Welcome to HIV this month! In this issue, we cover the following topics:

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   - Weekend breaks on efavirenz-based ART non-inferior in adolescents
   - HIV-exposed uninfected children – why the increased mortality risk?
   - Getting to 90-90-90 in China: where are the gaps?
   - Showing they care: lay-counsellors, home-based testing and the value of follow-up support
   - Patient navigators and financial incentives have no effect on HIV viral suppression in people with substance use disorders

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   - Identifying important proximal epidemiological parameters for HIV prevention

3. Combination prevention
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• Accurate country-level data necessary to inform HIV incidence estimates

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UNAIDS

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HIV this month, published by UNAIDS, is a selective scan of new HIV-related information found in scientific journals. The Editors of HIV this month interpret original abstracts and provide editorial comment, so that information may be easily understood by people responding to the HIV epidemic in many diverse settings. The selection of material, its abridgement and other editorial changes, and also the original editorial comment are the responsibility of the Editors and do not represent any official statement of UNAIDS. It should be noted that (except for open access journals, e.g. PLoS) the authors and/or publishers retain copyright in the original published material to which HIV this month refers.
1. HIV testing and treatment

Antiretroviral therapy for the prevention of HIV-1 transmission.


Background: An interim analysis of data from the HIV Prevention Trials Network (HPTN) 052 trial showed that antiretroviral therapy (ART) prevented more than 96% of genetically linked infections caused by human immunodeficiency virus type 1 (HIV-1) in serodiscordant couples. ART was then offered to all patients with HIV-1 infection (index participants). The study included more than 5 years of follow-up to assess the durability of such therapy for the prevention of HIV-1 transmission.

Methods: We randomly assigned 1763 index participants to receive either early or delayed ART. In the early-ART group, 886 participants started therapy at enrollment (CD4+ count, 350 to 550 cells per cubic millimeter). In the delayed-ART group, 877 participants started therapy after two consecutive CD4+ counts fell below 250 cells per cubic millimeter or if an illness indicative of the acquired immunodeficiency syndrome (i.e., an AIDS-defining illness) developed. The primary study end point was the diagnosis of genetically linked HIV-1 infection in the previously HIV-1-negative partner in an intention-to-treat analysis.

Results: Index participants were followed for 10,031 person-years; partners were followed for 8509 person-years. Among partners, 78 HIV-1 infections were observed during the trial (annual incidence, 0.9%; 95% confidence interval [CI], 0.7 to 1.1). Viral-linkage status was determined for 72 (92%) of the partner infections. Of these infections, 46 were linked (3 in the early-ART group and 43 in the delayed-ART group; incidence, 0.5%; 95% CI, 0.4 to 0.7) and 26 were unlinked (14 in the early-ART group and 12 in the delayed-ART group; incidence, 0.3%; 95% CI, 0.2 to 0.4). Early ART was associated with a 93% lower risk of linked partner infection than was delayed ART (hazard ratio, 0.07; 95% CI, 0.02 to 0.22). No linked infections were observed when HIV-1 infection was stably suppressed by ART in the index participant.

Conclusions: The early initiation of ART led to a sustained decrease in genetically linked HIV-1 infections in sexual partners. (Funded by the National Institute of Allergy and Infectious Diseases; HPTN 052 ClinicalTrials.gov number, NCT00074581.).

Abstract access

Editor’s notes: The HPTN 052 trial has been a landmark study in establishing antiretroviral therapy as a strategy for preventing onward transmission of HIV. It was a study of more than 800 couples. More than half of the couples were in African countries. In each couple, one sexual partner was HIV positive and the other HIV negative. The participants living with HIV were randomised either to receive immediate antiretroviral therapy or to delay until their CD4 count fell to 350, an approved approach at that time. The HIV negative partners were then monitored for acquisition of HIV. When new HIV infections occurred, the virus was studied for genetic similarity to the virus of the known positive partner. The interim analysis was published in 2011. It illustrated the programme to be so
effective that the randomisation was ended and all the participants living with HIV were offered antiretroviral therapy.

This article presents data after five years of follow-up, and if anything the results are even more remarkable. In more than 10 000 person-years of follow up, there were only eight transmissions of genetically linked virus from participants receiving antiretroviral therapy. Of these transmissions, four occurred early in treatment when the viral load would not be expected to be suppressed. The other four occurred after treatment failure. In this enormous study, there were therefore no linked transmissions from participants who were stable on treatment without detectable viraemia. The study provides powerful support for the UNAIDS 90-90-90 treatment target. The widest possible effective use of antiretroviral therapy will not only improve the health of people treated but could have a dramatic effect on new HIV infections.

BREATHER (PENTA 16) short-cycle therapy (SCT) (5 days on/2 days off) in young people with chronic human immunodeficiency virus infection: an open, randomised, parallel-group Phase II/III trial.


Background: For human immunodeficiency virus (HIV)-infected adolescents facing lifelong antiretroviral therapy (ART), short-cycle therapy (SCT) with long-acting agents offers the potential for drug-free weekends, less toxicity, better adherence and cost savings.

Objectives: To determine whether or not efavirenz (EFV)-based ART in short cycles of 5 days on and 2 days off is as efficacious (in maintaining virological suppression) as continuous EFV-based ART (continuous therapy; CT). Secondary objectives included the occurrence of new clinical HIV events or death, changes in immunological status, emergence of HIV drug resistance, drug toxicity and changes in therapy.

Design: Open, randomised, non-inferiority trial.

Setting: Europe, Thailand, Uganda, Argentina and the USA.

Participants: Young people (aged 8-24 years) on EFV plus two nucleoside reverse transcriptase inhibitors and with a HIV-1 ribonucleic acid level [viral load (VL)] of < 50 copies/ml for > 12 months.

Interventions: Young people were randomised to continue daily ART (CT) or change to SCT (5 days on, 2 days off ART).

Main outcome measures: Follow-up was for a minimum of 48 weeks (0, 4 and 12 weeks and then 12-weekly visits). The primary outcome was the difference between arms in the proportion with VL > 50 copies/ml (confirmed) by 48 weeks, estimated using the Kaplan-Meier method (12% non-inferiority margin) adjusted for region and age.

