

# Evaluation and Treatment of Obesity and Its Comorbidities: 2022 Update of Clinical Practice Guidelines for Obesity by the Korean Society for the Study of Obesity

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The goal of the 8th edition of the Clinical Practice Guidelines for Obesity is to help primary care physician provide safe, effective care to patients with obesity by offering evidence-based recommendations to improve the quality of treatment. The Committee for Clinical Practice Guidelines comprised individuals with multidisciplinary expertise in obesity management. A steering board of seven experts oversaw the entire project. Recommendations were developed as the answers to key questions formulated in patient/problem, intervention, comparison, outcomes (PICO) format. Guidelines underwent multi-level review and cross-checking and received endorsement from relevant scientific societies. This edition of the guidelines includes criteria for diagnosing obesity, abdominal obesity, and metabolic syndrome; evaluation of obesity and its complications; weight loss goals; and treatment options such as diet, exercise, behavioral therapy, pharmacotherapy, and bariatric and metabolic surgery for Korean people with obesity. Compared to the previous edition of the guidelines, the current edition includes five new topics to keep up with the constantly evolving field of obesity: diagnosis of obesity, obesity in women, obesity in patients with mental illness, weight maintenance after weight loss, and the use of information and communication technology-based interventions for obesity treatment. This edition of the guidelines features has improved organization, more clearly linking key questions in PICO format to recommendations and key references. We are confident that these new Clinical Practice Guidelines for Obesity will be a valuable resource for all healthcare professionals as they describe the most current and evidence-based treatment options for obesity in a well-organized format.

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**Key words:** Obesity, Practice guideline, Republic of Korea, Diagnosis, Therapeutics, Comorbidity

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## INTRODUCTION

The prevalence of obesity is rapidly increasing in Korea, with the current obesity epidemic in the country characterized by a rapid increase in morbid obesity and obesity in children, adolescents, and young adults.<sup>1</sup> This is a worrying trend as obesity is associated with a range of comorbidities such as diabetes and heart disease.<sup>2,3</sup> While prevention of obesity is important in managing the condition, treatment also becomes crucial in controlling obesity-related comorbidities.<sup>4</sup> It is vital that both prevention and treatment strategies be implemented to effectively combat the obesity epidemic in Korea. This will help to improve personal and public health in the long-term.<sup>5</sup>

The target audience of “Clinical Practice Guidelines for Obesity 2022” is primary healthcare professionals, including primary care physician who manage adults, children, and adolescents with obesity living in Korea. The guidelines have two main objectives. The first is to provide evidence-based recommendations that can assist primary care physicians in making safe and effective clinical decisions. To accomplish this, the guidelines are clear in their level of evidence and consider the balance between benefits and harms. The second objective is to improve the quality of care by providing high-quality, evidence-based information that helps primary care physicians avoid unnecessary and risky treatments, ultimately leading to better outcomes for patients.

## METHODS

### Development process

“Clinical Practice Guidelines for Obesity 2022” is the 8th edition of obesity management guidelines published by the Korean Society for the Study of Obesity (KSSO). To evaluate the 7th edition and gather opinions on appropriate updates for the 8th edition, a survey was conducted of members of the Committee of Clinical Practice Guidelines and executive members of KSSO. As a result, five new topics were added: diagnosis of obesity, obesity in women, obesity in patients with mental illness, weight maintenance after weight loss, and obesity treatment using information and communication technology (ICT)-based interventions. As a result, the 8th edition of the guidelines now includes 14 topics.

The development period of the guidelines was from January 2021 to November 2022. Adaptation guideline development was applied to develop this edition of the guidelines according to the manual of the Korean Ministry of Health & Welfare and Korean Academy of Medical Science.<sup>6</sup> The recommendations provided are clear and easy to understand.

### Steering board

A steering board comprising seven experts was established to oversee the entire project and planned and confirmed all processes. The adequacy of key questions was discussed with their authors and the steering board to ensure relevance and appropriateness. Conflicts among authors and reviewers regarding recommendations were resolved with the steering board’s guidance to ensure that all final recommendations are fair and unbiased. The steering board played a crucial role in ensuring the success and integrity of the project by providing oversight and resolving any issues.

### Personnel involved in the development of the guidelines

The Committee of Clinical Practice Guidelines comprised multidisciplinary experts in obesity management including family physicians, endocrinologists, clinical nutritionists, exercise specialists, pediatricians, surgeons, and psychiatrists. All members of the committee received education on developing clinical practice guidelines, developing key questions, and writing recommendations through literature review, through participation in multiple workshops. To effectively develop clinical practice guidelines, tasks such as literature and previous guidelines screening, evaluation of selected guidelines, and extraction of evidence for deriving recommendations were carried out by the committee members based on their professional areas of expertise. We used the extracted evidence to derive recommendations and develop clinical guidelines.

### Key questions

The key questions for each topic were developed using the patient/problem, intervention, comparison, outcomes (PICO) format so that the answers could be used as recommendations. This format clearly presents alternatives depending on the target population and clinical condition being addressed. Key questions and their corresponding recommendations are presented in Table 1.

