Sexual behaviour among users of antiretroviral pre-exposure prophylaxis

The pioneering trials of antiretroviral pre-exposure prophylaxis for HIV prevention have yielded a potent new strategy for the reduction of HIV incidence in at-risk populations.1–4 However, pre-exposure prophylaxis is inherently a combination approach: the intervention effect will depend not only on drug efficacy, but also on behaviours of users and providers. Before the first trial findings emerged, scientific researchers had already identified the potential for increased sexual risk-taking among pre-exposure prophylaxis users who feel protected from HIV.5 Concerns about risk compensation behaviour have persisted as the pre-exposure prophylaxis evidence base has grown. Although findings from trials consistently show reductions in risk behaviour of participants,1–4 controlled clinical trials are not an optimum setting to test the association between behaviour of pre-exposure prophylaxis users and their perceptions of drug protection.6

The study by the Partners PrEP team7 makes a crucial contribution to the scientific literature on risk compensation associated with pre-exposure prophylaxis. This analysis capitalised on the open-label extension of the Partners PrEP trial among serodiscordant heterosexual couples,1 which was stopped after definitive evidence of pre-exposure prophylaxis benefit was found. HIV-uninfected participants originally randomised to receive tenofovir alone or with emtricitabine continued to take pre-exposure prophylaxis without interruption, and questionnaires tracked sexual risk behaviours 12 months before and after unblinding. Compared with predicted behaviour trends, participants reported no significant change in the frequency of unprotected sex with their HIV-infected partners. Although most sex acts of participants continued to be with their primary HIV-infected partners, investigators also found a significantly increased frequency of unprotected sex and total sex with outside partners over time. However, no corresponding increase in incidence of sexually transmitted infections or pregnancy was reported. This study adds to analyses of behaviour among users of pre-exposure prophylaxis,6,9 and acceptability research among populations considering pre-exposure prophylaxis uptake.

Empirical data for risk compensation associated with pre-exposure prophylaxis are valuable for several purposes. These data should guide the development of pre-exposure prophylaxis implementation packages for users, which should include culturally tailored behavioural counselling and assessment strategies to minimise risk-taking and to maximise adherence. Results from the Partners PrEP analysis show the need for providers to counsel users on risks both within serodiscordant partnerships and with outside partners. Understanding pre-exposure prophylaxis user behaviour can assist in modelling the effect of implementation at the population level, improve cost-effectiveness calculations, and help address the structural issues integral to pre-exposure prophylaxis roll-out.

Empirical data for risk compensation should also contribute to pre-exposure prophylaxis education for providers. Findings from several studies suggest that providers’ predictions of risk compensation behaviour among patients might affect willingness to prescribe pre-exposure prophylaxis.10–12 If providers presume that some patients are more likely to increase risk-taking, and therefore should not receive pre-exposure prophylaxis, then anticipated risk compensation could also lead to unequal access.13 Incorporation of behavioural data into provider training might help to address perceived risk compensation as a deterrent to implementation of pre-exposure prophylaxis.

Open-label extension studies offer opportunities to analyse behaviour among pre-exposure prophylaxis users, but they also present methodological challenges. The notion of preventive misconception suggests that participants in prevention trials often formulate their own perceptions of group assignment and intervention benefit,8,14–17 which might affect behaviour before unblinding. That is, participants who believe they have received an effective drug might adjust their risk-taking before knowing their true assignment, which can affect analyses based on unblinding. Findings from several trials of pre-exposure prophylaxis show that participants hold beliefs about group assignment,2,3,8 and that perceived pre-exposure prophylaxis efficacy might increase over time and influence behaviour.8 Future open-label
extension trials should consider additional measures to quantify how unblinding changes the perceptions of participants. Assessment of the effect of new information might further clarify the beliefs of participants—e.g., the iPrEx study results1 were published 7–8 months before unblinding in the Partners PrEP study, which might have affected participants’ perceptions. Behavioural scientists might also explore how the shift in perception by trial participants from being uncertain to certain about pre-exposure prophylaxis efficacy compares with the shift in perception by real-world users from no pre-exposure prophylaxis to effective pre-exposure prophylaxis, now that proof of concept is established.

The Partners PrEP analysis provides an important advance in the measurement of behaviour among serodiscordant couples using pre-exposure prophylaxis. Future research should examine the behaviours of pre-exposure prophylaxis users outside trial settings, behavioural strategies for optimisation of pre-exposure prophylaxis uptake and adherence while decreasing risk-taking, methods for assessment of users’ behaviours over time, and methods for training providers. Researchers and implementers should also investigate the context of behaviour among pre-exposure prophylaxis users; individuals might have personally meaningful reasons to take risks, such as fertility desires, and understanding these motivations can strengthen efforts to support pre-exposure prophylaxis users before, during, and after use.

Kristen Underhill, Kenneth H Mayer
Yale Center for Interdisciplinary Research on AIDS, Yale Law School, New Haven, CT 06520, USA (KU); Fenway Health, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA (KHM)
kristen.underhill@yale.edu

KHM has received unrestricted research and educational grants from Gilead (Foster City, CA, USA).

Malaria in pregnancy: increasing access and improving delivery of interventions

The report by Anna Maria van Eijk and colleagues1 in The Lancet Infectious Diseases into coverage of interventions for malaria in pregnancy highlights the achievements and continuing challenges of global malaria control overall. The use of insecticide-treated nets by pregnant women and intermittent preventive treatment with sulfadoxine–pyrimethamine during pregnancy—shown to improve birth outcomes in endemic countries with moderate to high burden of disease2—are included in strategic plans for malaria