We declare no competing interests.

1 Curno MJ, Rossi S, Hodges-Mameletzis I, Johnston R, Price MA, Heidari S. A Systematic Review of the Inclusion (or Exclusion) of Women in HIV Research. *J Acquir Immune Defic Syndr* 2016; **71:** 181–88.
2 Gandhi M, Aweeka F, Greenblatt RM, Blaschke TF. Sex differences in pharmacokinetics and pharmacodynamics. *Annu Rev Pharmacol Toxicol* 2004; **44:** 499–523.
3 Berg KM, Demas PA, Howard AA, Schoenbaum EE, Gourevitch MN, Arnsten JH. Gender differences in factors associated with adherence to antiretroviral therapy. *J Gen Intern Med* 2004; **19:** 1111–17.
4 Lennox JL, Landovitz RJ, Ribaudo HJ, et al. Efficacy and tolerability of 3 nonnucleoside reverse transcriptase inhibitor-sparing antiretroviral regimens for treatment-naive volunteers infected with HIV-1: a randomized, controlled equivalence trial. *Ann Intern Med* 2014; **161:** 461–71.
5 Clotet B, Feinberg J, van Lunzen J, et al. Once-daily dolutegravir versus darunavir plus ritonavir in antiretroviral-naive adults with HIV-1 infection (FLAMINGO): 48 week results from the randomised open-label phase 3b study. *Lancet* 2014; **383:** 2222–31.
6 Squires KE, Kityo C, Hodder S, et al. Integrase inhibitor versus protease inhibitor based regimen for HIV-1 infected women (WAVES): a randomised, controlled, double-blind, phase 3 study. *Lancet HIV* 2016; published online May 27. http://dx.doi.org/10.1016/S2352-3018(16)30016-9.
7 Squires KE, Hodder SL, Feinberg J, et al. Health Needs of HIV-Infected Women in the United States: Insights from The Women Living Positive Survey. *AIDS Patient Care STDS* 2011; **25:** 279–85.
8 McComsey GA, Moser C, Currier J, et al. Body composition changes after initiation of raltegravir or protease inhibitors: ACTG A5260s. *Clin Infect Dis* 2016; **62:** 853–62.
9 Gibb DM, Kizito H, Russell EC, et al. Pregnancy and infant outcomes among HIV-infected women taking long-term ART with and without tenofovir in the DART trial. *PLoS Med* 2012; **9:** e1001217.
10 Regan L, Rai R. Epidemiology and the medical causes of miscarriage. *Baillieres Best Pract Res Clin Obstet Gynaecol* 2000; **14:** 839–54.
11 Dellicour S, Aol G, Ouma P, Yan N, Bigogo G. Weekly miscarriage rates in a community-based prospective cohort study in rural western Kenya. *BMJ Open* 2016; **6:** e011088.
12 The Interagency Task Team on the Prevention and Treatment of HIV Infection in Pregnant Women, Mothers and Children. Progress toward global plan targets: key data points for priority countries. http://emtct-iatt.org/priority-countries/ (accessed May 6, 2016).
13 Chen JY, Ribaudo HJ, Souda S, et al. Highly active antiretroviral therapy and adverse birth outcomes among HIV-infected women in Botswana. *J Infect Dis* 2012; **206:** 1695–705.
14 Zash R, Souda S, Chen JY, et al. Reassuring birth outcomes with tenofovir/emtricitabine/efavirenz used for prevention of mother-to-child transmission of HIV in Botswana. *J Acquir Immune Defic Syndr* 2016; **71:** 428–36.
15 Powis KM, Kitch D, Ogwu A, et al. Increased risk of preterm delivery among HIV-infected women randomized to protease versus nucleoside reverse transcriptase inhibitor-based HAART during pregnancy. *J Infect Dis* 2011; **204:** 506–14.

A breather from daily antiretroviral therapy for adolescents

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The global scale-up of antiretroviral therapy (ART) has resulted in HIV infection being transformed from an inevitably fatal disease to a chronic, albeit incurable, infection requiring life-long treatment.[1] Increasing numbers of children infected through mother-to-child HIV transmission, who would have died in infancy in the pre-ART era, are now reaching adolescence and face the prospect of having to take ART daily with optimum adherence for the rest of their lives.[2-4]

In *The Lancet HIV*, the PENTA 16 trial group report the findings of the BREATHER study, an open-label, non-inferiority trial, comparing continuous daily ART with short cycle treatment enabling 2 days off treatment every week.[5] 199 participants aged 8–24 years who had been virally suppressed for at least 12 months before enrolment and were taking an ART regimen containing the long-acting drug efavirenz were recruited from 11 countries worldwide. At 48 weeks, six (6%) of 99 children in the short cycle treatment group versus seven (7%) of 100 in the continuous treatment group had virological rebound (HIV viral load >50 copies per mL; difference –1·2%, 90% CI –7·3 to 4·9), showing that short cycle treatment is non-inferior to continuous treatment. There was no statistical difference between the groups in the proportion of participants who developed major resistance mutations or in the proportion of adverse events. This is the first trial to show that controlled interruption seems to be safe in terms of both maintenance of viral suppression and emergence of drug resistance. Notably, the trial was done in geographically diverse settings and achieved an impressive retention rate with only one participant lost to follow-up.

