ISSN 1472-4863

HTB: vol 23 no 11/12: November/December 2022

hiv treatment bulletin (e)

Glasgow 2022, UK statistics & guidelines (16 December 2022)

CONTENTS

Contents continued inside...

Published by HIV i-Base

Supporting Ukraine

Simon Collins, HIV i-Base

The significant challenges to support people who remain in Ukraine and those who migrated involves both international and community-based organisations.

HTB includes the following two online resources: one to donate unused medicines and the other to highlight a range of organisations that can benefit from direct financial support.

Sending unused meds to Ukraine: emergency appeal

https://i-base.info/htb/42694

The call for HIV and other meds, and medical supplies is still important. This is even though International agencies and drug manufacturers are also organising to meet this demand.

This project is led by EACS and BHIVA and supported by the UK-CAB.

Medicines need to be in original packaging, ideally in unopened packs. All HIV and related meds are acceptable, ***even if they are past the use-by date.***

All donations will be screened beforehand to make sure they are suitable.

The link page includes further details, including postal addresses in the UK, Europe and the US.

Organisations to help support Ukraine

https://i-base.info/htb/42633

This page including 14 organisations that are helping people affected by the crisis in Ukraine.

This includes organisations that are supporting people living with HIV that are still in Ukraine or who have migrated to other countries.

EDITORIAL

The final issue of HTB for 2022 includes a review of the latest HIV statistics in the UK, conference news from Glasgow, the launch of updated guidelines, including from BHIVA, and other related reports.

We also pay tribute to two leading activists – Giulio Maria Corbelli and Chris Sandford – who were friends of i-Base for many years and who recently died.

This has been a difficult year with complications from COVID continuing and against the backdrop of the Russian invasion of Ukraine.

And just as we were emerging from two years dominated by COVID, early cases of monkeypox – now newly renamed as mpox – were reported in the UK. This rapidly expanded to thousands of cases in the UK and more that 80,000 cases globally, often with 40–50% of cases in people living with HIV.

Over the last six months, HTB included more that 40 reports on mpox including five special reports due to the lack of emergency funding to support health services in the UK.

Luckily mpox cases have now dramatically dropped in the UK and many other countries, even where vaccine access is limited. This is good news, although it makes it difficult to evaluate vaccine efficacy. Although it is difficult to predict the risk of further outbreaks, most health authorities still urge caution. With less than a handful of cases now being reported each week in the UK, enrolment into the PLATINUM study is still recommended, to hopefully find out the benefits of tecovirimat as mpox treatment.

We lead this issue with a report on the latest UK data on HIV diagnoses, care and prevention. This remarkable body of information is meticulously compiled every year from multiple sources and is the basis for understanding the UK epidemic. Significant differences by demographics include rates of late and very diagnoses, which also correlate with access to PrEP. For example, the median CD4 count for gay and bisexual men is double that of straight men (443 vs 221), linked to more frequent HIV testing with PrEP.

While >70% of gay and bisexual men who could benefit from PrEP are able to access PrEP, these rates drop to 33% of straight men and only 23% of women.

We include six reports from Glasgow and a final article on metabiolic complications of latest HIV drugs from the IAS meeting in Meontreal.

We cover the latest CHAI report on global access to ART which includes both impressive advances in reducing generic drug prices but worryiing data on how badly children's care falls below that of adults.

Other news includes the launch of several updated guidelines, notably the main UK (BHIVA) guidelines on management of HIV in adults. These now recommend ART based on second-generation integrase inhibitors (dolutegravir or bictegravir) both for first-line treatment and in annual evaluations of people stable on other ART.

The UK has also now moved to national prescribing for each country which should make access to choice of ART more equitable, although some combination formulations will no longer be available or widely used, when generic components are available.

As we approach the upcoming holidays, i-Base would like to wish all readers best wishes for the upcoming year ahead, and to thank all contributors, editors, advisers and funders for all your support for HTB and other i-Base projects.

In memory: Giulio Maria Corbelll and Chris Sandford

Simon Collins, HIV i-Base

It is with great sadness we report that two leading HIV activists died this Autumn and these short tributes in memory are to recognise their work over many years.

Both were remarkable people who in different ways affected the lives of many thousands of people living with HIV.

Our thoughts are with their families and friends.

Giulio Maria Corbelll

Giulio Maria Corbelli was a leading Italian HIV and LGBT activist since his diagnosis in 1997, based in Rome.

He brought an amazing energy for both HIV prevention – helping to establish and run the Checkpoint clinics in Bologna and Rome where his good looks made him a natural model for posters about safer sex – and HIV treatment – where he was a community representative on the national treatment guidelines.

Guilio was also a European activist and as a long-standing member of the European AIDS Treatment Group he focussed on treatment, using his understanding of HIV science to chair the European Community Advisory Board (ECAB) for four years, represented the EATG at the European Medicines Agency and was invovled with many scientific conferences including EACS and Glasgow. More recently he became a leading activist involved in cure-related research,

I was lucky enough to work with Giulio on two large international studies, both of which ended up running for around ten years. One of these - the PARTNER study - produced the largest dataset to prove that havinf an undetectable viral load on ART prevented sexual transmission even without condoms. The second - the START study - proved there were cinical benefits of ART even at high CD4 counts, and changed national and international treatment guidelines overnight, generating data to support universl access to ART in every country.

Giulio contributing as many comments to scientific papers, as to the original study design and the wording of patient information. And he continued to be active even though he had complications from cancer for the last two years.

Most importantly Giulio brought an amazing warmth and enthusiam to everyone he met and every project he was involved in, shown by messages posted by activists and researchers from dozens of countries in trubute from the many groups he had worked with, that were collected for his family.

As one colleauge from the PARTNER study said: “things happened when Giulio got involved. I will miss his smile and his insights”.

Giulio leaves a long history of achievements as an activist and many memories for his spirit as a friend with a smile and the warmth he brought with him wherever he went.

Links

EATG: HIV activist Giulio Maria Corbelli has died

https://www.eatg.org/news/hiv-activist-giulio-maria-corbelli-has-died/

Chris Sandford

Chris Sandford found out he was living with HIV before there was a name or a test, and as one of the first people to be diagnosed he spent over 40 years commited to support others.

Chris brought the experiences from that impossible period, including caring for his partners when stigma and discrimination were at their highest, and his knowledge of managing his own health care, to developing peer advocacy.

At an age when many people were happy to retire, Chris became a peer advocate for ten years at the Mortimer Market clinic in central London, where he supported hundreds of people slowly take control of their HIV diagnoses.

Even after leaving this post (in his seventies) Chris continued to be an active member of the Bloomsbury Network, taught medical students for the university and server as a Governor for Central & North West London (CNWL) NHS Foundation Trust. He was an active member of the UK-CAB and a trustee of two other HIV charities.

Chris was also committed to keeping the history of HIV alive and not forgotten. He brought four decades of lived experience to support and develop projects that recognised the important of our histories. He was one of the first people to be interviewed for the National HIV Story Trust and went on to become Education Director, volunteering as a speaker for schools and colleges with qualities that let him easily connect with people of all ages and backgrounds. He talked movingly of his personal experiences as a carer for his lover and his own history with HIV.

Chris also brought his experience from being a gay man and living with HIV to understand the importance of overcoming stigma, especially in older people and he contributed to a recent campaign focussed on older people living with HIV.

Memory Sachikonye, a long term friend and colleague, remembered Chris: “for always checking about my health first, even if contacting me about work. We were both living with HIV and a kidney transplant and we always supported each other. I will always value his kindness and caring personality and will be missed by me and the HIV community.”

Even though his own health was difficult, Chris always brought such positive energy to his work and confidence that he still had a huge amount to offer. Like so many other people, I had seen Chris only a few week before he died, to talk about the importance of oral histories, when it was clear he was still deeply affected by the early loss of his partner and equally committed to making sure our stories continue to be told.

Links

Remembering Chris Sandford

https://www.cnwl.nhs.uk/news/remembering-chris-sandford

Growing older with HIV: CNWL’s Governor Chris Sandford shares his story

https://www.cnwl.nhs.uk/news/growing-older-hiv-cnwls-governor-chris-sandford-shares-his-story

National HIV Story Trust

https://www.nhst.org.uk/team/chris-sandford

Latest statistics on HIV in the UK: data for 2021

Simon Collins, HIV i-Base

In October 2022, UKHSA published an online summary online of HIV statistics for 2021, together with supporting data tables and the final report on 1 December 2022. [1]

Data is for 2021 and covers the second year that COVID-19 affected sexual health services including HIV testing, diagnoses and overall treatment. Although COVID likely led to some delayed HIV diagnoses, the report suggests that the steady reduction in new infections before the epidemic is still continuing.

Clinics responded remarkably well under very difficult circumstances, often restructuring and developing improved new services, including expanding the option for home testing and easier access to PrEP. For example, more than 61,000 people in the UK started or continued PrEP (70% of the 87,000 identified as having need), although even amongst those with a clear need, access to PrEP varied from 71% in gay and bisexual men to only 23% in women.

The report is accompanied by six sets of data tables including for PEP and PrEP, and two slide set presentations. [2]

This essential and impressive surveillance dataset is detailed, with breakdowns of figures by all key demographics (age, sex, race, sexuality, geographical region and HIV risk).

Selected results are included in Table 1 below. Differences in reporting each year means that some values are different to those included in reports from earlier years, Please refer to data tables in addition to the summary report.

Table 1: Selected results from 2021 HIV surveillance data

	2021	2020	2019	comments
Testing				
Total tests in all sexual health clinics England	1,053,169	913,383	1,319,915	Numbers increased more in gay men (50% now online) than other groups.
Positive tests from specialist sexual health clinics - n (%) (from GUMCAD)	1076 (0.10%)	1,005 (0.11%)	1523 (0.11%)	Reducing % in gay men (0.25% now from 52% in 2019). Stable in women (0.04%) and MSW (0.09%).
Internet tests	560,130	423,287	NA **	Increase in tests driven by online testing but disproportionally accessed by GBMSM.
HIV tests in GBMSM (England)	178,466	144,800	156,631	
HIV tests in women (England)	489,727	441,017	628,607	
HIV tests in heterosexual men (England)	248,355	242,813	419,501	
% of eligible people tested in clinics	46%	46%	65%	
% of eligible people not offered a test	38%	38%	16%	
PrEP and PEP in England *(data tables include demographic details)*				
% of clinic population defined as being in need of or able to benefit from PrEP.	7.4% (87,828 out of	NA	NA	Need was identified in 64.5% of GBMSM vs 1.4% of heterosexual men vs 0.5% of women.

