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hiv treatment bulletin (e)

AIDS 2022 and MPX responses (3 October 2022)

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Introduction to ART: i-Base guide (June 2022)

The widely used i-Base guide to ART has been updated to include recommendations in the 2022 BHIVA guidelines.

Both online and print versions are now updated.

This guide covers information for people newly diagnosed, those about to start ART, and also those who have been living with HIV for many years and who want to learn more about treatment.

https://i-base.info/guides/starting

PrEP for women (June 2022)

A new leaflet about PrEP produced by and for women (with the Sophia Forum).

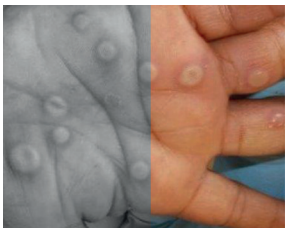
These small 16-page A7 leaflets were produced to raise awareness of access to PrEP.

Translations into key European and African languages are online and will be included on this page when available.

https://i-base.info/htb/43453

EDITORIAL

This issue of HTB includes further reports from the 24th International AIDS Conference (AIDS 2022) and the International Paediatric HIV Workshop, both held in Montreal.



Notable news includes first PK data using a paediatric combination of dolutegravir with TAF-based backbone.

We also include another special report on monkeypox (MPX) (our fifth this year) with another six articles later in the issue. The importance of the continued focus on MPX is because more than 40% of cases have been reported in men who are living with HIV. This has been reported as a potential factor for hospitalisations out other worse outcomes in some cohorts (notably in the US).

Other news includes that research into islatravir as a novel HIV treatment will now restart although not for HIV prevention, which will move to a second-generation compound called MK-8537.

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

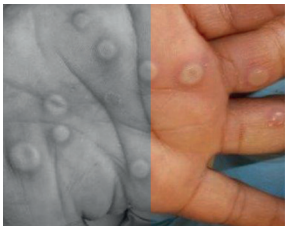
This page including 14 organisations that are helping people affected by the crisis in Ukraine.

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

SPECIAL REPORT: MONKEYPOX IN THE UK

Monkeypox into Autumn: still no emergency funding, vaccine efficacy and UK cancels vaccine orders

Simon Collins



This is the fifth consecutive issue of HTB to include a special report that summarises developments about monkeypox (MPX) in the UK and introducing additional articles.

Each report has covered the remarkable responses from sexual health services and community organisations that unfortunately contrast to that from the UK government.

MPX continues to be an infection that is affecting gay and bisexual men and disproportionately affecting those who are living with HIV.

The good news is that MPX cases have been rapidly dropping since August. The latest UK epidemiology report dated October reports 3673 confirmed or likely cases since May 2022, with the majority in England (only 46, 94 and 34 are reported in Wales, Scotland and Northern Ireland, respectively). [1]

The notifiable disease register list only 13 cases in England for the week ending 16 October, and steadily reducing numbers for each of the previous five weeks (62, 45, 25, 25, 20, respectively). [2]

This is likely due to several reasons. One is that during the summer many gay and bisexual men changed their levels of personal risk – generally limiting situations where MPX is most easily transmitted. Another is likely to due immune responses developed by those who were exposed to, and then cleared MPX. A third is hopefully due to the impact of MPX vaccination, even though most people have only received a single shot of the two-dose recommended schedule.

However, the studies reporting fewer infections in people who have been vaccinated, are all based on retrospective observational data in a population where significant behavioural differences would be expected in the vaccinated group. Many of those who were vaccinated were actively health-seeking who might have initially been at low risk – and they might also be avoiding risk now while waiting for a second shot.

These include an MMWR study of 5,402 cases in men aged 18 to 49 years old where MPX was 14-fold more likely in those who were unvaccinated. [3]

A second US study, published as a research letter in JAMA, reported 90 MPX cases from a cohort of 7339 people who had received at least one MPX vaccine. Of these, 37 were diagnosed within the first week, 32 within the second and 13 during the third and fourth weeks post vaccination. [4]

While cautiously optimistic, both studies showed that infections still occur, especially in the few weeks after a single shot, but also several weeks after a second shot.

A small Israeli study, not yet peer reviewed, reported a 79% protective impact of vaccination, but only involved 18 cases: 3 vaccinated (>25 days after a single shot) and 15 unvaccinated, and with significant differences in baseline demographics between the two groups. [5]

In response to the limited supply of vaccines which ran out by mid-August, the UK has now adopted intradermal vaccination using the new supply delivered in late September. This is in an attempt to reach greater vaccine cover with single shots, with no announcement yet on receiving second doses.