Results: In total, 199 young people (11 countries) were randomised (n = 99 SCT group, n = 100 CT group) and followed for a median of 86 weeks. Overall, 53% were male; the median age was 14 years (21% ≥ 18 years); 13% were from the UK, 56% were black, 19% were Asian and 21% were Caucasian; and the median CD4% and CD4 count were 34% and 735 cells/mm³, respectively. By week 48, only one participant (CT) was lost to follow-up. The SCT arm had a 27% decreased drug exposure as measured by the adherence questionnaire and a MEMSCap™ Medication Event Monitoring System (MEMSCap Inc., Durham, NC, USA) substudy (median cap openings per week: SCT group, n = 5; CT group, n = 7). By 48 weeks, six participants in the SCT group and seven in
the CT group had a confirmed VL > 50 copies/ml [difference -1.2%, 90% confidence interval (CI) -7.3% to 4.9%] and two in the SCT group and four in the CT group had a confirmed VL > 400 copies/ml (difference -2.1%, 90% CI -6.2% to 1.9%). All six participants in the SCT group with a VL > 50 copies/ml resumed daily ART, of whom five were resuppressed, three were on the same regimen and two with a switch; two others on SCT resumed daily ART for other reasons. Overall, three participants in the SCT group and nine in the CT group (p = 0.1) changed ART regimen, five because of toxicity, four for simplification reasons, two because of compliance issues and one because of VL failure. Seven young people (SCT group, n = 2; CT group, n = 5) had major non-nucleoside reverse transcriptase inhibitor mutations at VL failure, of whom two (n = 1 SCT group, n = 1 CT group) had the M184V mutation. Two young people had new Centers for Disease Control B events (SCT group, n = 1; CT group, n = 1). There were no significant differences between SCT and CT in grade 3/4 adverse events (13 vs. 14) or in serious adverse events (7 vs. 6); there were fewer ART-related adverse events in the SCT arm (2 vs. 14; p = 0.02). At week 48 there was no evidence that SCT led to increased inflammation using an extensive panel of markers. Young people expressed a strong preference for SCT in a qualitative substudy and in pre- and post-trial questionnaires. In total, 98% of the young people are taking part in a 2-year follow-up extension of the trial.

Conclusions: Non-inferiority of VL suppression in young people on EFV-based first-line ART with a VL of <50 copies/ml was demonstrated for SCT compared with CT, with similar resistance, safety and inflammatory marker profiles. The SCT group had fewer ART-related adverse events. Further evaluation of the immunological and virological impact of SCT is ongoing. A limitation of the trial is that the results cannot be generalised to settings where VL monitoring is either not available or infrequent, nor to use of low-dose EFV. Two-year extended follow-up of the trial is ongoing to confirm the durability of the SCT strategy. Further trials of SCT in settings with infrequent VL monitoring and with other antiretroviral drugs such as tenofovir alafenamide, which has a long intracellular half-life, and/or dolutegravir, which has a higher barrier to resistance, are planned.

Trial registration: Current Controlled Trials ISRCTN97755073; EUDRACT 2009-012947-40; and CTA 27505/0005/001-0001.

Funding: This project was funded by the National Institute for Health Research (NIHR) Health Technology Assessment programme (projects 08/53/25 and 11/136/108), the European Commission through EuroCoord (FP7/2007/2015), the Economic and Social Research Council, the PENTA Foundation, the Medical Research Council and INSERM SC10-US19, France, and will be published in full in Health Technology Assessment; Vol. 20, No. 49. See the NIHR Journals Library website for further project information.

Abstract Full-text [free] access

Editor’s notes: Adherence to ART has been shown to deteriorate in adolescence, with missed doses occurring particularly at weekends. Pharmacokinetic properties of some ART drugs, such as efavirenz, allow for a break in pill taking without a break in effective treatment. Non-inferiority trials evaluating five days on, two days off in adults have shown continuous ART to be non-inferior with low rates of virologic rebound. This formed the rationale for this global, randomised Phase II/III trial in young people.

In the BREATHER trial, non-inferiority of viral suppression in adolescents on efavirenz-based first-line ART was shown for short-cycle treatment compared with continuous treatment. Overall 93% of adolescents remained virally suppressed. Findings from the two-year long-term follow-up phase will confirm if short-cycle treatment is effective and safe in this population. Further studies are required to
confirm the applicability of this strategy in real-life settings where viral load monitoring is likely to be less frequent than in a trial setting.

HIV-exposed children account for more than half of 24-month mortality in Botswana.


Background: The contribution of HIV-exposure to childhood mortality in a setting with widespread antiretroviral treatment (ART) availability has not been determined.

Methods: From January 2012 to March 2013, mothers were enrolled within 48 h of delivery at 5 government postpartum wards in Botswana. Participants were followed by phone 1-3 monthly for 24 months. Risk factors for 24-month survival were assessed by Cox proportional hazards modeling.

Results: Three thousand mothers (1499 HIV-infected) and their 3033 children (1515 HIV-exposed) were enrolled. During pregnancy 58% received three-drug ART, 23% received zidovudine alone, 11% received no antiretrovirals (8% unknown); 2.1% of children were HIV-infected by 24 months. Vital status at 24 months was known for 3018 (99.5%) children; 106 (3.5%) died including 12 (38%) HIV-infected, 70 (4.7%) HIV-exposed uninfected, and 24 (1.6%) HIV-unexposed. Risk factors for mortality were child HIV-infection (aHR 22.6, 95% CI 10.7, 47.5), child HIV-exposure (aHR 2.7, 95% CI 1.7, 4.5) and maternal death (aHR 8.9, 95% CI 2.1, 37.1). Replacement feeding predicted mortality when modeled separately from HIV-exposure (aHR 2.3, 95% CI 1.5, 3.6), but colinearity with HIV-exposure status precluded investigation of its independent effect. Applied at the population level (26% maternal HIV prevalence), an estimated 52% of child mortality occurs among HIV-exposed or HIV-infected children.

Conclusions: In a programmatic setting with high maternal HIV prevalence and widespread maternal and child ART availability, HIV-exposed and HIV-infected children still account for most deaths at 24 months. Lack of breastfeeding was a likely contributor to excess mortality among HIV-exposed children.

Abstract Full-text [free] access

Editor’s notes: It has been known for some time that HIV-exposed but uninfected children have a higher risk of death than HIV-unexposed children. There is now a need for prospective studies to explore the mechanisms underlying this observation. In this study from Botswana, one of every 20 HIV-exposed but uninfected children had died by 24 months. Four in every five deaths in the HIV-exposed but uninfected children were attributed to infectious diseases, most commonly diarrhoeal illness and respiratory infections.

The analysis was unfortunately not able to unpick the effect of infant feeding on mortality in the HIV-exposed uninfected children. Only 16% of HIV-exposed children were breastfed. This is consistent with national guidelines at the time, where formula feeding was recommended for mothers living with HIV. It is reassuring that in recently updated national guidelines, exclusive breastfeeding for six months is now recommended for mothers living with HIV on ART with virologic suppression.