**Table 1.** Key questions and recommendations

1. Diagnosis of obesity	
Q1-1. Is measuring BMI in adults an appropriate way to evaluate the risk of obesity-related comorbidities?	R1-1-1. It is recommended to measure BMI at least once a year in all adults (I, B). <sup>21,60</sup> R1-1-2. Considering the risk of obesity-related comorbidities, the criterion for adult obesity in Korea is a BMI of 25 kg/m <sup>2</sup> or higher (IIa, B). <sup>15,61-69</sup>
Q1-2. Does dividing obesity into grades help evaluate the risk of obesity-related diseases in adults?	R1-2. Obesity is divided into class 1 obesity (BMI 25.0–29.9 kg/m <sup>2</sup> ), class 2 obesity (BMI 30.0–34.9 kg/m <sup>2</sup> ), and class 3 obesity (severe obesity, BMI 35.0 kg/m <sup>2</sup> or higher) in Korea, considering the risk of obesity-related comorbidities (IIa, B). <sup>38,63</sup>
Q1-3. Does measuring WC in addition to BMI help evaluate the risk of obesity-related comorbidities in adults?	R1-3. The criteria for determining abdominal obesity by measuring WC are 90 cm or more for men and 85 cm or more for women in Korea (IIa, B). <sup>70</sup>
2. Pre-treatment evaluation of obesity	
Q2-1. Is it necessary to confirm the cause of obesity in adults before treatment?	R2-1. Before starting treatment, consider conducting a medical interview and screening tests for genetic diseases, endocrinologic diseases, and medications that may cause obesity (IIa, B). <sup>16,17</sup>
Q2-2. Is it necessary to confirm the presence of obesity-related comorbidities before treating adult patients with obesity?	R2-2. Because obesity increases the risk of hypertension, type 2 diabetes, dyslipidemia, gout, arthritis, cardiovascular disease, and cancer and increases mortality rate, it is recommended to conduct a medical interview and screening test for these diseases (I, A). <sup>18,38,39</sup>
Q2-3. What should the weight loss goal for adults with obesity be before treatment?	R2-3. It is recommended to set a primary goal of losing 5%–10% of initial body weight within 6 months (I, A). <sup>18-20</sup>
3. Diet therapy	
Q3-1. How much should energy intake be restricted for weight loss in adults with obesity or overweight?	R3-1-1. It is recommended to individualize the amount of energy restriction for weight loss in adults with obesity or overweight based on personal characteristics and medical conditions (I, A). <sup>38,39</sup> R3-1-2. Very low energy diets should only be performed under supervision of trained professionals under limited circumstances and should be implemented along with intensive lifestyle interventions (I, A). <sup>40,71,72</sup>
Q3-2. Do differences in macronutrient content in nutritional approaches affect the efficacy of weight loss and improvement of metabolic markers in adults with obesity?	R3-2-1. While diverse types of diets (low energy, low carbohydrate, low-fat, high protein, etc.) can be chosen, it is recommended to use a diet that is nutritionally appropriate and achieves an energy deficit, emphasizing healthy eating habits (I, A). <sup>38-40</sup> R3-2-2. It is recommended to individualize the composition of macronutrients (carbohydrates, fats, proteins) based on personal characteristics and medical conditions (I, A). <sup>38-40</sup>
4. Exercise therapy	
Q4-1. How should the decision of exercise participation be made before exercise therapy in adults with obesity?	R4-1. If there are symptoms of cardiovascular, metabolic, or renal diseases or if there are no symptoms but there is a history of cardiovascular, metabolic, or renal diseases and regular exercise is not performed, exercise should be started after consulting a doctor. In other cases, low to moderate intensity exercise without prior medical permission is appropriate (I, A). <sup>73,74</sup>
Q4-2. What is the amount and method of exercise that can help lose weight in adults with obesity?	R4-2. For weight loss, it is recommended to perform aerobic exercise for at least 150 minutes per week, 3–5 times a week and resistance exercise using large muscle groups, 2–3 times a week (I, A). <sup>75-81</sup>
Q4-3. What is the difference in weight loss effect between the combination of aerobic and resistance exercise versus aerobic exercise alone in adults with obesity?	R4-3. Exercise that combines aerobic exercise and resistance exercise is more effective for weight loss than either aerobic exercise alone or resistance exercise alone. Therefore, it is recommended to perform a combination of both aerobic and resistance exercise for weight loss (I, A). <sup>80,82</sup>
Q4-4. What is the difference in weight loss effect between exercise alone and exercise performed in combination with diet therapy in adults with obesity?	R4-4. For effective weight loss, it is recommended to combine exercise with diet therapy (I, A). <sup>76,83</sup>
5. Behavioral therapy	
Q5-1. Are comprehensive lifestyle interventions that incorporate behavioral therapy techniques more effective for weight loss and its maintenance in adults with obesity than typical treatments (e.g., providing advice and educational materials)?	R5-1-1. For weight loss, comprehensive lifestyle improvement such as reducing energy intake and increasing physical activity based on behavioral therapy is recommended (I, A). <sup>84,85</sup> R5-1-2. For effective weight loss, it is recommended that a trained therapist conduct face-to-face behavioral therapy for at least 6 months (I, A). <sup>71,86,87</sup> R5-1-3. For effective maintenance of weight loss, it is recommended that a trained therapist conduct behavioral therapy for at least 1 year (I, A). <sup>86,88-90</sup> R5-1-4. If a 2.5% weight loss is not achieved within 1 month of behavioral therapy, consider reinforcing the lifestyle interventions based on behavioral therapy (IIa, B). <sup>21,91,92</sup>
Q5-2. What measures are necessary for weight loss and its maintenance in adults with obesity who drink alcohol?	R5-2. It is recommended to evaluate alcohol consumption during behavioral therapy for weight loss and its maintenance (I, A). <sup>93-95</sup>
Q5-3. What treatment is needed to reduce weight gain when trying to quit smoking during obesity treatment?	R5-3. When attempting to quit smoking during obesity treatment, consider using smoking cessation medications in conjunction with behavioral therapy to prevent weight gain (IIa, B). <sup>96-98</sup>

