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Grant and Glidden present interesting data from the iPrEx trial [1]. In contrast to their findings, the PROUD study did not show a major reduction over time in risky sexual behaviour. The Figure shows the number of different partners with whom participants reported condomless receptive anal sex in the 90 days prior to visits at enrolment, 12 months, and 24 months. In both the immediate and deferred PrEP groups, about 80% of participants reported one or more partners at 12 months and at 24 months (not necessarily the same individuals). Thus for most men it was appropriate to continue prescribing PrEP, suggesting that subpopulations might exist who need the drug for a longer time than suggested by the iPrEx data. We note (1) the iPrEx analysis is limited to seroconverters who, by definition, were at especially high risk of HIV infection; (2) the PROUD analysis [2] excludes men who stopped attending clinic and who may have been at lower risk. These factors may partially explain the difference between the findings of these two analyses.

Nonetheless, we agree with Grant's and Glidden's key point about individual variation in the risk of acquiring HIV infection, including periods of no or low risk. Given this, we were surprised that they did not mention the IPERGAY study [3], which found that intermittent PrEP (two tablets before sex and a further two tablets after sex) was highly effective. This is arguably a more logical and cost-effective approach than daily dosing for individuals who "pass through HIV risk moments" rather than being at continuous significant risk. PrEP guidelines for the MSM population at risk of HIV currently lack uniformity: US guidelines recommend daily dosing only [4], whereas the European AIDS Clinical Society recommend either daily or intermittent dosing [5]. Further evaluation is required to determine the optimal way to promote and deliver PrEP in different populations, taking account of the wide range of behaviours and the need to tailor regimens to individual circumstances.

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References

1. Grant, RM, Lama, JR, Anderson, PL et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. N Engl J Med. 2010; 363: 2587–2599
2. McCormack, S, Dunn, DT, Desai, M et al. Pre-exposure prophylaxis to prevent the acquisition of HIV-1 infection (PROUD): effectiveness results from the pilot phase of a pragmatic open-label randomised trial. Lancet. 2016; 387: 53–60
3. Molina, JM, Capitant, C, Spire, B et al. On-demand preexposure prophylaxis in men at high risk for HIV-1 infection. N Engl J Med. 2015; 373: 2237–2246
4. US Public Health Service. Preexposure prophylaxis for the prevention of HIV infection in the United States—2014: a clinical practice guideline. http://www.cdc.gov/hiv/pdf/guidelines/PrEPguidelines2014.pdf. ((accessed March 22, 2016).)
5. European AIDS Clinical Society. Guidelines version 8.0. www.eacsociety.org/guidelines/eacs-guidelines/eacs-guidelines.html; October, 2015. ((accessed March 22, 2016).)

Figure legend
Number of partners with whom participants reported condomless receptive anal sex in previous 90 days.

Footnote: Based on 515 values at baseline, 406 values at 12 months, 244 values at 24 months. Further data will become available at 24 months with continued follow-up.
Figure

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