Depot medroxyprogesterone acetate (DMPA) is known to potentially cause a reversible decrease in bone mineral density (BMD), leading to recommendations to consider cautionary use in some at-risk groups. However, there is no evidence that reversible loss of BMD leads to fragility fractures in premenopausal women. No studies have determined whether there is an increased fracture risk from use of DMPA.

Lanza et al. have conducted a retrospective cohort analysis to determine whether there is a relationship between DMPA use and fracture risk, and whether the level of exposure to DMPA is relevant. They studied over 312,000 women from the General Practice Research Database and compared users of DMPA with users of other prescribed contraceptives, with average follow-up of nearly 6 years. Crude fracture rates were converted to incidence rate ratios (IRR).

A subcohort analysis was performed for potential confounding risk factors. However, as the IRR was unchanged by these factors, the full study cohort was used for analysis. DMPA users were found to have a higher fracture incidence than non-users (IRR 1.28). However, this did not increase in either group after commencing treatment (DMPA IRR 1.08, non-users 1.12). Those with low DMPA exposure had a higher fracture incidence than those in a high exposure group. There was no apparent relationship with time from commencing DMPA to fracture. DMPA users were more likely to have traumatic and appendicular fractures than non-users. There was no difference between groups for axial fractures. These results support the conclusion that fractures in the DMPA group are unlikely to be related to decreased BMD.

Lanza et al. have provided new evidence that fracture risk is not increased by DMPA use. This is the largest cohort analysis of DMPA, looking at a clinical endpoint rather than BMD as in previous studies. Although conducted via a UK database, the conclusions are likely to be relevant to other populations where DMPA is offered. Retrospective cohort studies such as this are known to be limited by questions of bias and confounding, and whilst the authors have addressed this in the study design, they have acknowledged that some confounding variables may remain.

However, the finding that there is a higher fracture risk in users than non-users overall requires further clarification. The authors have suggested this may be due to increased reporting or unexamined factors in this group. More work is needed to identify why this should be the case and whether we need to be more cautious about which patients are offered DMPA.
Use of depot medroxyprogesterone acetate contraception and incidence of bone fracture

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