It is therefore disturbing to hear that in October, Health secretary Thérèse Coffey rejected expert advice to order an additional 70,000 doses of the vaccine. [6]

This is even given the global demand for limited vaccines, currently supplied by a single company (Bavarian Nordic), the limited protection from single doses and that online slots for booking a first dose in London clinics are already over-booked. [7]

On 20 October, a new online vaccine appointment finder for the rest of England was launched that includes more than 100 clinics. Both sites currently only offer first vaccines. [8]

So far, second doses are only being offered in Manchester, through a third online portal. [9]

The accompanying information, however, refers to only expecting to vaccinate 100,000 people, including health workers. Many community organisations, including i-Base, believe this to significantly underestimate the numbers for what is now expected to be an endemic STI among gay and bisexual men.

Lower case numbers with challenge enrolment into the UK tecovirimat study. We include information about the UK PLATINUM study (also in the previous HTB) and encourage anyone diagnosed with MPX to enrol. No clinic visits are required but doctors need to email a standard referral than confirms MPX. There is only a short window period to prospectively collect information from a randomised study. [10]

Other MPX reports include a review of the most serious and complex cases referred to the US CDC. These include involvement of many major organ systems requiring specialist management and hospitalisation and a caution that the risk of severe outcomes might be higher in people with significantly reduced immune function, including having a CD4 count <200 cells/mm^3. They are a caution that MPX can be extremely serious and sometimes fatal. [11]

We also include letters from leading professional organisations involved in the frontline response to MPX that challenge the UK Government's refusal to acknowledge the exceptional impact on sexual health services which remain threatened unless supported with emergency funding. [12]

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CONFERENCE REPORTS

14th International Workshop on HIV & Pediatrics

27–28 July 2022, Montreal, Canada

The 14th International Workshop on HIV & Pediatrics was a hybrid meeting held just before AIDS 2022.

This is a very focused annual international workshop on the prevention and treatment of paediatric HIV infection.

The workshop materials (including programme, abstracts, slides and videos) are available at:

https://academicmedicaleducation.com/hiv-pediatrics-2022

The following meeting report is included in this issue of HTB.

- First paediatric pharmacokinetic data of dolutegravir in combination with a TAF-based NRTI backbone

First paediatric pharmacokinetic data of dolutegravir in combination with a TAF-based NRTI backbone

Polly Clayden, HIV i-Base

Dolutegravir (DTG) exposure in children was 20–30% lower when combined in ART regimens with tenofovir alafenamide (TAF) compared with standard of care. These data from a sub study of CHAPAS-4 were presented at the International Workshop on HIV & Pediatrics 2022.

DTG plus two NRTI, is the preferred treatment for children living with HIV. TAF is under investigation in this population but there are currently no pharmacokinetic (PK) data on DTG exposure when these drugs are given in combination. There are also limited data in children taking DTG with food.

CHAPAS-4 (Children with HIV in Africa: Pharmacokinetics and Acceptability of Simple novel second-line antiretroviral regimens) is a 96 week, randomised controlled trial in children aged 3–13 years (n=690) failing first-line ART. It compares TAF versus standard of care (SOC; abacavir or zidovudine) and DTG versus ritonavir-boosted protease inhibitors in a factorial design. The data presented were from a nested PK sub study.

DTG dosing is according to WHO weight bands: children weighing 14–19.9 kg, 25 mg as dispersible tablets and children >20 kg, 50 mg film-coated tablets with food. DTG concentrations were measured (LC-MS/MS method). Samples were at t=per-dose (0.5), 1, 2, 4, 6, 8, 12, 24 hours post DTG dose. The target C-trough was 0.32 mg/L.

Forty-one children taking DTG were included in this PK sub study: 21 (median 10.8 years and 28.5 kg) taking DTG plus SOC and 20 (median 10.9 years and 25.9 kg) taking DTG plus TAF.

Those taking DTG with SOC had (mean with coefficient of variation %): AUC0–24h 63.2 (32.6) h.mg/L and C-trough 0.9 (50.6) mg/L. Those taking DTG with TAF: AUC0–24h 48.5 (41.9) h.mg/L and Ctrough 0.7 (77.6) mg/L.