Mother-to-child HIV transmission at 24 months was still around 2%, and further infections may have been undiagnosed in children who died before being tested. More than one in three children living with HIV died within 24 months. This reminds us that while there is increasing interest in HIV-exposed
uninfected children, our priority for now should still be achieving elimination of mother-to-child HIV transmission.

Disparities in HIV care along the path from infection to viral suppression: a cross-sectional study of HIV/AIDS patient records in 2013, Shandong province, China.


Background: The 90-90-90 targets recommended by the Joint United Nations Programme on HIV/AIDS require strengthening human immunodeficiency virus (HIV) care, which includes diagnosis, linkage to and retention in care, assessment for treatment suitability, and optimization of HIV treatment. We sought to quantify patient engagement along the continuum, 10 years after introduction of Chinese HIV care policies.

Methods: We included patients from Shandong, China, who were diagnosed with HIV from 1992 to 2013. Records were obtained from the HIV/AIDS Comprehensive Response Information Management System to populate a 7-step HIV care continuum. Pearson chi² test and multivariate logistic regression were used for analysis.

Results: Of 6500 estimated HIV-infected persons, 60.1% were diagnosed, of whom 41.9% received highly active antiretroviral therapy (HAART). Only 59.6% of patients on HAART and 15% of all infected persons achieved viral suppression. Children infected by mother-to-child transmission (MTCT) and persons infected by intravenous drug use were less likely to be linked to and retained in care (odds ratio [OR], 0.33 [95% confidence interval {CI}, .14-.80] and OR, 0.58 [95% CI, .40-.90], respectively). Persons tested in custodial institutions were substantially less likely to be on HAART (OR, 0.22 [95% CI, .09-.59]) compared with those tested in medical facilities. Patients on HAART infected by homosexual or heterosexual transmission and those infected by MTCT were less likely to achieve viral suppression (OR, 0.18 [95% CI, .09-.34]; OR, 0.12 [95% CI, .06-.22]; OR, 0.07 [95% CI, .02-.20], respectively).

Conclusions: Our report suggests, at the current rate, Shandong Province has to accelerate HIV care efforts to close disparities in HIV care and achieve the 90-90-90 goals equitably.

Abstract access

Editor’s notes: The UNAIDS treatment target set for 2020 aim for at least 90 percent of all people living with HIV to be diagnosed, at least 90 percent of people diagnosed to receive antiretroviral therapy, and for treatment to be effective and consistent enough in at least 90 percent of those people on treatment to suppress the virus. This would result in about 73% of all people living with HIV being virally suppressed.

This study estimated coverage of HIV diagnosis, antiretroviral treatment and viral suppression in Shandong Province in 2013, 10 years after the introduction of a Chinese HIV care policy.

The authors found that overall, only about 60% of people on ART and 15% of all people living with HIV achieved viral suppression (defined in this analysis as having a viral load of less than HIV RNA 50 copies per mL). This is in sharp contrast with recently published figures from Botswana where 97% of people on ART, and about 70% of persons living with HIV were virally suppressed (there defined as having a viral load of less than 400 copies per mL).

With only 15% of persons with HIV being virally suppressed in Shandong Province, a big gap remains for reaching the UNAIDS target of 73%. The authors demonstrate that despite a free, inclusive,
nationwide HIV care policy, significant inequalities in HIV testing and treatment exist in Shandong Province. For example people who inject drugs and people in custodial institutions were much less likely to be initiated on ART.

The authors conclude that to achieve the 90-90-90 UNAIDS treatment target, Shandong Province needs to close these disparities in HIV care.

How home HIV testing and counselling with follow-up support achieves high testing coverage and linkage to treatment and prevention: a qualitative analysis from Uganda.


Introduction: The successes of HIV treatment scale-up and the availability of new prevention tools have raised hopes that the epidemic can finally be controlled and ended. Reduction in HIV incidence and control of the epidemic requires high testing rates at population levels, followed by linkage to treatment or prevention. As effective linkage strategies are identified, it becomes important to understand how these strategies work. We use qualitative data from The Linkages Study, a recent community intervention trial of community-based testing with linkage interventions in sub-Saharan Africa, to show how lay counsellor home HIV testing and counselling (home HTC) with follow-up support leads to linkage to clinic-based HIV treatment and medical male circumcision services.

Methods: We conducted 99 semi-structured individual interviews with study participants and three focus groups with 16 lay counsellors in Kabwohe, Sheema District, Uganda. The participant sample included both HIV+ men and women (N=47) and HIV-uncircumcised men (N=52). Interview and focus group audio-recordings were translated and transcribed. Each transcript was summarized. The summaries were analyzed inductively to identify emergent themes. Thematic concepts were grouped to develop general constructs and framing propositional statements.

Results: Trial participants expressed interest in linking to clinic-based services at testing, but faced obstacles that eroded their initial enthusiasm. Follow-up support by lay counsellors intervened to restore interest and inspire action. Together, home HTC and follow-up support improved morale, created a desire to reciprocate, and provided reassurance that services were trustworthy. In different ways, these functions built links to the health service system. They worked to strengthen individuals' general sense of capability, while making the idea of accessing services more manageable and familiar, thus reducing linkage barriers.

Conclusions: Home HTC with follow-up support leads to linkage by building "social bridges," interpersonal connections established and developed through repeated face-to-face contact between counsellors and prospective users of HIV treatment and male circumcision services. Social bridges link communities to the service system, inspiring individuals to overcome obstacles and access care.

Abstract Full-text [free] access

Editor’s notes: How can people be encouraged once they have received a positive HIV-test result to link and stay in treatment? This is a crucial question as the momentum for everyone living with HIV to be on antiretroviral therapy grows. The authors of this paper demonstrate clearly and succinctly the value of personal contact in supporting people to test and the link to care. Lay-counsellors paying visits to people’s homes provided the encouragement to help some people to link to care. The home visits were seen by people visited as a sign that 'someone cared'. The personal attention and
information provided promoted trust. The visits also created a sense of obligation: the person visited felt they should do something in return to please the counsellor.

Increasing numbers of people living with HIV does not necessarily mean that it is easier for someone coping with a positive-test result to link to care. We should not underestimate the continued burden that an HIV-positive test result places on individuals. Many barriers remain both to testing and sustaining a link to care. The authors of this paper provide examples of how to overcome some of those barriers. However, while this paper provides encouraging findings on the value of the home-based activity, the findings also pose a challenge. Can such follow-up support services, which demand more than a single visit, be provided widely enough to benefit all people who need such attention and support?

