Welcome to the 6th issue of HIV this month! In this issue, we cover the following topics:

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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

90-90-90: a clear roadmap for HIV treatment. But each 90 brings with it opportunities and challenges.

Editor’s notes: The discovery of effective antiretroviral therapy (ART) will go down in history as the greatest success of biomedical science of the past decades. Landmark studies have shown that the earlier people living with HIV start ART, not only is their clinical outlook improved, but also their likelihood of transmitting infection to their sexual partners falls dramatically. People who take their ART effectively and in whom the virus is suppressed to undetectable levels are no longer infectious. A massive public health and social justice response has led to unprecedented scale up of this miraculous treatment. There is widespread adoption of the UNAIDS 90-90-90 treatment target. The target is easy to recite: 90% of people living with HIV know their status; 90% of people who know their status are on ART and 90% of people taking ART have suppressed their viral load. Many mathematical models show that if these targets are achieved, there should be a substantial impact on the trajectory of the epidemic with a large reduction in new HIV infections and HIV-related deaths, leading to huge cost-savings in the future.

Several large community based studies have been established to examine both the necessary processes to reach these goals and the impact at community level of the wider coverage with effective ART. We have commented in previous editions on the ANRS Treatment as Prevention (TasP) study in rural Kwazulu-Natal and on papers from the SEARCH study in rural Kenya and Uganda. Not surprisingly, given the different contexts, approaches, methods and definitions, the studies each shed light on different aspects of the 90-90-90 target.

This month, there are two new papers from the PopART (HPTN071) study, along with an accompanying commentary from the TasP study team. PopART is the largest of the large community randomized studies of the universal test and treat approach, nested within a broader combination prevention package. The population covered by the trial is around one million people living in largely urban or peri-urban communities in Zambia and the Western Cape province of South Africa. The approach used in two of the three arms of the trial, is to deliver HIV testing and other prevention services by means of community health workers. These so called CHiPs (Community HIV care Providers) also encourage linkage of people either known to be or newly found to be living with HIV to the local government health facilities, where ART is started regardless of CD4 count in one arm of the study, or in line with government guidelines (which is now also regardless of CD4 count in both countries) in the other. In the third arm of the trial, there are no CHiPs and HIV testing and linkage to treatment is performed by routine services, with treatment also offered to all, regardless of CD4 count.

The papers in this month’s edition cover only the four Zambian communities receiving the most intensive package during the first year of the intervention. Shanaube and colleagues focus on the first 90, while Hayes and colleagues focus on the second 90. The overall conclusion is that the CHiPs approach leads to a very high uptake of HIV testing, but that linkage to care still takes longer than expected. However, there is a wealth of detail in both the process and the ways to measure these apparently straightforward statistics. When the CHiPs actually see people, acceptance of HIV testing is very high, unless people have recently had an HIV test. Even then, almost three quarters of women are happy to have another test four to six months after their most recent negative test, whereas for men, there is somewhat more reluctance. The main challenges for the CHiPs are that people may need more than one visit to decide to test and that men are often not at home, despite multiple visits and scheduled appointments. Furthermore, as Iwuju and Newell point out in their slightly pessimistic commentary, people move around and migration makes it hard to define a reliable denominator (a challenge also faced by the SEARCH team in Uganda and Kenya). Around 20% of
the people who knew they were HIV positive were not able to be seen at one year follow-up, so it is not possible to know whether they were linked to care or not. The TasP study also found that the second 90 was the real challenges, with a very high coverage of HIV testing, but not enough linkage to lead to a reduction in incidence at the community level.

The PopART study is ongoing, and recent presentations suggest that with time, a larger proportion of people are indeed linking to care. The lesson may be that it requires ongoing and continuing support in an urban and peri-urban community to achieve high levels of coverage. We await eagerly the next instalments and final results demonstrating whether there is a wider public health impact which will not be available before 2019!

These huge longitudinal studies also remind us that the 90-90-90 target is defined as cross-sectional measurements, and does not take into account directly the length of time that it takes to start treatment or to become virally suppressed. The information from large cross-sectional studies, such as ICAP and PEPFAR's population-based HIV impact assessments (PHIA) give a direct measurement of 90-90-90. However, in contrast to PopART and the other community-based studies, gives no insight into the dynamics of the processes through which people decide to get tested, link to care and remain in care.

McCreesh and colleagues used an individual-based mathematical model of the flow through testing, linkage to treatment and retention based on data from Uganda and using a novel method of calibration. They show that removing the CD4 threshold (as is recommended by WHO and the UNAIDS 90-90-90 target) is very likely to be the most cost-effective approach to reduce the burden of HIV over the years up to 2030. However, they also found that their model predicts that efforts to improve linkage to and retention in care are likely to be more cost-effective than increased coverage of testing in Uganda. This is in part because many Ugandans already know their HIV status as a result of previous efforts, so it should not be taken as a general recommendation not to work to improve the first 90 as well as the second two! The authors state clear conclusions: “Our results strongly suggest that an increase in the rates of HIV testing in the general population in Uganda ….. should not be prioritized above interventions to improve linkage to, and retention in, care….. In Uganda, interventions to improve retention in and movement through the HIV care pathway should be prioritized over case finding interventions in the general population.”

In rural Kwazulu-Natal, the challenge of retention among populations that are by necessity mobile was also shown in a study by Arnesen and colleagues. In this study of risk factors for people on ART being lost to follow up they found that more than one quarter of the 3242 people on the treatment register in 15 primary care clinics were thought to be lost. However, the authors found that one-third of these people labelled as lost were in fact taking treatment at another clinic. As in other similar studies men were more likely to discontinue treatment, as were people with advanced immunosuppression (who are at high risk of dying in the absence of treatment) and being on ART for less than six months. This is a useful reminder of priorities. Providing more support to men, and the sickest patients, maintaining closer supervision for the first year, might lead to better programme outcomes and (as predicted by the Ugandan model) save money in the medium term.

By comparison, a large records-based study in the United States of America by Youn and colleagues examined time trends in retention on treatment (persistence in the authors’ terminology). The author used insurance claims for prescriptions for ART and for other medicines for heart disease, hypertension or diabetes taken regularly over a long time by both HIV positive and HIV-negative people. They were able to examine persistence in over 40 000 people living with HIV starting treatment in 2001-2003 (when ART was more cumbersome and more toxic) compared to 2004-2006 and 2007-2010. Persistence improved dramatically over this time period for ART, but hardly changed
at all for the other medicines studied. This demonstrates that the changes were not merely secular trends in the likelihood of remaining on treatment. Interestingly, in people living with HIV, persistence on the non-HIV related medicines also improved, suggesting that HIV care provided additional benefits in terms of retention and adherence to medicines that went beyond ART.

There was also good news from Australia, where Medland and colleagues used records from the two largest HIV treatment clinics in the state of Victoria to examine time trends in the delay from HIV diagnosis to starting ART. Among 729 people started on ART, the proportion of patient in care and on ART within one year of diagnosis increased from 43.4% to 78.9% from 2011 to 2014. By 2014, 50% of people were starting ART within 77 days of being diagnosed. The authors point out that this is a key measurement of programme effectiveness that is not routinely captured. Nor does it form part of the 90-90-90 targets. Of course, it is important to remember that the period prior to HIV diagnosis is probably even more important in terms of risks of transmission, as there have been numerous studies showing that people who know their HIV status are less likely to transmit HIV. So we really need to know the period from infection to HIV diagnosis, as well as the time from diagnosis to treatment, and perhaps also the time to become virally suppressed. Viral suppression can take months or even more than a year depending on an individual’s initial virological and immunological state and variations in response to treatment as well as with the choice of ART regimen.

Despite massive scale up of ART, there are still many people living with HIV who present to services late with a CD4 count of <200 cells per ml. A recent report in MMWR, showed that in 10 PEPFAR supported countries, there are still as many as one third of people presenting late. Many of these people have opportunistic infections that have characterised HIV infection since the earliest days of the AIDS epidemic. Botswana has made huge progress towards 90-90-90, but Tenforde and colleagues show that cryptococcal meningitis is still a major health problem. They were able to collect laboratory based data over the past decade, as well as more detailed records from the two largest referral centres. Although the number of cases of cryptococcal meningitis has halved since 2004, when the scale up of ART in Botswana really got going, the two referral hospitals still see more than 150 cases per year. Mortality is still horribly high. Overall, the authors explored data from more than 5000 episodes of cryptococcal meningitis in 4702 individuals over the period 2004-2014. For people who could be linked to their clinical medical records, they demonstrate that the risk rises dramatically as the CD4 count falls – people with a CD4 count of < 50 cells per ml have an incidence of around 2000/100 000 person years, whereas the rates of people with 50-100 or 100-200 cells per ml are around 350 and 80 respectively. More than 90% of the cases identified occurred in people whose CD4 cell count was <200 cells per ml. As other studies might have predicted, men are more affected, as they tend to present to services later. The most useful medicines for cryptococcal meningitis, i.e., liposomal Amphotericin and 5 flucytosine, remain too expensive or not available in most African countries. Not only do we need to bring the prices of these commodities down to affordable levels, but we also need continued efforts to engage men (and other populations who get left behind) earlier in the course of their HIV infection.

The improvements in overall survival and life expectancy for people living with HIV if they have access to effective treatments are well known. A large collaborative study (the ART Cohort Collaboration) has brought together 18 European and North American cohorts in order to look at the mortality experienced in the first years after starting ART. They found the biggest improvements in people who started treatment in the last period that they studied (2008-2010). There were also greater changes in mortality in the second and third years after starting ART. Even so, they conclude that life expectancy is still not as good as that of HIV negative people. Previous studies have sometimes been biased towards people who survive longer, partly through not including as many people in the first year after ART when mortality is at its highest. They propose that much of the
What works-reaching universal HIV testing: lessons from HPTN 071 (PopART) trial in Zambia


Objective: To determine the uptake of home-based HIV counselling and testing (HCT) in four HPTN071 (PopART) trial communities (implementing a ‘full’ combination HIV prevention package that includes universal HIV testing and treatment) in Zambia. We also explore factors associated with uptake of HCT in these communities.