*(Continued to the next page)*

Table 1. Continued

6. Pharmacotherapy	
Q6-1. Is it appropriate to only use medication to treat obesity in adults with obesity?	R6-1. The basic treatment for obesity is diet therapy, exercise therapy, and behavioral therapy, and it is recommended to use medication as an additional treatment method only in combination with these (I, A). <sup>99-112</sup>
Q6-2. What are the indications for obesity pharmacotherapy in adults with obesity?	R6-2. In Korean adults with a BMI of 25 kg/m <sup>2</sup> or more who have failed to lose weight with non-medicinal treatment, pharmacotherapy should be considered (IIa, B). <sup>21,40,61,113</sup>
Q6-3. What medications should be used for weight loss in adults with obesity?	R6-3. For long-term weight management, it is recommended to use medications that have been approved based on large-scale clinical trials (I, A). <sup>99,114</sup>
Q6-4. Should anti-obesity medication be maintained in case of an insufficient response?	R6-4. If at least 5% weight loss is not achieved within 3 months of maintenance dosage of anti-obesity medication, it is recommended to change or stop the medication (I, A). <sup>115-120</sup>
7. Bariatric surgery	
Q7-1. Which group of patients will benefit the most from weight loss or show improvement in obesity-related comorbidities if they undergo bariatric/metabolic surgery compared to non-surgical treatment?	R7-1-1. Bariatric/metabolic surgery should be considered in Korean adults with a BMI of 35 kg/m <sup>2</sup> or more, or a BMI of 30 kg/m <sup>2</sup> or more with obesity-related comorbidities, who have failed to lose weight with non-surgical treatment (IIa, B). <sup>40,48</sup> R7-1-2. Bariatric/metabolic surgery should be considered in individuals with type 2 diabetes mellitus with a BMI of 27.5 kg/m <sup>2</sup> or more and a blood sugar level that is not properly controlled with non-surgical treatment (IIa, B). <sup>40,48</sup>
Q7-2. What should be evaluated before performing bariatric/metabolic surgery in patients who need it?	R7-2-1. It is recommended to collect a medical and psychosocial history, conduct a physical examination, and run diagnostic tests to evaluate the safety of the potential bariatric/metabolic surgery (I, A). <sup>121,122</sup> R7-2-2. Appropriate evaluation of nutritional status should be considered before bariatric/metabolic surgery (IIa, B). <sup>123</sup> R7-2-3. It is recommended to quit smoking at least 6 weeks prior to bariatric/metabolic surgery (I, B). <sup>124</sup>
Q7-3. What type of bariatric/metabolic surgery should be performed in patients who need it?	R7-3. It is recommended to choose from among standard procedures that have been proven to be effective and safe, such as sleeve gastrectomy, Roux-en-Y gastric bypass, adjustable gastric banding, and biliopancreatic diversion/duodenal switch, taking into account the individual's status (I, A). <sup>40</sup>
Q7-4. Does continuous follow-up management after bariatric/metabolic surgery affect the outcome? If so, what is the appropriate follow-up method for management and evaluation?	R7-4-1. It is recommended to conduct multidisciplinary follow-up management for all patients who have undergone bariatric/metabolic surgery (I, B). <sup>47-50</sup> R7-4-2. It is recommended to supplement micronutrients and conduct regular follow-up examinations according to the surgical procedure after bariatric/metabolic surgery (I, B). <sup>76,81,84</sup>
8. Obesity in the elderly	
Q8-1. What should be considered when evaluating obesity in the elderly?	R8-1. It is recommended to evaluate WC in conjunction with BMI when diagnosing obesity in the elderly (I, A). <sup>8-10</sup>
Q8-2. When does weight loss help in the elderly?	R8-2. Weight loss should be considered when the benefits outweigh the risks for the elderly (IIa, B). <sup>21-32</sup>
Q8-3. What should be considered for effective and safe obesity treatment in the elderly?	R8-3-1. In managing obesity in the elderly, it may be necessary to evaluate osteoporosis and sarcopenia (IIb, B). <sup>21,35-37</sup> R8-3-2. For treatment of obesity in the elderly, it is recommended to prioritize a low energy diet rich in protein and to increase physical activity (I, A). <sup>125-128</sup> R8-3-3. When treating obesity in the elderly, pharmacotherapy and surgical treatments may be considered with caution, taking into account the presence of accompanying diseases and medications to ensure patient safety (IIb, B). <sup>21,40,56-59,129</sup>
9. Obesity in children and adolescents	
Q9-1. How is obesity diagnosed in children and adolescents?	R9-1-1. It is recommended to prevent and treat childhood and adolescent obesity, because obesity in this age group easily progresses to adult obesity and is associated with a high risk of obesity-related comorbidities (I, A). <sup>130-132</sup> R9-1-2. When diagnosing obesity for children and adolescents older than 2 years, it is recommended to use the BMI percentile for age and sex based on the 2017 Korean National Growth Chart for Children and Adolescents. A BMI in the 85th percentile or higher should be considered to indicate pre-obesity (overweight), while a BMI in the 95th percentile or higher should be considered to indicate obesity (I, A). <sup>12-14,130</sup> R9-1-3. Individualized medical risk assessment should be considered in children and adolescents with pre-obesity or obesity (IIa, B). <sup>14,130,132</sup>
Q9-2. What are the treatment goals and principles for obesity in children and adolescents?	R9-2. Treatment of obesity in children and adolescents is recommended to maintain appropriate weight while supplying the energy and nutrients necessary for normal growth and to habituate a healthy lifestyle (I, A). <sup>14,52,130,132-135</sup>
Q9-3. What are safe and effective treatment strategies for obesity in children and adolescents?	R9-3-1. Comprehensive lifestyle modifications including diet, exercise, and behavioral therapy are recommended for treatment of obesity in children and adolescents (I, A). <sup>14,52,130</sup> R9-3-2. In cases where weight gain and obesity-related comorbidities are sustained even with intensive diet, exercise, and behavioral therapy, obesity pharmacotherapy by an experienced specialist should be considered (IIa, B). <sup>130,133,134,136</sup> R9-3-3. In cases where weight gain and obesity-related comorbidities are sustained even with intensive multidisciplinary treatment and pharmacotherapy for obesity, surgical therapy may be considered in limited cases, only after completion of growth and puberty (IIb, C). <sup>52-55</sup>

(Continued to the next page)

Table 1. Continued

10. Obesity in women
Q10-1. Does weight loss help in reducing pregnancy complications in women with obesity who are preparing for pregnancy? R10-1. Women who are considering pregnancy are recommended to maintain a normal weight to reduce obstetric and perinatal risks (I, A). <sup>137-145</sup>
Q10-2. What are the appropriate lifestyle habits for weight management during pregnancy and after delivery in women with obesity? R10-2-1. In pregnant women with obesity, a balanced diet and regular physical activity should be considered for appropriate rather than excessive weight gain during pregnancy (IIa, B). <sup>146-150</sup> R10-2-2. Active lifestyle interventions, such as modification of diet and an increase in physical activity, are recommended for weight management after delivery in women with obesity (I, A). <sup>151</sup>
Q10-3. Does menopause increase the risk of obesity and its comorbidities? R10-3. Because menopause can lead to abdominal obesity, which increases the risk of obesity-related comorbidities, appropriate weight management is recommended for menopausal women with obesity (I, A). <sup>152-158</sup>
Q10-4. Should hormone therapy be used to aid weight loss or to prevent weight gain in menopausal women? R10-4. Hormone therapy is not recommended for the purpose of weight loss in menopausal women (III, A). <sup>159</sup>
11. Obesity in patients with mental illness
Q11-1. Is it necessary to conduct screening tests for obesity and metabolic diseases in patients with severe mental illness for proper management? R11-1. It is recommended to conduct screening tests for obesity and metabolic diseases in patients with severe mental illness who are taking medications related to weight gain for prevention and management of metabolic diseases (I, B). <sup>160</sup>
Q11-2. For patients with obesity and severe mental illness, is it effective and mentally safe to implement comprehensive lifestyle interventions, obesity pharmacotherapy, and bariatric surgery? R11-2. For weight loss in patients with obesity and severe mental illness, comprehensive lifestyle interventions are recommended (I, A). <sup>161-166</sup>
Q11-3. Is distinguishing whether a patient with obesity also has binge eating disorder useful in predicting the effectiveness of obesity treatment? R11-3. Because patients with obesity in conjunction with binge eating disorder may experience less weight loss in response to typical obesity treatments, the presence of binge eating disorder should be considered for evaluation when treating obesity (IIa, C). <sup>167,168</sup>
Q11-4. What kind of obesity treatment is effective at inducing weight loss and improving symptoms of obstructive sleep apnea in patients with obesity and obstructive sleep apnea? R11-4. Comprehensive lifestyle interventions for weight loss are recommended for patients with obesity and obstructive sleep apnea (I, A). <sup>169-174</sup>
12. Weight maintenance after weight loss
Q12-1. Are there different long-term outcomes for obesity-related comorbidities in adults with obesity who have successfully maintained weight loss compared to those who have not? R12-1. It is recommended to maintain weight loss for more than 1 year to prevent and manage obesity-related comorbidities (I, A). <sup>88,175-184</sup>
Q12-2. What treatment is effective for long-term weight management and outcomes in adults with obesity? R12-2-1. It is recommended to use a combination of diet, exercise, and cognitive behavioral therapy for weight maintenance after weight loss (I, A). <sup>185-193</sup> R12-2-2. The use of anti-obesity medications that are approved for long-term use may also be considered (IIb, B). <sup>88,107,194</sup>
Q12-3. Is additional obesity pharmacotherapy helpful for long-term weight management in patients with morbid obesity who have regained weight after bariatric/metabolic surgery? R12-3. In patients who have regained weight after bariatric/metabolic surgery, the use of anti-obesity medications in conjunction with lifestyle modifications may be considered (IIb, B). <sup>195-198</sup>
13. Metabolic syndrome
Q13-1. What are the diagnostic criteria for metabolic syndrome in Korean adults? R13-1. In Korea, adults are diagnosed with metabolic syndrome if they meet three or more of the following criteria (-, A). <sup>70,199,200</sup> (1) Abdominal obesity (WC $\geq$ 90 cm in men and $\geq$ 85 cm in women) (2) Elevated blood pressure ( $\geq$ 130/85 mmHg or use of hypertension medications) (3) Elevated fasting blood sugar ( $\geq$ 100 mg/dL or use of diabetes medications) (4) Elevated triglycerides ( $\geq$ 150 mg/dL or use of lipid-lowering drugs) (5) Low HDL cholesterol ( $<$ 40 mg/dL in men and $<$ 50 mg/dL in women or use of lipid-lowering drugs)
Q13-2. What are effective interventions for treating and managing metabolic syndrome in adults? R13-2. To treat and manage metabolic syndrome, lifestyle modifications and, if necessary, drug interventions for individual components are recommended (I, A). <sup>201-211</sup>
14. Obesity treatment using ICT-based interventions
Q14-1. Can information and communication technology-based methods be used to modify lifestyle to manage obesity and metabolic syndrome? R14-1. ICT-based interventions should be considered for managing obesity and metabolic syndrome (IIa, B). <sup>212,213</sup>
Q14-2. Are ICT-based interventions effective at inducing weight loss and maintenance compared to conventional treatment in adults with obesity? R14-2. ICT-based interventions may be considered as part of a comprehensive strategy for weight loss (IIb, B). <sup>214-216</sup>