Effect of patient navigation with or without financial incentives on viral suppression among hospitalized patients with HIV infection and substance use: a randomized clinical trial.


Importance: Substance use is a major driver of the HIV epidemic and is associated with poor HIV care outcomes. Patient navigation (care coordination with case management) and the use of financial incentives for achieving predetermined outcomes are interventions increasingly promoted to engage patients in substance use disorders treatment and HIV care, but there is little evidence for their efficacy in improving HIV-1 viral suppression rates.

Objective: To assess the effect of a structured patient navigation intervention with or without financial incentives to improve HIV-1 viral suppression rates among patients with elevated HIV-1 viral loads and substance use recruited as hospital inpatients.

Design, setting, and participants: From July 2012 through January 2014, 801 patients with HIV infection and substance use from 11 hospitals across the United States were randomly assigned to receive patient navigation alone (n = 266), patient navigation plus financial incentives (n = 271), or treatment as usual (n = 264). HIV-1 plasma viral load was measured at baseline and at 6 and 12 months.

Interventions: Patient navigation included up to 11 sessions of care coordination with case management and motivational interviewing techniques over 6 months. Financial incentives (up to $1160) were provided for achieving targeted behaviors aimed at reducing substance use, increasing engagement in HIV care, and improving HIV outcomes. Treatment as usual was the standard practice at each hospital for linking hospitalized patients to outpatient HIV care and substance use disorders treatment.

Main outcomes and measures: The primary outcome was HIV viral suppression (≤200 copies/mL) relative to viral nonsuppression or death at the 12-month follow-up.

Results: Of 801 patients randomized, 261 (32.6%) were women (mean [SD] age, 44.6 years [10.0 years]). There were no differences in rates of HIV viral suppression versus nonsuppression or death among the 3 groups at 12 months. Eighty-five of 249 patients (34.1%) in the usual-treatment group experienced treatment success compared with 89 of 249 patients (35.7%) in the navigation-only group for a treatment difference of 1.6% (95% CI, -6.8% to 10.0%; P = .80) and compared with 98 of 254 patients (38.6%) in the navigation-plus-incentives group for a treatment difference of 4.5%
(95% CI -4.0% to 12.8%; P = .68). The treatment difference between the navigation-only and the navigation-plus-incentives group was -2.8% (95% CI, -11.3% to 5.6%; P = .68).

Conclusions and relevance: Among hospitalized patients with HIV infection and substance use, patient navigation with or without financial incentives did not have a beneficial effect on HIV viral suppression relative to nonsuppression or death at 12 months vs treatment as usual. These findings do not support these interventions in this setting.

Trial registration: clinicaltrials.gov Identifier: NCT01612169.

Abstract access

Editor’s notes: Substance use in people living with HIV has consistently been shown to be associated with poor clinical outcomes. Within this population, management often requires a combination of treatment for both HIV and substance use disorders. It is evident that it is the poor engagement in one or both of these treatment approaches that contributes significantly to poor clinical outcomes. The author’s group aimed to fill a gap in current evidence and explore whether two activities, patient navigation and financial incentives, could potentially motivate engagement with both treatment approaches and ultimately improve HIV viral suppression.

This study tested, among people living with HIV in hospital, with substance use disorders, six months of patient navigation alone (care co-ordination and case management), or six months of patient navigation alongside a financial incentive plan. While overall uptake and retention to the programme schedules were high, no differences in HIV-1 viral suppression rates (which were generally poor) or death by 12 months were noted.

One factor that must be highlighted is that the participation in actual substance use treatment programmes post hospital discharge was low across all groups (average 24.8%), primarily due to a lack of available services in the regions. It may be that the programme may have been more effective in a different population of people already established in substance use treatment programmes, or if treatment had been more easily accessible.

The study serves as a reminder that such key populations are extremely vulnerable with a number of comorbidities and competing priorities. While not supporting health care navigation or financial incentives in their defined setting, the study findings emphasise a need to develop and tailor, cost-effective activities to improve health outcomes in this group.

2. Elimination of childhood infections

Prospects for HIV control in South Africa: a model-based analysis.


Background: The goal of virtual elimination of horizontal and mother-to-child HIV transmission in South Africa (SA) has been proposed, but there have been few systematic investigations of which interventions are likely to be most critical to reducing HIV incidence.

Objective: This study aims to evaluate SA’s potential to achieve virtual elimination targets and to identify which interventions will be most critical to achieving HIV incidence reductions.

Design: A mathematical model was developed to simulate the population-level impact of different HIV interventions in SA. Probability distributions were specified to represent uncertainty around 32
epidemiological parameters that could be influenced by interventions, and correlation coefficients \((r)\) were calculated to assess the sensitivity of the adult HIV incidence rates and mother-to-child transmission rates (2015-2035) to each epidemiological parameter.

Results: HIV incidence in SA adults (ages 15-49) is expected to decline from 1.4% in 2011-2012 to 0.29% by 2035 (95% CI: 0.10-0.62%). The parameters most strongly correlated with future adult HIV incidence are the rate of viral suppression after initiating antiretroviral treatment (ART) \((r=-0.56)\), the level of condom use in non-marital relationships \((r=-0.40)\), the phase-in of intensified risk-reduction counselling for HIV-positive adults \((r=0.29)\), the uptake of medical male circumcision \((r=0.24)\) and the phase-in of universal ART eligibility \((r=0.22)\). The paediatric HIV parameters most strongly associated with mother-to-child transmission rates are the relative risk of transmission through breastfeeding when the mother is receiving ART \((r=0.70)\) and the rate of ART initiation during pregnancy \((r=-0.16)\).

Conclusions: The virtual elimination target of a 0.1% incidence rate in adults will be difficult to achieve. Interventions that address the infectiousness of patients after ART initiation will be particularly critical to achieving long-term HIV incidence declines in South Africa.

Abstract  Full-text [free] access

**Editor’s notes:** Despite substantial progress in controlling HIV in South Africa, incidence rates remain very high. There is a continued need to identify and prioritise HIV prevention programmes to improve the impact of existing programmes. A deterministic compartmental model was used to simulate the impact of HIV programmes in South Africa. The modeling study aimed at identifying proximal epidemiological parameters that are important in reducing HIV incidence. The authors of this paper also aimed to evaluate the possibility of achieving the ‘virtual elimination’ targets that have been suggested for both heterosexual and mother-to-child transmission and the UNAIDS 90-90-90 treatment target. The model was parameterised using behavioural and demographic data for South Africa. The results from the study suggest that for the purpose of preventing heterosexual and mother-to-child transmission of HIV in South Africa, the most important proximal epidemiological parameter to focus on is the infectiousness of people receiving antiretroviral therapy. The model predicts that the virtual elimination target of a 0.1% incidence rate in adults will be difficult to achieve. The authors emphasized on the need to scale-up existing HIV prevention and treatment programmes in order to reduce HIV incidence in South Africa.