Design: HPTN071 (PopART) is a 3-arm community-randomized trial in 12 communities in Zambia and 9 communities in South Africa evaluating the impact of a combination HIV prevention package, including universal HIV testing and treatment, on HIV incidence.

Methods: Using a door-to-door approach that includes systematically re-visiting households, individuals were offered participation in the intervention and verbal consent was obtained. Data were analysed for the first 18 months of the intervention, December 2013 to June 2015 for individuals 18 years and older.

Results: Among 121 130 enumerated household members, 101 102 (83.5%) accepted the intervention. HCT uptake was 72.2% (66 894/92 612), similar by sex but varied across communities. HCT uptake was associated with younger age, sex, community, being symptomatic for TB and STI and longer time since previous HIV test. Knowledge of HIV status due to the intervention increased by 36% overall and by 66% among HIV positives; the highest impact was among 18-24 year olds.

Conclusion: Overall acceptance of HIV-testing through offering a door-to-door-based combination HIV prevention package was 72.2%. The intervention increased knowledge of HIV status from ~50% to ~90%. However, challenges still remain and a one-off intervention is unlikely to be successful but will require repeated visits and multiple strategies.

A universal testing and treatment intervention to improve HIV control: One-year results from intervention communities in Zambia in the HPTN 071 (PopART) cluster-randomised trial


Objective: The Joint United Nations Programme on HIV/AIDS (UNAIDS) 90-90-90 targets require that, by 2020, 90% of those living with HIV know their status, 90% of known HIV-positive individuals receive sustained antiretroviral therapy (ART), and 90% of individuals on ART have durable viral suppression. The HPTN 071 (PopART) trial is measuring the impact of a universal testing and treatment intervention on population-level HIV incidence in 21 urban communities in Zambia and South Africa. We report observational data from four communities in Zambia to assess progress towards the UNAIDS targets after 1 y of the PopART intervention.
Methods and Findings: The PopART intervention comprises annual rounds of home-based HIV testing delivered by community HIV-care providers (CHiPs) who also support linkage to care, ART retention, and other services. Data from four communities in Zambia receiving the full intervention (including immediate ART for all individuals with HIV) were used to determine proportions of participants who knew their HIV status after the CHIP visit; proportions linking to care and initiating ART following referral; and overall proportions of HIV-infected individuals who knew their status (first 90 target) and the proportion of these on ART (second 90 target), pre- and post-intervention. We are not able to assess progress towards the third 90 target at this stage of the study. Overall, 121,130 adults (59,283 men and 61,847 women) were enumerated in 46,714 households during the first annual round (December 2013 to June 2015). Of the 45,399 (77%) men and 55,703 (90%) women consenting to the intervention, 80% of men and 85% of women knew their HIV status after the CHIP visit. Of 6197 HIV-positive adults referred by CHiPs, 42% (95% CI: 40%-43%) initiated ART within 6 mo and 53% (95% CI: 52%-55%) within 12 mo. In the entire population, the estimated proportion of HIV-positive adults who knew their status increased from 52% to 78% for men and from 56% to 87% for women. The estimated proportion of known HIV-positive individuals on ART increased overall from 54% after the CHIP visit to 74% by the end of the round for men and from 53% to 73% for women. The estimated overall proportion of HIV-positive adults on ART, irrespective of whether they knew their status, increased from 44% to 61%, compared with the 81% target (the product of the first two 90 targets). Coverage was lower among young men and women than in older age groups. The main limitation of the study was the need for assumptions concerning knowledge of HIV status and ART coverage among adults not consenting to the intervention or HIV testing, although our conclusions were robust in sensitivity analyses.

Conclusions: In this analysis, acceptance of HIV testing among those consenting to the intervention was high, although linkage to care and ART initiation took longer than expected. Knowledge of HIV-positive status increased steeply after 1 y, almost attaining the first 90 target in women and approaching it in men. The second 90 target was more challenging, with approximately three-quarters of known HIV-positive individuals on ART by the end of the annual round. Achieving higher test uptake in men and more rapid linkage to care will be key objectives during the second annual round of the intervention.

Abstract Full-text [free] access

Universal test, treat, and keep: improving ART retention is key in cost-effective HIV control in Uganda


Background: With ambitious new UNAIDS targets to end AIDS by 2030, and new WHO treatment guidelines, there is increased interest in the best way to scale-up ART coverage. We investigate the cost-effectiveness of various ART scale-up options in Uganda.

Methods: Individual-based HIV/ART model of Uganda, calibrated using history matching. 22 ART scale-up strategies were simulated from 2016 to 2030, comprising different combinations of six single interventions (1. increased HIV testing rates, 2. no CD4 threshold for ART initiation, 3. improved ART retention, 4. increased ART restart rates, 5. improved linkage to care, 6. improved pre-ART care). The incremental net monetary benefit (NMB) of each intervention was
calculated, for a wide range of different willingness/ability to pay (WTP) per DALY averted (health-service perspective, 3% discount rate).

Results: For all WTP thresholds above $210, interventions including removing the CD4 threshold were likely to be most cost-effective. At a WTP of $715 (1 × per-capita-GDP) interventions to improve linkage to and retention/re-enrolment in HIV care were highly likely to be more cost-effective than interventions to increase rates of HIV testing. At higher WTP (> ~ $1690), the most cost-effective option was 'Universal Test, Treat, and Keep' (UTTK), which combines interventions 1-5 detailed above.

Conclusion: Our results support new WHO guidelines to remove the CD4 threshold for ART initiation in Uganda. With additional resources, this could be supplemented with interventions aimed at improving linkage to and/or retention in HIV care. To achieve the greatest reductions in HIV incidence, a UTTK policy should be implemented.

Abstract  Full-text [free] access

Predictors of loss to follow-up among patients on ART at a rural hospital in KwaZulu-Natal, South Africa.


Introduction: Improved HIV outcomes as a result of expanded antiretroviral therapy (ART) access is threatened by increasing rates of loss to follow up (LTFU) among those on ART, largely reported in urban populations. Some reports suggest that LTFU rates are overestimated due to patient movement to other facilities and inadequate medical records.

Study Objective: To define the proportion disengaging from HIV care as well as the characteristics of those LTFU in order to design and implement appropriate interventions to increase retention.

Methods: We performed a retrospective review of patients who discontinued ART at a central hospital ART clinic in rural South Africa and compared with patients receiving care at the 15 primary health clinics (PHCs) to determine the true proportion of those who were LTFU. We also compared those who discontinued ART with those who did not at the central hospital ART clinic to determine predictors of loss to follow up.

Results: Among 3242 patients on ART, 820 were originally marked as LTFU. Among all patients, 272 (8.4%) were found at a clinic on treatment, 56 (1.7%) were found at a clinic from which they had since discontinued treatment, and 10 (0.3%) returned to care between June and July 2016, leaving 475 (14.7%) unaccounted for and thus categorized as ‘true’ LTFU. Factors found to be associated with discontinuation include being male, age 18-35, having a CD4 count under 200 cells/μL, and being on ART for under six months.

Conclusions: Young men with low CD4 counts early after ART initiation are at highest risk of ART disengagement in this rural South African HIV clinic. Novel interventions targeting this group are needed to improve retention in care.

Abstract  Full-text [free] access

Ten-year trends in anti-retroviral therapy persistence among US Medicaid beneficiaries, 2001-2010

Objective: Whether the rate of HIV antiretroviral therapy (ART) persistence has improved over time in the U.S. is unknown. We examined ART persistence trends between 2001 and 2010, using non-HIV medications as a comparator.

Methods: We conducted a retrospective cohort study using Medicaid claims. We defined persistence as the duration of treatment from the first to the last fill date before a 90-day permissible gap, and used Kaplan-Meier curves and Cox proportional hazard models to assess crude and adjusted non-persistence. The secular trends of ART persistence in 43,598 HIV patients were compared with the secular trends of persistence with angiotensin-converting enzyme inhibitors (ACE) or angiotensin receptor blockers (ARB), statins, and metformin in (1) non-HIV-infected patients and (2) subgroups of HIV patients who started these control medications while using ART.

Results: Median time to ART non-persistence increased from 23.9 months in 2001-2003 to 35.4 months in 2004-2006, and was not reached for those starting ART in 2007-2010. In adjusted models, ART initiators in 2007-2010 had 11% decreased hazards of non-persistence compared with those who initiated in 2001-2003 (p<0.001). For non-HIV patients initiating ACE/ARB, statins, and metformin, the hazard ratios (HR) for non-persistence comparing 2007-2010 to 2001-2003 were 1.07, 0.94, and 1.02, respectively (all p<0.001). For HIV patients initiating the three control medications, the HRs of non-persistence comparing 2007-2010 to 2001-2003 were 0.71, 0.65, and 0.63, respectively (all p<0.001).

Conclusions: Persistence with ART improved between 2001 and 2010. Persistence with control medications improved at a higher rate among HIV patients using ART than HIV-negative controls.

Abstract

Time from HIV diagnosis to commencement of antiretroviral therapy as an indicator to supplement the HIV cascade: Dramatic fall from 2011 to 2015


Introduction: The HIV care cascade is increasingly used to evaluate HIV treatment programs at the population level. However, the cascade indicators lack the ability to show changes over time, which reduces their utility to guide health policy. Alternatives have been proposed but are complex or result in a delay in results. We propose a new indicator of ART uptake, the time from HIV diagnosis to commencement of ART, and compare it to the existing cascade indicator of proportion of patients on treatment and the WHO proposed cohort cascade indicator of proportion of patients on treatment within one year of diagnosis.

