to prepare GRADE evidence-to-decision frameworks allowed the guideline panel to follow a structured consensus process in order to transparently document decisions made during the meeting. External peer review was conducted by a methodological expert independent of the guideline development process.

As a quality measure prior to publication, the final report has been externally peer reviewed by a methodological expert who has not been involved in this guideline development.

The guideline is considered as guidance to general practitioners, family doctors, allied health professionals, and other relevant specialists. In addition, policy makers may refer to recommendations and judgments made in this guideline. As such it is expected to exert a beneficial impact in the area of management for overweight, obesity, and associated comorbidities and mortality.

Recommendations were developed by the Saudi expert panel members and facilitated by McMaster methodologists. Panel members deliberated over prepared evidence profiles for each key question, and reached consensus on recommendations while documenting their decision making processes following the GRADE evidence to decision framework.

Methods. This CPG is part of a second wave of a larger initiative by the Saudi MOH to ensure quality and consistency of care across the KSA. The MOH's, EBHC, in collaboration with McMaster University guideline group worked together to publish and disseminate CPG with the aim of improving the quality and safety of health care in the KSA. Through this program, the Obesity Research Center at King Saud University, Riyadh, KSA was contacted to nominate expert Saudi panelists in the field of obesity management. A brief description of the methods used to develop recommendations is described, details are available in a separate publication.[7]

Topic selection. Topics for this guideline were selected by the panel members and all healthcare questions were prioritized using a formal online consensus process.

Literature search. We updated an existing systematic review on the management of obesity for adults from 2013, published by the National Health and Medical Research Council (NHMRC), Canberra, ACT Australia.[8] Questions were grouped into categories of pharmacological, non-pharmacological, and surgical approaches to management of obesity in adults. For each question, the McMaster guideline-working group (lead by AM for this guideline) updated the search strategy to identify new studies, or new systematic reviews and updated meta-analyses when relevant. The McMaster group also conducted systematic searches for contextual information necessary to develop the full guideline for the KSA, including searches for information on patients' values and preferences, and costs and resource use specific to the Saudi setting (**Appendix 1***).

Evidence to decision. For each question, one evidence profile was developed as well as an evidence-to-decision (EtD) table following the GRADE approach.[9,10] Profiles and tables were shared with the panel members. The guideline panel was invited to provide additional information, particularly when published evidence was lacking.

Recommendations. Final recommendations were formulated during an in-person meeting of the guideline panel members and McMaster guideline working group members in Riyadh on March 17th and 18th 2015. The GRADE evidence-to-decision framework was followed. This allowed a structured consensus process and transparent documentation of all decisions made during the meeting. Potential conflicts of interests of all panel members were managed according to the World Health Organization (WHO) rules.[11]

Interpreting recommendations. *Grading the quality of evidence.* To facilitate the interpretation of these guidelines, the GRADE working group defines the quality of evidence as the degree of confidence that the estimate of an effect is adequate to support a particular decision, or recommendation.[9] We assessed the quality of evidence using the GRADE approach.

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*The full text including Appendix is available in PDF format on Saudi Medical Journal website (www.smj.org.sa)

Quality of evidence is classified as "high", "moderate", "low", or "very low" based on panel decisions on methodological characteristics of the available evidence for a specific health care problem. The definition of each category is as follows:

- **High:** We are very confident that the true effect lies close to that of the estimate of the effect.
- **Moderate:** We are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
- **Low:** Our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of the effect.
- **Very low:** We have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.

Grading the strength of recommendations. The GRADE working group defines the strength of recommendation as the degree to which we can be confident that desirable effects of an intervention outweigh undesirable effects. According to the GRADE approach, the strength of a recommendation is either strong, or conditional (also known as weak) and has explicit implications.[12] Understanding the interpretation of these 2 grades, either strong or conditional, of the strength of recommendations is necessary for sound clinical decision-making (**Table 1**).

Results. The guideline has discussed 11 questions in the management of obesity. These questions were divided into 3 sections: I. non-pharmacological management (questions 1-8), II. pharmacological management (questions 9-10), and III. surgical management (question 11). Upon reaching a recommendation, the panel members made a consistent judgment regarding obesity as a priority problem due to the high prevalence of obesity in KSA. Similarly, with respect to values and preferences, panel members agreed that there was probably no important uncertainty on how much people value the main outcomes (namely, mortality, cardiovascular disease, weight loss, and change in BMI).