% (n) in need who had consultation.	79.1% (69,507 out of 87,828)	NA	NA	Percentage consulted: 81.0% of GBMSM, 49.4% of heterosexual men and 33.0% of women.
% in need who used PrEP ***(sexuality data not always available).***	69.6% (61,092 out of 87,828)	NA	NA	71.6% of GBMSM (n=50,152) 34.2% heterosexual men (n=1068) 23.3% women (n=1221).
PEP use.	8,115	7,193	12,038	PEP use significantly dropped in all groups during COVID years.
HIV treatment and care				
New diagnoses UK (includes testing in all settings).	2,955	2,961	4,408	Steep drop in 2020 likely due to reduced testing during COVID. Approx 25% each year first diagnosed abroad.
Median CD4 in England (cells/mm^3). Data is based on ~ 80% who had a CD4 count within 3 months of diagnoses).	337	NA **	NA **	2021 breakdown: MSM: 443. MSW: 260. People of Black African ethnicity: 265, Those age >65 years old: 167. ***Significant differences by demographic group are driven by more frequent testing in people using PrEP, notably gay and bisexual men.***
Late diagnosis (CD4 <350).	46% (786 of 1,715)	44% (724 of 1,643)	41% (961 out of 2,343)	2021 breakdown: GBMSM: 37%, MSW: 63%, women 50%, Black African: 56%, White: 45%. ***Late diagnosis was associated with an 11-fold increased risk of death in the following year. Risk was highest in those over 65 years old.***
Very late diagnosis (CD4 <200).	NA **	NA **	NA **	Breakdown for this important lower threshold is not included in the summary report. However, the majority of late diagnoses <350 are actually <200.
Total HIV+ in care (England) .	91,432	88,786	90,504	
% in care >50 yrs old	48%	NA **	NA **	This was 25% in 2012.
% on ART	99%	98%	98%	Consistently high in all groups.
% <50 copies/mL (England).	98% (80,250)	97% (70,632) **	97% (79,242)	High is all groups by sex, race and sexuality, but 92% linked with vertical transmission (1,325 out of 1,434), and 94% injecting drug use (1,076 out of 1,143).
Deaths	797	814	584	Increases since 2019 are likely due directly to COVID-19 or indirectly from reduced access to health care services,
New diagnoses of advanced HIV (AIDS) ***	177	178	216	Few details are included about this field which is underreported. It only refers to AIDS-defining infections, not CD4 <200.

* This value seems like an error but will be confirmed and corrected if appropriate.

** Data to be added or confirmed shortly by UKHSA.

*** Advanced HIV disease is now a more appropriate term than AIDS for symptomatic HIV-related infection. It is now used by WHO instead of the term AIDS, and perhaps could also be adopted by UKHSA in future reports.

NA - Data either not included in the summary report or difficult to locate in the tables. Will be corrected if appropriate.

C O M M E N T

The data tables are impressive and the summary report includes a narrative of selected data.

Although not included in the summary report, this is now the fourth year that trans and non-binary data has been collected in England and this is available in the tables on key populations. Limited baseline data are now reported for the approximately 170 trans and nonbinary people who are living with HIV and there were less than five new diagnoses among this group in both 2020 and 2021.

However, the PEP and PrEP datasets combine trans men with men and trans women with women in binary datasets. The separated data is needed to develop and fund services.

The summary report does describe demographic differences in access to care, but doesn't comment critically on these, perhaps needing to be neutral.

The differences in CD4 count at diagnosis is particularly notable as being twice as high in gay and bisexual men compared to men who only have sex with women (443 vs 221), driven by more frequent HIV testing when using PrEP.

Similarly, and related, approximately 71% of gay and bisexual men attending sexual health clinics who could benefit from PrEP either started or continued to use PrEP, but this percentage dropped to 33% for straight men and only 23% for women.

Including separate data on very late diagnosis (CD4 <200) would also highlight that this accounts for the majority of people diagnosed late (<350). [3]

The UK HIV Action Plan published in 2021 aims to reduce HIV transmission by 80% by 2025 and to reduce it completely by 2030. Further details on this strategy are published to include progress over the last three years. [4, 5]

Including a similar at-a-glance table each year to highlight the main changes might also be useful in future reports.

References
1. UKHSA. HIV testing, PrEP, new HIV diagnoses, and care outcomes for people accessing HIV services: 2022 report. (1 December 2022). https://www.gov.uk/government/statistics/hiv-annual-data-tables
2. UKHSA. HIV Official Statistics. (1 December 2022). https://www.gov.uk/government/statistics/hiv-annual-data-tables
3. Collins S et al. Late diagnosis of HIV in 2022: Why so little change? HIV Med. 2022; 23(11): 1118- 1126. doi: 10.1111/hiv.13444.
4. Department of Health and Social Care. 'Towards Zero - An action plan towards ending HIV transmission, AIDS and HIV-related deaths in England - 2022 to 2025'. (2021) https://www.gov.uk/government/publications/towards-zero-the-hiv-action-plan-for-england-2022-to-2025/towards-zero-an-action-plan-towards-ending-hiv-transmission-aids-and-hiv-related-deaths-in-england-2022-to-2025
5. UKHSA. HIV action plan monitoring and evaluation framework. 1 December 2022. https://www.gov.uk/government/publications/hiv-monitoring-and-evaluation-framework/hiv-action-plan-monitoring-and-evaluation-framework

CONFERENCE REPORTS

Glasgow HIV Congress (2022)

23–26 October 2022, Glasgow and virtual

Introduction

This year the HIV Glasgow Congress was held from 23–26 October 2022, overcoming the difficult challenges of being both an in-person and virtual meeting, at a time when organising medical conferences is especially difficult.

The planning and work involved to enable such meetings is often under-appreciated (and under-acknowledged) especially as they are now vulnerable to underlying shifts in COVID dynamics that are impossible to predict months beforehand.

And yet these meetings play a vital role in connecting us to the latest research and in generating new ideas and projects that only come from face-to-face conversations. As a comment, over recent years, an increasing number of delegates use their annual leave to attend and are self-financing.
The progamme is available online at the conference website:
https://www.hivglasgow.org

The abstract book is available as a supplement to the Journal of the IAS.
https://onlinelibrary.wiley.com/doi/10.1002/jia2.26009

As always, this meeting had a lively and very current programme.

Highlights from the oral sessions in this year's programme include:

- The opening session rightly highlighted the impact of the ongoing war against Ukraine and shows the resilience of doctors and other health workers both in Ukraine (for example, by continuing to develop and PrEP services) and in neighbouring countries that are supporting new migrants (in structuring emergency access to ART).
- Rethinking approaches to PEP based on efficacy data from PrEP.
- ART strategies, including same-day and very early ART.
- Studies that help to understand risk of virological failure with CAB-LA/RPV-LA despite perfect adherence to this long-acting injectable combination.
- Understanding monkeypox (MPX) and the impact of different health responses to the recent outbreak.
- Changing patterns of pregnancies in women living with HIV in the UK, including the women who have lived with HIV since birth and are now becoming mothers.
- Patterns of comorbidities, including cardiovascular complications and especially as people living with HIV get older.
- The impact of SARS CoV-2 in people living with HIV.
- Durability of dual ART using dolutegravir and lamivudine.
- Updates on a reduced daily dose islatravir – now 0.25 mg/day – to enable research to continue in combination with daily doravirine.
- First virological data on the NIH-developed bNAb N6LSa, now being developed by ViiV as VH3810109.

The following meeting reports are included in this issue of HTB.

- Vertical transmission rate below 0.3% among women living with HIV in the UK
- Better re-suppression after viral rebound with DTG-based ART compared to EFV- or PI-based regimens
- Impact of islatravir on lymphocyte counts in a dose-ranging study: a post-hoc analysis
- Islatravir studies to use 0.25 mg daily dose to overcome risk of reducing CD4 and total lymphocytes

- Fostemsavir 240 week results from BRIGHTE study
- Fostemsavir: QT prolongation and drug-drug interactions
- Glasgow 2022: Mpox updates on epidemiology, treatment and prevention

GLASGOW 2022: PREGNANCY

Vertical transmission rate below 0.3% among women living with HIV in the UK

Polly Clayden, HIV i-Base

Vertical HIV transmission in the UK remains very low, according to data presented at HIV Glasgow 2022. Changes in the characteristics of women living with HIV accessing antenatal care have implications for service provision and need continued monitoring. [1]

The low transmission rate reflects both the antenatal screening programme – that includes HIV testing and has an uptake rate of 99% – as well as effective clinical management of HIV in pregnancy.

HIV population level surveillance has been in place for over 30 years in the UK and enables the monitoring of trends. The oral presentation showed recent trends in characteristics and outcomes of pregnancies among women living with HIV, using data from the NHS Integrated Screening Outcomes Surveillance Service (ISOSS).

ISOSS is conducted as part of the NHS Infectious Diseases in Pregnancy Screening Programme, UCL Great Ormond Street Institute of Child Health. All pregnancies in women living with HIV in the UK, their infants and any children living with HIV are reported to ISOSS (this changed to England only in 2020).

The dataset and analyses covered pregnancies in women diagnosed before delivery with estimated date of delivery during 2014–2019 and reported by 31 December 2021.

There were 5858 pregnancies among 3353 women during the surveillance period. The annual number decreased from approximately 1100 in 2014–2015 to 800–900 in 2018–2019. The proportion of women diagnosed during pregnancy declined over time.

From 2014–2019 the median age at estimated date of delivery was 34 years (IQR: 30 to 38) – this increased over time.

There were several shifts in maternal characteristics in 2014–2015 compared to 2018–2019. All were statistically significant ($p<0.001$):

- Maternal age >40 years increased from 12.5% to 19.1%
- Pregnancies in women born in sub-Saharan Africa decreased from 72.0% to 64.1%
- Pregnancies in women born in Eastern Europe increased from 4.3% to 6.9%
- Pregnancies in women with vertically-acquired HIV increased from 1.7% to 3.7%

Maternal diagnosis before pregnancy increased from 86.8% in 2014–2015 to 90.6% in 2018–2019. And the percentage on ART at conception among this group increased from 77.8% to 89.0% during the same time periods. (Both $p<0.001$).

The overall proportion of pregnancies conceived on ART increased from 67.2% in 2014–2015 to 81.0% in 2018–2019 ($p<0.001$).

Women diagnosed in pregnancy started ART increasingly earlier: from 19 weeks' gestation (IQR 16 to 23) in 2014– 2015 to 16 weeks (14 to 20) in 2018–2019.

The proportion of women with first antenatal CD4 count >500 cells/mm^3 increased from 51.2% in 2014–2015 to 58.5% in 2018–2019 ($p=0.001$).

Over the surveillance period, there were 5117 (87.1%) live births and 44 (0.75%) still births. Overall, 92.1% of deliveries were to women with viral load <50 copies/mL. For those on ART from conception, this proportion was 95.5%. There were no statistically significant differences between to two time periods.

Vaginal deliveries increased from 44.3% in 2014–2015 to 47.4% in 2018–2019. And emergency caesareans decreased from 26.9% to 22.3%, respectively. (Both p<0.001). The preterm delivery rate remained approximately 12%.

Supported breastfeeding cases – in line with BHIVA guidelines – increased from 1.5% in 2014–2015 to 5.8% in 2018–2019 (p<0.001).

The vertical transmission rate for infants born to diagnosed women (in England) declined steadily from 2.86% reported in 2000–2001 to a plateau of approximately 0.3% since 2012.

Two related posters ISOSS showed results from further analyses of characteristics and outcomes of pregnancies among women with vertically-acquired HIV and with supported breastfeeding in the UK. [2,3]

Women with vertically-acquired HIV are an emerging cohort in the UK. This dataset and analysis was from pregnancies with known outcomes reported to ISOSS between 2006 and 2021 (no pregnancies were reported in this population before 2006).

There were 17,478 pregnancies overall, of which 202 (1.6%) were among women with vertically-acquired HIV. There was a 10-fold increase in the proportion of pregnancies in with vertically-acquired HIV – from 0.3% in 2006–2009 to 3.5% in 2018–2021. In the same surveillance period, there was a decrease in the proportion of pregnancies among women with heterosexually-acquired HIV (p<0.001).

