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Broadening the debate over HIV and hormonal contraception

The question of whether hormonal contraception, particularly depot medroxyprogesterone acetate, increases a woman's risk of acquiring HIV has been debated since an association was first noted in 1991.[1] Subsequent data from observational studies, secondary analyses of trials, and systematic reviews[2–4] largely support the view that depot medroxyprogesterone acetate makes a moderate contribution to HIV risk. Efforts to synthesise existing evidence, however, have shown significant heterogeneity and serious, uncontrolled risk of confounding.[5–7]

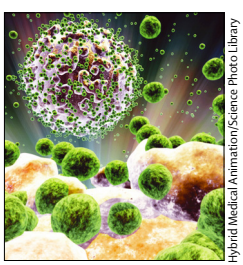
In *The Lancet Infectious Diseases*, Lauren Ralph and colleagues[8] extend this debate by providing the first pooled estimate of the association between depot medroxyprogesterone acetate and HIV acquisition, drawn from a meta-analysis of the most up-to-date observational evidence. They conclude that depot medroxyprogesterone acetate use increases a woman's chance of acquiring HIV by 40% (pooled hazard ratio 1·40, 95% CI 1·16–1·69). In studies with women already at high risk of infection, much higher effects of depot medroxyprogesterone acetate on HIV risk were reported, although heterogeneity prevented calculation of a pooled estimate. Ralph and colleagues also did a priori secondary analyses to test and substantiate the robustness of their pooled estimates.

Ralph and colleagues' findings add an important element to the longstanding debates about the HIV and depot medroxyprogesterone acetate relation, and the growing calls for further evidence about the magnitude, mechanisms, and health effects of this link. The investigators argue that their findings confirm those from previous research of an increased risk and suggest that their pooled estimates can be used immediately to guide decision making about the use of depot medroxyprogesterone acetate.

Currently, the increasingly narrow and fierce debates over the HIV and depot medroxyprogesterone acetate link have focused on whether a large randomised controlled trial should be done to better understand this link.[5] Like many scientific controversies, views have become hardened, personal, financial, or political agendas have been suggested, and there has even been intrigue in the form of leaked copies of articles under peer review.[9] Both sides have raised important, compelling arguments, but their partisan character can weaken the quality of the debates and restrict the view of the complex relation between evidence, policy, and practice.

Trial proponents have argued that only a randomised trial can be used to answer the question about a link in a way that is both scientifically valid and credible to policy makers.[10,11] They argue that equipoise exists as to whether hormonal contraception affects HIV risk, and that a trial is feasible (or at least its feasibility is an open question). Their focus on the quality of the evidence from randomised controlled trials, however, tends to sidestep the many serious methodological challenges of trials like these, challenges recently faced in the VOICE and MIRA trials.[12] Proponents have argued convincingly about the urgent need to avoid thousands of preventable HIV infections in women using depot medroxyprogesterone acetate. In doing so, however, they have tended to downplay other health risks of not using depot medroxyprogesterone acetate.

Critics of the proposed randomised controlled trial maintain that, with the existing evidence, there is no equipoise and the trial would be unethical. They argue that existing policy options and further modelling research could effectively mitigate the risk of depot medroxyprogesterone acetate and that the opportunity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costs of the trial would be huge. Additionally, there are complex tradeoffs between effective HIV prevention and effective family planning. Also they point out that hard-fought progress in increasing access to contraception, especially in sub-Saharan Africa, will be threatened if governments and health-care workers abandon support for depot medroxyprogesterone acetate based on insufficient evidence. Critics, however, tend to gloss over problems with existing evidence, assume too easily that resources are finite and research funding is fungible, and can overestimate the ability of modelling studies to answer policy questions. Like proponents, they also often frame the stakes here in the language of women's lives and bodies, emphasising maternal mortality and other pregnancy-related risks.

We believe rhetorical arguments[13,14] about protecting the lives of women are not the best way to address this issue. Neither are generic arguments about the value and hierarchies of different forms of evidence. Ralph and colleagues' signature contribution is their nuanced discussion of what their research adds and what is possible with current and future evidence. They synthesise and evaluate the existing observational data and identify many ways in which further modelling, epidemiological studies, behavioural and clinical research, and basic biological science could work synergistically to increase our knowledge. Additionally, they address the complicated policy decision points and local contextual factors that always complicate the path from evidence to policy and practice. They describe an approach to evidence, policy, and practice rooted in an "ecology of evidence"[15] as the foundation for thinking through the next steps. The current polarised environment around the proposed trial makes this more holistic approach all the more difficult, but necessary.

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The natural history of molluscum contagiosum in children

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Molluscum contagiosum, a common viral cutaneous infection in children, is caused by a poxvirus of the molluscipox genus. The infection accounts for roughly 1% of all diagnosed skin disorders.[1] Despite its common occurrence, little has been published on the natural history of molluscum contagiosum.[2–4] The natural history can be deduced from the time the lesions initially appear until the time of documented spontaneous resolution of the lesions.

In *The Lancet Infectious Diseases*, Jonathan Olsen and colleagues[5] report a 13·3 month (SD 8·2) mean time to resolution of molluscum contagiosum lesions in children aged 4–15 years. Lesions had not resolved by 18 months in 30% of cases and by 24 months in 13% of cases. Previously, Hawley[2] investigated 14 Fijian children with molluscum contagiosum and reported that the mean duration of the lesions was 16 months (range 6-28 months). Overfield and Brody[4] studied