No cost effectiveness studies were identified specific to Saudi Arabia. Studies from other countries were identified in the literature update for orlistat and bariatric surgery.[13,14] Panel members provided their estimate of average unit costs for the specific intervention in Saudi Arabian Riyal (SR).

I. Non-pharmacological management:

Question 1. Should lifestyle interventions compared to other interventions be used for overweight and obese adults?

Lifestyle interventions are the cornerstone of obesity treatment. These interventions are multi-component treatments that involve promoting healthy lifestyle habits, dietary interventions, dietary counseling, physical exercise training as well as psychological and behavioral interventions. Pharmacotherapeutic agents are often supplementing lifestyle interventions; however, they are not considered as a part of the lifestyle interventions.[15] The question was primarily based on the NHMRC systematic review published in 2013.[8] The updated literature search identified a Canadian systematic review and meta-analysis.[15] The benefits of lifestyle interventions clearly outweigh the harms, and the resources required are small. As such, the option was judged to be cost-effective. The option is both feasible and acceptable and has no impact on health inequities.[15] Generation of local evidence for lifestyle modification is recommended (the research evidence used in this guideline involving behaviors may not be applicable

Table 1 - Interpretation of strong and conditional (weak) recommendations.

Implications	Strong recommendation	Conditional (weak) recommendation
For patients	Most individuals in this situation would want the recommended course of action and only a small proportion would not. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.	The majority of individuals in this situation would want the suggested course of action, but many would not.
For clinicians	Most individuals should receive the intervention. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator.	Recognize that different choices will be appropriate for individual patients and that you must help each patient arrive at a management decision consistent with his or her values and preferences. Decision aids may be useful helping individuals making decisions consistent with their values and preferences.
For policy makers	The recommendation can be adapted as policy in most situations	Policy making will require substantial debate and involvement of various stakeholders.

for Saudi population which could affect outcomes). Individualized package of lifestyle interventions should be prescribed to each patient according to his/her comorbidities.

Recommendation 1. The panel recommends lifestyle intervention rather than usual care alone in overweight and obese adults (strong recommendation, moderate quality evidence).

Question 2. Should intensive lifestyle interventions compared to usual care be used for overweight and obese adults?

Intensive lifestyle interventions (ILI) involve more extreme dietary, physical, and behavioral counseling, delivered by multidisciplinary teams of nutritionists, physicians, behavioral therapists, and exercise trainers.[16-18] Low calorie diet (800-1200 Kcal/day) and very low calorie diet (<800 Kcal/day) are typically included in the ILI. Also included are moderate to intense physical activity consisting of at least 30 minutes of activity a day, or the equivalent of consuming 1800-2500 Kcal/week; and individualized behavioral goal setting, delivered at weekly, or bi-monthly visits for one to several years. Intensive lifestyle interventions is therefore reserved for populations at high risk of obesity. Outcomes for this intervention are consequently longer-term, such as mortality and cardiovascular events, which are direct patient important end-points.[16-18] The question was primarily based on the Finnish, Diabetes Prevention Study (DPS), and the Look AHEAD (Action for Health in Diabetes) trial.[16-18] The updated literature search identified no new studies. Most panel members thought that the benefit in terms of prevention of diabetes and associated cost of care outweighs the downsides. The panel judged the option of ILI to be probably acceptable to key stakeholders and the feasibility to vary and perhaps not be possible on a population level. The panel judged the feasibility to be possible in selected settings where human and financial resources are available, as barriers include the resources and availability of health care professionals to support intensive lifestyle modification. The panel judged the provision of ILI to probably increase health inequity. Required resources were judged by the expert panel to not be small and probably not cost-effective. In addition, generation of local evidence for lifestyle modification is recommended (the research evidence used in this guideline involving behaviors that may not be applicable for Saudi population, which could affect outcomes).

Recommendation 2. The panel suggests using intensive lifestyle modification rather than usual, or minimal care in overweight and obese adults (conditional recommendation, moderate quality evidence).

Remarks. This recommendation pertains to those who are at higher risk for obesity-related comorbidities such as diabetes as they would benefit more from intensive lifestyle interventions. Well-organized and standardized programs dedicated for lifestyle intervention will be required for implementation.