Just over half (54%) of women with vertically-acquired HIV were African-born compared with 74% for women with heterosexually-acquired HIV; 37% were UK-born compared with 15%, respectively (p<0.001).

The median age at delivery among women with vertically-acquired HIV was 24 years of age compared with 33 years for those with heterosexually-acquired HIV.

Fewer women with vertically-acquired HIV had viral load less than 50 copies/mL at delivery compared with those with heterosexually-acquired HIV: 55% and 87% vs 74% and 93% during 2006–2010 and 2016–2021, respectively (p<0.05). ART at conception increased significantly over time among both groups of women as did earlier antenatal visits.

Of the 202 pregnancies among women with vertically-acquired HIV, there were: 170 (84%) live births, 10 (5%) miscarriages, 18 (9%) terminations, and 4 (2%) stillbirths.

Preterm birth and low birth weight were more common among women with vertically-acquired HIV (both <0.001). Of infants with complete follow up, 1/150 (0.66%) was diagnosed with HIV.

The number of women choosing supported breastfeeding in the UK is increasing. Although it remains comparatively small. BHIVA pregnancy guidelines recommend formula feeding but state that women with undetectable viral load and good adherence wishing to breastfeed may be supported to do so.

ISOSS has collected data on supported breastfeeding since 2012. Among 8526 live births there were 267 (3.1%) reports of intention to breastfeed and/or breastfeeding. Reports have increased 4-fold from less than 10 per year in 2012–2014 to 40 to 50 per year in 2019–2020. At the time of analysis, 203 women were confirmed to have breastfed (using linked paediatric reports).

Of 96 women with this information recorded, 77 were known to have had monthly mother and infant testing in line with BHIVA guidelines. About a quarter of this group had issues for mother/infant testing.

The median duration of breastfeeding among mother/infants who had stopped breastfeeding at time analysis (150/203) was 56 days. Of those reported to have stopped, 71% of infants had a negative18–24 month antibody test, with no transmissions to date. The HIV status for the remainder could not yet be determined based on 18–24 month testing as the majority of these infants are still in follow up (23%), discharged before antibody testing (3%) or lost to follow up (3%).

COMMENT

These outcomes for the approximately 900 pregnancies among women with HIV in the UK are reassuring – with the current vertical transmission rate below 0.3%.

Among the growing population of women with vertically-acquired HIV, as well as those with heterosexually-acquired HIV, all markers have improved over time. Though numbers are very small, there may be a slightly elevated risk of transmission

among the vertically-acquired group. The authors note that further work is needed to understand why fewer women with vertically-acquired HIV have undetectable viral load at delivery – to help to optimise outcomes in this cohort.

Supported breastfeeding is expected to continue to slowly increase in the UK. There are no vertical transmissions to date but a few are lost-to-follow-up and some are still being followed.

Importantly, among vertical transmissions occurring in the UK, a number are attributed to undisclosed and supported breastfeeding by women with undetectable viral load. So this option needs to be very carefully discussed and managed.

This excellent surveillance programme continues to inform future guidance and optimal clinical management of pregnant women living with HIV and their infants.

References
1. Peters H et al. Trends in maternal characteristics and pregnancy outcomes among women living with HIV in the UK: 2014 to 2019. HIV Glasgow 2022. 23–26 October 2022. Oral abstract MO46.
2. Peters H et al. Pregnancy characteristics and outcomes of women with vertically-acquired HIV in the UK. HIV Glasgow 2022. 23–26 October 2022. Poster abstract P001.
3. Francis K et al. Supported breastfeeding among women with diagnosed HIV in the UK – the current picture. HIV Glasgow 2022. 23–26 October 2022. Poster abstract P041.

GLASGOW 2022: TREATMENT STRATEGIES

Better re-suppression after viral rebound with DTG-based ART compared to EFV- or PI-based regimens

Polly Clayden, HIV i-Base

People receiving dolutegravir (DTG)-based HIV treatment were significantly more likely to re-suppress after initial viraemia compared to those on efavirenz (EFV)- or PI-based ART. These findings from a meta-analysis of four African trials were presented at HIV Glasgow 2022.

It compared rates of virological failure and re-suppression in four randomised trials of DTG, efavirenz (EFV) and protease inhibitors (PI/r). The trials were:

- ADVANCE, comparing DTG- to EFV-based ART, plus either tenofovir disoproxil fumarate (TDF)/emtricitabine (FTC) or tenofovir alafenamide (TAF)/FTC in treatment-naive participants in South Africa.
- NAMSAL, comparing DTG- to low dose EFV-based ART, plus TDF/lamivudine (3TC) in treatment naive participants in Cameroon.
- DolPHIN-2, comparing DTG- to EFV-based ART, plus TDF/3TC in treatment naive, pregnant women, starting ART in the third trimester, in South Africa and Uganda.
- VISEND, comparing DTG- to PI-based ART, plus tenofovir prodrugs to zidovudine (AZT) in four second-line regimens, in people who had failed NNRTI-based first-line in Zambia.

The analysis examined whether participants with virological failure during treatment with DTG should be switched or if adherence counselling led to re-suppression.

Virological failure was defined as viral load >1000 copies/mL at any visit after week 24. Re-suppression was defined as viral load <50 copies/mL at the next visit in ADVANCE, DolPHIN-2 and VISEND, or <200 copies/mL in NAMSAL.

In ADVANCE, participants had similar rates of virological failure: 11%, 13% and 8.8% in the TAF/FTC/DTG, TDF/FTC/DTG and TDF/FTC/EFV arms, respectively. But 41%, 59% and 23% of participants in the respective arms achieved re-suppression.

In NAMSAL, virological failure rates were also similar between the TDF/3TC/DTG and TDF/3TC/EFV arms: 15.7% and 17.2%. And, 60.4% and 27%, in the respective arms, re-suppressed.

In DolPHIN-2, virological failure rates were similar by treatment group: 33.1% and 30.4% in the TDF/FTC/DTG and TDF/FTC/EFV arms. But, in this study, re-suppression rates did not differ between arms: 34.1% and 34.2%, respectively.

Women in DolPHIN-2 women started ART in late stage pregnancy and experienced quite high rates of virological failure and a proportion stopped taking treatment after delivery. This is a very vulnerable population with complex psycho-social issues – which likely account for different results to the two previous studies.

Re-suppression results were significant across the three studies in ART naive participants: p<0.01, DTG vs EFV arms.

In VISEND, virological failure was less frequent in the DTG arms than the boosted PI ones: 18.75% and 12.3% vs 27.5% and 20.3% in the TDF/FTC/DTG, TAF/FTC/DTG, AZT/3TC/LPV/r and AZT/3TC/ATV/r arms respectively. Re-suppression was more frequent among participants receiving DTG: 41% and 34.6% vs 19.6% and 17.5%, in the respective arms. Re-suppression DTG vs PI, p<0.01.

Unsurprisingly, VISEND participants switching ART with <1000 copies/mL at baseline were less likely to experience virological failure.

In the meta-analysis, overall re-suppression rates were significantly higher for DTG vs EFV, p=0.04.

COMMENT

WHO guidelines currently recommend that people with persistent viral load above 1000 copies/mL, despite adherence counselling, switch treatment.

Presenting author, Andrew Hill, asked whether or not people receiving DTG-based ART should be switched to another class and after how much adherence counselling. The research group are continuing to look at these questions and including more studies in the analyses.

He noted that the new South African ART guidelines recommend people are only switched if resistance testing shows evidence of integrase inhibitor mutations.

Although other guidelines recommend switching, poor tolerability of PIs also requires consideration.

Discussion after the presentation focused on the implications of continuing treatment in people with unsuppressed viral load. Although a substantial proportion of people receiving DTG-based ART re-suppressed, that leaves 40–50% that did not. Dr Hill explained that so far the analysis does not suggest an increased risk of integrase inhibitor mutations (although not the case with EFV).

As follow up across these studies is still relatively short (although ADVANCE has reported week 192 results), a question was raised asking if those who re-suppressed were followed for long enough, would they eventually fail, as has been observed with NNRTI-based ART.

Not raised in this discussion but quite likely to be an issue in the not-too-distant future are the population level implications of possible emerging integrase inhibitor resistance for the introduction of cabotegravir as PrEP. Cabotegravir was approved for this indication in December 2022 in South Africa and earlier this year in Zimbabwe. Pilot programmes are starting in 2023.

Reference

Hill A et al. Virological failure and HIV RNA re-suppression rates in four randomised trials of dolutegravir, efavirenz or protease inhibitor-based treatment in 3116 participants. HIV Glasgow 2022. 23–26 October 2022. Oral abstract O42.

https://virtual.hivglasgow.org/programme/late-breakers-hot-topics (webcast, first presentation)

GLASGOW 2022: ANTIRETROVIRALS

Impact of islatravir on lymphocyte counts in a dose-ranging study: a post-hoc analysis

Kirk Taylor, HIV i-Base

HIV Glasgow included a late-breaking post-hoc analysis of islatravir (ISL) dose-ranging studies (0.25 mg, 0.75 mg and 2.25 mg) that led to most clinical studies of being stopped last December due to safety concerns over a decline of CD4 counts. [1, 2]

Total lymphocyte, CD4 and B cell counts were reduced by the greatest extent at the highest dose of ISL (2.25 mg). A 3-fold dose reduction from 2.25 to 0.75 mg improved cell counts. Changes in total lymphocyte and CD4 cell counts were comparable for 0.25 mg ISL and standard ART.

Other haematological parameters (haemoglobin, platelets, and neutrophils) were not affected.

Post-hoc analysis was performed for protocol 11, which included participants that received either ISL (0.25, 0.75 or 2.25 mg) plus DOR/3TC or DOR/3TC/TDF. ISL was standardised to 0.75 mg at week 60, and all participants were switched to ISL/DOR (0.75/100 mg) at week 144 and followed for a year.

At week 72, total lymphocytes counts were +20.5%, –0.4% and –15.9% compared to baseline for 0.25, 0.75 and 2.25 mg ISL, respectively. CD4 counts changed by +24.0% (2.25 mg ISL), +47.1% (0.75 mg ISL), +79.8% (0.25 mg ISL) and 60.1% (DOR/3TC/TDF).

A 3-fold reduction of ISL from 2.25 mg to 0.75 mg increased lymphocyte (21.2%) and CD4 (28%) counts. Conversely, a 3-fold increase of ISL (0.25 mg to 0.75 mg) led to reduced lymphocyte (10.8%) and CD4 (1.8%) counts.

Adverse events relating to other infections were common across all arms of the study with prevalence rates of 71% (DOR/3TC/TDF), 58.1% (2.25 mg ISL), 73.3% (0.75 mg ISL) and 65.5% (0.25 mg ISL).

There were two AIDS-defining events that were not linked to ISL.