Methods and Materials: Records from patients from the two largest HIV treatment centres in the state of Victoria, Australia (Melbourne Sexual Health Centre and The Alfred Hospital Department of Infectious Diseases) from 2011 to 2015 were extracted. The intervals between date of diagnosis, entry into care and initiation of ART were compared.

Results and Discussion: From 2011 to 2015 the proportion of in-care patients who were on ART rose from 87% to 93% (p<0.0001). From 2011 to 2014, the proportion of patients in care and on ART within one year of diagnosis increased from 43.4% to 78.9% (p = 0.001). The median time
from diagnosis to ART fell from 418 days (IQR: 91-1176) to 77 days (IQR: 39-290) (p<0.001) by calendar year in which ART was commenced.

Conclusions: From 2011 to 2015 there were substantial and clinically important falls in the median time from diagnosis to commencing ART in those that commenced ART. The size of this dramatic change was not apparent when only reporting the proportion of patients on ART. Time to ART is a useful indicator and can be used to supplement existing cascade indicators in measuring progress toward universal ART coverage.

Abstract Full-text [free] access

Trends in prevalence of advanced HIV disease at antiretroviral therapy enrollment — 10 countries, 2004–2015


Monitoring prevalence of advanced human immunodeficiency virus (HIV) disease (i.e., CD4+ T-cell count <200 cells/μL) among persons starting antiretroviral therapy (ART) is important to understand ART program outcomes, inform HIV prevention strategy, and forecast need for adjunctive therapies. To assess trends in prevalence of advanced disease at ART initiation in 10 high-burden countries during 2004-2015, records of 694,138 ART enrollees aged ≥15 years from 797 ART facilities were analyzed. Availability of national electronic medical record systems allowed up-to-date evaluation of trends in Haiti (2004-2015), Mozambique (2004-2014), and Namibia (2004-2012), where prevalence of advanced disease at ART initiation declined from 75% to 34% (p<0.001), 73% to 37% (p<0.001), and 80% to 41% (p<0.001), respectively. Significant declines in prevalence of advanced disease during 2004-2011 were observed in Nigeria, Swaziland, Uganda, Vietnam, and Zimbabwe. The encouraging declines in prevalence of advanced disease at ART enrollment are likely due to scale-up of testing and treatment services and ART-eligibility guidelines encouraging earlier ART initiation. However, in 2015, approximately a third of new ART patients still initiated ART with advanced HIV disease. To reduce prevalence of advanced disease at ART initiation, adoption of World Health Organization (WHO)-recommended “treat-all” guidelines and strategies to facilitate earlier HIV testing and treatment are needed to reduce HIV-related mortality and HIV incidence.

Abstract Full-text [free] access
Advanced HIV disease in Botswana following successful antiretroviral therapy rollout: Incidence of and temporal trends in cryptococcal meningitis


Background: Botswana has a well-developed antiretroviral therapy (ART) program which serves as a regional model. With wide ART availability, the burden of advanced HIV and associated opportunistic infections would be expected to decline. We performed a nationwide surveillance study to determine the national incidence of cryptococcal meningitis, and describe characteristics of cases 2000-2014 and temporal trends at two national referral hospitals.

Methods: Cerebrospinal fluid data from all 37 laboratories performing meningitis diagnostics in Botswana were collected 2000-2014 to identify cases of cryptococcal meningitis. Basic demographic and laboratory data were recorded. Complete national data from 2013-2014 were used to calculate national incidence using UNAIDS population estimates. Temporal trends in cases were derived from national referral centers 2004-2014.

Results: 5296 episodes of cryptococcal meningitis were observed in 4702 individuals; 60.6% were male, and median age was 36 years. Overall 2013-2014 incidence was 17.8 cases/100 000 person-years (95%CI 16.6 - 19.2). In the HIV-infected population, incidence was 96.8 cases/100 000 person-years (95%CI 90.0 - 104.0); male predominance was seen across CD4 strata. At national referral hospitals, cases decreased 2007-2009 but stabilized 2010-2014.

Conclusions: Despite excellent ART coverage in Botswana, there is still a substantial burden of advanced HIV, with 2013-2014 incidence of cryptococcal meningitis comparable to pre-ART era rates in South Africa. Our findings suggest a key population of individuals, often men, are developing advanced disease and associated opportunistic infections due to a failure to effectively engage in care, highlighting the need for differentiated care models.

Abstract

Survival of HIV-positive patients starting antiretroviral therapy between 1996 and 2013: a collaborative analysis of cohort studies


Background: Health care for people living with HIV has improved substantially in the past two decades. Robust estimates of how these improvements have affected prognosis and life expectancy are of utmost importance to patients, clinicians, and health-care planners. We examined changes in 3 year survival and life expectancy of patients starting combination antiretroviral therapy (ART) between 1996 and 2013.

Methods: We analysed data from 18 European and North American HIV-1 cohorts. Patients (aged ≥16 years) were eligible for this analysis if they had started ART with three or more drugs between 1996 and 2010 and had at least 3 years of potential follow-up. We estimated adjusted (for age, sex, AIDS, risk group, CD4 cell count, and HIV-1 RNA at start of ART) all-cause
and cause-specific mortality hazard ratios (HRs) for the first year after ART initiation and the second and third years after ART initiation in four calendar periods (1996-99, 2000-03 [comparator], 2004-07, 2008-10). We estimated life expectancy by calendar period of initiation of ART.

Findings: 88 504 patients were included in our analyses, of whom 2106 died during the first year of ART and 2302 died during the second or third year of ART. Patients starting ART in 2008-10 had lower all-cause mortality in the first year after ART initiation than did patients starting ART in 2000-03 (adjusted HR 0.71, 95% CI 0.61-0.83). All-cause mortality in the second and third years after initiation of ART was also lower in patients who started ART in 2008-10 than in those who started in 2000-03 (0.57, 0.49-0.67); this decrease was not fully explained by viral load and CD4 cell count at 1 year. Rates of non-AIDS deaths were lower in patients who started ART in 2008-10 (vs 2000-03) in the first year (0.48, 0.34-0.67) and second and third years (0.29, 0.21-0.40) after initiation of ART. Between 1996 and 2010, life expectancy in 20-year-old patients starting ART increased by about 9 years in women and 10 years in men.

Interpretation: Even in the late ART era, survival during the first 3 years of ART continues to improve, which probably reflects transition to less toxic antiretroviral drugs, improved adherence, prophylactic measures, and management of comorbidity. Prognostic models and life expectancy estimates should be updated to account for these improvements.

Abstract Full-text [free] access

How will we know when someone is cured of HIV?

Editor’s notes: The success of ART has led to life expectancy that approaches normality if people are diagnosed promptly and take treatment effectively for the rest of their lives. However, the goal of a cure remains elusive. The main challenge is that HIV becomes integrated into the DNA of the cells of individuals living with HIV. So while ART is taken, the virus is suppressed, but as soon as ART is stopped, the virus rebounds, possibly to high levels, and may cause additional immune and inflammatory consequences.

As discussed in previous issues, we are now beginning to test various approaches to drain this so-called reservoir of latent infection integrated into cellular DNA. This has led to the challenge of how to assess whether or not the “cure” has been successful. Many scientists prefer the term “remission” or “viral control in the absence of ART” to reflect this uncertainty. After all, the famous Mississippi baby remained free of virus (even in sophisticated tests of the reservoir) for a couple of years, before rebounding and needing to restart ART. Most people agree that the only practical way to be certain is to stop ART and watch closely to see what happens. This is known as an “analytical treatment interruption” (ATI). But for how long should we watch closely? Dube and colleagues undertook a qualitative inquiry to explore different stakeholder perceptions in the United States of America of the ethical and practical implications of ATIs. They found that there was little consensus on when ATIs would be ethically warranted. Secondly, many perceived that participating in the research on ATIs would be advancing science and contributing to society. Thirdly, the risks related to viral rebound were not yet well established and this caused concern to many. While more ethics research is needed, several of the stakeholders interviewed suggested ways to minimize the risks of ATIs in HIV cure research including full information; better assays for reservoirs; standardized protocols for follow up and ensuring that coercion is not used to recruit participants.

Watch this space!
‘We need to deploy them very thoughtfully and carefully’: Perceptions of analytical treatment interruptions in HIV cure research in the United States - a qualitative inquiry


**Strategies to control HIV in the absence of ART are needed to cure HIV.** However, such strategies will require *analytical treatment interruptions (ATIs)* to determine their efficacy. We investigated how U.S. stakeholders involved in HIV cure research perceive ATIs. We conducted 36 in-depth interviews with three groups of stakeholders: 12 people living with HIV (PLWHIV), 11 clinician-researchers, and 13 policy-makers/bioethicists. Qualitative data revealed several themes. First, there was little consensus on when ATIs would be ethically warranted. Second, the most frequent perceived hypothetical motivators for participating in research on ATIs were advancing science and contributing to society. Third, risks related to viral rebound were the most prevalent concerns related to ATIs. Stakeholders suggested ways to minimize the risks of ATIs in HIV cure research. Increased cooperation between scientists and local communities may be useful for minimizing risk. Further ethics research is necessary.

Abstract

2. Combination prevention

*How are we going to get to our prevention targets? Old tools, new tools and a more nuanced understanding of transmission dynamics.*

**Editor’s notes:** By 2020, the Fast-Track strategy is aiming to reduce new HIV infections to 200 000 per year. There is increasing recognition that if we are to succeed, we will need to do much more than simply putting people onto HIV treatment. Despite the massive impact of ART on infectiousness, the decline in new infections at the community level is still not fast enough, even in countries like Botswana (see above) where 90-90-90 has almost been reached. Renewed enthusiasm for primary prevention has also followed key trials of biomedical prevention tools including voluntary medical male circumcision and ARV-based prevention. It is all too easy for us to forget the crucial role that condoms have played from the early days of the epidemic. More recently, with HIV seen as a less terrifying infection, many programmes suffer from “condom fatigue”. So it is good to see papers on the key importance of condoms as well as perspectives on how they are perceived by young men.