Questions 3 & 4. Should physical activity and diet compared to diet, or physical activity alone be used for overweight and obese adults?

Reduced-energy diets and increased energy expenditure through physical activity are the main components of lifestyle intervention, which is first line treatment of choice for obesity management. Although evidence supporting the effectiveness of physical activity alone on weight loss is disappointing, studies do support physical activity effectiveness for preventing weight gain and incidence of diabetes. Additional potential benefits include: improved mobility, physical function (strength), decreased joint pain (associated with arthritis), decreased cardiovascular risk, and improved bone density. Studies informing these questions are derived from the NHMRC systematic review and include 2 Cochrane reviews[19,20] and 4 more recent randomized controlled trials (RCTs).[19-24] The updated literature search identified no new studies. Desirable consequences clearly outweigh undesirable consequences in most settings, and no harmful outcomes were identified. However, the panel judged that the desirable anticipated effects due to exercise, or diet alone are probably not large. As for the resource use out of pocket expense for cost and travel to indoor recreation centers are prohibitive (1000-3000 SR per month), hot weather is a barrier to outdoor exercise. For diet, costs are associated with the use of specialized diets. Purchasing low-energy diet items to replace meals may be costly for individuals and their use requires frequent monitoring by healthcare professionals. The relevant healthcare professional to monitor use may be a general practitioner, dietician, or specialist nurse, depending on access to the type of provider. Therefore, health professional visit fees would also need to be considered among the resources required. A per visit fee for such providers was estimated by the expert panel as follow: 300 SR for general practitioner, 250 SR for diabetic educator, or nutritionist, and 200 SR for behavioral specialist. The panel judged that exercise and

diet would be both feasible to implement and acceptable to most stakeholders. The panel also judged that there is no important uncertainty, or variability on how much people value this outcome.

Recommendations 3 & 4. The panel recommends physical activity rather than no physical activity in overweight and obese adults (strong recommendation, low quality evidence).

The panel recommends physical activity in addition to diet rather than a diet alone in overweight, or obese adults (strong recommendation, low quality evidence).

Question 5. Should nutrition and physical activity counseling compared to health education pamphlets be used for overweight and obese adults?

While counseling for nutrition and physical activity represents the core component of lifestyle interventions for obesity management, this brief and simple intervention (education pamphlets) is intended to be delivered by primary care physicians within constraints of limited office time and limited behavioral counseling skills. The emphasis on brevity, and less intensive behavioral/psychotherapeutic aspects may favor tolerability for both patients and practitioners as evidenced by the lower dropout rate (13%) compared to the traditional lifestyle interventions (>20%).[25] The question was based on one moderate sized trial,[25] derived from the NHMRC systematic review.[8] The updated literature search identified no new studies. The panel, judged the cost of providing nutrition and physical exercise information to probably not be small cost, as physicians must provide time to discuss tailored information and preparation of individualized information. However, the panel did judge the option to be cost effective. The panel judged the provision of nutrition and physical activity information to be acceptable and probably feasible with no impact on health inequities.

There is health benefit without downsides other than the cost of implementation and there is no doubt among members that an individualized approach in overweight and obese individuals is better than a generic approach. More research on the methods of individualized interventions is required.

Recommendation 5. The panel recommends individualized counseling interventions rather than generic educational pamphlets in overweight or obese adults (strong recommendation, low quality evidence).

Question 6. Should iso-caloric low-fat compared to moderate-fat diet be used for overweight and obese adults?

People with diabetes are advised to reduce fat intake in order to decrease their risk of cardiovascular disease. The practicality of adherence to a very low fat diets, which are usually less appetizing, and hence the benefits of such diet for reducing weight and improving cardiovascular risk, are a matter of debate. Three studies[26-28] informing this question are derived from the NHMRC systematic review.[8] There was no meta-analysis provided in the original review, but this analysis was undertaken for the current report to estimate the effect on weight reduction and lipid profile. One of the RCTs reported additional outcomes of systolic and diastolic blood pressure[26] that were not evaluated by the other trials.[27, 28] The updated literature search identified no new studies. Individual dietary programs to create an energy deficit may be more cost-effective than broad general practitioner advice if delivered by an accredited practicing dietitian. Costs are associated with the use of specialized diets. Purchasing very low-fat diet items to replace meals may be costly for individuals and their use requires frequent monitoring by healthcare professionals. The relevant healthcare professional to monitor use may be a general practitioner with special training, dietitian or specialist nurse, depending on access to the type of provider. The panel judged the use of low-fat diets both acceptable and feasible, and the impact on inequity to be not applicable. In addition, the panel judged that as far as how much people value this outcome, there is no important uncertainty, or variability. The panel judged the balance between desirable and undesirable consequences as uncertain due to lack of information on undesirable effects. Therefore, the panel suggests RCTs be carried out with adequate follow-up duration that compares iso-caloric diets with fat content lower than 20%, approximately 20%, and approximately 30%.