3. **Combination prevention**

Providing a conceptual framework for HIV prevention cascades and assessing feasibility of empirical measurement with data from east Zimbabwe: a case study.


Background: The HIV treatment cascade illustrates the steps required for successful treatment and is a powerful advocacy and monitoring tool. Similar cascades for people susceptible to infection could improve HIV prevention programming. We aim to show the feasibility of using cascade models to monitor prevention programmes.

Methods: Conceptual prevention cascades are described taking intervention-centric and client-centric perspectives to look at supply, demand, and efficacy of interventions. Data from two rounds of a population-based study in east Zimbabwe are used to derive the values of steps for cascades.
for voluntary medical male circumcision (VMMC) and for partner reduction or condom use driven by HIV testing and counselling (HTC).

Findings: In 2009 to 2011 the availability of circumcision services was negligible, but by 2012 to 2013 about a third of the population had access. However, where it was available only 12% of eligible men sought to be circumcised leading to an increase in circumcision prevalence from 3.1% to 6.9%. Of uninfected men, 85.3% did not perceive themselves to be at risk of acquiring HIV. The proportions of men and women tested for HIV increased from 27.5% to 56.6% and from 61.1% to 79.6%, respectively, with 30.4% of men tested self-reporting reduced sexual partner numbers and 12.8% reporting increased condom use.

Interpretation: Prevention cascades can be populated to inform HIV prevention programmes. In eastern Zimbabwe programmes need to provide greater access to circumcision services and the design and implementation of associated demand creation activities. Whereas, HTC services need to consider how to increase reductions in partner numbers or increased condom use or should not be considered as contributing to prevention services for the HIV-negative adults.

Abstract Full-text [free] access

**Editor’s notes:** UNAIDS has set an ambitious goal of reducing new adult HIV infections below 500 000 per year by 2020. Achieving this goal relies on increased coverage of primary HIV prevention programmes, including pre-exposure prophylaxis and voluntary medical male circumcision (VMMC). The HIV treatment cascade is a well known tool to monitor the performance of services for people living with HIV, and to identify gaps in care. An HIV prevention cascade could provide a similarly useful tool to inform prevention programmes. The tool would define the steps necessary for an effective HIV prevention programme, estimating the proportion of people lost at each step, and hence identifying the barriers to effective HIV prevention in populations. The authors propose a framework for HIV prevention cascades, differentiating between availability, uptake, adherence, and efficacy. The framework would estimate the proportion of the population protected by a given strategy or combination of strategies. Population survey data from rural Zimbabwe are used to illustrate the prevention cascade for VMMC and behaviour change driven by HIV testing and counselling (HTC). These data are used to highlight the barriers impacting on reducing HIV incidence. As the authors acknowledge, there are limitations to the cascade approach for HIV prevention. The cascade is more difficult to define and to estimate for HIV prevention than for HIV treatment. In order for the cascade to be useful, it is necessary to have a good understanding of who is at risk of acquiring HIV. However, the prevention needs of HIV negative adults change over time as people move in and out of risk. Although the authors illustrate the use of the cascade for an individual programme, it is more difficult to assess the combined effect of several prevention strategies. Still, the cascade approach may provide a useful tool to help guide HIV prevention efforts, by identifying gaps and prioritising areas for action.

Interventions to strengthen the HIV prevention cascade: a systematic review of reviews.


Background: Much progress has been made in interventions to prevent HIV infection. However, development of evidence-informed prevention programmes that translate the efficacy of these strategies into population effect remain a challenge. In this systematic review, we map current evidence for HIV prevention against a new classification system, the HIV prevention cascade.
Methods: We searched for systematic reviews on the effectiveness of HIV prevention interventions published in English from Jan 1, 1995, to July, 2015. From eligible reviews, we identified primary studies that assessed at least one of: HIV incidence, HIV prevalence, condom use, and uptake of HIV testing. We categorised interventions as those seeking to increase demand for HIV prevention, improve supply of HIV prevention methods, support adherence to prevention behaviours, or directly prevent HIV. For each specific intervention, we assigned a rating based on the number of randomised trials and the strength of evidence.

Findings: From 88 eligible reviews, we identified 1964 primary studies, of which 292 were eligible for inclusion. Primary studies of direct prevention mechanisms showed strong evidence for the efficacy of pre-exposure prophylaxis (PrEP) and voluntary medical male circumcision. Evidence suggests that interventions to increase supply of prevention methods such as condoms or clean needles can be effective. Evidence arising from demand-side interventions and interventions to promote use of or adherence to prevention tools was less clear, with some strategies likely to be effective and others showing no effect. The quality of the evidence varied across categories.

Interpretation: There is growing evidence to support a number of efficacious HIV prevention behaviours, products, and procedures. Translating this evidence into population impact will require interventions that strengthen demand for HIV prevention, supply of HIV prevention technologies, and use of and adherence to HIV prevention methods.

Abstract  Full-text [free] access

Editor's notes: Demand, supply and use of programmes are crucial for the uptake and effective use of HIV prevention strategies. This paper presents an impressive undertaking in which the authors conducted a review of systematic reviews on the evidence for the effectiveness of HIV prevention programmes across the multiple steps in an HIV prevention cascade. This particular prevention cascade allocates programmes into demand-side, supply-side, adherence, and direct HIV prevention technologies. This was published in a separate paper in conjunction with this review. The review found that there is strong evidence with regards to which direct HIV prevention technologies are efficacious, as well as maps where adherence and supply-side programmes have been effective. A primary gap was noted on the demand-side of the cascade (e.g. information, education and communication, and peer-based activities to increase demand for medical male circumcision) where studies have not resulted in reducing HIV incidence or prevalence. There remains a need to understand why, despite supply, there is low uptake of some HIV prevention strategies, and for evaluation of novel activities to increase demand.

4. Key populations

Policing practices as a structural determinant for HIV among sex workers: a systematic review of empirical findings.


Introduction: Sex workers are disproportionately infected with HIV worldwide. Significant focus has been placed on understanding the structural determinants of HIV and designing related interventions. Although there is growing international evidence that policing is an important
structural HIV determinant among sex workers, the evidence has not been systematically reviewed.