References

1. Correll T et al. Total lymphocyte and lymphocyte subset changes in participants receiving islatravir (0.25, 0.75 and 2.25mg QD) and doravirine (DOR) +/- lamivudine (3TC): post-hoc analysis from a phase 2b dose-ranging study (P011). Oral 46. HIV Glasgow, 23 to 26 October 2022. Weblink: https://virtual.hivglasgow.org/programme/late-breakers-hot-topics
2. Collins S. FDA further limit use of islatravir in ongoing studies. HTB (20December 2021) https://i-base.info/htb/41866

Islatravir studies to use 0.25 mg daily dose to overcome risk of reducing CD4 and total lymphocytes

Kirk Taylor, HIV i-Base

HIV Glasgow included a late-breaking presentation of a model to explain the unexpected drop in CD4 cells and total lymphocytes that led to most clinical studies of islatravir (ISL) being stopped in December 2021. [1, 2]

ISL is a highly potent NRTTI under development for HIV treatment and prevention. After dosing, it it is phosphorylated to ISL-TP in enters lymphocytes. However, the extremely long half-life of ISL led to accumulation of high levels of ISL-TP that were cytotoxic to CD4 and total lymphocytes.

Total lymphocyte and CD4 counts were modelled using data from four clinical studies of ISL that used QD (0.25 to 2.25 mg) or QM (60 to 120 mg) regimens. The greatest drops in lymphocyte and CD4 counts were associated with the 0.75 mg dose. Using 0.25 mg gave comparable lymphocyte counts to other ART regimens.

The present study aimed to establish an optimal dose that does not impact lymphocyte counts, whilst maintaining efficacy against HIV. Data were collected from trials with HIV negative (protocol P016; 60 mg and 120 mg QM), treatment naïve (P011; 0.25, 0.75 and 2.25 mg QD) and virologically suppressed (P017

and P018; 0.75 mg QD) participants. There was a minimum of 36 weeks of data for each trial and participant numbers ranged from 30 to 330 per arm.

Two models were built to assess ISL-related changes in total lymphocyte and CD4 counts. Efficacy was evaluated for wild-type (WT) and M184I/V HIV-1 strains. ISL (0.25mg QD) achieved efficacy against both strains with 4 days of initiation.

Changes in CD4 counts were benchmarked against 50 published ART switch studies that included >19,000 participants. Change in CD4 counts fell mostly within the range -5% to +10% and this was used for ISL studies.

Modelling predicted a dose-dependent decrease of total lymphocyte and CD4 counts with the greatest reduction seen with 2.25 mg ISL. For 0.25 mg QD ISL, total lymphocyte and CD4 counts at week 48 were 97.5% (95% PI: 92.7% to 103%) and 98.4% (95% CI: 91.4% to 105.0%) of control, respectively. Predicted total CD4 counts were 700 cells/mm^3 (95% PI: 649 to 753) for 0.25mg ISL and 719 cells/mm^3 (95% PI: 664 to 766) for comparator ART.

A phase 3 study is underway to evaluate efficacy of DOR/ISL (100/0.25mg) for people living with HIV that are virally suppressed or treatment naïve. Safety monitoring will include quarterly CD4 counts.

References

1. Vargo R et al. Modelling and simulation to optimize islatravir doses in HIV treatment naïve and virologically suppressed populations. Oral 45. HIV Glasgow, 23 to 26 October 2022.
https://onlinelibrary.wiley.com/doi/10.1002/jia2.26009 (abstract)
https://virtual.hivglasgow.org/programme/late-breakers-hot-topics (webcast)
2. Collins S. FDA further limit use of islatravir in ongoing studies. HTB (20 December 2021)
https://i-base.info/htb/41866

Fostemsavir 240 week results from BRIGHTE study

Kirk Taylor, HIV i-Base

HIV Glasgow included two posters from the BRIGHTE study on the week 240 efficacy of fostemsavir (FTR) in participants with extensive multidrug resistance. [1, 2]

Virologic efficacy at week 96 (79%) was maintained through week 240 (82%). Viral load was <200 copies/mL for 92% and 77% of participants in the randomised (RC) and non-randomised (NRC) cohorts, respectively. Virological failure was more common for the NRC (54%) that were on functional FTR monotherapy due to failing optimised background therapy (OBT). [1]

Multivariate analysis showed that virologic response correlates with baseline viral load and CD4 count. Virologic failures were associated with GP120 mutations, baseline CD4 count and viral load but these were not predictive factors. [2]

Participants were enrolled into the RC (n=272, 3:1 FTR:placebo) or open-label NRC (n=99) arms and followed over five years. Participants were highly treatment experienced (HTE) with resistance to ≥1 class. Median baseline viral load and CD4 count was 4.6 log copies/mL (IQR: 1.6 to 6.9) and 80 cells/mm^3 (IQR: 0 to 1160), with 30% of participants having a CD4 count <20 CD4 cells/mm^3.

Week 240 interim analysis was performed to determine efficacy and safety of FTR + OBT beyond week 96. At week 240 virologic efficacy was maintained at 82% and viral load was <200 copies/mL for 92% and 77% of participants in the RC and NRC arms, respectively.

Virologic failure was higher in the NRC arm (54% vs 29%) reflecting greater baseline resistance. In the RC arm CD4 counts at week 240 were >200 cells/mm^3 for 78% of participants, which included 22/33 participants that had <20 CD4 cells/mL at baseline. 60% of RC participants remained on FTR beyond week 240 and >80% had a viral load >40 copies/mL.

The safety profile was consistent with week 96 data. Six participants became pregnant during the study period with 3 normal pregnancies, 2 with complications (1 with foetal growth restriction and 1 premature birth) without congenital abnormalities and 1 pregnancy ended after an elective abortion.

The second poster included a post-hoc multivariate analysis considered factors influencing virologic outcomes where 65% of participants in the RC achieved >0.5 log copies/mL decrease of viral load by day 8. For those with stable viraemia in the RC (n=141), better virologic outcomes were associated with higher baseline CD4 count and viral load. GP120 mutations (S375H/I/M/N/Y, M426L and M434K) were associated with lower chance of viral load decrease. [2

Protocol-defined virologic failure rates were 8% and 25% in the RC and NRC, respectively. Virologic response for both arms was associated with baseline CD4 count, viral load and PK parameters. GP120 mutations and lower efficacy of the OBT were associated with virologic failure in the NRC.

References:

1. Aberg J et al. Efficacy and safety of fostemsavir plus optimized background therapy in heavily treatment-experienced adults with HIV-1: Week 240 results of the phase 3 BRIGHTE study. Poster 061 HIV Drug Therapy, Glasgow 23 to 26 October 2022.
   https://virtual.hivglasgow.org/posters-exhibitions/posters/efficacy-and-safety-fostemsavir-plus-optimized-background-therapy
2. Gartland M et al. A multivariate analysis of the phase 3 BRIGHTE trial, trough week 24, to identify predictors of virologic response to fostemsavir in heavily treatment-experienced people living with HIV. Poster 064 HIV Drug Therapy, Glasgow 23 to 26 October 2022.
   https://virtual.hivglasgow.org/posters-exhibitions/posters/multivariate-analysis-phase-iii-brighte-trial-through-week-24-identify

Fostemsavir: QT prolongation and drug-drug interactions

Kirk Taylor, HIV i-Base

HIV Glasgow included a poster on the risk of QT prolongation with fostemsavir (FTR) as this has previously been reported with both FTV and its active metabolite temsavir (TMR) when administered at supratherapeutic doses. [1]

QT prolongation was reported for 7 (2%) participants in the phase 3 registrational BRIGHTE study who discontinued due to QT prolongation by week 96. Analysis of drug-drug interactions indicate that consideration should be given when FTR is co-administered with other drugs that influence QT interval (e.g. EFV, LPV and antiarrhythmics).

Therapeutic doses of FTR have not been linked to QT prolongation and the Liverpool database does not indicate potential interactions with other commonly used ART (i.e. INSTI, NRTI, or DOR). [2]

FTR is approved for twice daily dosing (600 mg BD) for people with multidrug-resistant HIV, in combination with other active ARVs. Pre-clinical studies of FTR noted QT prolongation (8 to 18ms) at supratherapeutic doses. Above therapeutic dosing, FTR has a dose-dependent impact on QT interval.

FTR is metabolised to TMR by cytochrome p450 and co-administration with other drugs may alter the PK profile, leading to higher plasma concentrations. QT prolongation threshold (>10ms) is met when plasma TMR levels are >7,500ng/mL (>4x reported Cmax for BD regimens).

The 7 participants in BRIGHTE discontinued due to prolonged QT of >450ms. Of these, 6/7 remained on FTR outside of the study and no cardiovascular events were reported. No participants discontinued due to QT prolongation from a phase 2b dose-escalation study (range 400 mg to 1,200 mg QD).

The University of Liverpool HIV drug database did not indicate any significant or high potential for prolonged QT interval for co-administration of FTR with other commonly used HIV drugs (e.g. INSTI, NRTI or DOR). [2]

Combining FTR with other ARVs does not require dose adjustment. Consideration should be given to potential interactions when FTR is combined with drugs known to influence QT interval (e.g. EFV, LPV and antiarrhythmics).

References

1. Patel S et al. Fostemsavir and QT prolongation: Clinical Applications for co-administration with other drugs. Poster 030. HIV Drug Therapy, Glasgow (23rd to 26th October 2022).
   https://virtual.hivglasgow.org/posters-exhibitions/posters/fostemsavir-and-qt-prolongation-clinical-applications-co-administration
2. Liverpool University Drug Interaction Website.
   https://www.hiv-druginteractions.org/checker

Mpox updates on epidemiology, treatment and prevention

Kirk Taylor, HIV i-Base

HIV Glasgow 2022 included an in-depth symposium on the monkeypox outbreak - newly renamed mpox - that included talks from healthcare professionals, reflections from a patient and survey data. [1–6]

Although by 28 November 2022, 3,575 confirmed cases of mpox had been reported in the UK, numbers have dramatically dropped to less than 30 over the last month. [7] Mpox case numbers across Europe peaked in the summer and are now in similar decline. [1]

Guidelines for mpox presentation have been updated to include anogenital and mucosal lesions and reference sexual transmission routes. [2]

People living with HIV account for 38% of mpox cases and CDC guidelines state that those with <200 CD4 cells/mm^3 should be prioritised for both vaccination and access to tecovirimat. [2, 3]

Harun Tulunay gave a powerful account of his experience with mpox and stressed the need to promote vaccine uptake and adequately support sexual health services. [4]

Survey results cited high levels of early mpox awareness but highlight inequities in the mpox response linked to education and employment status. [5, 6]

Epidemiology of the mpox outbreak

As of October 2022, WHO figures include 25,036 confirmed mpox cases across 41 European countries. [1, 2]

Countries with the greatest number of cases are Spain (7,277), France (4,084), United Kingdom (3,686) and Germany (3,651). Mpox evolution has been quicker than anticipated with 50 mutations to date (compared to the expected 4). Mutations within APOBEC3 likely account for reduced pathogenicity and increased mpox distribution.

Across Europe, 39% of cases were reported for people aged between 31 to 40 and males account for 98% of all cases. Of those, the majority were gay and bisexual men (96%) and 38% were PLWH.

International case definitions were updated in May 2022 to include sexually active gay and bisexual men.

Case data from the UK, Spain, CDC and a global study were used to explore mpox presentation and symptoms. Early associations were drawn between mpox and transmission, sexual contact, sex-on-premises venues, HIV, large gatherings (e.g. pride) and travel.

Onset of mpox symptoms took a median of 7 days and included rash (96%), systemic symptoms (68%) and anogenital lesions (49%). Hospitalisation rates were 6.3% (n=736) with 5 people admitted to the ICU and 4 deaths.

Clinical definitions have been updated to include anogenital and mucosal lesions.