Recommendation 6. The panel makes no clinical recommendation regarding iso-caloric low-fat versus moderate-fat diets. The panel suggests randomized controlled trials be carried out with adequate follow-up duration that compare iso-caloric diets with fat content lower than 20%, approximately 20% and approximately 30% (low quality evidence).

Remarks. Panel members judged that there was not enough evidence to choose one option over another. If any diet is used, fat content should be determined according to the Acceptable Macronutrient Distribution Range (AMDR) and fatty acids subtypes should be

defined (saturated fatty acids, trans fatty acids, and Omega 3 and 6 fatty acids) in order to evaluate benefits or harms.

Question 7. Should portion-controlled diet compared to non-portion controlled diet be used for obese and overweight adults?

The meals of portion-controlled diet are expected to improve long-term adherence to diet since they are easily incorporated into individuals' lifestyle due to their commercial availability, and specific convenient design. This question addresses the effect of portion-controlled diet against standard diet and was based on a single long-term (36 months) RCT identified in the NHMRC systematic review.[29] The updated literature search identified no new studies. Costs are associated with the use of specialized diets. The monthly estimates for resources required for commercial preparation of portion-controlled diet are judged by the panel to be most likely not small. As for the home-made portion controlled diets, due to lack of data on resources required, the panel was uncertain if such resources are small. Purchasing diet items to replace meals may be costly for individuals and their use requires frequent monitoring by healthcare professionals. The relevant healthcare professional to monitor use may be a general practitioner, dietician or specialist nurse, depending on access to the type of provider. Therefore, health professional visit fees would also need to be considered (their estimated costs were previously mentioned in questions 3 and 4). The balance between desirable and undesirable consequences is closely balanced, or uncertain as it is not clear whether the desirable anticipated effects are large and whether the overall undesirable effects are small. The panel judged the option both feasible and acceptable to key stakeholders to implement. The panel also judged that increased associated costs would likely cause health inequities to increase. The panel judged that there is no important uncertainty regarding the variability on how much people value this outcome. More research on portion controlled diet strategies for weight loss is suggested.

Recommendation 7. The panel does not make a clinical recommendation on portion-controlled diets. The panel suggests that more research be carried out (very low quality evidence).

Standardization of diet if made at home may be a barrier for successful implementation.

Question 8. Should psychotherapy-cognitive behavioral therapy (CBT) compared to no cognitive behavioral therapy be used for overweight and obese adults?

Multicomponent lifestyle interventions that include diet, exercise, and behavior modification are a common strategy for weight loss, associated with moderate weight reduction.[15] Psychotherapy is a core component of behavioral modification. In order to understand the role of psychotherapy, this question focuses on cognitive behavioral therapy (CBT), which is an established psychotherapeutic treatment of choice for weight loss.[4] Cognitive behavioral approaches offer individuals the opportunity to identify behavioral and thinking patterns that relate to their particular weight problems.[30] Cognitively oriented weight programs have been developed to reach the growing number of overweight men and women since the 1970's. More recently, RCTs evaluating the impact of psychotherapy have identified CBT to be superior for reducing binge-eating, compared to other psychotherapies.[31] Findings in the NHMRC systematic review (2013) was the reference for this question, and the group did not find new studies in the literature related to CBT. There are probably large beneficial effects of CBT, and other than the high required resources, there are no anticipated adverse consequences. The panel judged that the resources are probably not small in Saudi Arabia because psychologists, or well-trained primary care physicians are required for this intervention and training in psychotherapy would be required. The panel judged the provision of CBT to be cost effective, for overweight and obese adults. However, the panel was concerned about applying this recommendation to complex populations with suspected, or confirmed eating disorders who would require specialized psychiatric assessment. In addition, there is a need to conduct a systematic review of observational studies in Saudi Arabia among both men and women to assess the role of CBT in the management of obesity.