Children are expected to take ART for 20 years longer on average than adults and strategies that enable time off ART could be an effective way to reduce treatment fatigue.[6] Additionally, reduced ART usage through short cycle treatment might provide potential cost savings. The short cycle treatment strategy was highly acceptable to participants, particularly because it enabled socialising at weekends, which is otherwise a key barrier to taking medication. Even patients who are virologically suppressed report intermittently missing drugs, and short cycle treatment provides regulated time off medication and a legitimate way to miss doses.[7] Of concern is that such a strategy might give out the message that missing doses is acceptable and seems not to affect viral load. Therefore, appropriate counselling is crucial to ensure that the results are not misinterpreted and that patients understand that there is a maximum break in treatment of the designated 2 days per week.

Notably, the findings of this study are only generalisable to patients who are stable and well established on ART. The median time on ART before randomisation in this trial was 6 years and children had been virally suppressed for at least 12 months. Additionally, the results cannot be extrapolated to children who have had previous treatment failure, or to ART containing reduced doses of efavirenz (equivalent to 400 mg for adults) or indeed to other long-acting ART regimens. The follow-up period was short and the planned 2 year trial extension will provide data for longer term sustainability of the short cycle treatment strategy. Other questions remain to be answered before short cycle treatment can become a viable option. The trial was done in tightly controlled conditions with intensive viral load monitoring. Research is needed to understand whether the trial could be safely implemented in resource-constrained settings where routine viral load monitoring is unavailable or infrequent. Further research could also assess short cycle treatment with the newer long-acting drugs becoming available that have a higher barrier to resistance and are more tolerable, such as tenofovir alafenamide and dolutegravir.[8]

Viral suppression is the ultimate goal to improve health outcomes and reduce HIV transmission, thus conferring individual and public health benefits.[9,10] Optimum adherence to ART is crucial to ensure sustained virological suppression. Adherence to treatment of chronic illnesses drops off during adolescence and unfortunately HIV is no exception.[11] Adolescents face several barriers to adherence, and our experience is that no single intervention will be sufficient to ensure the high levels of adherence needed to maintain virological suppression.[12] Therefore, we need several different approaches in our armamentarium to support adherence in this age group. We now have a promising and innovative option on the horizon that could be offered to young people who face the prospect of taking lifelong ART.

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1 UNAIDS. How AIDS Changed Everything—MDG6: 15 years, 15 lessons of hope from the AIDS responses. Geneva: UNAIDS, 2015.
2 Newell M-L, Coovadia H, Cortina-Borja M, Rollins N, Gaillard P, Dabis F. Mortality of infected and uninfected infants born to HIV-infected mothers in Africa: a pooled analysis. *Lancet* 2004; **364:** 1236–43.
3 Hazra R, Siberry GK, Mofenson LM. Growing up with HIV: children, adolescents, and young adults with perinatally acquired HIV infection. *Annu Rev Med* 2010; **61:** 169–85.
4 Foster C, Judd A, Tookey P, et al. Young people in the United Kingdom and Ireland with perinatally acquired HIV: the pediatric legacy for adult services. *AIDS Patient Care STDS* 2009; **23:** 159–66.
5 Weekends-off efavirenz-based antiretroviral therapy in HIV-infected children, adolescents, and young adults (BREATHER): a randomised, open-label, non-inferiority, phase 2/3 trial. *Lancet HIV* 2016; published online June 20. http://dx.doi.org/10.1016/S2352-3018(16)30054-6.
6 Lowenthal ED, Bakeera-Kitaka S, Marukutira T, Chapman J, Goldrath K, Ferrand RA. Perinatally acquired HIV infection in adolescents from sub-Saharan Africa: a review of emerging challenges. *Lancet Infect Dis* 2014; **14:** 627–39.
7 Bernays S, Seeley J, Paparini S, Rhodes T. 'I am scared of getting caught up in my lie': challenges to self-reported adherence for young people living with HIV. AIDS Impact; Amsterdam, Netherlands; July 28–31, 2015.
8 Elliot E, Amara A, Jackson A, et al. Dolutegravir and elvitegravir plasma concentrations following cessation of drug intake. *J Antimicrob Chemother* 2016; **71:** 1031–36.
9 Attia S, Egger M, Muller M, Zwahlen M, Low N. Sexual transmission of HIV according to viral load and antiretroviral therapy: systematic review and meta-analysis. *AIDS* 2009; **23:** 1397–404.
10 Mills EJ, Bakanda C, Birungi J, et al. Life expectancy of persons receiving combination antiretroviral therapy in low-income countries: a cohort analysis from Uganda. *Ann Intern Med* 2011; **155:** 209–16.
11 Nachega JB, Hislop M, Nguyen H, et al. Antiretroviral therapy adherence, virologic and immunologic outcomes in adolescents compared with adults in southern Africa. *J Acquir Immune Defic Syndr* 2009; **51:** 65–71.
12 Adejumo OA, Malee KM, Ryscavage P, Hunter SJ,Taiwo BO. Contemporary issues on the epidemiology and antiretroviral adherence of HIV-infected adolescents in sub-Saharan Africa: a narrative review. *J Int AIDS Soc* 2015; **18:** 20049.

Time to accommodate antiretroviral-based HIV prevention

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In *The Lancet HIV*, Aghaizu and colleagues[1] present results from their analysis of repeated, cross-sectional surveys coupled with anonymous HIV testing to try to explain why HIV incidence remains high in gay and bisexual men in London, UK. The authors sought to explain why incidence might be sustained, despite improvements in frequency of HIV testing and treatment uptake since 2000.

The findings show the value of repeated, behavioural surveillance of an HIV-affected population, not only in the identification of behaviours that explain epidemic trends, but also to suggest potential areas for intervention.[2,3] Sadly, few jurisdictions have initiated or sustained investment in behavioural surveillance,[4] so, in many locations, the direction in which community norms are shifting and the practices that need attention