The magic of ARVs does not end with treatment. We are finally moving to wider use of pre-exposure prophylaxis (PrEP). There is no doubt that PrEP works when taken, but there are still plenty of questions for policy-makers about how to adopt it whole-heartedly into their national strategic plans and for financiers about how to pay for it. Papers this month cover a range of experiences with PrEP from the US, where the huge majority of PrEP users still live, to Europe and Australia, where policies are finally moving towards wider use. Long acting PrEP remains a key objective for many, as it might improve regular adherence, which has proved the Achilles’ heel of oral and topical PrEP in several of the large studies.

One of the ways to make PrEP most cost-effective is to ensure that it is available to people who are most likely to acquire HIV. So the hope continues that phylogenetic analyses will allow more sophisticated understanding of the dynamics of the multiple overlapping networks of HIV transmission in communities. Papers this month cover Australia and the PANGEA consortium of African research sites along with a cautionary comment about establishing the ethical framework for such studies, particularly among populations who are already subject to discrimination and criminalization.
When used correctly and consistently, condoms are highly effective not only to prevent HIV but also to prevent pregnancy and to prevent sexually transmitted infections. Stover and colleagues have tried to capture all three benefits in one model. They explore three potential scenarios for condom programming between now and 2030 in 81 countries that are priorities for family planning or HIV programmers or both. The benefits of greater investment in condoms are huge. In their most optimistic scenario, the authors suggest that if the entire gap between people who would like to use condoms and people who currently use them was filled (almost 11 billion condoms over the period), this could prevent up to 400 million unwanted pregnancies; 16.8 million new HIV infections and more than 700 million sexually transmitted infections. The costs are quite modest, and at $115 per DALY averted this is an investment that everyone should support. There are of course limitations in such a broad brush model, but it provides an excellent starting point.

The challenges in provision of condoms to young people go well beyond the cost and effectiveness considerations that underpin the previous analysis. In an interesting qualitative study in South Africa, de Bruin and Panday-Soobrayan report their findings from focus group discussions with learners in 33 public schools. Most of the learners were not in favour of provision of condoms at school, although they were keen on more youth friendly sexual and reproductive health and rights services within the public sector. Many thought that provision of condoms would lead to earlier and more frequent sexual contacts, despite considerable experience showing that this is not the case in other settings.

Multiple trials have shown that PrEP is extremely effective when it is used consistently and correctly. Many countries in all continents are now beginning to work out where it fits within their combination prevention package. To date, the large majority of PrEP users are in the United States of America (USA), where more than 140 000 people have started. It is much harder to measure how many are still taking it regularly. Patel and colleagues analysed utilization at three months after the initial prescription of PrEP in three major PrEP clinics in three states in the USA. 18% of the 201 people (90% male) seen at baseline did not use their PrEP and this was strongly predicted by insurance status, with around a four-fold risk of dropping out among those who were not insured. Although the numbers are small, this is an important study. The authors suggest that increased insurance cover might make PrEP have a greater impact. More broadly it raises the challenge that PrEP is often needed most by people least able to access it. This will be a real challenge in countries where people most at risk, such as gay men and other men who have sex with men and sex workers, are criminalized or discriminated against in many health care settings.

In Australia, PrEP has been provided through large demonstration projects while awaiting decisions about how to include it in routine practice. Lal and colleagues report results from 114 (one transgender woman, the rest male) people taking PrEP in the Victorian PrEP Demonstration project. Participants have to pay an equivalent of an insurance co-payment, in order to make the situation more like the “real world”. The participants were recruited because they were at high risk of HIV engaging in condomless anal sex with partners who were known to be living with HIV or of unknown status. Adherence to PrEP was excellent as measured by a variety of reported and biological measures. They observed one seroconversion in a man with exposure two weeks before starting PrEP who was already in the process of seroconverting and whose virus was found to be resistant to emtricitabine. The only other seroconversion occurred in someone who had not yet started PrEP. The authors found a substantial increase in rates of gonorrhoea and chlamydia once participants were “stable” on PrEP after three months. There was also a significant reduction in condom use with both regular and casual partners. This is one of the first studies to document important risk compensation among PrEP users. Of course, preventing HIV is a huge benefit that generally outweighs the harms of additional treatment for sexually transmitted infections. However, the study emphasizes the importance of enhancing sexual health services alongside PrEP and reminds us that
people most at risk of HIV are also at high risk of other infections (and also of pregnancy in the context of heterosexual transmission.) If PrEP is integrated within a broad sexual health service, there could be considerable synergistic benefits.

Gay men and men who have sex with men who enrolled in the PrEP demonstration project in Amsterdam also had high concomitant rates of hepatitis C virus (HCV). Hoorenborg and colleagues found that around 5% of the 375 men enrolled in the project were co-infected. The HCV found among these men were genetically similar to those circulating in the population of gay men and other men who have sex with men living with HIV, and more distinct from HCV from other risk groups. This is good evidence that HCV and HIV both circulate in this population, and emphasizes once again the need for more integrated services, including hepatitis screening.

The ÉCLAIR study is a phase 2a trial of cabotegravir injections in healthy HIV-negative male volunteers. As noted, adherence is a major challenge in many PrEP trials; although notably less of a problem when people choose to take PrEP in demonstration projects. It is hoped that cabotegravir could be the first long acting PrEP. Markowitz and colleagues presented the results of this study at CROI 2017. The authors point out that although the injections are painful, many men stated that they would be happy to continue if the injections were effective. No serious safety challenges emerged. The pharmacokinetics suggests that a dose given more frequently will be needed – and subsequent trials will use a two monthly regimen.

One group for whom PrEP has been recommended by WHO for some years are serodiscordant couples (SDCs). The Partners PrEP study, which forms one of the cornerstones for the evidence that PrEP works for both men and women, was conducted in SDCs. The idea is to protect the HIV-negative partner from infection until such time as the partner living with HIV has been on ART consistently and suppressed their viral load. So a study from the Centers for Disease Control USA is relevant to discussions of PrEP. Crepaz and colleagues found that around 6000 new HIV infections occur each year in the USA among men and women having heterosexual sex and are aware that their partner is living with HIV. They point out that viral suppression is achieved by only around 50% of heterosexuals living with HIV and that an additional proportion does not know their HIV status. So the importance of HIV testing, and of focusing efforts on serodiscordant couples is clear. Such efforts include both improving HIV treatment effectiveness, and providing a range of prevention choices including PrEP until viral suppression is achieved.

While the study above used traditional epidemiological surveillance reports, phylogenetics may provide additional insights into the dynamics of transmission. In Australia, where notifications with HIV are rising steadily, Castley and colleagues have examined the sequence data from almost 5000 viruses collected across the country from 2005-2012. This sample is drawn from around 1200 new HIV infections per year (and around 27 000 people living with HIV). The sample is not random, but reflects samples that were sent for sequencing to determine drug resistance. Around one quarter of sequences are found in tight clusters (pairs, triplets or more) with other sequences, making it likely that they are closely connected by transmission. Of course, all HIV sequences have been transmitted, so a longer time period and complete sampling would be expected to give a much higher proportion in clusters. Indeed the more recent samples are around twice as likely to be in clusters as those collected at the start of the time period. Nonetheless, the large sample and the time period of collection allows some clear observations to be made. In all states, the proportion of non-B subtypes is increasing, which must relate to travel and migration to and from Asia and Africa. There is little evidence that the C subtypes (originally from Africa) are found in all male clusters suggesting little spill over into the community of gay men and other men having sex with men. Larger clusters are more common among younger, all male networks. Like most molecular epidemiological studies, there are a
small number of large clusters which represent highly active transmission. These clusters are also most likely to be all male. Taken together, the results suggest that the steady rise in notifications in Australia is probably due to increasing migration and travel and to ongoing active transmission networks among young gay men. The challenge is to turn this sort of analysis into clear policy recommendations that can improve HIV prevention.

UNAIDS joined an interesting meeting on the ethics of phylogenetic studies in Africa organised by the PANGEA consortium. Many of the issues discussed are also covered in a comment by Cohen on the importance of thinking through the risks inherent in these studies. A key issue is to ensure that systems are reinforced to monitor any unexpected harms and to establish mitigation strategies to minimize them. The challenges are not necessarily different to traditional epidemiological studies which may highlight networks and locations of groups that are criminalized or discriminated against. In community consultations, prior to agreeing to go forward with phylogenetic studies, some potential participants even say that they would be keen to “know who infected them” in order to punish them. This is clearly NOT the aim of such studies and emphasizes the importance of clear information about the limitations of the techniques which cannot usually rule out the possibility of additional links in the transmission chain. Issues of anonymised information and what to do if clinically relevant results such as drug resistance mutations are uncovered as incidental findings also need to be discussed.

Furthermore, Ratmann and colleagues, reporting on the first 4000 sequences from the PANGEA consortium (largely from the Rakai project in Uganda), also emphasize some of the technical challenges that may lead to erroneous results in creating phylogenies. There is little doubt that as the cost of sequencing falls and as the technologies and software become increasingly straightforward, we will see more and more studies of sequence data. It is likely that analysis of these data will lead to more nuanced approaches to HIV prevention, particularly as the overall incidence falls, and sharper tools are needed to dissect the pathways of ongoing transmission.