Recommendation 8. The panel suggests CBT rather than no such therapy in overweight and obese adults (conditional recommendation, low quality evidence).

Remarks. This recommendation pertains to general obese populations. Individuals with suspected or confirmed eating disorders or depression require specialized psychiatric assessment and management. Cognitive behavioral therapy, as interpreted in this intervention, is delivered by a health care worker with special competence in CBT and therefore, requires

consideration in terms of implementation and the need for health professional training. Psychotherapy should not be a substitute for psychiatric assessment in any individual with suspected, or confirmed eating disorder, or depression.

II. Pharmacological management

Question 9. Should metformin compared to no metformin be used for overweight and obese adults?

The cornerstone of obesity treatment is lifestyle changes. In view of the low success rate in achieving weight loss and even lower success rate for maintaining this weight loss, drug therapy for obesity in conjunction with lifestyle changes are often used.[3-5,15,32] Evidence suggests that metformin therapy alone contributes to weight loss,[15] although its use for obesity is considered off-label in most jurisdictions. Evidence informing this question is derived from the NHMRC review and includes a meta-analysis on insulin-sensitizing drugs for weight loss in women pooled across 8 trials,[33] as well as the Diabetes Prevention Program Outcomes Study.[34] Our literature update also identified one RCT on hypertensive patients using low dose metformin.[35] The panel judged resources required for metformin to be small and cost effectiveness to be uncertain. The monthly cost for an adult taking 850 mg BID is estimated to be 20SR. The panel judged metformin to be feasible and acceptable and that benefits may be larger in patients with pre-diabetes and those with risk factors for diabetes. Because the desirable anticipated benefits of metformin are not large, and those individuals with pre-diabetes and other diabetes risk factors may experience larger benefits; the panel judged that desirable consequences probably outweigh undesirable consequences in most settings. The undesirable side-effects vary. Future RCTs are required on unselected obese and overweight populations that report all patient-important outcomes (namely, quality of life, function, morbidity and mortality) rather than surrogate outcomes only. Economic analysis in the KSA health care system is also recommended.

Recommendation 9. The panel suggests metformin in obese or overweight adults (conditional recommendation, low quality evidence).

Question 10. Should orlistat compared to no orlistat be used for overweight and obese adults?

Orlistat is a lipase inhibitor, which prevents absorption of approximately 25% of fat consumed and is the main anti-obesity drug approved for long-term treatment of obesity.[36] Evidence suggests that orlistat therapy alone contributes to weight loss.[8] Its high safety profile is implied by its availability over the counter in some jurisdictions as in the US. This question was informed by a meta-analysis (of 11 trials) included the NHMRC review, and a Cochrane review (4 RCTs) also derived from the NHMRC; where the adverse events, mortality and myocardial infarction rates are summarized.[13,37] The panel judged that overall, benefits of orlistat probably outweigh anticipated important adverse events and that implementation is feasible and acceptable. The panel recommends that patients be advised to expect adverse events, to avoid fatty meals and to consider vitamin supplementation (since orlistat decreases absorption of fat soluble vitamins). Regarding health inequities, the panel judged that there is a probable increase impact on health inequities; and therefore in situations with limited resources it would be also reasonable not using orlistat. The panel judged resource use associated with orlistat to be small and probably cost effective, and that economic analyses in the Saudi Arabian context be undertaken. Studies investigating whether and when to use multivitamin supplementation with orlistat are also recommended.

Recommendation 10. The panel suggests orlistat in obese and overweight adults (conditional recommendation, moderate quality evidence).

III. Surgical management

Question 11. Should bariatric surgery compared to non-surgical therapies be used for overweight and obese adults?