BMI, body mass index; WC, waist circumference; HDL, high-density lipoprotein; ICT, information and communication technology.

## Literature review

A medical librarian developed literature search strategies and formulas specifically tailored to each database search engine. Utilizing these strategies, the librarian systematically searched through literature-search software for selected topics and established key questions. These searches were executed in PICO format. The publication date range of the literature searched was between January 2010 and May 2021. Report types searched were systematic reviews, meta-analyses, randomized clinical trials, cohort studies, and guidelines. Narrative reviews were also included for topics lacking randomized clinical trials. Electronic databases of Pubmed (Medline), Embase, Cochrane Library, KoreaMed, RISS (KERIS), ScienceOn, Guidelines International Network (GIN), National Institute for Health and Care Excellence (NICE), Scottish Intercollegiate Guidelines Network (SIGN), National Health and Medical Research Council (NHMRC), and Google were searched.

## Level of evidence and recommendations

The level of evidence of the literature (or guidelines) used for developing the recommendations was classified into four categories (A, B, C, and D in Supplementary Table 1). The Committee of

Clinical Practice Guidelines used the modified Grading of Recommendation Assessments, Development, and Evaluation (GRADE) method to determine the strength of the recommendations considering the level of evidence, benefits and harms, feasibility, acceptability, and level of applicability in primary care practice. There were four grades of recommendations (I, IIa, IIb, and III in Supplementary Table 1)<sup>7</sup>. Even if the level of evidence was low, recommendations that were considered to have clear benefits or high applicability in clinical practice were upgraded by agreement of the Committee of Clinical Practice Guidelines.

## Employment of multi-level reviews and cross-checks

After initial development of the recommendations, a small group discussion method was used to review these recommendations. Review and cross-checking by the steering board and writing members resulted in revision of the initial recommendations and explanations. Then, at KSSO congresses, two public hearings on the updated management guidelines were held. The revised version after the public hearings was reviewed by executive members of KSSO who were not members of the guidelines committee. Finally, the steering board supervised and confirmed the final version. Endorse-

**Table 2.** Diagnostic criteria for obesity, abdominal obesity, and metabolic syndrome and risk of comorbidity according to BMI and WC in Koreans

Classification*	BMI (kg/m <sup>2</sup> )	Risk of comorbidity according to WC	
		< 90 cm (men), < 85 cm (women)	≥ 90 cm (men), ≥ 85 cm (women)
<b>Adults (≥ 18 years)</b>			
Underweight	< 18.5	Low	Average
Normal	18.5–22.9	Average	Increased
Pre-obesity	23–24.9	Increased	High
Class 1 obesity	25–29.9	High	Severe
Class 2 obesity	30–34.9	Severe	Very severe
Class 3 obesity	≥ 35	Very severe	Very severe
<b>Metabolic syndrome in adults</b>			
Adults are diagnosed with metabolic syndrome if they meet three or more of the following criteria.			
(1) Abdominal obesity (WC ≥ 90 cm in men and ≥ 85 cm in women)			
(2) Elevated blood pressure (≥ 130/85 mmHg or use of hypertension medications)			
(3) Elevated fasting blood sugar (≥ 100 mg/dL or use of diabetes medications)			
(4) Elevated triglycerides (≥ 150 mg/dL or use of lipid-lowering drugs)			
(5) Low HDL-cholesterol (< 40 mg/dL in men and < 50 mg/dL in women or use of lipid-lowering drugs)			
<b>Children and adolescents (2–18 years old)</b>			
Pre-obesity	BMI percentile for sex and age based on 2017 Korean National Growth Chart for Children and Adolescents		
Obesity	85th–94.9th		
	≥ 95th		

\*Pre-obesity may be defined as overweight or at-risk weight, and class 3 obesity may be defined as extreme obesity. BMI, body mass index; WC, waist circumference; HDL, high-density lipoprotein.

ment was requested and received from relevant scientific societies and associations.

## DIAGNOSTIC CRITERIA FOR OBESITY, ABDOMINAL OBESITY, AND METABOLIC SYNDROME

Diagnostic criteria for obesity, abdominal obesity, and metabolic syndrome remain the same as in the previous version (Table 2). Diagnosis of obesity based on body mass index (BMI) applies regardless of age in adults. However, in the elderly, the same BMI may indicate a higher body fat percentage due to changes in body composition caused by decreased muscle and bone mass, as well as a decrease in height. Therefore, we recommended evaluation of waist circumference (WC) in conjunction with BMI when diagnosing obesity in the elderly (I, A).<sup>8-10</sup> For children and adolescents older than 2 years, use of the BMI percentile for age and sex based on the 2017 Korean National Growth Chart for Children and Adolescents is recommended; a BMI in the 85th percentile or higher is considered to indicate pre-obesity (overweight), while that in the 95th percentile or higher is considered to indicate obesity (I, A).<sup>11-14</sup> Obesity in adults is divided into class 1, class 2, and class 3 obesity (extreme obesity) (BMI 35.0 kg/m<sup>2</sup> or higher) in Korea (IIa, B).<sup>12,15</sup> Criteria used to diagnose obesity and abdominal obesity have been established, taking into account the risk of obesity-related comorbidities.