The AUC GM ratio TAF/SOC was 0.77 (90% CI: 0.63 to 0.93). The C-trough GM ratio TAF/SOC was 0.74 (90% CI: 0.54 to 1.01). DTG C-tough target was achieved with TAF in all but two children.

To evaluate the effect of food the investigators compared these data with that from the fasting ODYSSEY trial. They noted that DTG exposure increases 30–60% when taken with food. Also, that this sub study of CHAPAS-4 is the first DTG evaluation of fed children

They reported an AUC GM ratio (fed/fasted) of 1.02 (90% CI: 0.9 to 1.16). There was no difference in Cmax and Ctrough.

C O M M E N T

This sub-study shows exposure of DTG in combination with TAF in children to be 20–30% lower than with abacavir or AZT (SOC). These evaluations are important as TAF has been highlighted (including by Paediatric Antiretroviral Working Group [PAWG] of the WHO) as a possible NRTI option for children.

The investigators noted that the clinical relevance of this sub study has yet to be determined.

So far, the reduction in drug levels in children is not thought to be clinically significant, and this isn't seen in adults

As the main CHAPAS-4 study has still to be completed, viral load and safety data are not presently available. They also noted that the mechanism for the reduced DTG exposure with TAF is not clear.

The extra PK comparison of fed DTG in CHAPAS-4 versus fasted in ODYSSEY had several limitations including different trial schedule, not a randomised comparison and different sample schedule. The investigators concluded that they could not confirm a food effect in children on DTG exposure.

Reference

Bevers L et al. First pharmacokinetic data of dolutegravir in combination with a TAF containing backbone in children living with HIV. International Workshop on HIV & Pediatrics 2022. Hybrid Meeting Montreal, Canada. 27–28 July 2022. Oral abstract 1.

https://academicmedicaleducation.com/hiv-pediatrics-2022

CONFERENCE REPORTS

24th International AIDS Conference (AIDS 2022)

29 July to 2 August 2022, Montreal, Canada

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.

- Efficacy of DTG- vs EFV-based first-line ART in advanced HIV with CD4 <50 cells/mm^3
- Gender-affirming hormones, weight gain and ART

Efficacy of DTG- vs EFV-based first-line ART in advanced HIV with CD4 <50 cells/mm^3

Kirk Taylor, HIV i-Base

AIDS 2022 included results from an observational study conducted in five Brazilian cities comparing DTG- and EFV-containing ART therapy in 184 people who were treatment-naïve and diagnosed with advanced HIV. [1]

Data were collected prospectively for the DTG arm (2018 to 2021) and compared to retrospective data (2013 to 2016) for the EFV control arm. There were 92 participants in each arm and results were presented by Carlos Brites, from the University of Bahia. Salvator, Brazil.

The primary objective was to monitor efficacy of DTG- or EFV-containing regimens for people with advanced AIDS. 184 participants were randomised 1:1 to either 3TC/TDF/DTG or 3TC/TDF/EFV across five AIDS referral centres in Brazil. Inclusion criteria also included having CD4 count >50 cells/mm^3 and being diagnosed of AIDS-defining illness. These included pneumonia (n=64), oesophageal candidiasis (n=53), neurotoxoplasmosis (n=42) and tuberculosis (n=30).

Baseline demographics were similar in each arm. Participants in the DTG arm were female (32%) with median age 39 years (SD: 4.7). Median CD4 counts and viral load were 21 cells/mm^3 (IQR: 9 to 34) and 5.5 log copies/mL (5.1 to 5.9). In the EFV arm, 36% were females with median age of 37 years (SD: 5.4). Median CD4 counts and viral load at entry were 20 cells/mm^3 (IQR: 12 to 33) and 5.5 log copies/mL (5.1 to 5.9).

At week 48, viral load and CD4 count responses were both significantly better in the DTG vs EFV arms. HIV viral load was suppressed to <200 copies/mL in 74% vs 48% and to <50 copies/mL in 65% vs 45% in the DTG vs EFV arms respectively, (p<0.001). CD4 count increased to >200 cells/mm^3 in 45% vs 29% (p=0.03).

There were also 25% fewer deaths in the DTG arm (n=9 vs 12) although this was not statistically significant (HR: 0.70; 95%CI: 0.30 to 1.66). More males than females died during the trial (22% vs 10%, p=0.04). The leading causes of death were sepsis (38%) and neurotoxoplasmosis (24%).

DTG was also associated with significantly fewer side effects and treatment-related changes (1% vs 17%), p=0.001.

