

# Obesity and Reproduction

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## Abstract

**Objective:** To provide a comprehensive review and evidence-based recommendations for the delivery of fertility care to women with obesity.

**Outcomes:** The impact of obesity on fertility, fertility treatments, and both short and long-term maternal fetal outcomes was carefully considered.

**Evidence:** Published literature was reviewed through searches of MEDLINE and CINAHL using appropriate vocabulary and key words. Results included systematic reviews, clinical trials, observational studies, clinical practice guidelines, and expert opinions.

**Values:** The Canadian Fertility & Andrology Society (CFAS) is a multidisciplinary, national non-profit society that serves as the voice of reproductive specialists, scientists, and allied health professionals working in the field of assisted reproduction in Canada. The evidence obtained for this guideline was reviewed and evaluated by the Clinical Practice Guideline (CPG) Committee of the CFAS under the leadership of the principal authors.

**Benefits, Harms, and Costs:** The implementation of these recommendations should assist clinicians and other health care providers in counselling and providing reproductive care to women with obesity.

**Validation:** This guideline and its recommendations have been reviewed and approved by the membership, the CPG Committee and the Board of Directors of the CFAS.

**Sponsors:** Canadian Fertility & Andrology Society.

**Recommendations:** Twenty-one evidence based recommendations are provided. These recommendations specifically evaluate the

impact of obesity on natural fertility, fertility treatments, and maternal-fetal outcomes. Strategies to lose weight and BMI cut-offs are also addressed.

## Résumé

**Objectif :** Présenter une revue exhaustive ainsi que des recommandations fondées sur des données probantes en matière de soins de fertilité offerts aux femmes présentant une obésité.

**Résultats :** L'incidence de l'obésité sur la fertilité, les traitements de fertilité et les issues maternelles et fœtales à court et à long terme a été analysée avec soin.

**Données :** Des études publiées récupérées au moyen de recherches dans MEDLINE et CINAHL à l'aide d'une terminologie appropriée et de mots-clés ont été évaluées. Les documents retenus comprenaient des revues systématiques, des essais cliniques, des études observationnelles, des directives cliniques et des opinions d'experts.

**Valeurs :** La Société canadienne de fertilité et d'andrologie est une organisation multidisciplinaire nationale à but non lucratif qui se veut la voix des spécialistes de la procréation, des scientifiques et des professionnels de la santé alliés qui travaillent dans le domaine de la procréation assistée au Canada. Les résultats obtenus ont été évalués par le Comité des lignes directrices de pratique clinique de la Société canadienne de fertilité et d'andrologie, sous la direction des auteurs principaux.

**Avantages, inconvénients, coûts :** La mise en œuvre de ces recommandations devrait aider les cliniciens et les autres fournisseurs de soins de santé à offrir du counseling et des soins de fertilité aux femmes qui présentent une obésité.

**Validation :** Cette directive clinique et les recommandations qu'elle contient ont été révisées et approuvées par les membres de la Société canadienne de fertilité et d'andrologie, ainsi que par son Comité des lignes directrices de pratique clinique et son conseil d'administration.

**Commanditaire :** Canadian Fertility & Andrology Society.

**Recommandations :** Vingt et une recommandations fondées sur des données probantes sont proposées. Plus précisément, ces recommandations décrivent les conséquences de l'obésité sur la fertilité naturelle, les traitements de fertilité et les issues maternelles et fœtales. Des stratégies pour la perte de poids et les seuils d'IMC sont aussi abordés.

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This document is based on available evidence to date, often in a rapidly advancing field of study. Recommendations may not reflect emerging evidence and are subject to change. Clinical guidelines are intended as an aid to clinical judgement, and not to replace it. Clinical guidelines do not prevent clinicians from exercising freedom in their good clinical practice, nor relieve them of their responsibility to make appropriate decisions based on their own knowledge and experience.

**Table 1. Internationally recognized BMI cut-off values for underweight, normal weight, overweight and obese<sup>3</sup>**

BMI	Category
<18.5	Underweight
18.5–24.9	Normal Weight
25–29.9	Overweight
30–34.9	Obesity Class I
35–39.9	Obesity Class II
≥40	Obesity Class III

BMI: body mass index.