Methods: We conducted a systematic review of quantitative studies to examine the effects of policing on HIV and STI infection and HIV-related outcomes (condom use; syringe use; number of clients; HIV/STI testing and access) among cis and trans women sex workers. Databases included PubMed, Embase, Scopus, Sociological Abstracts, Popline, Global Health (OVID), Web of Science, IBSS, IndMed and WHOLIS. We searched for studies that included police practices as an exposure for HIV or STI infection or HIV-related outcomes.

Results: Of the 137 peer-reviewed articles identified for full text review, 14 were included, representing sex workers' experiences with police across five settings. Arrest was the most commonly explored measure with between 6 and 45% of sex workers reporting having ever been arrested. Sexual coercion was observed between 3 and 37% of the time and police extortion between 12 and 28% across studies. Half the studies used a single measure to capture police behaviours. Studies predominantly focused on "extra-legal policing practices," with insufficient attention to the role of "legal enforcement activities". All studies found an association between police behaviours and HIV or STI infection, or a related risk behaviour.

Conclusions: The review points to a small body of evidence that confirms policing practices as an important structural HIV determinant for sex workers, but studies lack generalizability with respect to identifying those police behaviours most relevant to women's HIV risk environment.

Abstract Full-text [free] access

Editor’s notes: The paper reports on a systematic review, which explored how quantitative research to date has operationalized the measurement of law enforcement practices as a structural determinant of HIV for female (including transgender) sex workers. The authors reviewed 14 quantitative studies using policing practices as a micro-structural determinant for HIV risk among sex workers. They found substantial heterogeneity in both the police measures and the health outcomes considered by the different studies. Overall, the studies found that police measures were regularly reported by sex workers, with an average of 34% of sex workers experiencing at least one police measure. They found that arrest was the most commonly explored measure in the studies. Following this, sexual coercion and then police extortion were important.

The studies reported that these police measures were consistently, positively, associated with either HIV infection or STI symptoms or with inconsistent condom use. Having ever been arrested, sexual coercion, police extortion, and syringe confiscation was associated with an increased risk of acquiring an HIV infection or an STI. These measures, and displacement by the police, were also associated with inconsistent condom use. Intervening on interactions between sex workers and the police reduced HIV risk over the time of the programme.

The authors argue that these findings point to the potentially pivotal role that the police have as a structural determinant for HIV in vulnerable populations. However, they argue that nearly all the papers identified in this review fail to take account of the complexities of the risk environment in which law enforcement occurs. The authors thus suggest a need for better measures for legal and extra-legal enforcement practices as mechanisms through which sex workers' HIV risk is mediated.
5. Elimination of gender inequalities

Ethical challenges of randomized violence intervention trials: examining the SHARE intervention in Rakai, Uganda.


Objective: We identify complexities encountered, including unanticipated crossover between trial arms and inadequate 'standard of care' violence services, during a cluster randomized trial (CRT) of a community-level intimate partner violence (IPV) and HIV prevention intervention in Uganda.

Methods: Concepts in public health ethics - beneficence, social value of research, fairness, standard of care, and researcher responsibilities for post-trial benefits - are used to critically reflect on lessons learned and guide discussion on practical and ethical challenges of violence intervention CRTs.

Results: Existing ethical guidelines provide incomplete guidance for responding to unexpected crossover in CRTs providing IPV services. We struggled to balance duty of care with upholding trial integrity, and identifying and providing appropriate standard of care. While we ultimately offered short-term IPV services to controls, we faced additional challenges related to sustaining services beyond the 'short-term' and post-trial.

Conclusion: Studies evaluating community-level violence interventions, including those combined with HIV reduction strategies, are limited yet critical for developing evidence-based approaches for effectively preventing IPV. Although CRTs are a promising design, further guidance is needed to implement trials that avoid introducing tensions between validity of findings, researchers’ responsibilities to protect participants, and equitable distribution of CRT benefits.

Abstract access

Editor’s notes: Data from 81 countries indicate that 30% of women aged 15 and above have experienced physical and/or sexual intimate partner violence in their lifetime. Settings with the highest intimate partner violence prevalence were found to be in sub-Saharan Africa, the region most affected by HIV. Intimate partner violence is now widely accepted to be both a precursor to and sequelae of HIV infection. In response, a growing number of combination intimate partner violence and HIV prevention programmes have been implemented and systematically evaluated through randomised trials. The authors of this paper discuss some of the practical, ethical and safety challenges introduced by randomised trials on violence prevention, drawing on experience from a project in rural Uganda.

International guidelines have been established for the ethical conduct of biomedical research involving human subjects. The subject of violence against women and the method of randomised controlled trials are not easily resolved with these standard guidelines. In response, specialised recommendations for conducting safe and ethical population-based survey research on violence against women have been developed. These guidelines are an important development, but randomised trials to evaluate intimate partner violence prevention programmes face practical challenges in responding to common research ethics and safety considerations. These include: what to offer control communities in a trial investigating the optimal delivery approach for an activity likely to be effective in a setting with no standard of care. This needs to be done while maintaining the integrity of the study.
Drawing from their experience of the SHARE trial in the Rakai District in Uganda, the authors offer three reflections from lessons learned. (1) Ongoing need to formally update programmes that address multiple and overlapping vulnerabilities of individuals experiencing intimate partner violence and at risk of, or living with, HIV. (2) Cluster-randomised trials are a promising approach for programme evaluation but introduce numerous challenges with practical and ethical implications. (3) Given widespread underreporting of intimate partner violence, evaluation of violence programmes may have particularly high levels of unanticipated demand. The authors advocate for a framework of relevant considerations to be developed to guide researchers working on activities to reduce intimate partner violence. These guidelines should address potentially common challenges. They also encourage researchers to share field lessons arising from their studies in order to a) contribute to the development of this framework b) for revising and improving guidelines for the ethical conduct of intimate partner violence programmes in low resource settings.

6. Elimination of stigma

Examining the associations between HIV-related stigma and health outcomes in people living with HIV/AIDS: a series of meta-analyses.


Objective: To conduct a systematic review and series of meta-analyses on the association between HIV-related stigma and health among people living with HIV.

Data sources: A structured search was conducted on 6 electronic databases for journal articles reporting associations between HIV-related stigma and health-related outcomes published between 1996 and 2013.

Study eligibility criteria: Controlled studies, cohort studies, case-control studies and cross-sectional studies in people living with HIV were considered for inclusion.