The case for investing in the male condom


When used correctly and consistently, the male condom offers triple protection from unintended pregnancy and the transmission of sexually transmitted infections (STIs) and human immunodeficiency virus (HIV). However, with health funding levels stagnant or falling, it is important to understand the cost and health impact associated with prevention technologies. This study is one of the first to attempt to quantify the cost and combined health impact of condom use, as a means to prevent unwanted pregnancy and to prevent transmission of STIs including HIV. This paper describes the analysis to make the case for investment in the male condom, including the cost, impact and cost-effectiveness by three scenarios (low in which 2015 condom use levels are maintained; medium in which condom use trends are used to predict condom use from 2016-2030; and high in which condom use is scaled up, as part of a package of contraceptives, to meet all unmet need for family planning by 2030 and to 90% for HIV and STI prevention by 2016) for 81 countries from 2015-2030. An annual gap between current and desired use of 10.9 billion condoms was identified (4.6 billion for family planning and 6.3 billion for HIV and STIs). Under a high scenario that completely reduces that gap between current and desired use of 10.9 billion condoms, we found that by 2030 countries could avert 240 million DALYs. The additional cost in the 81 countries through 2030 under the medium scenario is $1.9 billion, and $27.5 billion under the high scenario. Through 2030, the cost-effectiveness ratios are $304 per DALY averted for the medium and $115 per DALY averted for the high scenario. Under the three scenarios
described above, our analysis demonstrates the cost-effectiveness of the male condom in preventing unintended pregnancy and HIV and STI new infections. Policy makers should increase budgets for condom programming to increase the health return on investment of scarce resources.

Abstract Full-text [free] access

Learners' perspectives on the provision of condoms in South African public schools.


A stubborn health challenge for learners in South African public schools concerns sexual and reproductive health and rights (SRHR). In 2015, the Department of Basic Education (DBE) proposed the provision of condoms and SRHR-services to learners in schools. This study aimed to contribute to the finalisation and implementation of DBE’s policy by exploring learners’ perspectives on the provision of condoms and SRHR-services in schools. Sixteen focus group discussions were conducted with learners (n = 116) from 33 public schools, to assess their attitudes, social influences, and needs and desires regarding condom provision and SRHR-services in schools. The majority of learners did not support condom provision in schools as they feared that it may increase sexual activity. Contrarily, they supported the provision of other SRHR-services as clinics fail to offer youth-friendly services. Learners’ sexual behaviour and access to SRHR-services are strongly determined by their social environment, including traditional norms and values, and social-pressure from peers and adults. Learners’ most pressing needs and desires to access condoms and SRHR-services in school concerned respect, privacy and confidentiality of such service provision. Implementation of DBE’s policy must be preceded by an evidence-informed advocacy campaign to debunk myths about the risk of increased sexual activity, to advocate for why such services are needed, to shift societal norms towards open discussion of adolescent SRHR and to grapple with the juxtaposition of being legally empowered but socially inhibited to protect oneself from HIV, STIs and early pregnancy. Provision of condoms and other SRHR-services in schools must be sensitive to learners’ privacy and confidentiality to minimise stigma and discrimination.

Abstract Full-text [free] access

Impact of insurance coverage on utilization of pre-exposure prophylaxis for HIV prevention


Pre-exposure prophylaxis (PrEP) can reduce U.S. HIV incidence. We assessed insurance coverage and its association with PrEP utilization. We reviewed patient data at three PrEP clinics (Jackson, Mississippi; St. Louis, Missouri; Providence, Rhode Island) from 2014-2015. The outcome, PrEP utilization, was defined as patient PrEP use at three months. Multivariable logistic regression was performed to determine the association between insurance coverage and PrEP utilization. Of 201 patients (Jackson: 34%; St. Louis: 28%; Providence: 28%), 91% were male, 51% were White, median age was 29 years, and 21% were uninsured; 82% of patients reported taking PrEP at three months. Insurance coverage was significantly associated with PrEP utilization. After adjusting for Medicaid-expansion and individual socio-demographics, insured patients were four times as likely to use PrEP services compared to the uninsured (OR: 4.49,
95% CI: 1.68-12.01; p = 0.003). Disparities in insurance coverage are important considerations in implementation programs and may impede PrEP utilization.

Abstract

Medication adherence, condom use and sexually transmitted infections in Australian PrEP users: interim results from the Victorian PrEP demonstration project


Objective: HIV Pre-exposure prophylaxis (PrEP) decreases risk of HIV acquisition however its efficacy is closely dependent on adherence. There is also concern that the preventive effect of PrEP may be offset by risk compensation, notably an increase in condomless anal sex.

Design: Multi-site, open-label demonstration study that recruited people at current or recent risk of HIV infection in Melbourne, Australia.

Methods: Participants were recruited from three general practice clinics and one sexual health clinic in Melbourne and consented to take daily tenofovir/emtricitabine for 30 months. Sexual practice data, HIV and sexually transmitted infection (STI) test results were collected at baseline and 3-monthly during follow up. PrEP adherence was evaluated by self-report at clinical visits, online surveys, refill-based assessments and dried blood spot (DBS) testing. We present a 12-month interim analysis.

Results: 114 people were recruited. We observed a significant decline in condom use which occurred concomitantly with a significant increase in STIs over the first 12 months of PrEP. Incidence (per 100PY) of any STI was 43.2 and 119.8 at m0-3 and M3-12, respectively (IRR 2.77 (1.52, 5.56)). Adherence to PrEP medication was high by all measures, including six month TDF-FTC levels in DBS.

Conclusions: We found significant reduction in condom use and an increase STIs over the first 12 months of follow-up. High medication adherence rates coupled with a decline in condom use and a rise in STIs, suggests that prevention, early detection and treatment of STIs is a chief research priority in the current era of HIV PrEP.

Men who have sex with men starting pre-exposure prophylaxis (PrEP) are at risk of HCV infection: evidence from the Amsterdam PrEP study


Objectives and Design: Hepatitis C virus (HCV) has been recognised as an emerging sexually transmitted infection (STI) among HIV-positive men who have sex with men (MSM). However, HIV-negative MSM at high risk for HIV might also be at increased risk for HCV. We studied the HCV prevalence in HIV-negative MSM who start pre-exposure prophylaxis (PrEP) in Amsterdam. Phylogenetic analysis was used to compare HCV strains obtained from HIV-negative and HIV-positive MSM.
Methods: At enrolment in the Amsterdam PrEP (AMPPrEP) demonstration project, HIV-negative MSM were tested for the presence of HCV antibodies and HCV RNA. If positive for HCV RNA, an HCV NS5B gene fragment (709bp) was sequenced and compared with HCV isolates from HIV-positive MSM (n=223) and risk groups other than MSM (n=153), using phylogenetic analysis.

Results: Of 375 HIV-negative MSM enrolled in AMPPrEP, 18 (4.8%, 95%CI 2.9%-7.5%) of participants were anti-HCV and/or HCV RNA positive at enrolment; 15/18 (83%) had detectable HCV RNA. HCV genotyping showed genotype 1a (73%), 4d (20%) and 2b (7%). All HCV-positive MSM starting PrEP were part of MSM-specific HCV clusters containing MSM with and without HIV.

Conclusion: HCV prevalence among HIV-negative MSM who started PrEP was higher than previously reported. All HIV-negative HCV-positive MSM were infected with HCV strains already circulating among HIV-positive MSM. The increasing overlap between sexual networks of HIV-positive and HIV-negative MSM might result in an expanding HCV-epidemic irrespective of HIV-status. Hence, routine HCV testing should be offered to MSM at high risk for HIV, especially for those enrolling in PrEP programs.

Abstract

Safety and tolerability of long-acting cabotegravir injections in HIV-uninfected men (ECLAIR): a multicentre, double-blind, randomised, placebo-controlled, phase 2a trial.


Background: Cabotegravir (GSK1265744) is an HIV-1 integrase strand transfer inhibitor with potent antiviral activity and a long half-life when administered by injection that prevented simian-HIV infection upon repeat intrarectal challenge in male macaques. We aimed to assess the safety, tolerability, and pharmacokinetics of long-acting cabotegravir injections in healthy men not at high risk of HIV-1 infection.

Methods: We did this multicentre, double-blind, randomised, placebo-controlled, phase 2a trial at ten sites in the USA. Healthy men (aged 18-65 years) deemed not at high risk of acquiring HIV-1 at screening were randomly assigned (5:1), via computer-generated central randomisation schedules, to receive cabotegravir or placebo. Participants received oral cabotegravir 30 mg tablets or matching placebo once daily during a 4 week oral lead-in phase, followed by a 1 week washout period and, after safety assessment, three intramuscular injections of long-acting cabotegravir 800 mg or saline placebo at 12 week intervals. Study site staff and participants were masked to treatment assignment from enrolment through week 41 (time of the last injection). The primary endpoint was safety and tolerability from the first injection (week 5) to 12 weeks after the last injection. We did analysis in the safety population, defined as all individuals enrolled in the study who received at least one dose of the study drug. This study is registered with ClinicalTrials.gov identifier, NCT02076178.

Findings: Between March 27, 2014, and Feb 23, 2016, we randomly assigned 127 participants to receive cabotegravir (n=106) or placebo (n=21); 126 (99%) participants comprised the safety population. Most participants were men who have sex with men (MSM; n=106 [83%]) and white (n=71 [56%]). 87 (82%) participants in the cabotegravir group and 20 (95%) participants in the placebo group completed the injection phase. Adverse events (n=7 [7%]) and injection intolerability (n=4
were the main reasons for withdrawal in the cabotegravir group. The frequency of grade 2 or higher adverse events was higher in participants in the long-acting cabotegravir group (n=75 [80%]) than in those in the placebo group (n=10 [48%]; p=0.0049), mostly due to injection-site pain (n=55 [59%]). No significant differences were noted in concomitant medications, laboratory abnormalities, electrocardiogram, and vital sign assessments. Geometric mean trough plasma concentrations were 0.302 μg/mL (95% CI 0.237-0.385), 0.331 μg/mL (0.253-0.435), and 0.387 μg/mL (0.296-0.505) for injections one, two, and three, respectively, indicating lower than predicted exposure. The geometric mean apparent terminal phase half-life estimated after the third injection was 40 days. Two (2%) MSM acquired HIV-1 infection, one in the placebo group during the injection phase and one in the cabotegravir group 24 weeks after the final injection when cabotegravir exposure was well below the protein-binding-adjusted 90% inhibitory concentration.