Bariatric surgery in general carries risk of morbidity and peri-operative mortality. It is therefore considered when other treatments have failed. Risks with bariatric surgery include; bleeding (0.5%), thromboembolic events (0.8%), wound complications (1.8%), deep infection-abscess or leak (2.1%), pulmonary complications (6.2%), miscellaneous complications (4.8%), cholecystitis and mortality (0.52%).[38] Large observational studies of bariatric surgery, confirms effectiveness for major weight reduction and improvement in comorbidities, which are reported in small, randomized trials.[39] Our literature update identified a meta-analysis of bariatric surgery within the 2014 Cochrane review by Colquitt.[38] Nevertheless, comparing sleeve gastrectomy to medical therapy, which is the comparison of interest to the panel members, was not included in this review. Panel members identified the RCT by Schauer et al,[40] 2014 that specifically

evaluated sleeve gastrectomy in comparison to medical therapy as important for consideration in the Saudi context and this RCT informs this question. The panel judged that health inequities would probably increase in relation to surgical interventions, that implementation considerations need to address pre-operative screening requirements by trained physicians for evaluation of comorbidities and other causes of obesity, including eating disorders and depression and that post-operative lifelong follow-up by interdisciplinary teams (trained physician, surgeon, clinical nutritionist, psychotherapist) are required to prevent and manage dietary deficiencies and other complications. These health professional resource requirements represent additional implementation considerations. The panel judged that this option is feasible and acceptable to implement. All in all, and in most settings, the desirable consequences of this surgical intervention were judged by the panel to probably outweigh the undesirable ones. Anticipated beneficial effects are large, risks are probably small. Costs are judged to be not small and probably cost-effective. The intervention is acceptable and feasible. Certain points were clearly identified by the panel. These include: the data are limited to sleeve gastrectomy, there are associated inequities, and implementing this intervention needs consideration of screening resources and integrated postoperative follow up care. Long-term evaluation of benefits and complications related to bariatric surgery are required, as well as evidence from studies involving obese individuals with lower BMI (30-35 kg/m^2).

Recommendation 11. The panel suggests using bariatric surgery in obese adults (BMI ≥40 or ≥35 kg/m^2 with comorbidities). (conditional recommendation, moderate quality evidence).

Remarks. This recommendation pertains to individuals with larger BMI since anticipated benefits are larger in the setting of individuals who are at higher health risk due to obesity when considering risks associated with surgery. It also considers implementation requirements of interdisciplinary teams to prevent and manage lifelong dietary deficiencies, operative complications and weight management.

Discussion. Obesity is considered a disease, and as such national and international efforts have to be intensified for its prevention and management. Weight loss results in numerous health benefits even if it is modest (5-10% of body weight), however greater weight loss produces greater health benefits.[41]

The magnitude of the health problem of overweight and obesity is enormous in the KSA, and therefore management of overweight and obesity in adult Saudis became an essential part of the larger initiative of the MOH to establish a program of rigorous development of guidelines. The ultimate goals are to provide guidance for clinicians and other healthcare decision makers and reduce unnecessary variability in clinical practice across the Kingdom.

Clinicians, patients, third-party payers, institutional review committees, other stakeholders, or the courts should never view these recommendations as dictates. As described in other guidelines following the GRADE approach, no guideline or recommendation can take into account all of the often-compelling unique features of individual clinical circumstances. Therefore, no one charged with evaluating clinicians' actions should attempt to apply the recommendations from these guidelines by rote or in a blanket fashion.

The panel members of this CPG emphasized the local context, patients values and preferences and culture. This is expected to increase acceptance by patients and relevant health care providers. The recommendations in this guideline shared some similarities with other internationally available recommendations. Previous reports such as American Heart Association/American College of Cardiology/The Obesity Society guidelines,[2] and the Endocrine Society CPG on the pharmacological management of obesity,[32] all share the Saudi CPG focus on diets, exercise and behavioral approaches, for obesity in adults.

Lifestyle interventions, which are considered the cornerstone of obesity management, are multi-component treatments that involve promoting healthy lifestyle habits, dietary interventions, dietary counseling, physical exercise training as well as psychological and behavioral interventions. Although the current guideline focuses on lifestyle modifications as a means for managing of overweight and obesity, the panel members recognize that permanent weight loss could be difficult to achieve based on lifestyle interventions alone. Therefore pharmacological and surgical approaches for weight management were included in the current guideline.