Outcome measures: Mental health (depressive symptoms, emotional and mental distress, anxiety), quality of life, physical health, social support, adherence to antiretroviral therapy, access to and usage of health/social services and risk behaviours.

Results: 64 studies were included in our meta-analyses. We found significant associations between HIV-related stigma and higher rates of depression, lower social support and lower levels of adherence to antiretroviral medications and access to and usage of health and social services. Weaker relationships were observed between HIV-related stigma and anxiety, quality of life, physical health, emotional and mental distress and sexual risk practices. While risk of bias assessments revealed overall good quality related to how HIV stigma and health outcomes were measured on the included studies, high risk of bias among individual studies was observed in terms of appropriate control for potential confounders. Additional research should focus on elucidating the mechanisms behind the negative relationship between stigma and health to better inform interventions to reduce the impact of stigma on the health and well-being of people with HIV.

Conclusions: This systematic review and series of meta-analyses support the notion that HIV-related stigma has a detrimental impact on a variety of health-related outcomes in people with HIV. This review can inform the development of multifaceted, intersectoral interventions to reduce the impact of HIV-related stigma on the health and well-being of people living with HIV.

Abstract  Full-text [free] access
Editor’s notes: There is a growing body of research documenting the negative impact of stigma and discrimination on the health of people living with HIV. Stigma is associated with poorer mental health, including emotional distress, depression and reduced psychological functioning. It has also been linked to intermediate health outcomes such as seeking healthcare and adherence to antiretroviral therapy. This paper reports a comprehensive systematic review and meta-analyses summarising the published evidence on the relationship between HIV-associated stigma and a wide range of health outcomes, including intermediate health outcomes. Results illustrate associations between HIV-associated stigma and depressive symptoms, lower levels of social support, ART adherence and use of health services. However, the majority of studies in the review were cross-sectional and longitudinal studies are necessary to explore the complex relationship between these factors, including the role of moderating factors, such as coping strategies. In addition, more research is necessary from low- and middle-income countries given that much of the published research is from North America. Further, there is also a need to better understand the intersection of HIV-associated stigma with other types of stigma experienced by people living with HIV, including homophobia, racism and gender discrimination.

7. Financing

Comparative cost of early infant male circumcision by nurse-midwives and doctors in Zimbabwe.


Background: The 14 countries that are scaling up voluntary male medical circumcision (VMMC) for HIV prevention are also considering early infant male circumcision (EIMC) to ensure longer-term reductions in HIV incidence. The cost of implementing EIMC is an important factor in scale-up decisions. We conducted a comparative cost analysis of EIMC performed by nurse-midwives and doctors using the AccuCirc device in Zimbabwe.

Methods: Between August 2013 and July 2014, nurse-midwives performed EIMC on 500 male infants using AccuCirc in a field trial. We analyzed the overall unit cost and identified key cost drivers of EIMC performed by nurse-midwives and compared these with costing data previously collected during a randomized noninferiority comparison trial of 2 devices (AccuCirc and the Mogen clamp) in which doctors performed EIMC. We assessed direct costs (consumable and nonconsumable supplies, device, personnel, associated staff training, and waste management costs) and indirect costs (capital and support personnel costs). We performed one-way sensitivity analyses to assess cost changes when we varied key component costs.

Results: The unit costs of EIMC performed by nurse-midwives and doctors in vertical programs were US$38.87 and US$49.77, respectively. Key cost drivers of EIMC were consumable supplies, personnel costs, and the device price. In this cost analysis, major cost drivers that explained the differences between EIMC performed by nurse-midwives and doctors were personnel and training costs, both of which were lower for nurse-midwives.

Conclusions: EIMC unit costs were lower when performed by nurse-midwives compared with doctors. To minimize costs, countries planning to scale up EIMC should consider using nurse-midwives, who are in greater supply than doctors and are the main providers at the primary health care level, where most infants are born.
Abstract  Full-text [free] access

Editor’s notes: The evidence behind the efficacy for male circumcision in HIV prevention has been proven beyond a reasonable doubt, and 14 countries with a high HIV prevalence are currently scaling up voluntary medical male circumcision. To improve future HIV prevention, WHO and UNICEF also recommend that early infant male circumcision be performed within the first 60 days of life in countries with a high HIV prevalence. In countries such as Zimbabwe, an acute shortage of human resources for health has the potential to hinder scale-up of early infant male circumcision. However, with new devices such as the AccuCirc®, early infant male circumcision can be performed without advanced surgical skills – raising the potential for task shifting as a way to alleviate pressure on human resources.

This study compares the unit cost of early infant male circumcision using the AccuCirc®, as performed by doctors and by nurse-midwives. Nurse-midwives on average took a longer time to complete a circumcision (average 18 minutes) as compared to doctors (average 16 minutes). However, the reductions in salary costs offset this increased time, reducing the unit cost of early infant male circumcision overall. Integrating early infant male circumcision into a public health facility (as compared to a vertical programme) would further reduce the costs.

This study suggests that countries seeking to scale up early infant male circumcision should consider task shifting as a way to reduce costs. Task shifting does pose the risk of increasing workload for lower-level personnel; more nurse-midwives will need to be trained to cope with additional responsibilities to avoid over-burdening existing personnel. However, this is a promising solution to enable scale-up of early infant male circumcision quickly and affordably in settings such as Zimbabwe.

Changing HIV treatment eligibility under health system constraints in sub-Saharan Africa: Investment needs, population health gains, and cost-effectiveness.


Objective: We estimated the investment need, population health gains, and cost-effectiveness of different policy options for scaling-up prevention and treatment of HIV in the 10 countries that currently comprise 80% of all people living with HIV in sub-Saharan Africa (Ethiopia, Kenya, Malawi, Mozambique, Nigeria, South Africa, Tanzania, Uganda, Zambia, and Zimbabwe).

Design: We adapted the established STDSIM model, to capture the health system dynamics: demand-side and supply-side constraints in the delivery of antiretroviral treatment (ART).

Methods: We compared different scenarios of supply-side (i.e. health system capacity) and demand-side (i.e. health seeking behavior) constraints, and determined the impact of changing guidelines to ART eligibility at any CD4 cell count within these constraints.

Results: Continuing current scale-up would require US$178 billion by 2050. Changing guidelines to ART at any CD4 cell count is cost-effective under all constraints tested in the model, especially in demand-side constrained health systems because earlier initiation prevents loss to follow-up of patients not yet eligible. Changing guidelines under current demand-side constraints would avert 1.8 million infections at US$208 per life-year saved.