C O M M E N T

DTG is recommended by most treatment guidelines as first-line ART irrespective of CD4 count. However, data on responses in people with advanced HIV are limited as most trials enroll people with CD4 counts >200 cells/mm^3.

Even though this was not a randomised study and used historical controls, the results support the change in standard of care from EFV- to DTG-based first-line ART.

It is also useful to see the overall results from using DTG-based ART in such advanced HIV.

Although not strictly related to this study, the panel discussion afterwards asked about whether it is ethical to still use low-dose EFV 400 mg now that DTG is becoming widely available.

Dr Mireille Mpoudi Ngole from Cameroon stressed that access to EFV remains essential given the percentage of women in low-income settings who have significant wight gain with DTG which in some cases can be +20 kg within two years.

References

Brites C. Survival in advanced AIDS patients treated with efavirenz or dolutegravir in Brazil: a multicenter, observational study. ART in evidence. AIDS 2022 (Montreal). 29 July to 2 August 2022.

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

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AIDS 2022: Gender-affirming hormones, weight gain and ART

Kirk Taylor, HIV i-Base

An overview on gender-affirming hormone therapy, weight gain and ART presented by Emilia Jalil from FIOCRUZ, Brazil, included a report that trans women (TW) gain more weight on INSTI or TAF-based regimens than trans men (TM). [1]

This is important as transgender people have disproportionate risk of becoming HIV positive and are considered a priority group for prevention and care strategies. ART studies tend to recruit low numbers of trans participants and lack disaggregated trans data.

Approximately 50% of transgender people take gender-affirming hormones, with a further 30% having considered hormone therapy. TW receive anti-androgen plus oestrogen therapies that cause physical changes (ie reduced muscle mass and body fat redistribution), and favourable lipid profile changes.

Testosterone therapy for TM drives development of masculine secondary characteristics. Testosterone increases muscle mass, redistributes body fat, and worsens lipid profiles (raising LDL, cholesterol and triglycerides and lowering HDL).

Weight gain is associated with gender affirming hormones with increases seen within 4 months for TM and after 22 months for TW. TM report higher rates of obesity and weight gain.

Although many HIV drugs do not interact with hormone therapy, it is important to be aware of drug-drug interactions with some drugs and to consider potential adverse effects. Doctors need to understand these data in order to reduce the risk of altered adherence by trans people. [2]

The ADVANCE study reported weight gain in trans people using three commonly-used first-line combinations. At week-144, weight gain occurred with all regimens with the greatest increases observed for TW: TAF/FTC/DTG (+12.3 kg for TW vs +7.2 kg for TM) >TDF/FTC/DTG (+7.4 kg for TW vs +5.5 kg for TM) >TDF/FTC/EFV (+5.5 kg for TW vs +2.6 kg for TM). [3]

Although CAB-LA injections were not associated with weight gain in HIV negative participants in the HPTN 077 PrEP study, when used as treatment, injectable CAB-LA/RPV-LA in people living with HIV, weight increases were similar to dolutegravir-based ART. [4, 5]

More work is required to overcome knowledge gaps due to trials not enrolling enough trans people and/or lack of trans-specific analyses.

C O M M E N T

Liverpool University publish a comprehensive resource on potential drug interactions between ART and hormone treatment which is also updated id new data become available. [2]

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ANTIRETROVIRALS

Islatravir update: treatment studies to use a lower dose but PrEP research discontinued in favour of MK-8537

Simon Collins, HIV i-Base

On 29 September 2022, Merck announced that studies using the investigational NRTTI islatravir as HIV treatment will continue, but using a new lower dose. [1]

This will hopefully overcome the reduction in total lymphocyte and CD4 counts that led to most islatravir studies being stopped at the end of 2021. [2, 3, 4]

The earlier unexpected effect is now being explained by an accumulation of intracellular concentrations of islatravir triphosphate that will hopefully be avoided by using a reduced dose.

New studies will include:

- Phase 3 studies using once-daily oral islatravir plus doravirine as initial ART and as a switch therapy.
- Phase 2 research into once-weekly oral islatravir in combination with once-weekly oral lenacapavir (being developed by Gilead).

However, dose reductions are not appropriate for the longer-acting formulations of islatravir including a monthly oral tablet and an annual implant that were both being studied as PrEP. Instead, the company is planning to continue long-acting PrEP studies using MK-8527, a second NRTTI at an earlier stage of development, in the hope that it might have a different side effect profile and that this might not be a class effect.