Decline in mpox cases is likely due to early diagnosis, contact tracing, awareness programmes and vaccinations. The impact of each measure and how the mpox outbreak will develop remains unclear.

Data from London indicate that the reduction of mpox cases preceded peak vaccine uptake, suggesting behavioural changes were likely a key factor in reducing case numbers. [3]

Mpox and people living with HIV

Given that mpox virus has been detected in semen, swabs (urethral and anal), and type of sex correlates with lesion sites, Professor Chloe Orkin was one of the leading doctors proposing that mpox should be classified as an STI. This was reflected in an updated Swiss statement on mpox that says, “MPX must for now be considered an STI but it is important to note that transmission can still occur outside of sex”. [2]

People living with HIV are disproportionately affected by mpox and whilst the underlying reasons are unclear, this may arise through behavioural differences relating to risk, easier access to testing and biological factors.

Although a retrospective review of people hospitalised with mpox in Nigeria reported 9/40 cases were people living with HIV, the majority were not virally suppressed and 4/9 had <200 CD4 cells/mm^3. People living with HIV had more prolonged illness with larger and more widespread lesions and higher incidence of bacterial superinfection. [8]

Data from the US CDC report no differences in clinical presentation or hospital admissions for those who were

HIV positive (n=201) that had median CD4 count of 680 cells/mm^3 and virological suppression rate of 97%. There were two cases with significant complications of epiglottitis and myocarditis.

Racial disparities are highlighted within the CDC data with higher than expected case rates for Black, Asian and Latinx populations. 82% of people in the data series were virologically suppressed but those who were HIV positive were more likely to be hospitalised with mpox than HIV negative people (8% vs 3%).

US CDC guidelines indicate that PLWH <200 CD4 cells/mm^3 are at higher risk of severe complications and should be prioritised for vaccination and tecovirimat. Intradermal dosing is not recommended with <200 CD4 cells/mm^3. Vaccination in the UK has been prioritised for healthcare workers and sexually-active gay and bisexual men. [2, 3]

Mpox vaccines and therapies for treatment and prevention

Orthopox viruses have shared immune epitopes and three smallpox vaccines are licenced for use against mpox. The MVA-BN-Jynneos formulation (non-replicating virus) is most widely used and is non-inferior to the live vaccine (ACAM2000) which is not being used due to higher toxicity. A single dose generates T and B cell responses but efficacy data against mpox are limited. Open-label observational data on mpox vaccination from the US CDC show that unvaccinated individuals were 14 times more likely to contract mpox, but this doesn't account for behavioural differences and vaccine use. A much smaller observational cohort in Israel reported vaccine efficacy of 80% after a single dose, but with similar cautions about interpretation of non-randomised data. [3]

Interestingly, healthcare workers who had previously been vaccinated against smallpox had neutralising antibody responses to mpox. Neutralisation titres were lower for people that had not previously been vaccinated against smallpox.

Antivirals for mpox include tecovirimat, cidofovir and brincidofovir and interactions with ART are available through the University of Liverpool site. [9]

Tecovirimat has been used in the UK for people hospitalised with mpox. Although the UK PLATINUM and US STOMP trials are ongoing to evaluate the of tecovirimat, enrolment is now challenged by having dramatically fewer cases.

Living with mpox, the patient perspective

Harun Tulunay, an HIV-positive advocate at Positively UK in London gave a powerful talk, outlining his early experience of mpox, symptom progression, and the difficulty in getting a diagnosis. Harun's first symptom in June 2022 was a single facial lesion on his nose accompanied by a high fever. He ascribed the lesion to impetigo and tested several times for COVID, all were negative. [4]

Ibuprofen was used to manage early symptoms and he began to experience muscle pains and a sleep-disturbing rash. This was diagnosed as a fever rash it took 2.5 weeks and six calls to emergency services before paramedics came to his flat. They advised him to take analgesics, anti-inflammatories, and penicillin for tonsilitis. Harun's GP wrongly suggested his ART may have stopped working.

After he was hospitalised due to oropharyngeal lesions that prevented him swallowing food and fluids, he received tecovirimat. After three days he was able to swallow and was discharged on day 10.

Harun was very open and transparent about his experiences, and broadcasting a blog on YouTube, contributed to early behaviour changes in the community. He then developed online support groups and awareness campaigns.

This led to both positive and negative messages in response to his campaigns. He stressed that five months into the mpox outbreak, half of those eligible are unvaccinated and that sexual health services should have been more adequately supported.

Perceptions of mpox

Between June and July 2022, two UK community surveys examined awareness and understanding of mpox. [5, 6]

Surveys were distributed through social media and Grindr. Respondents (n=1932) were male (91%), aged <40 (39%), White (71%), Asian (8%), Black (3%) and Latinx (2%). 90% of respondents were cis or trans men who have sex with men and 77% of all respondents identified as gay or lesbian and 7% were living with HIV.

Awareness was high with only 31 individuals reporting that they had not heard about mpox. News outlets were

the most common source of information (57%), followed by Twitter (21%), dating apps (13%) and healthcare professionals (11%). Concerns were raised that those talking about mpox do not represent them (45%).

Healthcare professionals and government websites were considered the most credible sources of information. Social media and private group chats scored low on trustworthiness.

Only 17% of respondents said that they understood mpox 'very well' and understanding was greater for Latinx than Black respondents (35% vs 12%). Greater educational attainment and being employed also correlated with understanding.

Over half of respondents considered themselves at risk of mpox and 50% said that they would attend a sexual health clinic if they experienced mpox symptoms. 38% said they would be unable to isolate for 21 days, citing lack of support and disability amongst their reasons. 6% of people said that they would not receive a vaccine if it was available to them.

A sub-analysis of cis (n=88) and trans (n=15) women was conducted. [6] Although this group had high rates of vaccine acceptability, public health information and advice were neither universally accepted nor correctly understood. There is a risk of compounding health inequalities and engagement with all communities is required.

C O M M E N T

References

Presentations 1-6 were part of a symposium on the mpox outbreak presented at HIV Drug Therapy, Glasgow, 23 to 25 October 2022. The session webcast is available through the conference platform:

https://virtual.hivglasgow.org/programme/monkeypox-where-are-we-now-and-what-have-we-learned

1. Noori T et al. Epidemiology of monkeypox and public health response. HIV Drug Therapy, Glasgow, 23 to 25 October 2022.
2. Orkin C et al. Case definitions, evolution and HIV presentation. HIV Drug Therapy, Glasgow, 23 to 25 October 2022.
3. Bhagani S et al. Treatment, vaccines and guidelines. HIV Drug Therapy, Glasgow, 23 to 25 October 2022.
4. Tulunay H et al. The patient perspective. HIV Drug Therapy, Glasgow, 23 to 25 October 2022.
5. Paparini S et al. Perceptions and understandings of media and public health messaging about the monkeypox outbreak in the UK: Findings from a rapid response, co-produced survey. HIV Drug Therapy, Glasgow, 23 to 25 October 2022. Oral abstract 41A.
6. Paparini S et al. Including women in the public health response to the monkeypox (MPXV) outbreak in the UK: Findings from a rapid response, co-produced survey. HIV Drug Therapy, Glasgow, 23 to 25 October 2022. Oral abstract 41B.
7. UKHSA. Monkeypox outbreak: epidemiological overview, 29 November 2022. https://www.gov.uk/government/publications/monkeypox-outbreak-epidemiological-overview/monkeypox-outbreak-epidemiological-overview-29-november-2022
8. Ogoina D. Clinical course and outcome of human monkeypox in Nigeria. Clin. Inf. Dis. 71(8). (13 February 2020). DOI: https://doi.org/10.1093/cid/ciaa143
9. Liverpool University drug interaction website. https://www.hiv-druginteractions.org/checker

CONFERENCE REPORTS

24th International AIDS Conference (AIDS 2022)

29 July to 2 August 2022, Montreal, Canada

Simon Collins, HIV i-Base

Introduction

This year the IAS conference was held in Montreal and also as an impressive fully hybrid conference online.

As usual, the conference had a strong programme that covered all aspects of HIV treatment, prevention, activism and policy. Many specialist workshops were also held in the few days before the main conference.

The full programme for the meeting is available online, with open access to all posters, webcasts and other conference resources.

https://programme.aids2022.org

Webcasts are posted online but are sometimes easier to find from this progamme link:

https://programme.aids2022.org/#youtubevideoEnglishFalse

The following reports are included in this issue.

- Metabolic complications of newer HIV drugs in older people

Metabolic complications of newer HIV drugs in older people

Kirk Taylor, HIV i-Base

AIDS 2022 included a presentation by Tristan Barber on the metabolic complications of new HIV drugs in older people, defined as being >50 years old, noting the lack of data in this population. [1]

The lack of data is compounded by much of the research on natural ageing being based in high income countries, and control populations for health complications often being overrepresented by cisgender white men.

This is despite more than half of people living with HIV being older than 50 in many cohorts, including at the Royal Free Hospital in London, where for the last four years Dr Barber helped establish and run the Sage clinic to promote and support healthy ageing, with a focus on comorbidities and frailty.

Good metabolic health can be defined as covering five main goals: (i) having a good and stable appetite, (ii) minimal belly fat, (iii) normal blood sugar, (iv) normal blood pressure, and (v) having good enough muscle, bone and joints to be physically active. These targets are to achieve and maintain a good quality of life, rather than simply meeting good chemical and physiological markers.

Ideally, this is with minimal need for medications, but ART is clearly essential in people living with HIV and the newer ARVs from five drug classes include TAF, dolutegravir, bictegravir, doravirine, injectable cabotegravir-LA and rilpivirine-LA, ibalizumab and fostemsavir. Registrational studies for new drugs, however, generally include low numbers of people older than 50, unless they are specifically developed to overcome multidrug resistance.

Weight gain

Although weight gain has been an important new research focus since 2017, when the ADVANCE study reported significant associations with both dolutegravir and TAF, especially in Black women, few of these studies focus on older people. An Italian study in people older than 65 years old did not report weight gain after switching to dolutegravir, but this was in a largely male Caucasian cohort. [2]

Any discussion on weight changes in people living with HIV needs to relate to changes in the general population, where weight commonly increases during middle age and is linked to a wide range of health complications. These include cardiovascular disease and stroke, diabetes, NAFLD, some cancers, joint pains, general mortality, depression and lower quality of life. It is also associated with low self-image and stigma.

After the age of 60, weight starts to decrease, visceral abdominal fat increases and lean muscle declines (affecting the interpretation of BMI). But although the complications of high BMI are less pronounced (compared to when younger), excess weight still remains a concern, increasing pressure on the respiratory system and joints and increasing the risk of cancers, cardiovascular and liver diseases. In older people, low BMI and weight loss are associated with increased mortality.

Frailty

Frailty is a critical issue in the management of older people. It is not just a measure of physical activity, strength and quality of life, but a diagnosis that is independently linked to mortality.

Two people with a similar chronological age, medical history, BMI and biomarkers can have very different levels of frailty based on lifestyle factors that achieve and maintain higher levels of activity.

Healthier lifestyle changes make it easier to have stronger responses to future complications.

HIV-related age and ART experience

The talk also introduced the importance of HIV-related age. Ageing with HIV will be very different for a man aged 70 who was diagnosed in 1994 compared to 2017.