Interpretation: Despite high incidence of transient, mild-to-moderate injection-site reactions, long-acting cabotegravir was well tolerated with an acceptable safety profile. Pharmacokinetic data suggest that 800 mg administered every 12 weeks is a suboptimal regimen; alternative dosing strategies are being investigated. Our findings support further investigation of long-acting injectable cabotegravir as an alternative to orally administered pre-exposure prophylaxis regimens.

Abstract

Examination of HIV infection through heterosexual contact with partners who are known to be HIV infected in the United States, 2010-2015


Using data from the National HIV Surveillance System, we examined HIV infections diagnosed between 2010 and 2015 attributed to heterosexual contact with partners previously known to be HIV infected. More than four in 10 HIV infections among heterosexual males and five in 10 HIV infections among heterosexual women were attributed to this group. Findings may inform the prioritization of prevention and care efforts and resource allocation modeling for reducing new HIV infection among discordant partnerships.

Abstract

A national study of the molecular epidemiology of HIV-1 in Australia 2005–2012


Introduction: Rates of new HIV-1 diagnoses are increasing in Australia, with evidence of an increasing proportion of non-B HIV-1 subtypes reflecting a growing impact of migration and travel. The present study aims to define HIV-1 subtype diversity patterns and investigate possible HIV-1 transmission networks within Australia.

Methods: The Australian Molecular Epidemiology Network (AMEN) HIV collaborating sites in Western Australia, South Australia, Victoria, Queensland and western Sydney (New South Wales), provided baseline HIV-1 partial pol sequence, age and gender information for 4873
patients who had genotypes performed during 2005-2012. HIV-1 phylogenetic analyses utilised MEGA V6, with a stringent classification of transmission pairs or clusters (bootstrap ≥98%, genetic distance ≤1.5% from at least one other sequence in the cluster).

Results: HIV-1 subtype B represented 74.5% of the 4873 sequences (WA 59%, SA 68.4%, w-Syd 73.8%, Vic 75.6%, Qld 82.1%), with similar proportion of transmission pairs and clusters found in the B and non-B cohorts (23% vs 24.5% of sequences, p = 0.3). Significantly more subtype B clusters were comprised of ≥3 sequences compared with non-B clusters (45.0% vs 24.0%, p = 0.021) and significantly more subtype B pairs and clusters were male-only (88% compared to 53% CRF01_AE and 17% subtype C clusters). Factors associated with being in a cluster of any size included; being sequenced in a more recent time period (p<0.001), being younger (p<0.001), being male (p = 0.023) and having a B subtype (p = 0.02). Being in a larger cluster (>3) was associated with being sequenced in a more recent time period (p = 0.05) and being male (p = 0.008).

Conclusion: This nationwide HIV-1 study of 4873 patient sequences highlights the increased diversity of HIV-1 subtypes within the Australian epidemic, as well as differences in transmission networks associated with these HIV-1 subtypes. These findings provide epidemiological insights not readily available using standard surveillance methods and can inform the development of effective public health strategies in the current paradigm of HIV prevention in Australia.

Abstract Full-text [free] access

HIV-1 full-genome phylogenetics of generalized epidemics in sub-Saharan Africa: impact of missing nucleotide characters in next-generation sequences.


To characterize HIV-1 transmission dynamics in regions where the burden of HIV-1 is greatest, the ‘Phylogenetics and Networks for Generalised HIV Epidemics in Africa’ consortium (PANGEA-HIV) is sequencing full-genome viral isolates from across sub-Saharan Africa. We report the first 3985 PANGEA-HIV consensus sequences from four cohort sites (Rakai Community Cohort Study, n=2833; MRC/UVRI Uganda, n=701; Mochudi Prevention Project, n=359; Africa Health Research Institute Resistance Cohort, n=92). Next-generation sequencing success rates varied: more than 80% of the viral genome from the gag to the nef genes could be determined for all sequences from South Africa, 75% of sequences from Mochudi, 60% of sequences from MRC/UVRI Uganda, and 22% of sequences from Rakai. Partial sequencing failure was primarily associated with low viral load, increased for amplicons closer to the 3’ end of the genome, was not associated with subtype diversity except HIV-1 subtype D, and remained significantly associated with sampling location after controlling for other factors. We assessed the impact of the missing data patterns in PANGEA-HIV sequences on phylogeny reconstruction in simulations. We found a threshold in terms of taxon sampling below which the patchy distribution of missing characters in next-generation sequences has an excess negative impact on the accuracy of HIV-1 phylogeny reconstruction, which is attributable to tree reconstruction artifacts that accumulate when branches in viral trees are long. The large number of PANGEA-HIV sequences provides unprecedented opportunities for evaluating HIV-1 transmission dynamics across sub-Saharan Africa and identifying prevention opportunities. Molecular
epidemiological analyses of these data must proceed cautiously because sequence sampling remains below the identified threshold and a considerable negative impact of missing characters on phylogeny reconstruction is expected.

Abstract  Full-text [free] access

3. Key populations

**Key populations need so much more than HIV-specific services – involve them at every stage of planning and programming**

**Editor's notes:** This month sees a welcome set of papers covering female sex workers in West Africa; gay men and other men who have sex with men in the Middle East and in East Africa; people who inject drugs in the USA and eastern Europe.

Sex work is legal in Côte d’Ivoire although soliciting and pandering are criminalized, which creates legal barriers to practicing sex work. Legalization does not necessarily prevent widespread abuse of power. Lyons and colleagues recruited 466 female sex workers in Abidjan through a respondent driven sampling approach. A structured interview and rapid HIV test was performed. Around 11% of the women were found to be living with HIV and it is clear that there are large unmet needs for HIV-specific services. Only one quarter of those living with HIV reported that they knew their status and of these, only a few were already taking ART. However, the focus of this study was on violence, both physical and sexual, which was alarmingly common, with around 54% of women reporting physical violence and 43% sexual violence. The violence was most often perpetrated by spouses and boyfriends as well as by paying customers. Other sex workers, pimps or managers and uniformed officers were also responsible for violence, both physical and sexual. 16% of women said that they had been tortured. Collecting reliable data on sensitive areas with vulnerable populations is challenging. The sampling method may introduce biases, and the interviews may lead to reported behaviours to “please” the interviewer. However, this study included major efforts to work with the community of sex workers and their networks, and considerable trust has been built, so the results seem credible. The authors call for structural interventions and policy reforms that have little to do with HIV directly, but would lead to an environment where HIV and other harms were greatly reduced. There is also a direct need to ensure that sex workers have good access to HIV and other sexual and reproductive health services.

People who inject drugs also have many needs besides HIV services. In the USA, the number of people who inject drugs is increasing. This has led to a rising number of deaths from opioid overdose (around 30,000 in 2014), as well as increased HIV transmission, which makes the headlines of the news, when it occurs in settings where HIV is otherwise rare. Cost-effective HIV prevention programmes for people who inject drugs are essential to the long-term health outcomes for this population and other high-risk groups in the USA. Bernard and colleagues used a mathematical model and economic analysis to identify the most cost-effective interventions for HIV prevention programmes for people who inject drugs in the USA.

The authors found that under many likely assumptions about potential scale up, the best buy was always to provide opioid agonist therapy, which reduces injecting frequency and results in multiple, immediate quality-of-life improvements. Needle and syringe exchange programmes are less expensive, but in these models produced fewer benefits, making them the next most cost-effective intervention, alone or in combination. PrEP was not likely to be cost-effective in this population except in the very highest risk settings. This is in line with the values and preference expressed by many people who use drugs around the world. The priority should be for “standard” harm reduction
approaches, which will reduce HIV transmission, but have far wider benefits on the health and well-being of drug users and their communities.

Relatively little research is carried out with key populations in the Middle East. Heimer and colleagues also used respondent driven sampling (with the same potential biases as above) to recruit 292 men who have sex with men in Beirut. Although one quarter of the participants had been born in Syria and moved recently to Lebanon, the sampling method does reduce the precision of this estimate. Of 36 people living with HIV identified, 32 were on HIV treatment, which is encouraging. If the 32 on treatment were virally suppressed, the prevalence of “infectious HIV” in the survey was around 1.4%. As we move forward into the viral load era, notions of risk for sexual behaviour will change, and we need to think about explicit descriptions such as “condomless sex” rather than simply referring to “unprotected sex”. As stated above, the benefits of condoms for other sexually transmitted infections as well as for HIV need to be emphasized and the full range of ARV-based prevention made available in order to minimize the epidemic of HIV among gay men and other men who have sex with men in Lebanon and beyond.

The dynamics of the HIV epidemic in Ukraine are shifting. Increasingly sexual transmission is becoming more common, and transmission through injecting drug use reducing. Fearnhill and colleagues’ study of phylogenetics and recent infections among 876 newly diagnosed people living with HIV in Kiev highlights these trends. The study also demonstrates plenty of uncertainty and suggests that the stigma associated with both injecting drug use and with gay men and other men having sex with men may lead to significant under-reporting of both in traditional epidemiological surveillance. Although phylogenetics cannot prove misclassification, it is highly suggestive when large clusters of HIV from known gay men and other men who have sex with men include no women, but do include other men, who self-report to be heterosexual. Transmission was most common among gay men and other men who have sex with men, and from those with recent infections. HIV strains from women often cluster with those from people who inject drugs. In a complex and dynamic environment with overlapping risk factors for HIV infection, phylogenetics adds a useful lens through which to examine what is happening. Yet again, the challenge is to translate more granular understanding of the epidemics into clear public health policy and practice.