## INTRODUCTION

The purpose of this guideline is to provide a framework for the delivery of fertility care to women with obesity. In Canada, as in many other countries, the prevalence of obesity in adults is increasing. More than half of Canadian men and women are overweight, and from 1978 to 2011 the rate of obesity increased from 14 to 26%.<sup>1</sup> Furthermore, the proportion of Canadians who are obese now exceeds the proportion of Canadians who regularly smoke (11%) or drink alcohol to excess (16%).<sup>2</sup>

The World Health Organization (WHO) defines obesity as abnormal or excessive fat accumulation that impairs health.<sup>3</sup> Obesity is most commonly defined using body mass index (BMI). BMI is the weight in kilograms divided by the square of height in metres ( $\text{kg}/\text{M}^2$ ). The international cut-off values for defining underweight, normal weight, overweight and obese using BMI are listed in Table 1. It should be noted that other measures of obesity such as waist circumference, waist-to-hip ratio and the Edmonton obesity scoring

system have merit,<sup>4,5</sup> but that this guideline focuses primarily on BMI as this is the measure most commonly used in the obesity and reproductive medicine literature.

Excessive caloric intake is the fundamental cause of obesity. Globally we are seeing an increase in the consumption of energy-dense foods, and a reduction in physical activity.<sup>2</sup> The health consequences of this imbalance include cardiovascular disease, diabetes, musculoskeletal disorders, sleep apnea and an increased risk of certain malignancies, such as breast, endometrial and colon cancer.<sup>6,7</sup> It has been estimated that in young adults a BMI >45 reduces life expectancy by as much as 5 to 20 years.<sup>8</sup>

Obesity also has a profound impact on reproductive health. Women who have obesity are at increased risk for menstrual dysfunction, anovulatory infertility and pregnancy-related complications.<sup>9</sup> In this guideline we will highlight the current literature related to obesity and reproduction, and present evidence-based recommendations using GRADE (Table 2).

## WHAT IS THE IMPACT OF OBESITY ON FEMALE FERTILITY?

The impact of obesity on fecundity is complex.<sup>10,11</sup> Perhaps the best understood association is that between obesity and anovulation. Obesity induces a hormonal milieu consisting of insulin resistance, hyperinsulinemia, low sex hormone-binding globulin, elevated androgens, increased peripheral conversion of androgens to estrogens, increased free insulin-like growth factor 1 and high leptin.<sup>12,13</sup> The combined effect of these changes causes hypothalamic dysfunction, aberrant gonadotropin secretion, reduced folliculogenesis and lower luteal progesterone levels.<sup>14–16</sup>

**Table 2. GRADE**

Recommendations are graded according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system. GRADE offers two strengths of recommendation: strong and weak. The strength of the recommendation is based on the quality of supporting evidence, degree of uncertainty about the balance between desirable and undesirable effects, degree of uncertainty or variability in patient values and preferences and degree of uncertainty about whether the intervention represents a wise use of resources.
Strong recommendations are those for which the Canadian Task Force on Preventive Health Care is confident that the desirable effects of an intervention outweigh its undesirable effects (strong recommendation for an intervention) or that the undesirable effects of an intervention outweigh its desirable effects (strong recommendation against an intervention). A strong recommendation implies that most individuals will be best served by the recommended course of action.
Weak recommendations are those for which the desirable effects probably outweigh the undesirable effects (weak recommendation for an intervention) or undesirable effects probably outweigh the desirable effects (weak recommendation against an intervention), but appreciable uncertainty exists. Weak recommendations result when the balance between desirable and undesirable effects is small, the quality of evidence is lower, or there is more variability in the values and preferences of patients. A weak recommendation implies that most people would want the recommended course of action but that many would not. Clinicians must recognize that different choices will be appropriate for each individual, and they must help each person arrive at a management decision that is consistent with his or her values and preferences. Policy-making will require substantial debate and involvement of various stakeholders.
Quality of evidence is graded as high, moderate, low or very low, based on how likely further research is to change the task force's confidence in the estimate of effect.

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