Time of HIV diagnosis is important for experience of both HIV and treatment and can be split into the following four categories:

Before 1996: before effective ART, longer time with detectable viral load, opportunistic infections, possible AIDS diagnosis, bereavement from partners and friends and being less financially prepared.

1996 to 2005: early ART was effective but had difficult side effects, sometimes permanently reducing quality of life, longer periods of viraemia, UK guidelines at one point had a CD4 threshold to start ART at 200 cells/mm3.

2005 to 2015: ART became better and easier, and was started earlier at CD4 350 cells/mm3.

After 2015: ART has been routinely recommended after diagnosis at any CD4 count (although at least 40% of people are still diagnosed late after the CD4 count is <350 cells/mm3).

Metabolic health

Duration of HIV and use of ART contributes to a complex pattern of factors that impact on metabolic health. These can make the underlying mechanisms and pathogenesis of ageing very different in people living with HIV. [3]

Both HIV and ART can cause or enhance:

- Genetic damage (epigenetic ageing, mitochondrial dysfunction, oxidative stress, telomere length).
- Cellular changes (senescence, altered autophagy, protein responses).
- Inflammation (detectable HIV, coinfections including CMV, inverted CD4:CD8 ratio).
- Biological changes (altered microbial balance, increased gut permeability, endocrine decline).
- Environmental (sexual history, smoking, use of drugs and alcohol, exercise and diet).

Individual HIV drugs can have different side effects that affect metabolic health.

Older people living with HIV need to consider effects of long-term ART uses, viral factors (reservoir and HIV proteins) and biological changes.

However, one review shows similar levels of viral suppression rates for people aged ≥ 50 years initiating ART compared to those under 50 (range: 85% to 100%) when using newer drugs as first-line ART. These studies include data for dolutegravir, bictegravir and TAF, but not so far for long-acting therapies.

Prescribing and polypharmacy

Several cohorts, including the AGEhIV cohort study, have reported that comorbidities (e.g. cardiovascular and renal disease) and polypharmacy increase with age. People aged >65 years report more comorbidities (40% report ≥2 non-HIV conditions) and polypharmacy (20% report taking ≥3 non-ART medications). [4]

The choice of ART needs to have the least potential for drug-drug interactions (DDIs). Drug handling changes with age, as hepatic and renal changes may alter ARV processing and clearance differently in older people.

Even though many people living with HIV report wanting to remain on the same therapy because they see it as effective, they might not understand that age-related changes in drug handling may make them more susceptible to side effects over time, especially with efavirenz. This should be considered alongside a review of comedications at every appointment.

There is an ethical imperative to evaluate ART and consider alternatives at least annually. This can involve switching from an “it’s working” mentality and considering better alternatives that often come with newer drugs. This review should focus on whether each current treatment is still the best option for each individual. Recent UK guidelines support routine use of integrase inhibitors rather than boosted protease inhibitors, that can have better tolerability, fewer DDIs and often overcome earlier drug resistance.

Recommendations

- Prescribe ART with least potential for DDIs.
- Counsel people about their drugs and blood results.

- Review ART for ageing people as co-medications will change.
- Consider impact of altered renal and hepatic function on drug handling and metabolism.
- Take accurate measurements of waist to hip ratio, blood pressure, BMI.
- Accurately record these results and monitor over time to look for unexpected changes.
- Motivate behavioural changes to increase exercise or modify diet to improve health.

C O M M E N T

This excellent talk stressed that ageing is a dynamic process and the importance of actively managing HIV in older age.

This involves recognising that people who are generally perceived as being stable on long-term ART, actually present new medical challenges as we age.

References
1. Barber TJ. Older people. Metabolic consequences of new classes of ART. AIDS 2022, 29 July to 2 August 2022, Montreal. https://programme.aids2022.org/Programme/Session/23
2. Guaraldi G et al. Dolutegravir is not associated with weight gain in antiretroviral therapy experienced geriatric patients living with HIV. AIDS. (01 May 2021). DOI: 10.1097/QAD.0000000000002853. https://journals.lww.com/aidsonline/Fulltext/2021/05010/Dolutegravir_is_not_associated_with_weight_gain_in.10.aspx
3. 10.1097/QAD.0000000000001441. https://pubmed.ncbi.nlm.nih.gov/28471941
4. Schouten J, et al. Cross-sectional comparison of the prevalence of age-associated comorbidities and their risk factors between HIV-infected and uninfected individuals: the AGEhIV cohort study. CID 2014;59:1787–97. https://pubmed.ncbi.nlm.nih.gov/25182245

ANTIRETROVIRALS

EU recommends approval of dispersible dolutegravir FDC for children weighing 14 to >25 kg

Simon Collins, HIV i-Base

On 16 December 2022, the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) issued a positive opinion to approve Triumeq PD as a dispersible fixed dose combination (FDC) for children weighing 14 to <25 kg. [1]

The committee also lowered the minimum weight for using the adult non-dispersible tablet from 40 kg to 25 kg.

Triumeq PD is a dispersible tablet formulation of the fixed dose combination of abacavir, dolutegravir and lamivudine.

It was approved by the US FDA in March 2022. [2]

C O M M E N T

Paediatric HIV remains one of the global areas of unmet need. Only 52% of children (880k/1.3 million) are on ART and only 40% on ART are undetectable. [3]

WHO preferred first-line ART is already ViiV's fixed dose dispersible paediatric formulation of abacavir/lamivudine/dolutegravir (pALD), given without genetic HLA testing for abacavir hypersensitivioty. This is approved for weight 10 to 25 kg, with a plan to file for 6 kg lower weight. The US FDA approved different weight eligibility to the EU (down to 10 kg in US).

Originator products are rarely introduced in LMIC but CHAI and ViiV are working with generic manufacturers. Last I heard was filings are expected in the new year + tentative approval mid 2023. [3]

Given the wide use of dual ART without abacavir, the D3 study (PENTA 21) is also investigating DTG/3TC in children.

https://penta-id.org/hiv/d3

C O M M E N T

ViiV press release. ViiV Healthcare announces CHMP positive opinion for Triumeq PD, the first dispersible single tablet regimen containing dolutegravir, a once-daily treatment for children living with HIV in Europe. (16 December 2022).

viivhealthcare.com/hiv-news-and-media/news/press-releases/2022/december/viiv-healthcare-announces-chmp-positive-opinion-for-triumeq-pd

FDA approves dispersible dolutegravir/abacavir/3TC for children. HTB May 2022.

i-base.info/htb/42815

CHAI. Highlighting the latest updates in HIV treatment, prevention, and diagnostics

https://www.clintonhealthaccess.org/webinar/2022-hiv-market-report (report)

https://www.youtube.com/watch?v=GKay_ifczWE&t=70s (webinar)

Reference
1. ViiV press release. ViiV Healthcare announces CHMP positive opinion for Triumeq PD, the first dispersible single tablet regimen containing dolutegravir, a once-daily treatment for children living with HIV in Europe. (16 December 2022). https://viivhealthcare.com/hiv-news-and-media/news/press-releases/2022/december/viiv-healthcare-announces-chmp-positive-opinion-for-triumeq-pd
2. FDA approves dispersible dolutegravir/abacavir/3TC for children. HTB May 2022. https://i-base.info/htb/42815
3. CHAI. Highlighting the latest updates in HIV treatment, prevention, and diagnostics https://www.clintonhealthaccess.org/webinar/2022-hiv-market-report (report) https://www.youtube.com/watch?v=GKay_ifczWE&t=70s (webinar)

Early HIV diagnosis and treatment are important for better long-term health

NIAID press release

Starting antiretroviral treatment (ART) early in the course of HIV infection when the immune system is stronger results in better long-term health outcomes compared with delaying ART, according to findings presented at the IDWeek Conference in Washington, D.C. [1]

The findings are based on an extended follow-up of participants in the National Institutes of Health-funded Strategic Timing of Antiretroviral Treatment (START) study. In 2015, START demonstrated a 57% reduced risk of AIDS and serious non-AIDS health outcomes among participants who began ART when their CD4+ T-cell counts—a key indicator of immune system health—were greater than 500 cells per cubic millimeter (mm^3) compared with those who did not begin ART until either their CD4+ counts fell below 350 cells/mm^3 or they developed AIDS. [2]

Following the 2015 report of these findings, the participants in the deferred treatment arm were advised to begin ART.

Approximately, 1.2 million people in the United States are living with HIV, and roughly 13% do not know they are infected, according to the Centers for Disease Control and Prevention. When HIV diagnosis and treatment are delayed, HIV continues to replicate. This can negatively impact the infected individual's health and increase the risk of transmitting the virus to others.

The international START study proved the benefit of early ART initiation, but longer-term follow-up of 4,446 participants was undertaken to determine whether the health benefits of early ART compared with deferred ART increased, remained constant, or declined after the participants in the deferred arm were advised to begin ART. The primary study endpoints included the number of participants who developed AIDS; those who developed serious non-AIDS health conditions, such as major cardiovascular disease, kidney failure, liver disease and cancer; and those who died.

For participants who began ART before the end of 2015, the median CD4 cell count at the time of ART initiation was 648 cells/mm^3 for the immediate arm and 460 cells/mm^3 for the deferred arm. The analysis

presented in October 2022 compared the primary study endpoints before the end of 2015, with those in the extended follow-up period, from January 2016 to December 2021.

In the latter period, most deferred-arm participants were taking ART. During the second period, people initiating ART in the deferred group had rapid and sustained declines in HIV viral load (less than or equal to 200 copies/mL); however, CD4+ cell counts remained, on average, 155 cells lower compared with that of individuals in the immediate ART group. While the risk of serious health outcomes was substantially diminished soon after ART was initiated in the deferred treatment group, some excess risk remained compared with the immediate treatment group.

The deferred ART group continued to have a somewhat greater risk (21%) of serious health consequences or death in comparison to the immediate treatment group. Twenty-seven cases of AIDS occurred in the five-year follow-up period in the deferred treatment group compared with 15 cases in the early treatment group. Similarly, 88 cases of serious non-AIDS health issues occurred in the deferred treatment arm compared with 76 cases in the immediate treatment arm. Lastly, there were 57 deaths in the deferred treatment group compared to 47 in the immediate treatment arm.

These findings confirm that ART significantly improves the health of an individual with HIV and reduce the person's risk of developing AIDS and serious health issues, and that early diagnosis and treatment are key to maximizing these benefits and reducing risk, according to the presenters.

The START study and its extended follow up was conducted by the International Network for Strategic Initiatives in Global HIV Trials (INSIGHT), funded in part by the National Institute of Allergy and Infectious Diseases (NIAID), part of NIH. It was led by principal investigator James D. Neaton, Ph.D., of the University of Minnesota, Minneapolis, and START study co-chairs Abdel Babiker, Ph.D., of the University College London, and Jens Lundgren, M.D., of the University of Copenhagen.

C O M M E N T

This additional follow-up from the START study produces a unique dataset that supports the importance of early ART.

Even though the statistical significance of these results is not reported the numerical trend clearly favours earlier diagnosis and treatment of HIV.