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Low levels of RPV-LA might explain failure with injectable ART despite perfect adherence

Kirk Taylor, HIV i-Base

BHIVA guidelines caution that long-acting (LA) CAB/RPV regimens have virologic failures rates of 1 in 70 at 12 months, rising to 1 in 60 at 24 months. [1] Inter-person variability in PK parameters, especially of RPV-LA could be one explanation.

Early data from a sub-study of the Swiss HIV Cohort Study (SHCS) reports high inter-person variability in Cmin levels for CAB and RPV. [2] Whilst Cmin values were above their respective IC_{90} levels, some readings were close to this threshold prompting concerns about safety and efficacy. [1]

Therapeutic dose monitoring (TDM) can help to identify real-world variations in PK parameters to inform dosing and monitoring intervals.

The ATLAS-2M and FLAIR studies showed that LA-CAB/RPV can effectively manage HIV but real-world PK data is also required outside of stringent clinical studies. This prospective observational sub-study of the SHCS reports LA-CAB/RPV PK data in people living with HIV.

Most PK samples (84%) were collected prior to Q8W dosing when participants were expected to be close to Cmin levels. Blood samples were collected at routine visits (n=61) or during the oral lead-in period (n=30). In line with Swiss treatment guidelines, two participants that were on Q4W schedules transitioned to Q8W regimens.

Inter-participant variability of Cmin was reported as 101% and 94% for CAB and RPV, respectively. Intra-participant variability was significantly lower at 50% for CAB ($p=0.002$) and 27% for RPV ($p<0.0001$). The range of Cmin values for CAB and RPV were approximately 250 to 1,100 ng/mL and 18 to 300 ng/mL, respectively.

All reported PK values exceeded the IC90 values for CAB (166 ng/mL) and RPV (12 ng/mL). However, RPV levels were close to the IC90 for some participants, raising concerns of efficacy and safety.

Data collected up to July 2022 (n=46) were from participants that were female (17%), with median age of 45 years (range: 28 to 62), Caucasian (63%), Black (13%), Hispanic (7%) or Asian (7%). HIV viral load was below 200 copies/mL for all participants and <50 copies/mL (94%). Median CD4 counts 667 cells/mm^3 (range: 191 to 1192).

BHIVA guidelines indicate that obesity can be a risk factor for virologic failure on LA-CAB/RPV regimens. Median BMI was 26 kg/m^2 (range: 19 to 37) with 15% and 54% classified as obese or overweight, respectively.

Low grade adverse events, such as injection site reactions, were reported by 30% of participants. No virologic failures were reported.

C O M M E N T

Currently, based on the current BHIVA guidelines, a large proportion of people are contraindicated from using CAB-LA/RPC/LA due to obesity.

Although the risk of viral failure was lower with monthly dosing, the added inconvenience of more frequent injections makes this an unlikely choice, even if it was recommended in guidelines.

The study aims to enroll 200-300 people over the next two years.

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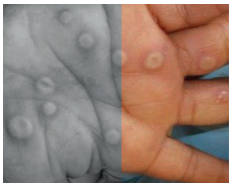
COMPLICATIONS: MONKEYPOX

Tecovirimat treatment for monkeypox in the UK: importance of the PLATINUM study

Simon Collins, HIV i-Base



The PLATINUM study in the UK is currently running in the UK for anyone diagnosed with mild-moderate monkeypox (MPX) and who is currently not being seen as an inpatient. [1]

Enrolment only requires a standard email from a doctor to confirm the MPX diagnosis.

No clinic visits are required and study meds are posted and responses are collected virtually.

Tecovirimat is the most promising antiviral against MPX and access outside this study is generally limited to severe cases that require hospitalisation.

Information about tecovirimat was included in the previous issue of HTB, also highlighting this study.

The reduced cases in the UK make enrolment into this study extremely important, in addition to offering potentially better treatment than the current standard of care.

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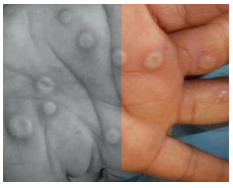
Levels of monkeypox viral load in different body sites supports highest risk from body contact

Simon Collins, HIV i-Base



The largest prospective study on the viral dynamics of monkeypox in multiple tissue types and samples provides an important dataset to help understand the relative risks of transmission. Skin and anal lesions were more likely to positive and at higher levels than other samples, including in semen where only half were positive and at much lower levels.