What do men who have sex with men in Kenya think about participating in HIV prevention research, such as a vaccine trial? Doshi and colleagues used a social network-based approach to conduct in-depth interviews with 70 gay men and other men who have sex with men. Here is what some of them said:

“He [the potential study participant] keeps hearing there is a research [study] that is starting, that there is money – one thousand or two, three thousand – he will run for the money…because it is someone’s life you have to be sure of what is going on…. You run for the better option because research comes in every type and researchers are everywhere in town.”

“Ok, you know most of the research coming to Kenya starts with MSM. Those are the ones that are tested on first so if there are side effects, those will be the first victims”

“It will benefit many of us…on my side…because sometimes I’m drunk I go out and meet people and they tell me they do not use condom…or… I’m drunk, I don’t know myself and I have already come to the bed with someone. Even I don’t know what he will do to me, if he will do me with a condom or if he will do me without a condom. Now the [HIV] vaccine…will be beneficial to me and the whole community”

This is a rich paper, giving insights into the reasons that people do or do not want to participate in vaccine trials. It raises plenty of ethical questions about the balance between self-interest, altruism,
coercion and consent. It is encouraging that on the whole most participants saw the potential benefits to the wider community and would consider volunteering their time despite the associated risks. Their perceptions were also coloured by previous research studies and how researchers had met their responsibilities for the care and well-being of their participants. A good advertisement for the UNAIDS-AVAC Good Participatory Practice guidance!

Physical and Sexual Violence Affecting Female Sex Workers in Abidjan, Côte d’Ivoire: Prevalence, and the Relationship with the Work Environment, HIV, and Access to Health Services


Background: Violence is a human rights violation, and an important measure in understanding HIV among female sex workers (FSW). However, limited data exist regarding correlates of violence among FSW in Côte d’Ivoire. Characterizing prevalence and determinants of violence and the relationship with structural risks for HIV can inform development and implementation of comprehensive HIV prevention and treatment programs.

Methods: FSW > 18 years were recruited through respondent driven sampling (RDS) in Abidjan, Côte d’Ivoire. In total, 466 participants completed a socio-behavioral questionnaire and HIV testing. Prevalence estimates of violence were calculated using crude and RDS-adjusted estimates. Relationships between structural risk factors and violence were analyzed using χ² tests and multivariable logistic regression.

Results: The prevalence of physical violence was 53.6% (250/466), and sexual violence was 43.2% (201/465) among FSW in this study. Police refusal of protection was associated with physical (adjusted Odds Ratio [aOR]: 2.8; 95% confidence interval [CI]: 1.7 to 4.4) and sexual violence (aOR: 3.0; 95% CI: 1.9 to 4.8). Blackmail was associated with physical (aOR: 2.5; 95% CI: 1.5 to 4.2) and sexual violence (aOR: 2.4; 95% CI: 1.5 to 4.0). Physical violence was associated with fear (aOR: 2.2; 95% CI: 1.3 to 3.1) and avoidance of seeking health services (aOR: 2.3; 95% CI: 1.5 to 3.8).

Conclusions: Violence is prevalent among FSW in Abidjan and associated with features of the work environment and access to care. These relationships highlight layers of rights violations affecting FSW, underscoring the need for structural interventions and policy reforms to improve work environments, and to address police harassment, stigma, and rights violations to reduce violence and improve access to HIV interventions.

Abstract


Background: The risks of HIV transmission associated with the opioid epidemic make cost-effective programs for people who inject drugs (PWID) a public health priority. Some of these programs have benefits beyond prevention of HIV-a critical consideration given that injection drug use is increasing across most United States demographic groups. To identify high-value HIV prevention program
portfolios for US PWID, we consider combinations of four interventions with demonstrated
efficacy: opioid agonist therapy (OAT), needle and syringe programs (NSPs), HIV testing and
treatment (Test & Treat), and oral HIV pre-exposure prophylaxis (PrEP).

Methods and Findings: We adapted an empirically calibrated dynamic compartmental model and
used it to assess the discounted costs (in 2015 US dollars), health outcomes (HIV infections
averted, change in HIV prevalence, and discounted quality-adjusted life years [QALYs]), and
incremental cost-effectiveness ratios (ICERs) of the four prevention programs, considered
singly and in combination over a 20-y time horizon. We obtained epidemiologic, economic, and
health utility parameter estimates from the literature, previously published models, and expert opinion.
We estimate that expansions of OAT, NSPs, and Test & Treat implemented singly up to 50%
coverage levels can be cost-effective relative to the next highest coverage level (low, medium,
and high at 40%, 45%, and 50%, respectively) and that OAT, which we assume to have immediate
and direct health benefits for the individual, has the potential to be the highest value investment,
even under scenarios where it prevents fewer infections than other programs. Although a model-
based analysis can provide only estimates of health outcomes, we project that, over 20 y, 50%
coverage with OAT could avert up to 22 000 (95% CI: 5200, 46 000) infections and cost US$18
000 (95% CI: US$14 000, US$24 000) per QALY gained, 50% NSP coverage could avert up to 35
000 (95% CI: 8900, 43 000) infections and cost US$25 000 (95% CI: US$7000, US$76 000) per
QALY gained, 50% Test & Treat coverage could avert up to 6700 (95% CI: 1200, 16 000)
infections and cost US$27 000 (95% CI: US$15 000, US$48 000) per QALY gained, and 50%
PrEP coverage could avert up to 37 000 (22 000, 58 000) infections and cost US$300 000 (95%
CI: US$162 000, US$667 000) per QALY gained. When coverage expansions are allowed to
include combined investment with other programs and are compared to the next best
intervention, the model projects that scaling OAT coverage up to 50%, then scaling NSP
coverage to 50%, then scaling Test & Treat coverage to 50% can be cost-effective, with each
coverage expansion having the potential to cost less than US$50 000 per QALY gained relative to the
next best portfolio. In probabilistic sensitivity analyses, 59% of portfolios prioritized the addition
of OAT and 41% prioritized the addition of NSPs, while PrEP was not likely to be a priority nor
a cost-effective addition. Our findings are intended to be illustrative, as data on achievable
coverage are limited and, in practice, the expansion scenarios considered may exceed feasible levels.
We assumed independence of interventions and constant returns to scale. Extensive sensitivity
analyses allowed us to assess parameter sensitivity, but the use of a dynamic compartmental model
limited the exploration of structural sensitivities.

Conclusions: We estimate that OAT, NSPs, and Test & Treat, implemented singly or in
combination, have the potential to effectively and cost-effectively prevent HIV in US PWID.
PrEP is not likely to be cost-effective in this population, based on the scenarios we evaluated. While
local budgets or policy may constrain feasible coverage levels for the various interventions, our
findings suggest that investments in combined prevention programs can substantially reduce
HIV transmission and improve health outcomes among PWID.

Abstract Full-text [free] access

HIV risk, prevalence, and access to care among men who have sex with men in Lebanon


Objective: Little is known about HIV prevalence and risk among men who have sex with men in much
of the Middle East, including Lebanon. Recent national level surveillance has suggested an increase
in HIV prevalence concentrated among men in Lebanon. We undertook a biobehavioral study to provide direct evidence for the spread of HIV.

Design: MSM were recruited by respondent driven sampling, interviewed, and offered HIV testing anonymously at sites located in Beirut, Lebanon from October 2014 through February 2015. The interview questionnaire was designed to obtain information on participants’ sociodemographic situation, sexual behaviors, alcohol and drug use, health, HIV testing and care, experiences of stigma and discrimination. Individuals not reporting an HIV diagnosis were offered optional, anonymous HIV testing.

Results: Among the 292 MSM recruited, we identified 36 cases of HIV (12.3%). A quarter of the MSM were born in Syria and recently arrived in Lebanon. Condom use was uncommon; 65% reported unprotected sex with other men. Group sex encounters were reported by 22% of participants. Among the 32 individuals already aware of their infection, 30 were in treatment and receiving antiretroviral therapy.

Conclusions: HIV prevalence was substantially increased over past estimates. Efforts to control future increases will have to focus on reducing specific risk behaviors and experienced stigma and abuse, especially among Syrian refugees.

Abstract

A Phylogenetic Analysis of HIV-1 Sequences in Kiev: Findings among Key Populations


Background: The HIV epidemic in Ukraine has been driven by a rapid rise among people who inject drugs, but recent studies have shown an increase through sexual transmission.

Methods: Protease and RT sequences from 876 new HIV diagnoses (April 2013 - March 2015) in Kiev were linked to demographic data. We constructed phylogenetic trees for 794 subtype A1 and 64 subtype B sequences and identified factors associated with transmission clustering. Clusters were defined as ≥ 2 sequences, ≥ 80% local branch support and maximum genetic distance of all sequence pairs in the cluster ≤ 2.5%. Recent infection was determined through the LAg avidity EIA assay. Sequences were analysed for transmitted drug resistance (TDR) mutations.

Results: 30% of subtype A1 and 66% of subtype B sequences clustered. Large clusters (maximum 11 sequences) contained mixed risk groups. In univariate analysis, clustering was significantly associated with subtype B compared to A1 (OR 4.38 [95% CI 2.56-7.50]), risk group (OR 5.65 [3.27-9.75]) for men who have sex with men compared to heterosexual males, recent, compared to long-standing, infection (OR 2.72 [1.64-4.52]), reported sex work contact (OR 1.93 [1.07-3.47]) and younger age groups compared to age ≥36 (OR 1.83 [1.10-3.05] for age ≤25). Females were associated with lower odds of clustering than heterosexual males (OR 0.49 [0.31-0.77]). In multivariate analysis, risk group, subtype and age group were independently associated with clustering (p<0.001, p=0.007 and p=0.033). 18 sequences (2.1%) indicated evidence of TDR.

Conclusions: Our findings suggest high levels of transmission and bridging between risk groups.

