Comment on journal review of ‘Use of depot medroxyprogesterone acetate contraception and incidence of bone fracture’

We thank Dr Curry for an accurate summary1 of our study entitled ‘Use of depot medroxyprogesterone acetate contraception and incidence of bone fracture’.2 Nevertheless, we do not recommend more selective use of depot medroxyprogesterone acetate (DMPA) on account of fracture risk, as we believe that this recommendation would reduce access to an effective, safe contraceptive without actually reducing fracture risk. As we reported, in those subjects with at least 6 months of pre-DMPA medical history (176 pre-treatment fractures among 41,876 future DMPA users and 1,574 fractures after starting DMPA) the incidence rate ratio (IRR) for fracture ‘after’ vs ‘before’ DMPA use was 1.08 [95% confidence interval (CI) 0.92–1.26]. We subsequently expanded that analysis to include up to 2 years of fracture history in the same subpopulation of 41,876 women (582 pre-treatment fractures in 64,737 patient-years; 1,574 fractures after starting DMPA), which yielded IRR ‘after’ vs ‘before’ of 1.01 (95% CI 0.92–1.11), supporting our conclusion that DMPA had no meaningful effect on fracture risk in women who chose to use it.

In contrast, considering only the post-treatment follow-up period, our study confirmed the findings of others3 4 that women who are offered and choose to use DMPA do tend to have more fractures than women who are not offered, or decline to use, DMPA. We agree with Dr Curry that reporting bias might play a role, because DMPA patients return to clinic every 3 months rather than annually. Possibly more important, however, is our observation that the incidence of peripheral fractures, most likely resulting from trauma, showed the greatest differential between DMPA users and non-users during follow-up, suggesting that the women to whom physicians tend to recommend DMPA may well experience more trauma than non-users. Several studies5 6 have noted demographic, economic and other sociological differences between self-selected DMPA users and non-users, supporting the possibility that there is a higher underlying risk for trauma in women who choose DMPA.

The effect of DMPA on bone mineral density (BMD) has been clearly demonstrated in numerous studies, but like the effect of pregnancy and lactation on BMD, the BMD decline seen with DMPA use has been shown to be largely reversible and does not appear to cause any increase in fracture risk.

Lee L Lanza, ScD
Director of Epidemiology, RTI Health Solutions, Waltham, MA, USA; llanza@rti.org

Lisa J McQuay, MBoinf
Senior Research Epidemiologist, RTI Health Solutions, Research Triangle Park, NC, USA; lmcmquay@rti.org

Kenneth J Rothman, DrPH
Vice-President for Epidemiology Research, RTI Health Solutions, Research Triangle Park, NC, USA; krothman@rti.org

Henry G Bone, MD
Section Chief of the Endocrinology Department, St John Hospital and Medical Center; Michigan Bone & Mineral Clinic, Detroit, MI, USA; hgbone.mdi@att.net

Andrew M Kaunitz, MD
Professor and Associate Chair, Department of Obstetrics and Gynecology, University of Florida College of Medicine-Jacksonville, FL, USA; andrew.kaunitz@jax.ufl.edu

Zeev Harel, MD
Professor of Pediatrics, Division of Adolescent Medicine/Hasbro Children’s Hospital and Department of Pediatrics/Warren Alpert Medical School, Brown University, Providence, RI, USA; ZHarel@Lifespan.org

Quazi Ataher, PhD
Director of Epidemiology, Pfizer Inc., Collegeville, PA, USA; quazi.ataher@pfizer.com

Douglas Ross, MD
Senior Director of Medical Affairs, Pfizer Inc., Collegeville, PA, USA; douglas.ross@pfizer.com

Philip L Arena, BSPharm
Director of Safety Surveillance, Pfizer Inc., New York, NY, USA; philip.l.arena@pfizer.com

Kevin D Wolter,* MD
Senior Director of Clinical Development, Pfizer Inc., New York, NY, USA; kevin.d.wolter@pfizer.com

*Corresponding author

REFERENCES

Competing interests
Doctors Ataher, Arena, Ross and Wolter are employees of Pfizer, Inc.

Provenance and peer review
Not commissioned; internally peer reviewed.