Although the cut-off values for each criterion were the same as those used in the previous KSSO guidelines, levels of evidence and grades of recommendations were modified through evaluation.

## EVALUATING OBESITY STATUS AND RELATED COMORBIDITIES AND SETTING TREATMENT GOALS PRIOR TO TREATMENT INITIATION

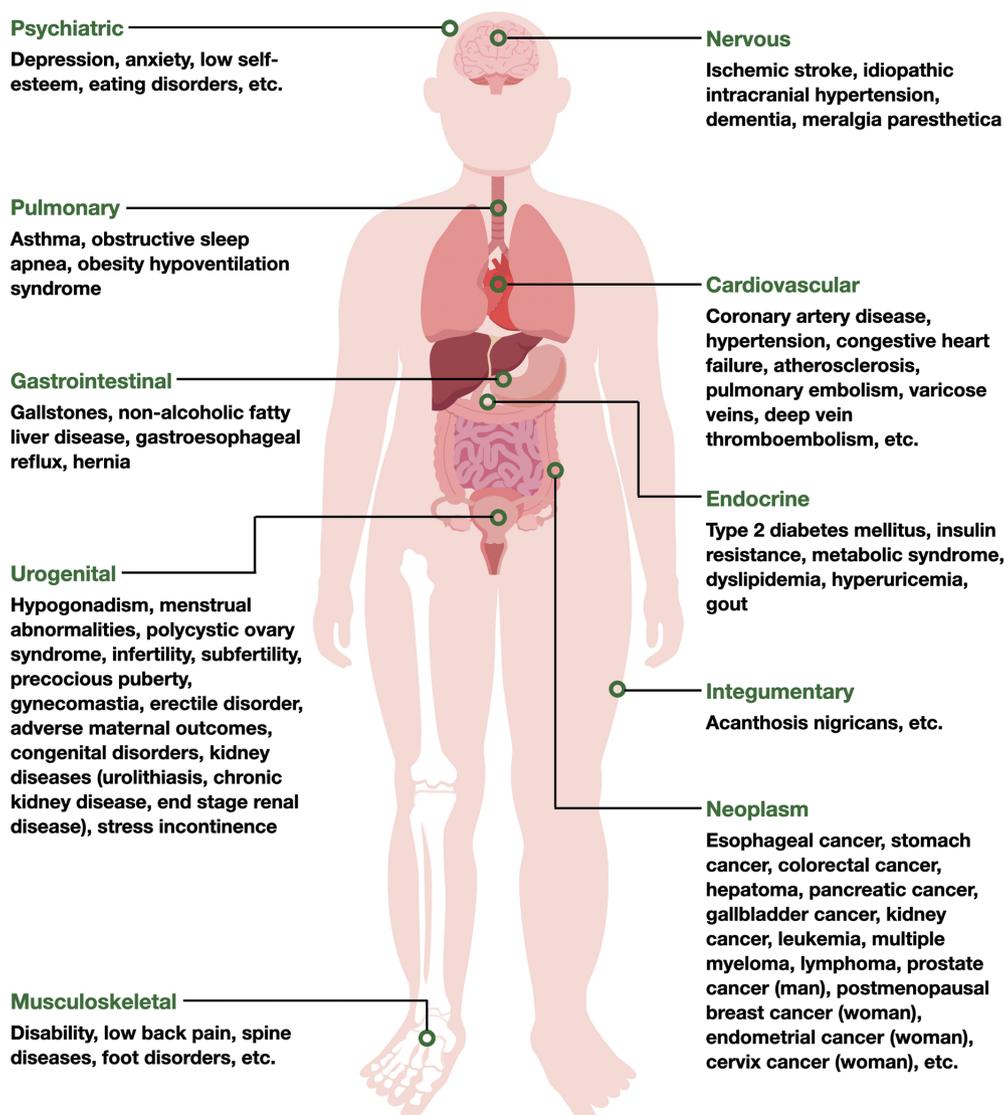
More than 90% of obesity cases are due to an imbalance between energy intake and expenditure, known as primary obesity. However, in some cases, secondary causes such as genetic and congenital disorders, medications, neurological and endocrine diseases, or psychiatric illnesses may be present (Table 3). Accurately identify-

**Table 3.** Causes of secondary obesity

Classification	Causes
Monogenic obesity	Leptin deficiency Leptin receptor deficiency Proopiomelanocortin (POMC) deficiency Melanocortin 4 receptor (MC4R) deficiency Other
Congenital syndromic obesity	Prader-Willi syndrome Laurence-Moon-Biedl syndrome Alström syndrome Cohen syndrome Carpenter syndrome Other
Drugs	Antipsychotics: thioridazine, olanzapine, clozapine, quetiapine, risperidone Tricyclic antidepressants: imipramine, amitriptyline, nortriptyline, doxepin Selective serotonin reuptake inhibitors: paroxetine Noradrenergic and specific serotonergic antidepressants: mirtazapine Mood stabilizers: lithium Anti-convulsants: valproate, carbamazepine, gabapentin, pregabalin Anti-diabetics: insulin, sulfonylurea, glinide, thiazolidinedione Serotonin receptor antagonists: pizotifen H1 antihistamines: cyproheptadine β-Blockers: propranolol, metoprolol, atenolol, nadolol α-Blockers: terazosin, prazosin, clonidine Steroids: oral contraceptives, glucocorticoids
Neuroendocrine diseases	Hypothalamic obesity: trauma, tumor, infective disorder, neurosurgery, elevated intracranial pressure Cushing's syndrome Insulinoma Polycystic ovary syndrome Growth hormone deficiency in adults Hypothyroidism
Psychiatric disorders	Affective disorder: major depression, bipolar disorder, seasonal affective disorder Anxiety disorder: panic disorder, agoraphobia Binge eating disorder Attention deficit hyperactivity disorder Alcohol dependency

ing and addressing these underlying causes can lead to more effective weight loss. Therefore, prior to initiating obesity treatment, a medical interview and screening tests should be considered to identify secondary obesity and its causes (IIa, B).<sup>16,17</sup>

People with obesity are at an increased risk for comorbidities stemming from metabolic abnormalities, such as hypertension, cardiovascular disease, type 2 diabetes, dyslipidemia, metabolic syndrome, gallbladder disease, gout, and some types of cancer. They



**Figure 1.** Comorbidities of obesity by body system.

also are at higher risk of developing weight-related conditions such as arthritis, low back pain, and obstructive sleep apnea compared to normal weight individuals. These obesity-related comorbidities are illustrated according to body system in Fig. 1. Refer to Table 4 for a list of tests used to evaluate obesity and its associated comorbidities.