The study included 356 samples from skin, anus, throat, blood, urine, and semen in 50 men with monkeypox (MPX) attending the Pitié-Salpêtrière Hospital in Paris. It reported whether samples at diagnosis (and after 14 days in 24 men) were positive, using PCR cycle thresholds [Ct] to indicate viral load (lower Ct = higher viral load).

Participants were recruited during May and June 2022. Median age was 34 (IQR: 29 to 40) and 44% (22/50) men were living with HIV, all with undetectable viral load on ART except one new diagnosis. Skin samples were taken from the same lesion at both timepoints and anal and throat swabs were not taken from lesions, even if present. Baseline samples were taken a median of 5 days (IQR: 3 to 6) from symptoms.

The results showed highest levels of detection and at significantly higher viral load in skin and anal samples compared to throat, blood and semen. Viral load in anal swabs was significantly high in those with anal lesions (Ct 19·6 vs 25·3, p=0·0073). Similarly, viral load was also higher in semen samples of patients with genital lesions (Ct 26·3 vs 30·2, p=0·022).

At Day 14, only 6/24 participants with paired samples had Ct values <35.0. This included 4 skin samples, 2 anal samples and 2 semen samples.

Importantly, detection in all samples significantly declined in all samples by Day 14, see Table 1.

Table 1: MPV in different sites at Day 0 and 14

	Detection at D 0 % (n)	Viral load at D0 (Ct)	Detection at D 14 % (n)
skin	88% (44/50)	Ct 19·8	22% (4/18)
anus	71% (30/42)	Ct 20·9	9% (2/22)
throat	77% (36/47)	Ct 27·2	0 (0/21)
blood	29% (13/45)	Ct 32·8	5% (1/21)
urine	22% (9/41)	Ct 31·1	0 (0/14)
semen	54% (13/24)	Ct 27·8	9% (2/11)

Key: D = day, Ct = cycle of transmission.

These results led the researchers to conclude that high viral load in skin and mucosa, including genital and anal sites, suggest that transmission most likely occurs through direct body contact rather than through the respiratory route or contact with body fluids, and that transmission is also possible through kissing, oral sex and breathing.

C O M M E N T

This is the largest prospective study to report on viral dynamics of MPX and the results are helpful for suggesting a scale of relative risk based on type of exposure. One caution is that the threshold levels for infection are not known and these might vary for different types of exposure.

It would be helpful if future studies could continue beyond 14 days to understand whether risk continues after skin lesions have healed, notably in semen.

Other studies have reported positive DNA results in blood and semen, albeit at low rates. [2, 3]

However, even though isolation of MPX DNA from semen has been reported it is unclear whether this is a risk of transmission. [4, 5]

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3. Tarín-Vicente EJ et al. Clinical presentation and virological assessment of confirmed human monkeypox virus cases in Spain: a prospective observational cohort study. Lancet. 2022; 400: 661-669.
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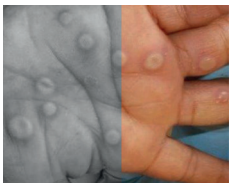
Severe complication of monkeypox reported to the US CDC: risks associated with HIV and other causes of immunosuppression

Simon Collins, HIV i-Base



Most cases in the current monkeypox (MPX) outbreak have been upsetting, difficult and are commonly painful, but still generally resolve within 2 to 4 weeks.

But there have been reports of extremely serious cases, including penile necrosis, amputation, the need for intensive care and approximately 30 deaths.

To highlight the range and severity of complications, the US CDC issued a health alert of cases that had been reported to them over up until September 2022. [1]

The alert highlight particular concern for people with significant immunosuppression related to HIV and other conditions, especially with low CD4 counts. However, severe cases are also reported in people who are HIV negative.

Examples of severe complications included but were not limit to the following conditions.

- Atypical or persistent rash with coalescing or necrotic lesions, or both, some which have required extensive surgical debridement or amputation of an affected extremity.
- Lesions on a significant proportion of the total body surface area, which may be associated with oedema and secondary bacterial or fungal infections among other complications.
- Lesions in sensitive areas (including mucosal surfaces such as, oropharynx, urethra, rectum, vagina) resulting in severe pain that interferes with activities of daily living.
- Bowel lesions that are exudative or cause significant tissue oedema, leading to obstruction.
- Severe lymphadenopathy that can be necrotising or obstructing (such as in airways).
- Lesions leading to stricture and scar formation resulting in significant morbidity such as urethral and bowel strictures, phimosis, and facial scarring.
- Involvement of multiple organ systems and associated comorbidities, including:
  - Oropharyngeal lesions inhibiting oral intake.
  - Pulmonary involvement with nodular lesions.
  - Neurologic conditions including encephalitis and transverse myelitis.
  - Cardiac complications including myocarditis and pericardial disease.
  - Ocular conditions including severe conjunctivitis and sight-threatening corneal ulcerations.
  - Urologic involvement including urethritis and penile necrosis.