Abstract Full-text [free] access
Contextualizing willingness to participate: recommendations for engagement, recruitment & enrolment of Kenyan MSM in future HIV prevention trials


Background: The HIV epidemic among men who have sex with men (MSM) continues to expand globally. The addition of an efficacious, prophylactic vaccine to combination prevention offers immense hope, particularly in low- and middle- income countries which bear the greatest global impact. However, in these settings, there is a paucity of vaccine preparedness studies that specifically pertain to MSM. Our study is the first vaccine preparedness study among MSM and female sex workers (FSWs) in Kenya. In this paper, we explore willingness of Kenyan MSM to participate in HIV vaccine efficacy trials. In addition to individual and socio-cultural motivators and barriers that influence willingness to participate (WTP), we explore the associations or linkages that participants draw between their experiences with or knowledge of medical research both generally and within the context of HIV/AIDS, their perceptions of a future HIV vaccine and their willingness to participate in HIV vaccine trials.

Methods: Using a social network-based approach, we employed snowball sampling to recruit MSM into the study from Kisumu, Mombasa, and Nairobi. A field team consisting of seven community researchers conducted in-depth interviews with a total of 70 study participants. A coding scheme for transcribed and translated data was developed and the data was then analysed thematically.

Results: Most participants felt that an HIV vaccine would bring a number of benefits to self, as well as to MSM communities, including quelling personal fears related to HIV acquisition and reducing/eliminating stigma and discrimination shouldered by their community. Willingness to participate in HIV vaccine efficacy trials was highly motivated by various forms of altruism. Specific researcher responsibilities centred on safe-guarding the rights and well-being of participants were also found to govern WTP, as were reflections on the acceptability of a future preventive HIV vaccine.

Conclusion: Strategies for engagement of communities and recruitment of trial volunteers for HIV vaccine efficacy trials should not only be grounded in and informed by investigations into individual and socio-cultural factors that impact WTP, but also by explorations of participants’ existing experiences with or knowledge of medical research as well as attitudes and acceptance towards a future HIV vaccine.

Abstract Full-text [free] access

4. Health systems and services

H’V – can we do better for HIV, HBV and HCV if we all work together?

Editor's notes: The Sustainable Development Goals (SDGs) signal a major shift in the way that the United Nations and her development partners aim to shape the next decades. Whereas the Millennium Development Goals reinforced specific programmes for HIV, tuberculosis and malaria, the SDGs call for a more integrated approach to health and well-being and encourage integration and synergy wherever it makes sense. Hepatitis is one obvious area in which better collaboration and coordination could yield benefits. Hepatitis B (HBV) and C (HCV) viruses are both more common in some of the populations most affected by HIV. HCV can now be cured with drugs that derive directly from the HIV portfolio, while some ARVs have a direct effect on HBV.
Rwanda is one of the first countries in sub-Saharan Africa to set up a control programme for viral hepatitis, building on the infrastructure established for HIV. Umutesi and colleagues report on results of screening almost 120 000 people living with HIV who entered care for markers of HBV and HCV. Around 5000 people (4.3%) were identified with a positive Hepatitis B surface antigen and a similar number (4.6%) were found to have antibodies against HCV. There was marked variation geographically with a range by district from 2%-11% for HBV, higher in more urban areas and in men. For HCV the range was from 3%-8% and was higher in more rural areas, and also in men. This study provides a good platform to estimate numbers of people who might need treatment and to plan the next steps in an integrated programme.

People who inject drugs are particularly severely affected by HCV, and so co-infection with both HIV and HCV is common in areas where both viruses circulate. Some estimates from Ho Chi Minh City in Viet Nam suggest that more than 40% of people who inject drugs are living with HIV and that essentially all of these people are also co-infected with HCV. Birger R and colleagues developed a mathematical model to explore the likely impact of interventions aimed at HIV, HCV or broad harm reduction [with methadone maintenance treatment (MMT)] on future mortality and incidence of both infections. While ART scale up reduces HIV incidence and mortality, it has no effect on HCV. MMT is effective at reducing incidence of both HIV and HCV (and has morbidity and mortality benefits beyond these viruses). However, MMT does not help the many people already living with HCV and so has little effect on HCV related mortality. So the model is clear that treatment for HCV needs to be an important part of a combined programme and that we urgently need to find ways to reduce the price of directly acting antivirals if we are to save more Vietnamese lives.

Haldane and colleagues have also focused on this intersection between HIV and substance use services. They carried out a systematic review to understand the models and implications of integration of service delivery. The authors expand their typology of integration models considering the point of entry of the client, and the degree to which services are co-located and delivered. Integration can be considered as “clinical”, “service” or “systems”. The first two can operate at the micro or meso level meaning that individual staff can deal with both situations, or that staff are trained to provide appropriate referrals. Systems level integration operates at a macro level and implies that programmes for each service make collaborations and coordinate in ways that may affect staffing, funding and fragmentation of services. Although there are theoretical advantages to coordination and integration (as shown by the mathematical model above), there are few good empirical studies of integrated service delivery reported outside the USA. The authors considered that most of the intervention studies had a risk of bias in the interpretation of their impact, although all demonstrated positive changes in outcomes. Furthermore, almost all the studies focussed on integration at the clinic or individual provider level (meso or micro) rather than addressing the larger systemic challenges that we need to consider. If we are to achieve the ideals laid out in the Sustainable Development Goals, we will need to overcome some of these systemic challenges, particularly for populations that are criminalized and marginalized by many of the public services.

Prevalence of hepatitis B and C infection in persons living with HIV enrolled in care in Rwanda.


Background: Hepatitis B (HBV) and C (HCV) are important causes of morbidity and mortality in people living with human immunodeficiency virus (HIV). The burden of these co-infections in sub-Saharan Africa is still unclear. We estimated the prevalence of the hepatitis B surface antigen
(HBsAg) and hepatitis C antibody (HCVAb) among HIV-infected individuals in Rwanda and identified factors associated with infection.

Methods: Between January 2016 and June 2016, we performed systematic screening for HBsAg and HCVAb among HIV-positive individuals enrolled at public and private HIV facilities across Rwanda. Results were analyzed to determine marker prevalence and variability by demographic factors.

Results: Overall, among 117,258 individuals tested, the prevalence of HBsAg and HCVAb was 4.3% (95% confidence interval [CI] 4.2-4.4) and 4.6% (95% CI 4.5-4.7) respectively; 182 (0.2%) HIV+ individuals were co-infected with HBsAg and HCVAb. Prevalence was higher in males (HBsAg, 5.4% [5.1-5.6] vs. 3.7% [3.5-3.8]; HCVAb, 5.0% [4.8-5.2] vs. 4.4% [4.3-4.6]) and increased with age; HCVAb prevalence was significantly higher in people aged ≥65 years (17.8% [16.4-19.2]). Prevalence varied geographically.

Conclusion: HBV and HCV co-infections are common among HIV-infected individuals in Rwanda. It is important that viral hepatitis prevention and treatment activities are scaled-up to control further transmission and reduce the burden in this population. Particular efforts should be made to conduct targeted screening of males and the older population. Further assessment is required to determine rates of HBV and HCV chronicity among HIV-infected individuals and identify effective strategies to link individuals to care and treatment.

The impact of HCV therapy in a high HIV-HCV prevalence population: A modeling study on people who inject drugs in Ho Chi Minh City, Vietnam.


Background: Human Immunodeficiency Virus (HIV) and Hepatitis C Virus (HCV) co-infection is a major global health problem especially among people who inject drugs (PWID), with significant clinical implications. Mathematical models have been used to great effect to shape HIV care, but few have been proposed for HIV/HCV.

Methods: We constructed a deterministic compartmental ODE model that incorporated layers for HIV disease progression, HCV disease progression and PWID demography. Antiretroviral therapy (ART) and Methadone Maintenance Therapy (MMT) scale-ups were modeled as from 2016 and projected forward 10 years. HCV treatment roll-out was modeled beginning in 2026, after a variety of MMT scale-up scenarios, and projected forward 10 years.

Results: Our results indicate that scale-up of ART has a major impact on HIV though not on HCV burden. MMT scale-up has an impact on incidence of both infections. HCV treatment roll-out has a measurable impact on reductions of deaths, increasing multifold the mortality reductions afforded by just ART/MMT scale-ups.

Conclusion: HCV treatment roll-out can have major and long-lasting effects on averting PWID deaths on top of those averted by ART/MMT scale-up. Efficient intervention scale-up of HCV alongside HIV interventions is critical in Vietnam.
Introduction: Substance use is an important risk factor for HIV, with both concentrated in certain vulnerable and marginalized populations. Although their management differs, there may be opportunities to integrate services for substance use and HIV. In this paper we systematically review evidence from studies that sought to integrate care for people living with HIV and substance use problems.

Methods: Studies were included if they evaluated service integration for substance use and HIV. We searched multiple databases from inception until October 2015. Articles were screened independently by two reviewers and assessed for risk of bias.

Results and discussion: 11 057 records were identified, with 7616 after removal of duplicates. After screening titles and abstracts, 51 met the inclusion criteria. Integration models were categorized by location (HIV, substance use and other facilities), level of integration from micro (integrated care delivered to individuals) to macro (system level integrations) and degree of integration from least (screening and counselling only) to most (care for HIV, substance use and/or other illnesses at the same facility). Most reported descriptive or cohort studies; in four randomized control trials integrated activities improved patient outcomes. There is potential for integrating services at all facility types, including mobile health services. While services offering screening only can achieve synergies, there are benefits from delivering integrated treatment for HIV and substance use, including ease of referral to other mental health and social services.

Conclusions: Our review used a wide range of databases and conference archives to increase representation of papers from low- and middle-income countries. Limitations include the overrepresentation of studies from the United States, and the descriptive nature of the majority of papers. The evidence reviewed shows that greater integration offers important benefits in both patient and service outcomes but further research and outcome reporting is needed to better understand innovative and holistic care models at the complex intersection of substance use and HIV services.

Abstract  Full-text [free] access