The goal of obesity treatment is not exclusively centered on achieving weight loss, but rather a reduction in the risk of obesity-related diseases and an increase in overall health. A weight loss of 5% to 10%, along with improvements in lifestyle, have been shown to have clinically significant benefits. We recommend losing 5% to 10% of initial body weight within 6 months (I, A).<sup>18-20</sup>

Obesity in the elderly increases the risk of various diseases and

medical costs, but there is insufficient evidence to show that weight loss can effectively prevent or treat obesity-related complications. Additionally, elderly individuals have a high incidence of osteopenia and osteoporosis, which increases the risk of fractures. Weight loss in this population may also be associated with decreased bone density and muscle mass. When treating obesity in older adults, evaluation of osteoporosis should be considered in high-risk groups, and weight loss should be considered when the benefits outweigh the risks (IIa, B).<sup>21-34</sup> Compared to the previous version of these guidelines, the current version recommends evaluation of osteoporosis and sarcopenia when treating obesity in the elderly (IIb, B).<sup>21,35-37</sup>

**Table 4.** Evaluation of obesity and its related comorbidities

Obesity		
1. BMI should be measured regularly at least once a year in all adults. People with a BMI between 23 and 24.9 kg/m <sup>2</sup> are classified as with pre-obesity, while those with a BMI of 25 kg/m <sup>2</sup> or above are classified as with obesity.		
2. WC should be measured to assess abdominal obesity. Individuals with abdominal obesity are considered at elevated risk for obesity-related comorbidities.		
3. Evaluate comorbidities in people with pre-obesity or obesity		
History taking	Obtain a comprehensive history, including past medical history, family history, current medications, smoking and alcohol use, social history, previous weight loss attempts, history of weight change, reason for weight gain, dietary habits, eating disorders, physical activity level, exercise habits, mental health status including depression and stress, desired weight, and motivation for weight loss	
Physical examination	Measure height, weight, WC, vital signs, body composition (using BIA or DXA if necessary), and visceral fat amount (using CT or MRI if necessary) and conduct a systemic physical examination to assess comorbidities	
Laboratory evaluation	Measure fasting blood glucose, serum lipid profile, uric acid, thyroid-stimulating hormone, liver function tests, complete blood count, renal function tests, and inflammatory markers and conduct tests for evaluation of secondary obesity (if necessary)	
Obesity-related comorbidities		
System	Comorbidities	Suggested tests
Cardio-cerebrovascular	Coronary artery disease, hypertension, ischemic stroke, congestive heart failure, atherosclerosis, pulmonary embolism, varicose veins, deep vein thromboembolism, etc.	Blood pressure, pulse rate, electrocardiography. Conduct a thorough examination for suspected diseases if necessary.
Gastrointestinal	Gallstone, nonalcoholic fatty liver disease, gastroesophageal reflux, hernia	Liver function tests. Conduct abdominal ultrasound and/or upper endoscopy if necessary.
Pulmonary	Asthma, obstructive sleep apnea, obesity hypoventilation syndrome	Chest X-ray, pulmonary function tests, measurement of neck circumference, polysomnography if necessary.
Endocrine	Type 2 diabetes mellitus, insulin resistance, metabolic syndrome, dyslipidemia, hyperuricemia, gout	Fasting blood glucose, serum lipid profile, uric acid. Glycated hemoglobin and/or fasting insulin if necessary.
Tumor	Esophageal cancer, stomach cancer, colorectal cancer, hepatoma, pancreatic cancer, gallbladder cancer, kidney cancer, leukemia, multiple myeloma, lymphoma, prostate cancer (man), postmenopausal breast cancer (woman), endometrial cancer (woman), cervix cancer (woman)	Conduct a thorough examination for suspected diseases if necessary.
Urogenital	Hypogonadism, menstrual abnormalities, polycystic ovary syndrome, infertility, subfertility, precocious puberty, gynecomastia, erectile disorder, adverse maternal outcomes (gestational diabetes, preeclampsia, eclampsia, miscarriage, dystocia, elevated risk of cesarean sections), congenital disorders (neural tube defects, cleft lip and cleft palate, hydrocephalus, congenital heart diseases), stress incontinence	Conduct a thorough examination for suspected diseases if necessary.
Musculoskeletal	Disability, low back pain, osteoarthritis, spine diseases, foot disorders	Conduct a thorough examination for suspected diseases if necessary.
Nervous	Idiopathic intracranial hypertension, dementia, meralgia paresthetica	Conduct a thorough examination for suspected diseases if necessary.
Psychiatric	Depression, anxiety, low self-esteem, eating disorder, decreased work performance, low quality of life, body dissatisfaction	Conduct a thorough examination for suspected diseases if necessary.
Other	Acanthosis nigricans, skin infections, periodontal disease, increased risk of anesthesia complications, lymphedema	Conduct a thorough examination for suspected diseases if necessary.

BMI, body mass index; WC, waist circumference; BIA, bioelectrical impedance analysis; DXA, dual-energy X-ray absorptiometry; CT, computed tomography; MRI, magnetic resonance imaging.

## LIFESTYLE-RELATED THERAPY

Diet, exercise, and behavioral therapy that induce lifestyle improvements are the mainstays of obesity treatment. General principles in this field remain unchanged from the previous edition of the guidelines. See Table 1 for detailed recommendations.

This edition of the guidelines recommends individualizing the amount of energy restriction and the composition of macronutri-

ents (carbohydrates, fats, proteins) for weight loss. Adequate protein intake is important to prevent sarcopenic obesity in the treatment of elderly obesity. A very low energy diet (VLED) that severely restricts calorie intake to 800 kcal or less per day can result in significant short-term weight loss; however, this rapid weight loss method can cause various medical problems. Therefore, VLED should only be performed under the supervision of trained professionals under limited circumstances. In the 8th edition guidelines,

**Table 5.** Summary of the characteristics of diverse diet therapies

Diet therapy	Characteristic
Low energy diet	Energy intake reduction by 500-1,000 kcal per day This enables the consumption of a nutritionally appropriate meal. 0.5–1.0 kg/week of weight loss is expected. A maximum effect on weight loss may be attained within 6 months, with a gradual decrease thereafter.
Very low energy diet	Energy restriction to 800 kcal/day or less Rapid weight loss is possible in a short period of time, but there is no significant difference in the long-term compared to a low energy diet. Medical supervision is necessary to prevent serious medical outcomes. Should be accompanied by interventions for long-term lifestyle improvements.
Very low carbohydrate diet	Limit carbohydrate consumption to less than 130 g/day or 30% of total energy (restrict to less than 50 g or 10% of total energy at start and increase gradually) Initial weight loss effect is greater than with a low energy diet, but the long-term effect is either similar or minimally better. This may improve serum triglyceride level but also increase the risk of cardiovascular disease due to elevation of LDL cholesterol.
Low carbohydrate diet	Limit carbohydrate consumption to 40%–45% of total energy typically Initial weight loss effect is greater than the low energy diet, but the long-term effect is either similar or minimally better. This may improve serum triglyceride level but also increase the risk of cardiovascular disease due to elevation of LDL cholesterol.
High protein diet	Usual protein intake of 25%–30% of total energy Helpful to prevent excessive carbohydrate intake, loss of lean mass, and maintain an appropriate protein nutrition status Effective for weight loss/maintenance compared to a low energy diet but not to a large extent
Intermittent energy restriction	Alternative dietary approach to the conventional continuous energy-restricted diet - Intermittent fasting: an eating pattern that alternates between periods of fasting and non-fasting days - Time-restricted diet: a type of eating pattern that allows eating within a particular window of time each day There is no significant or minimal difference in the degree of weight loss compared to continuous energy restriction methods. There is limited evidence on the long-term effects of this diet type on obesity.