The percentage of people diagnosed late is also much higher at >40% in the UK and most other countries. [3]

Source

NIAID press release. Early HIV diagnosis and treatment important for better long-term health outcomes. (2 November 2022).
https://www.hiv.gov/blog/early-hiv-diagnosis-treatment-important-better-long-term-health-outcomes

References

1. Babiker A for the START study writing group. Long term benefits from early antiretroviral therapy initiation in HIV infection: findings from the extended follow up of the START trial. IDWeek, 22 October 2022, Washington DC.
2. The INSIGHT START Study Group. Initiation of Antiretroviral Therapy in Early Asymptomatic HIV Infection, N Engl J Med 2015; 373:795-807. DOI: 10.1056/NEJMoa1506816
   ttps://www.nejm.org/doi/full/10.1056/nejmoa1506816
3. Collins S er al. Late diagnosis of HIV in 2022: Why so little change? HIV Med. 2022; 23(11): 1118–1126. doi: 10.111/hiv.13444.

TREATMENT ACCESS

CHAI 2022 report on global access to ART

Simon Collins, HIV i-Base

On 13 November 2022, Clinton Health Access Initiative (CHAI) published their annual global HIV market report, with UNITAID and the Bill & Melinda Gates Foundation.

These organisations continue to playing a leading role in global access by using economies of scale and bulk purchasing agreements to negotiate lower prices for better HIV medicines in lower and middle-income copuntries (LMICs).

Globally, 95:95:95 targets by 2025 at 88:90:92, with COVID-19 leading to fewer HIV tests for 2019 and 2020.

Key highlights include:

- Only 52% of children are on ART (880,000/1.7 million) compared to 76% adults in LMICs.
- Only 40% on ART have undetectable viral load
- There are still 160,000 new paediatric infections each year
- Only 30% of children in LMICs access early infant diagnosis (EID) - and many children with positive results are lost to care within the next year..
- 98,000 children died of HIV-related causes.
- Undiagnosed syphilis during pregnancy still causes 200,000 preventable stillbirths or newborn deaths.
- Deaths from advanced HIV (AHD) are not dropping quickly enough. Although 650,000 people (11% children) died of AHD in 2021, this is only 6% per esch year compared to the 20% annual drop needed to reach the 2025 target of 200,000.
- One-third of deaths are related to TB (incluiding 11% of children).
- COVID-19 disproportionally affects people living with HIV, but by July 2022, only 21% of people in Africa had completed a primary course of vaccines (and coverage wanes after 6 months). CHAI and partners negotiated for a course of Paxlovid to be available for high risk patients at $25.
- Continued investment is still needed to enable access to latest and upcoming HIV drugs. Most people globally are treated with generic medicines which has a market of US$1..2 billion.
- Generic TLD (tenofovir D/lamivudine/dolutegravir) is now available for less than US$ 50 per year using 6-monthly 180-pack cartonless packs. (By comparison, people living in the US are often still restricted to having to get a new prescription every month).
- 80% of people in LMICs now use DTG-based ART, although differentiation between first/second-line and adult/paediatric data are unclear, making monitoring difficult.
- Generic darunavir/ritonavir (400/50 mg) is now US$ 17.50 per month. This is less than lopinavir/r although WHO still lists LPV/r as a second-line option). This is WHO approved but not available for PEPFAR because it is expected to be FDA prequalified until 2024.
- Generic paediatric dolutegravir is US$ 4.50 for 90-pill pack.
- HIV self-testing now US$ 1.00 per test for public purchasing in 140 LMICs including a dual HIV/syphilis test.
- Generic TDF/FTC for oral PrEP is US$ 4.00 a month.
- Point-of-care CD4 test to diagnose advanced HIV (Visitect, with a 350 c/mm3 threshold) is < US$ 4.00 and availabvle for publicpurchasing in 130 LMOCs.
- Low pricing agreements have also been negotiated for TB preventative treatment preventive therapy three-month weekly rifapentine and isoniazid (3HP) and one-month daily rifapentine and isoniazid (1HP)..

- Access programmes for liposomal amphotericin B (L-AmB) for cryptococcal meningitis are also being developed. This includes the important example of an FDA-approved generic biosimilar formulation of a liposomal nanomedicine.

Information is also included on long-acting cabotegravir and rilpivirine. Also for lenacapavir and islatravir, although neither compound has been included in a generic access option.

The report also highlights increases in global uptake of PrEP and developments for access to injectable PrEP.

References
CHAI 2022 HIV Market Report: The state of the HIV market in low- and middle-income countries

https://www.clintonhealthaccess.org/webinar/2022-hiv-market-report (report)

CHAI. Highlighting the latest updates in HIV treatment, prevention, and diagnostics

https://www.youtube.com/watch?v=GKay_ifczWE&t=70s (webinar)

PREVENTION

Cabotegravir-LA submitted to EMA for use as PrEP in Europe

Simon Collins, HIV i-Base

On 28 October 2022, ViiV Healthcare announced that the European Medicine's Agency had registered it's application for cabotegravir-LA (CAB-LA) to be used as PrEP.

CAB-LA is a long-acting formulation that is given by intramuscular injection every two months to prevent HIV transmission, irrespective of condom use.

The application is largely based on results from two large international phase 3 studies called HPTN 083 and 084. Both studies randomised participants to either CAB-LA or to daily oral PrEP using TDF/FTC and reported significantly fewer people receiving CAB-LA became HIV positive. These results have previously been reported in HTB. [2, 3]

CAB-LA is already approved for PrEP in the US, Australia and, most-recently, Zimbabwe. [4]

It is marketed under the brand name Apretude.

C O M M E N T

This is important news. Submitting CAB-LA recognises that access in the EU is essential – and that ViiV want to find a European market for new PrEP formulations.

Although ViiV has previously stated a commitment to submitting for approval in the EU, regulatory documents were submitted first in South Africa, Malawi, Botswana, Brazil, Kenya, Uganda, Vietnam, Malaysia, Myanmar, Philippines and China. [5]

Access however is also dependent on having an affordable price, which in Europe will be compared to generic oral PrEP.

It is unclear how this will be reconciled with the significantly higher price for CAB-LA when used as treatment, not just in the EU but in all regions. In the US, CAB-LA for PrEP is currently listed at $22,000 pa,

The lack of an effective market for high-priced PrEP is the reason that Gilead cancelled their PrEP application for F/TAF (Descovy) in the EU. [6]

References

1. ViiV press release. European Medicines Agency validates ViiV Healthcare's marketing authorisation application for cabotegravir long-acting injectable for HIV Prevention. (28 October 2022).
   https://viivhealthcare.com/hiv-news-and-media/news/press-releases/2022/october/european-medicines-agency-validates-viiv-healthcare
2. Cabotegravir long-acting injections prevent HIV as PrEP. HTB (June 2020).
   https://i-base.info/htb/37961
3. Two-monthly cabotegravir injections prevent HIV infection in African women: HPTN 084 study recommends early unblinding. HTB (November 2020).
   https://i-base.info/htb/39327

4. ViiV press release. Progress in our commitment to enabling access to cabotegravir long-acting for hiv prevention, as first sub-Saharan African country approves Apretude. (Undated, but likely 20 October 2022).
https://viivhealthcare.com/hiv-news-and-media/news/company-statements/progress-in-our-commitment-to-enabling-access/
5. ViiV Healthcare. Worldwide registration: cabotegravir PrEP. [Accessed 28 October 2022]
https://viivhealthcare.com/content/dam/cf-viiv/viivhealthcare/en_GB/files/cab-prep-wwrs-10oct2022-for-external-use.pdf

COMPLICATIONS: MONKEYPOX

Updates and links to new studies on mpox

Simon Collins, HIV i-Base

The following links are to selected news and research about mpox.

WHO recommends mpox as new name for monkeypox disease

On 28 November 2022, WHO recommended using mpox due to racist and stigmatizing language associated with the name monkeypox.

Both terms can continue to be used over the next year as monkeypox is being phased out.

The new name involved broad consultation as part of the International Classification of Diseases (ICD), usually a process that takes several years.

"The issue of the use of the new name in different languages was extensively discussed. The preferred term mpox can be used in other languages. If additional naming issues arise, these will be addressed via the same mechanism. Translations are usually discussed in formal collaboration with relevant government authorities and the related scientific societies.

WHO will adopt the term mpox in its communications, and encourages others to follow these recommendations, to minimise any ongoing negative impact of the current name and from adoption of the new name."

Ref: WHO News release. WHO recommends new name for monkeypox disease. (28 November 2022).

https://www.who.int/news/item/28-11-2022-who-recommends-new-name-for-monkeypox-disease

Waning infections but still a need to understand implications of mutations

This editorial in JID reviews genetic evolution of mpox during the current global outbreak and includes a caution over the potential for later outbreaks, even though current numbers have dropped in most countries.

Ref: Kohli RM et al. Has the current monkeypox outbreak revealed a pox on 'U'?, Journal of Infectious Diseases, 2022; jiac471, https://doi.org/10.1093/infdis/jiac471

US CDC recommend early use of tecovirmat to treat mpox in people living with HIV especially if not on ART

This paper from the US CDC includes details of people liviniong with HIV.

"During August–October 2022, CDC *provided clinical consultation for 57 hospitalised patients with severe manifestations of monkeypox, most of whom were Black men with AIDS. Delays were observed in initiation of monkeypox-directed therapies. Twelve patients died, and monkeypox was a cause of death or contributing factor in five patients to date, with several other deaths still under investigation."*

Ref: Miller MJ et al. Severe monkeypox in hospitalized patients — United States, August 10–October 10, 2022. MMWR Morb Mortal Wkly Rep. ePub: 26 October 2022. DOI: 10.15585/mmwr.mm7144e1.

https://www.cdc.gov/mmwr/volumes/71/wr/mm7144e1.htm

MPX in women and people who are non-binary

This international collaboration that published the largest cohort of mpox cases early in the epidemic presents greater details on the data on 136 individuals with mpox who presented between May and October 2022, across 15 countries.

The cohort comprised 62 trans women, 69 cis women, and five non-binary individuals (who were, because of small numbers, grouped with cis women to form a category of people assigned female at birth for the purpose of comparison).

"The clinical features of monkeypox in women and non-binary individuals were similar to those described in men, including the presence of anal and genital lesions with prominent mucosal involvement. Anatomically, anogenital lesions were reflective of sexual practices: vulvovaginal lesions predominated in cis women and non-binary individuals and anorectal features predominated in trans women. The prevalence of HIV co-infection in the cohort was high."

Ref: Thornhill JO et al. Human monkeypox virus infection in women and non-binary individuals during the 2022 outbreaks: a global case series. The Lancet. DOI: 10.1016/S0140-6736(22)02187-0. (17 November 2022).
https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)02187-0/fulltext

UK study reports mpox transmission before symptoms

A UK study reported significant monkeypox transmission before symptoms appear or are detected (known as pre-symptomatic transmission).

Transmission was detected up to a maximum of four days before the onset of symptoms, and the researchers estimate that more than half (53%) of transmission occurred in this pre-symptomatic phase, meaning that many infections cannot be prevented by asking individuals to isolate after they notice their symptoms.

However this was a very small study and with only a small number of transmission pairs with sufficient data.

References

1. Ward T et al. Transmission dynamics of monkeypox in the United Kingdom: contact tracing study. BMJ 2022;379:e073153. doi: 10.1136/bmj-2022-073153. (2 November 2022).
   https://www.bmj.com/content/379/bmj-2022-073153
2. Freeman EE. The dynamics of monkeypox transmission. BMJ 2022;379:o2504. doi: 10.1136/bmj.o2504. (02 November 2022).
   https://www.bmj.com/content/379/bmj.o2504

Replication competent mpox only detected at high viral load levels: implications for sexual transmission

"In immunocompetent patients with mild monkeypox disease, PCR data alone would suggest a contact isolation period of 3 to 6 weeks but, based on detection of replication-competent virus, this time could be reduced. Based on findings from this cohort of patients, semen testing and prolonged use of condoms after recovery from monkeypox might not be necessary."

