

# Canadian Contraception Consensus—Update on Depot Medroxyprogesterone Acetate (DMPA)

*This update was prepared by the Ad Hoc DMPA Committee of the Society of Obstetricians and Gynaecologists of Canada and approved by the Executive and Council of the Society of Obstetricians and Gynaecologists of Canada.*

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Depot medroxyprogesterone acetate (DMPA) is a highly effective contraceptive method. It has been used as a contraceptive agent by millions of women in more than 90 countries since 1967 and was approved for use in Canada in 1997. Approximately 2% of Canadian women who are using contraception use DMPA as their birth control method.<sup>1</sup> In Canada, during a one-year period from October 2003 to October 2004, more than 629 000 prescriptions for DMPA were filled. Recent concerns about its effect on bone mineral density (BMD) have prompted advisories from the company that manufactures DMPA (Depo-Provera, Pfizer), the US Food and Drug Administration (FDA), and Health Canada.

**Key Words:** Bone mineral density, contraceptive agents, depot medroxyprogesterone acetate, osteoporosis, fractures, risk and benefits

DMPA has a number of advantages as a contraceptive agent. Because DMPA does not contain estrogen, it may be a suitable contraceptive option for women who have absolute or relative contraindications to estrogen, for example women with thrombophilias, female smokers over the age of 35, hypertensive women, and women who suffer from migraine headaches with associated neurological symptoms. DMPA has also been used to treat certain medical conditions, including menorrhagia, dysmenorrhea, endometriosis, and chronic pelvic pain. DMPA-associated amenorrhea is an advantage for women who prefer not to have menses because of menses-related symptoms, risk of anemia, or hygienic concerns. DMPA has the added advantage of demanding less compliance: because it is given as an intramuscular injection once every 12 to 13 weeks, it does not require daily attention and therefore may be more suitable for women who have difficulty adhering to other birth control regimens.

Frequently reported side effects with DMPA include menstrual cycle disturbances, headache,<sup>2,3</sup> weight changes,<sup>4</sup> and mood effects.<sup>2</sup> Amenorrhea occurs in 55% to 60% of DMPA users at 12 months.<sup>2,4–7</sup> Although this is a reversible method of contraception, return of fertility may be delayed for an average of up to nine months.<sup>8–10</sup>

A potential long-term consideration for women choosing DMPA is whether, by reducing BMD, DMPA adversely affects the future risk of fracture. There is increasing evidence that DMPA use results in, at least transiently, a decrease in BMD, probably because of the estrogen deficiency accompanying its use. Although some cross-sectional studies have demonstrated no adverse effect of DMPA on BMD,<sup>11</sup> the majority of studies report a decrease in BMD in DMPA users.<sup>12–21</sup> Prospective studies have found mean losses of BMD at the lumbar spine of between 0.87% and 3.52%. The decrease in BMD appears to be proportional to the duration of DMPA use; the greatest

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**Criteria for quality of evidence assessment and classification of recommendations**


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Level of evidence*	Classification of recommendations†
I: Evidence obtained from at least one properly designed randomized controlled trial.	A. There is good evidence to support the recommendation that the condition be specifically considered in a periodic health examination.
II-1: Evidence from well-designed controlled trials without randomization.	B. There is fair evidence to support the recommendation that the condition be specifically considered in a periodic health examination.
II-2: Evidence from well-designed cohort (prospective or retrospective) or case-control studies, preferably from more than one centre or research group.	C. There is poor evidence regarding the inclusion or exclusion of the condition in a periodic health examination.
II-3: Evidence from comparisons between times or places with or without the intervention. Dramatic results from uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in this category.	D. There is fair evidence to support the recommendation that the condition not be considered in a periodic health examination.
III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.	E. There is good evidence to support the recommendation that the condition be excluded from consideration in a periodic health examination.

\*The quality of evidence reported in these guidelines has been adapted from the Evaluation of Evidence criteria described in the Canadian Task Force on the Periodic Health Exam.<sup>31</sup>

†Recommendations included in these guidelines have been adapted from the Classification of Recommendations criteria described in the Canadian Task Force on the Periodic Health Exam.<sup>31</sup>

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amount of loss is seen in new users,<sup>18</sup> and the greatest rate of decrease occurs during the first two years of use.<sup>17,19,21</sup> Although a variable decrease in BMD has been observed, it is not usually sufficiently large to cause the BMD to fall into the osteoporotic range. Furthermore, two cross-sectional studies of past DMPA users<sup>22,23</sup> did not demonstrate a measurable difference in BMD compared with controls, suggesting that there is an improvement in BMD after DMPA is discontinued. Prospective studies have reported a substantial recovery of BMD once DMPA was discontinued, regardless of age.<sup>16,18</sup> A similar effect on BMD is seen with lactation. The BMD of women who breastfeed for six months or longer can decrease by 4% to 5% but recovers to baseline once breastfeeding is discontinued.<sup>24</sup>

Although published studies suggest that the loss of BMD is reversible, the interim results from as yet unpublished clinical studies prompted the FDA to issue a “black box warning” for DMPA in November 2004,<sup>25</sup> and in June 2005, Health Canada also issued an advisory.<sup>26</sup> The interim analysis found that in adult women who were on DMPA for five years, the decrease in hip and spine BMD was 5% to 6%. The decline was most pronounced in the first two years of use. When DMPA was stopped, BMD increased but did not always return to baseline in the first two years after discontinuation. Preliminary data in a small group of adolescents found a 2.44% to 6.53% decrease in BMD. As with the adult group, only partial recovery of BMD to baseline was seen during the two years of follow-up after discontinuation.

The DMPA-associated changes in BMD may be particularly important for adolescents, who are in the process of attaining peak bone mass. It is not clear whether the loss in BMD among adolescents prevents them from attaining their potential ultimate peak bone mass or if it will increase their risk of osteoporosis and fracture later in life. There is also concern regarding the perimenopausal DMPA user who may not have the opportunity to regain BMD before entering menopause with its associated accelerated phase of bone loss. The increase in fracture risk associated with a decrease in BMD has been studied in postmenopausal women, but there is little information on the effect of BMD changes on fracture risk for younger women, either during their younger years or later in life.

The World Health Organization (WHO), in its 2005 Statement on Hormonal Contraception and Bone Health, emphasizes that the critical outcome of interest with regard to bone health is the *occurrence of fracture*.<sup>27</sup> Although BMD measurements can be used to assess fracture risk, the accuracy of measurements can be affected by changes in body composition, and fracture risk is related to many factors besides BMD. It is not known whether DMPA-related BMD loss places women at increased risk for osteoporosis and fracture following menopause. Any potential effect will depend on a number of issues, including the magnitude and sustainability of loss, the microarchitectural deterioration of the skeleton associated with the bone loss, the level of BMD at the time of DMPA initiation, and the likelihood that other factors, such as physical activity, weight gain, and the development of comorbidities, affect this loss.<sup>19</sup>

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