C O M M E N T

Several reports to the MMWR include more details on neurological and ocular complications, including in people living with HIV with very low CD4 counts, sometimes not on ART. [2. 3]

Neurological complications are also reviewed in a paper in JAMA. [4]

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   https://www.cdc.gov/mmwr/volumes/71/wr/mm7142e1.htm
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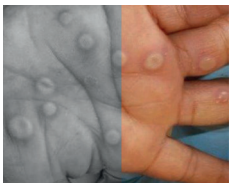
New reports on MPX vaccine efficacy suggest protection but cases are still reported after two shots

Simon Collins, HIV i-Base

As noted in the monkeypox (MPX) special report earlier in this issue of HTB, several analyses have reported fewer cases of MPX in people who have received a single shot of the MPX vaccine. [1]



However, although these results are tentatively optimistic, they are based on retrospective observational data in a population in which significant behavioural differences would be expected in the vaccinated group.

Many of those who were vaccinated could have been actively health-seeking and who were initially at very low risk. These people might also be avoiding risk now while waiting, for example, for a second shot.

These include an MMWR study of 5,402 cases in men aged 18 to 49 years old where MPX was 14-fold more likely in those who were unvaccinated. Among these, 4,606 (85%) were unvaccinated, 269 (5%) occurred ≤13 days a first shot, 77 (1.4%) ≥14 days after the first shot, and 450 (8.3%) had an unknown vaccination date. Of note, 14 cases were reported after a second shot (10 within 13 days and 2 more that 14 days after). [2]

A second US study, published as a research letter in JAMA, reported 90 MPX cases from a cohort of 7339 people who had received at least one MPX vaccine. Of these, 37 were diagnosed within the first week, 32 within the second and 13 during the third and fourth weeks post vaccination. However, 8 people were diagnosed more than four weeks after the first shot, including 2 cases more than three weeks after the second shot. [3]

These data support earlier i-Base reports to allow up to four weeks before relying on optimum vaccine protection and that infections are still possible two weeks after a second shot.

A small Israeli study, not yet peer reviewed, reported a similar protective impact of vaccination, but only involved 18 cases: 3/873 vaccinated (>25 days after a single shot) and 15/1097 unvaccinated (40 versus 6.4 per 100,000 person days). However, in addition to not being able to adjust for MPX risk, there were significant differences in baseline demographics between the two groups. [4]

The time to diagnosis in the three cases in the vaccination group was also interesting. Although the paper reports this as being more than two weeks after vaccination, the authors don't allow for the incubation period. Also, the incidence of MPX in Israel didn't show any overall declines in the period after the vaccines.

More cautious results from a study that measured antibody responses after MPX vaccination, also published as a pre-print before peer review, suggested that third doses might be needed. [5]

C O M M E N T

Results are cautiously optimistic - certainly better than if they were the other way round.

Observational data will be all we have for a while, so this is useful. If patterns of vaccine uptake were similar to London, for example, these results could easily just be a marker for health-seeking behaviour from men who are at lower overall risk. This is especially in studies where there were very few infections overall.

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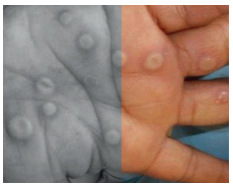
Other monkeypox studies of interest

Simon Collins, HIV i-Base

Although not summarised in detail, links are included as signposts to the following important resources and publications.



US CDC Science brief: updated research on MPX transmission

A comprehensive health briefing from the US CDC updates latest research about detection and transmission of MPX.

US CDC. Science brief: Detection and transmission of monkeypox virus. (18 October 2022).

https://www.cdc.gov/poxvirus/monkeypox/about/science-behind-transmission.html

Intradermal vaccination for monkeypox — benefits for individual and public health

This perspective article in the NEJM outlines the importance of using intradermal vaccine delivery for the MPX vaccine.