Ref: Suñer C et al. Viral dynamics in patients with monkeypox infection: a prospective cohort study in Spain. Lancet Inf Dis. DOI: 10.1016/S1473-3099(22)00794-0. (12 December 2022).

https://doi.org/10.1016/S1473-3099(22)00794-0

TREATMENT GUIDELINES

BHIVA 2022 ART guidelines: online with non-technical summary

Simon Collins, HIV i-Base

The 2022 antiretroviral therapy (ART) guidelines are now online, together with a non-technical summary. [1, 2]

They provide guidance on best clinical practice for ART and management of adults living with HIV.

The scope includes:

- Starting ART in those previously naïve to therapy.
- Support for people already on ART.
- Management of viral rebound.
- Changing ART for tolerability and/or toxicity issues.
- Recommendations for specific populations where other factors are important.

The guidelines are written for healthcare professionals directly involved with and responsible for the care of adults living with HIV, community advocates responsible for promoting the best interests and care of adults living with HIV, and people living with HIV for whom a non-technical summary is also available, if preferred.

They should be read in conjunction with other published BHIVA guidelines.

BHIVA also publishes the consultation comments received to the first draft of these guidelines and the responses from the guideline panel. [3]

References
1. BHIVA guidelines on antiretroviral treatment for adults living with HIV-1 2022
https://www.bhiva.org/HIV-1-treatment-guidelines
2. Non-technical community summaries.
https://www.bhiva.org/HIV-1-treatment-guidelines
3. BHIVA. Consultation comments on the initial draft and panel responses.
https://www.bhiva.org/file/635139fadbc5e/consultation-comments.pdf (PDF)

National HIV prescribing for England 2022: algorithms and policies

BHIVA

BHIVA have posted the following documents related to the reorganised structure for national HIV prescribing in the UK.

https://www.bhiva.org/NHSE-prescribing-documents

These changes were planned to have been launched announced much earlier in the year.

One main outcome is to provide equal access to ART throughout England, irrespective of HIV Trust or clinic.

Commissioning documents for health providers

National antiretroviral treatment prescribing toolkit

HIV CRG Drugs Subgroup (February 2022)

HIV National Prescribing Guide

Complex and Non Commissioned Regimens

HIV National Prescribing Guide

BHIVA-recommended regimens

Non-technical resources for people living with HIV

ART prescribing implementation toolkit on generics

Patient Information Leaflet: Generics (February 2022)

ART) prescribing implementation toolkit for prescribing ART

Patient Information Leaflet: Prescribing (February 2022)

National procurement for antiretrovirals for HIV treatment and prevention

Frequently Asked Questions (FAQ) for organisations supporting people living with HIV (September 2022)

National procurement for antiretrovirals for HIV treatment

Frequently Asked Questions (FAQ) for clinicians (July 2022)

https://www.bhiva.org/NHSE-prescribing-documents

EACS Guidelines update (2022)

EACS

The 11th edition of the EACS Guidelines for the management of people living with HIV in Europe were launched at the Glasgow HIV conference.

The English version is regularly updated by the guidelines panels with major revision every other year and minor revisions in the years in between. This year is a minor revision.

The EACS Guidelines are available in different formats: a PDF, a mobile app, and as a website. Translations are also available.

https://www.eacsociety.org/guidelines/eacs-guidelines (download page)

https://eacs.sanfordguide.com (interactive guide)

IAS–USA Guidelines on HIV Treatment and Prevention (2022)

IAS–USA

On 1 December 2022, the International Antiviral (formerly AIDS) Society–USA updated practice recommendations for managing HIV.

This includes:

- When to change ART.
- PrEP to prevent infection.
- Care of pregnant people with HIV during pregnancy.
- Care of people with substance use disorder and HIV.
- New challenges in people with HIV, including COVID-19 and mpox.

For some reason rhis document is only open access for one month on the JAMA website and requires a free account.

Reference

Antiretroviral Drugs for Treatment and Prevention of HIV Infection in Adults: 2022 Recommendations of the International Antiviral Society–USA Panel. JAMA. doi:10.1001/jama.2022.22246. (1 December 2022).

https://jamanetwork.com/journals/jama/fullarticle/2799240

ON THE WEB

Training webinar: 2nd HIV from A to Z

The 2nd EACS HIV:A to Z workshops are now available online.

This is a dynamic educational programme about the clinical management of HIV. The course includes 12 modules that will be available from September 2022 to August 2023.

It is primarily a resource and training for doctors, with talks given by global experts. As new modules are added, the earlier lectures will still remain available.

It is free and fully CME accredited.

Lectures will be available in English and Spanish.

- Link to access the webinar:

https://webinars.fls-science.com/courses/training-the-new-generation-of-hiv-physicians-eng

- Link to programme:

https://i-base.info/htb/wp-content/uploads/2022/10/Webinar-HIV-from-A-to-Z-Program.pdf (PDF)

MEETINGS & WORKSHOPS 2023

The following listing covers selected upcoming HIV-related meetings and workshops. Registration details, including for community and community press are included on the relevant websites.

Some meetings are in person, some are virtual and others offer both options.

Academic Medical Education (AME) meetings and workshops

Several AME workshops (previously Virology Education) are highlighted below but 35 meetings are planned each year. Many virtual meetings include free registrations for health workers, researchers and community.

https://academicmedicaleducation.com (meetings listings)

30th Conference on Retroviruses and Opportunistic Infections (CROI 2023)

19 – 22 February, 2023, Seattle

www.croiconference.org

BHIVA Annual Conference 2023

24 – 26 April 2023, Gateshead, UK

www.bhiva.org

12th IAS Conference on HIV Science

23 – 26 July 2023, Brisbane, Australia

https://iasociety.org

19th European AIDS Conference (EACS 2023)

18 – 21 October 2023, Warsaw, Poland

www.eacsociety.org

5th HIV Research for Prevention Conference (R4P 2023)

22 – 26 October 2023, Lima, Peru, and virtual.

www.iasociety.org/conferences/HIVR4P2023

6th Southern African HIV Clinicians Society Conference (SAHCS 2023)

8 – 10 November 2023, Cape Town, South Africa

www.sahcsconference.co.za

PUBLICATIONS & SERVICES FROM i-BASE

i-Base website

All i-Base publications are available online, including editions of the treatment guides.

http://www.i-Base.info

The site gives details about services including the UK Community Advisory Board (UK-CAB), our phone service and Q&A service, access to our archives and an extensive range of translated resources and links.

Publications and regular subscriptions can be ordered online.

The Q&A web pages enable people to ask questions about their own treatment:

http://www.i-base.info/qa

i-Base treatment guides

i-Base produces six booklets that comprehensively cover important aspects of treatment. Each guide is written in clear non-technical language. All guides are free to order individually or in bulk for use in clinics and are available online in web-page and PDF format.

http://www.i-base.info/guides

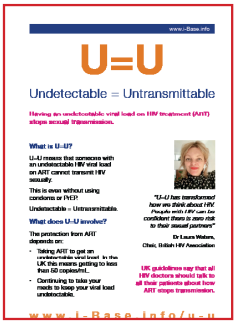
- Introduction to ART (May 2022)
- HIV & quality of life: side effects & long-term health (Sept 2016)
- Guide to PrEP in the UK (February 2022)
- HIV testing and risks of sexual transmission (June 2021)
- Guide to changing treatment and drug resistance (August 2021)
- Guide to HIV, pregnancy & women's health (April 2019)

Pocket guides

A series of pocket-size concertina folding leaflets that are designed to be a very simple and direct introduction to HIV treatment.

The five pocket leaflets are: Introduction to ART, HIV and pregnancy, ART and quality of life, UK guide to PrEP and HCV/HIV coinfection.

The leaflets use simple statements and quotes about ART, with short URL links to web pages that have additional information in a similar easy format.



U=U resources for UK clinics: free posters, postcards and factsheets

i-Base has produced a new series of posters, postcards and leaflets to help raise awareness about U=U in clincs.

This project was developed with the Kobler Centre in London.

As with all i-Base material, these resources are free to UK clinics.

Until our online order form is updated to include the U=U resources, more copies can be orded by email or fax.

email: subscriptions@i-base.org.uk

Customise U=U posters for your clinic

i-Base can customise U=U posters to include pictures of doctors, nurses, pharmacists, peer advocates or any other staff that would like to help publicise U=U.

Personalising these for your clinic is cheap and easy and might be an especially nice way to highlight the good news.

For further information please email: subscriptions@i-Base.org.uk

h-tb

HIV TREATMENT BULLETIN

HTB is published in electronic format by HIV i-Base. As with all i-Base publications, subscriptions are free and can be ordered using the form on the back page or directly from the i-Base website:

http://www.i-Base.info

by sending an email to: subscriptions@i-Base.org.uk

Editor: Simon Collins

Contributing Editor: Polly Clayden

HIV i-Base, 107 The Maltings,169 Tower Bridge Road, London, SE1 3LJ. T: +44 (0) 20 8616 2210. F: +44 (0) 20 8616 1250

http://www.i-Base.info

HIV i-Base is a registered charity no 1081905 and company reg no 3962064. HTB was formerly known as DrFax.

107 Maltings Place,169 Tower Bridge Road, London, SE1 3LJ
T: +44 (0) 20 7407 8488

Orders and subscriptions

Please use this form to amend subscription details for HIV Treatment Bulletin and to order single or bulk copies of publications. All publications are free, but donations are always appreciated - please see the form on the previous page.

Name _____ **Position** _____

Organisation _____

Address _____

_____

Telephone _____ **Fax** _____

e-mail _____

☐ I would like to make a donation to i-Base - *Please see inside back page*

- **HIV Treatment Bulletin (HTB) every two months** ☐ **by e-mail**
- **Pocket leaflets** - *A7 small concertina-folded leaflets (2017)*

  Pocket HCV coinfection quantity _____ **Pocket PrEP quantity** _____

  Pocket ART quantity _____ **Pocket pregnancy quantity** _____

  Pocket side effects quantity _____ **PrEP for women quantity** _____

- **Booklets about HIV treatment**

  Introduction to ART*: 44-page A5 booklet* **quantity** _____

  UK Guide To PrEP*: 24-page A5 booklet* **quantity** _____

  ART in pictures: HIV treatment explained*: 32-page A4 booklet* **quantity** _____

  Guide to HIV, pregnancy and women's health: *36-page A5 booklet* **quantity** _____

  Guide to changing treatment*: 16-p A5 booklet* **quantity** _____

  HIV and quality of life: side effects and long-term health*: 96-page A5* **quantity** _____

  Guide to HIV testing and risks of sexual transmission *52-page A5 booklet* **quantity** _____

- **Other resources**

  U=U resources:

  A3 posters quantity _____ **A5 leaflets quantity** _____ **A6 postcards quantity** _____

  HIV Treatment 'Passports' - Booklets to record your HIV medical history **quantity** _____

  Phoneline *posters (A4)* **quantity** _____

Please post to the above address, or email a request to HIV i-Base:

subscriptions@i-Base.org.uk