LDL, low-density lipoprotein.

we recommend a nutritionally appropriate diet and reduction of energy intake as was recommended in the previous edition of the guidelines and additionally emphasize “healthy eating habits” (I, A).<sup>38-40</sup> Refer to Table 5 for the diverse types of diets that can be implemented.

With regard to exercise therapy, individuals with symptoms of cardiovascular, metabolic, or renal diseases or those with a history of these diseases but who do not regularly exercise should consult a doctor before starting. In other cases, it is safe to start a low to mod-

erate intensity exercise regimen without obtaining medical clearance. This edition of the guidelines recommends aerobic exercise for at least 150 minutes per week, 3 to 5 times a week, and resistance exercise using large muscle groups 2 to 3 times per week for weight loss. Furthermore, increasing aerobic exercise to 250 to 300 minutes per week is suggested for more meaningful weight loss. Compared to exercise therapy alone, it has been shown that body weight, BMI, and WC are more improved when exercise therapy is combined with dietary therapy.

Comprehensive lifestyle improvement such as reducing energy intake and increasing physical activity based on behavioral therapy are recommended for weight loss in this edition of the guidelines, similar to the previous edition. Additionally, third-wave cognitive behavioral therapy, such as mindfulness-based cognitive therapy and acceptance and commitment therapy, is newly introduced in this edition of the guidelines.<sup>41-45</sup> Compared with the previous version of the guidelines, this edition recommends intensifying lifestyle interventions based on behavioral therapy if weight loss of 2.5% is not achieved within 1 month of starting therapy and highlights the roles of alcohol consumption and smoking during behavioral therapy for weight loss and maintenance.

## PHARMACOTHERAPY

Despite the development of many new peptide anti-obesity medications, with some of these currently under consideration for approval by the Korean Ministry of Food and Drug Safety, there have been no new approvals of anti-obesity medications for adults with obesity since the 7th edition of the guidelines (up to February 2023). However, liraglutide was newly approved during that period for patients with obesity aged 12 years or older. Therefore, currently available anti-obesity medications for children and adolescents in Korea are phentermine (for those aged 16 or older) for short-term treatment and orlistat (for those aged 12 or older) and liraglutide (for those aged 12 or older) for long-term treatment (Table 6).<sup>46</sup> In adults with obesity, orlistat, naltrexone/bupropion extended release (ER), liraglutide, and phentermine/topiramate ER are available for long-term weight loss, while phentermine, diethylpropion, phendimetrazine, and mazindol are available for short-term treatment in Korea.

**Table 6.** Anti-obesity medications for the pediatric population

Drug name	Mechanism of action	Indication	Considerations
Orlistat	Pancreatic and gastric lipase inhibitor	Obesity ≥ 12 years old	Flatulence, oily spotty stools, diarrhea, vitamin/mineral deficiencies
Phentermine	Sympathomimetic amine	Obesity > 16 years old Short-term use	Increases heart rate and blood pressure and causes dry mouth, insomnia, constipation, anxiety, irritability
Liraglutide 3.0 mg	GLP-1 receptor agonist	Adolescents (12–17-year-old) with a BMI corresponding to ≥ 30 kg/m <sup>2</sup> for adults and body weight > 60 kg	Abdominal pain, nausea, vomiting, diarrhea, potential hypoglycemia; contraindicated with history or family history of medullary thyroid carcinoma, MEN type 2, ESRD

Approved by the Korean Ministry of Food and Drug Safety.

GLP-1, glucagon-like peptide-1; BMI, body mass index; MEN, multiple endocrine neoplasia; ESRD, end-stage renal disease.

**Table 7.** Selection of anti-obesity medication according to comorbidities

Comorbidities		Anti-obesity medication			
		Orlistat	Naltrexone/bupropion ER	Liraglutide 3.0 mg	Phentermine/topiramate ER
Type 2 diabetes mellitus					
Hypertension			Monitor blood pressure and heart rate Contraindicated in uncontrolled hypertension	Monitor heart rate	Monitor heart rate
Coronary artery disease			Monitor blood pressure and heart rate		
Chronic kidney disease	Mild (eGFR 60–89 mL/min)				
	Moderate (eGFR 30–59 mL/min)		Do not exceed 8 mg/90 mg bid per day		Do not exceed 7.5 mg/46 mg per day
	Severe (eGFR < 30 mL/min)	Monitor for urolithiasis (oxalate stones)	Do not exceed 8 mg/90 mg bid per day Not recommended for end stage renal disease		Do not exceed 7.5 mg/46 mg per day Not recommended for end stage renal disease
Liver cirrhosis	Mild to moderate (Child-Pugh 5–9)	Monitor for gall stones	Do not exceed 8 mg/90 mg bid per day	Monitor for gall stones	Do not exceed 7.5 mg/46 mg per day
	Severe (Child-Pugh > 9)				
Obstructive sleep apnea					Recommend 15 mg/92 mg per day
Depression					Do not exceed 7.5 mg/46 mg per day
Glaucoma					
Pancreatitis					

■ Available; ■ With caution; ■ Not recommended or contraindicated; ■ Limited evidence.  
ER, extended release; eGFR, estimated glomerular filtration rate.

Obesity pharmacotherapy is recommended as an additional treatment method for Korean adults with a BMI of 25 kg/m<sup>2</sup> or higher after failure of non-pharmacological methods. Medication selection should consider accompanying diseases (Table 7). Given the diverse responses of individuals to these medications and the potential for adverse events, it is recommended to discontinue the medication in the event of a lack of response. In adults, if greater than 5% weight loss is not achieved within 3 months of maintenance dosage, the medication should be discontinued or changed.

In children and adolescents, if there is less than a 4% decrease in BMI or BMI z-score despite 12 weeks of medication, the medication should be considered ineffective and changed or discontinued.