Conclusions: Treatment eligibility at any CD4 cell count would be cost-effective, even under health system constraints. Excessive loss to follow up and mortality in patients not eligible for treatment can be avoided by changing guidelines in demand-side constrained systems. The financial
obligation for sustaining the AIDS response in sub-Saharan Africa over the next 35 years is substantial, and requires strong, long-term commitment of policy makers and donors to continue to allocate substantial parts of their budgets.

Abstract access

Editor’s notes: Recent WHO guidelines recommend that everyone who is diagnosed as HIV positive should be allowed to start treatment immediately, a change to the former guideline where their CD4 count (a measure of disease progression) was the main criteria for starting treatment. This paper uses a model to look at the costs and benefits of changing to this immediate treatment regimen in the sub-Saharan African countries most affected by the epidemic. The authors find that allowing all HIV people living with HIV to access treatment is cost-effective, and this finding does not change when the model assumptions are varied. However, the impact of this change on the health system budgets in these countries is very substantial, and the authors suggest that a large commitment is necessary from policymakers and donors to sustain this response as short-term spending will not be enough to make an impact.

8. Health systems and services


Background: Timely assessment of the burden of HIV/AIDS is essential for policy setting and programme evaluation. In this report from the Global Burden of Disease Study 2015 (GBD 2015), we provide national estimates of levels and trends of HIV/AIDS incidence, prevalence, coverage of antiretroviral therapy (ART), and mortality for 195 countries and territories from 1980 to 2015.

Methods: For countries without high-quality vital registration data, we estimated prevalence and incidence with data from antenatal care clinics and population-based seroprevalence surveys, and with assumptions by age and sex on initial CD4 distribution at infection, CD4 progression rates (probability of progression from higher to lower CD4 cell-count category), on and off antiretroviral therapy (ART) mortality, and mortality from all other causes. Our estimation strategy links the GBD 2015 assessment of all-cause mortality and estimation of incidence and prevalence so that for each draw from the uncertainty distribution all assumptions used in each step are internally consistent. We estimated incidence, prevalence, and death with GBD versions of the Estimation and Projection Package (EPP) and Spectrum software originally developed by the Joint United Nations Programme on HIV/AIDS (UNAIDS). We used an open-source version of EPP and recoded Spectrum for speed, and used updated assumptions from systematic reviews of the literature and GBD demographic data. For countries with high-quality vital registration data, we developed the cohort incidence bias adjustment model to estimate HIV incidence and prevalence largely from the number of deaths caused by HIV recorded in cause-of-death statistics. We corrected these statistics for garbage coding and HIV misclassification.

Findings: Global HIV incidence reached its peak in 1997, at 3.3 million new infections (95% uncertainty interval [UI] 3.1-3.4 million). Annual incidence has stayed relatively constant at about 2.6 million per year (range 2.5-2.8 million) since 2005, after a period of fast decline between 1997 and 2005. The number of people living with HIV/AIDS has been steadily increasing and reached 38.8 million (95% UI 37.6-40.4 million) in 2015. At the same time, HIV/AIDS mortality has been declining at a steady pace, from a peak of 1.8 million deaths (95% UI 1.7-1.9 million) in 2005, to 1.2 million deaths (1.1-1.3 million) in 2015. We recorded substantial heterogeneity in the levels and trends of HIV/AIDS across countries. Although many countries have experienced decreases in
HIV/AIDS mortality and in annual new infections, other countries have had slowdowns or increases in rates of change in annual new infections.

Interpretation: Scale-up of ART and prevention of mother-to-child transmission has been one of the great successes of global health in the past two decades. However, in the past decade, progress in reducing new infections has been slow, development assistance for health devoted to HIV has stagnated, and resources for health in low-income countries have grown slowly. Achievement of the new ambitious goals for HIV enshrined in Sustainable Development Goal 3 and the 90-90-90 UNAIDS targets will be challenging, and will need continued efforts from governments and international agencies in the next 15 years to end AIDS by 2030.

Abstract  Full-text [free] access

Editor’s notes: The global estimates for HIV incidence, prevalence, and deaths produced by the Global Burden of Disease (GBD) mathematical modelling approach for 2015 are somewhat higher than those published by UNAIDS in June 2016 prior to the International Conference on AIDS held in Durban in July. Both GBD and UNAIDS agree that as the scale-up of antiretroviral treatment (ART) continues, HIV-associated mortality is declining with the result that HIV prevalence is rising as the number of people living with HIV continues to grow. The metric of critical interest to policy makers and programme planners is HIV incidence, the number of new infections. Each new infection means ART for life, starting from HIV diagnosis now rather than later in disease progression. Both GBD and UNAIDS estimates suggest that globally annual HIV incidence stopped declining after 2005 and has remained persistently high at 2.5 million (2.2-2.7 million) according to GBD and 2.1 million (1.8-2.4 million) according to UNAIDS. Where the estimates differ is at country level, precisely where they can make the most difference to decision making. GBD estimates for HIV incidence for countries in the regions of northern America, Europe, Australasia, and central Asia are significantly lower than the reported numbers of newly diagnosed cases (see the comparison table in the Lancet commentary by Supervie and Costagliola: http://www.thelancet.com/journals/lanhiv/article/PIIS2352-3018(16)30089-3/abstract). For example, 85 252 people were newly diagnosed with HIV in the Russian Federation in 2014 whereas the GBD estimate for people newly acquiring HIV in 2015 was only 57 340, albeit with a wide range of uncertainty. For the United States of America, the uncertainly bounds around the GBD estimate of 23 040 do not include 44 073, the number of newly diagnosed cases. Furthermore, new diagnoses likely underestimate actual HIV incidence as they include people who acquired HIV in previous years. Estimates for some high prevalence countries are significantly higher than those produced by those countries with UNAIDS support. For example, http://aidsinfo.unaids.org/ illustrates South Africa as having 380 000 (330 000-430 000) new infections while GBD estimates 529 670 (440 940 to 630 390). Modelling estimates are simply estimates but they cannot be confirmatory or even complementary when they are so different. UNAIDS and IHME (GBD) are already working to understand the differences in the two mathematical modelling approaches - their methodologies, parameters, and assumptions – in order to explain important discrepancies at country level. More importantly, improved data collection by countries of the numbers of HIV diagnoses, people accessing and staying on ART, and the proportion of people living with HIV who achieve viral suppression is necessary to monitor progress towards the UNAIDS 90-90-90 treatment target. Enhanced clinical and epidemiological surveillance systems are also key to the creation of more accurate estimates of country HIV incidence, the metric that reflects HIV prevention programme progress and informs budget allocations and programme planning for HIV treatment.