The panel decided to focus on 2 of the most commonly used medications to promote weight loss in KSA; orlistat and metformin, and to postpone the inclusion of other US-FDA approved medications due to the lack of Saudi studies for their use. Although the Endocrine Society has recently published CPG on the pharmacological management of obesity, where several medications commonly prescribed in the United

States were discussed, they encouraged additional scrutiny of medications available in the United States by the European Medicines Agency and the funding of additional long-term clinical trials in the European Union and elsewhere to study the safety and efficacy of these medications.[32] As regards to the surgical approach in the management of obesity, the panel identified that data are limited to sleeve gastrectomy techniques. The implementation considerations need to address pre-operative screening requirements by trained physicians for evaluation of comorbidities and other causes of obesity, as well as post-operative lifelong follow-up by interdisciplinary teams (trained physician, surgeon, clinical nutritionist, psychotherapist), which are required to manage body weight and to prevent and manage dietary deficiencies and other complications.

It should be noted that this guideline did not address all the questions related to obesity and overweight management. During the initial phase of this project, 15 questions were prioritized as potentially relevant. However, only 11 questions were addressed for various reasons. For instance: the question of: "Should laparoscopic adjustable gastric band surgery rather than no laparoscopic adjustable gastric band surgery be used in obese adults?" was not addressed as the panel members agreed that this procedure was not relevant in the Saudi context as it has been replaced by other surgical procedures. Further questions were also not addressed such as: "Should intensive lifestyle intervention rather than group education sessions be used in overweight and obese adults?" and "Should motivational interviewing rather than no motivational interviewing be used in overweight and obese adults?" since group education and motivational interviewing were considered by the panel members to be a part of the intensive lifestyle modification already addressed in a separate question.

Developing a CPG with a rigorous approach is a challenging task.[42] To ensure neutrality and applicability of recommendations reached in these CPGs, and to avoid under-representing any pertinent angle or point of view, the EBHC of the MOH insured that pressing health issues were addressed, that a wide range of specialties in the expert panel were assembled, as well as collaboration with the McMaster Working Group, an internationally renowned specialized institution employing well-designed and standardized guideline development methods.

The following questions were identified by the panel members as priority to be answered in the future update of this guideline:

1. Should more novel anti-obesity drugs compared to classical anti-obesity drugs be used in overweight and obese adult patients?
2. Should specific types of bariatric surgery be offered to obese Saudi patients, as compared to the most commonly performed surgery?
3. Should herbal and traditional/cultural medicine (whether locally produced or imported) be encouraged in overweight and obese adult patients?
4. What are optimal intervention strategies for the prevention of obesity?
5. What are optimal strategies for the management and prevention of obesity in children and adolescents?

Due to the lack of data from Saudi Arabia in certain areas, the panel was not able to reach some recommendations. Therefore, the panel has highlighted that research is needed in certain fields, such as the use of portion-controlled diets, the generation of local evidence for lifestyle modification to be applicable for the Saudi population, and assessing the methods of individualized interventions as opposed to generic approaches. Other specific proposed ideas were agreed upon by the panel members, such as performing a systematic review of observational studies in Saudi Arabia among both men and women to assess the role of cognitive behavioral therapy in the management of obesity, RCTs to be designed with adequate follow-up duration that compare iso-caloric diets with fat content lower than 20%, approximately 20% and approximately 30%, RCTs are required on unselected obese and overweight populations that report all patient-important outcomes (namely, quality of life, function, morbidity and mortality) rather than surrogate outcomes only. In addition, economic analysis in the Saudi Arabian health care system, studies investigating whether and when to use multivitamin supplementation with orlistat, and long-term evaluation of benefits and complications related to bariatric surgery, as well as evidence from studies involving individuals with lower BMI (30-35 kg/m^2) are additional examples of recommended studies.

In conclusion, the current Saudi CPG is on the management of obesity and overweight in adults in Saudi Arabia. For the non-pharmacological management of overweight and obese adults, the panel members strongly suggests lifestyle intervention rather than usual care alone, individualized counseling interventions rather than generic educational pamphlet, physical activity rather than no physical activity, and physical activity in addition to diet rather than diet alone. Some

conditional recommendations were also reached, such as cognitive behavioral therapy rather than no such therapy, and using intensive lifestyle modification rather than usual or minimal care. As for the pharmacological management; metformin and orlistat were suggested as conditional recommendations for the management of overweight and obesity in adults. Finally, bariatric surgery was recommended, conditionally, for the management of obese adults (BMI ≥40 or ≥35 kg/m^2 with comorbidities).

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