## BARIATRIC AND METABOLIC SURGERY

The indications for bariatric/metabolic surgery for obesity are the same as in the previous version of the guidelines and are shown in Table 1. A standard procedure that has been proven to be effective

tive and safe, such as sleeve gastrectomy, Roux-en-Y gastric bypass, adjustable gastric banding, or biliopancreatic diversion/duodenal switch, is recommended based on patient condition (I, A).<sup>40,47</sup> After bariatric/metabolic surgery, multidisciplinary follow-up management should be scheduled for all patients (I, B).<sup>47-50</sup> In addition, micronutrient supplementation should be initiated, and regular follow-up examinations should be conducted according to the surgical procedure (I, B).<sup>47,48,51</sup> For children and adolescents with obesity, in cases where weight gain and obesity-related comorbidities remain despite intensive multidisciplinary treatment and pharmacotherapy for obesity, surgical therapy may be considered in limited cases, only after completion of growth and puberty (IIb, C).<sup>52-55</sup> In pediatric and adolescent cases, surgery may be considered if the BMI is 35 kg/m<sup>2</sup> or higher, the BMI is higher than 120% of the 95th percentile, and there are obesity-related comorbidities or if BMI is 40 kg/m<sup>2</sup> or higher or exceeds 140% of the 95th percentile. Bariatric surgery in the elderly is considered safe and effective; however, indications for bariatric surgery in obese elderly people in Asia, including Korea, have not been established. Age does not seem to increase the risk of complications after bariatric surgery. Therefore, if the risk of complications after surgery is not greater than the impact of obesity-related disabilities, surgical treatment for elderly people with obesity may be considered, taking into account accompanying diseases, medications, and safety (IIb, B).<sup>21,40,56-59</sup>

## NEW TOPICS INCLUDED IN THIS EDITION OF THE GUIDELINES

To stay current with the constantly evolving field of obesity, new main topics such as obesity in women, obesity in patients with mental illness, weight maintenance after weight loss, and the use of ICT-based interventions for obesity treatment are included in the 8th edition guidelines.

Women should maintain a normal weight before pregnancy due to the higher obstetric and perinatal risks associated with obesity. However, there is limited evidence to support the obstetric and perinatal benefits of non-pharmacological and pharmacological weight loss methods in women with obesity. Although a meta-analysis has shown positive impacts of bariatric surgery on spontaneous pregnancy in infertile women, these findings should be ap-

proached with caution due to the quality of the included data.

The current guidelines also address pregnancy-related weight gain and the relationship between obesity and menopause. During pregnancy, women with obesity should maintain a balanced diet and engage in regular physical activity to achieve appropriate weight gain. After delivery, active lifestyle interventions are recommended for weight management. Appropriate weight management is also recommended for women who are obese and in the menopausal period due to the increased risk of obesity-related comorbidities. Hormone therapy should not be used solely for the purpose of weight loss in menopausal women.

Severe mental illness has been linked to obesity and its comorbidities. Additionally, depression may also contribute to the development of obesity and an unhealthy metabolic state. Another important factor to consider in the clinical context is that many medications used to treat severe mental illness can cause weight gain. In light of this, the guidelines include key questions about screening tests for obesity and metabolic diseases and comprehensive lifestyle interventions for weight loss in patients with severe mental illness who are taking medications; recommendations are shown in Table 1.

Long-term maintenance after weight loss is more beneficial for overall health and well-being than is short-term weight loss. One of the most significant benefits of weight maintenance is prevention of diabetes. Additionally, it can improve the apnea-hypopnea index in individuals with obesity and obstructive sleep apnea, improve cerebral blood flow, and lower blood pressure. Furthermore, weight maintenance has been found to be associated with a lower mortality rate in individuals with obesity. The importance of long-term maintenance of weight loss and maintenance methods are highlighted in Table 1.

Another new area addressed in this edition of the guidelines is the use of ICT-based interventions for obesity. ICT-based interventions can supplement the lack of psychological and behavioral counseling provided by healthcare professionals and can facilitate achievement and maintenance of lifestyle modifications. Based on available evidence, technology-based interventions are recommended for obesity treatment (Table 1).

## CONCLUSION

The 8th edition of the Clinical Practice Guidelines for Obesity of KSSO was developed after reviewing all relevant scientific evidence and is intended for use by medical professionals, nutritionists, physical educators, and other related professionals in actual practice.

Methodologically, this edition of the guidelines features better links key questions in PICO format to recommendations and key references as answers to each key questions, increasing organization (Table 1). When developing clinical practice guidelines, it is important to involve stakeholders in the process, and our guideline development group included members from all relevant expert groups. However, a limitation of our work is the lack of investigation into the perspectives and preferences of the target population (patients, the general public, etc.) to whom the guidelines will be applied. Additional limitations include insufficient description of barriers and facilitators to executing the guidelines and lack of consideration of potential resources that may be required for application of the guidelines. In the future, clinical practice guidelines should address these methodological limitations.

The 8th edition of Clinical Practice Guidelines for Obesity has incorporated several new topics to keep up with the constantly evolving field of obesity. One of the new topics, 'obesity in women,' will be of great benefit to medical professionals treating women during their reproductive years, pregnancy, and postmenopausal stages. Additionally, two important topics, 'obesity in patients with mental illness' and 'weight maintenance after weight loss,' were added to provide strategies to address the most challenging issues faced by medical professionals treating obesity. The use of ICT is becoming increasingly important in medical fields, and the new topic 'obesity treatment using ICT-based interventions' will provide a foundation for further knowledge development in this area.

We are confident that the 8th edition of the Clinical Practice Guidelines for Obesity will be a useful tool for all healthcare professionals treating patients with obesity and will play a crucial role in improving the health of the Korean population.

## CONFLICTS OF INTEREST

In order to confirm the presence or absence of conflicts of inter-

est among all members involved in the development of these guidelines, a survey was conducted on whether they had received more than 10 million Korean won in sponsorship or consulting fees over the past 2 years on topics related to the development of these guidelines, whether they have rights to economic benefits such as stock options from specific institutions or pharmaceutical companies, and whether they hold official/unofficial positions in pharmaceutical companies. The survey results indicated no conflicting or potential conflicts of interest.

Ga Eun Nam has worked as an Associate Editor of the *Journal of Obesity and Metabolic Syndrome* since 2020. However, she was not involved in peer reviewer selection, evaluation, or the decision process for this article. There are no other potential conflicts of interest relevant to this article to report.

## SUPPLEMENTARY MATERIALS

Supplementary materials can be found online at <https://doi.org/10.7570/jomes23016>.

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## AUTHOR CONTRIBUTIONS

Study concept and design: KKK, JHH, BTK, EMK, JHP, SYR, JHK, and CBL; acquisition of data: all authors; analysis and interpretation of data: all authors; drafting of the manuscript: KKK, JHK, and JHH; critical revision of the manuscript: KKK and JHK; obtained funding: CBL; administrative, technical, or material support: KKK, JHK, and JHH; and study supervision: JHK.

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