Ref: Brooks JT. Intradermal vaccination for monkeypox — benefits for individual and public health. N Engl J Med 2022; 387:1151-1153. DOI: 10.1056/NEJMp2211311. (29 September 2022).

https://www.nejm.org/doi/full/10.1056/NEJMp2211311

Review of 546 MPX cases in German outbreak

Results from a retrospective study of all confirmed cases from May to 30 June 2022 from 42 centres.

The paper included clinical characteristics, comorbidities, and coinfections, including HIV, viral hepatitis, and sexually transmitted infections (STIs).

All cases were in gay men: 47% were living with HIV and 42% were taking PrEP. Median age was 39 (range: 20 to 67).

Ref: Hoffmann C et al. Clinical characteristics of monkeypox virus infections among men with and without HIV: A large outbreak cohort in Germany. (4 September 2022).

https://onlinelibrary.wiley.com/doi/full/10.1111/hiv.13378

Positive anorectal swabs in men with and without proctitis

This paper in CID on 18 gay men (10/18 were HIV positive) with MPX reported positive MPX DNA swabs in 9/9 with and 7/9 without proctitis. Testing was taken after a mean 4.6 days (range 1-8) after first symptoms.

Both the negative cases had received the MPX vaccines before symptoms.

All 9/9 participants with follow up had negative swabs taken a mean of 26 days from initial symptom onset (range 21 to 32), including six men who presented with protitis.

Ref: Meyerowitz EA et al. Anorectal testing for monkeypox virus infection in men who have sex with men with and without proctitis, Clinical Infectious Diseases, 2022; ciac825. (13 October 2022).

https://doi.org/10.1093/cid/ciac825

Monkeypox cases in children and infants including neonatal case

The US CDC has reported 27 confirmed cases of MPX in children aged **0** to **15 years**. [1]

Details of the complications and management of an infant <2 months old are detailed in a separate report. [2]

A UK case of perinatally acquired MPX and adenovirus coinfection in a 10-day-old infant was reported in a letter to the NEJM. [3]

The baby developed a rash nine days after birth. The likely route of inadvertent transmission was identified by the father have a disseminated rash nine days before the birth and the mother developing a rash four days after the birth. The baby was transferred to neonatal intensive care on day 15 and discharged after four weeks after recovery.

References
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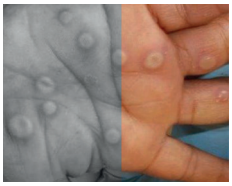


Monkeypox in pregnancy

A review in Lancet Infections Diseases that includes ten cases of MPX in pregnancy during the current outbreak. Luckily none have be severe but the articles highlights the importance of an international registry of cases.

Ref: Khalil A et a. Monkeypox in pregnancy: update on current outbreak Lancet Inf Dis. DOI: 10.1016/S1473-3099(22)00612-0. (14 September 2022).
https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00612-0/fulltext?dgcid=raven_jbs_aip_email

Monkeypox: challenging clinical questions

A free webinar from the Annals of Internal Medicine that includes three MPX case studies and a useful panel discussion.

https://www.acpjournals.org/doi/10.7326/M22-3040

Occupational needlestick MPX infection: single lesion despite vaccine

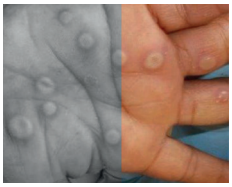
A case report published in the US MMWR included a health worker who developed MPX after recapping a needle (even though it recommended to not do this). The worker received a single shot of the MPX injection 16 hours after the exposure. However, 10 days later, a single PCR-confirmed MPX lesion occurred at the injury site.

Ref: Mendoza R et al. Monkeypox virus infection resulting from an occupational needlestick — Florida, 2022. MMWR Morb Mortal Wkly Rep. ePub: 17 October 2022.

http://dx.doi.org/10.15585/mmwr.mm7142e2

BHIVA, BASHH and others publish open letters on UK government response to monkeypox crisis

Simon Collins, HIV i-Base



On 8 October 2022, leading organisations responsible for providing frontline sexual health services wrote two open letters to highlight the lack of emergency support over the monkeypox (MPX) crisis.

Since May 2022, these services have dealt with more than 3,500 cases in this outbreak, without any additional support to either manage infections or provide an emergency vaccine programme.

The first letter, sent to Department of Health and Social Care (DHSC) and the UK Health Security Agency questions their refusal to recognise the impact of MPX and includes further evidence that, in some clinics, 30% of other sexual health services have been displaced due to the lack of financial support for MPX.

This has reduced access to services including PrEP, contraceptive and STI testing and treatment. This has led to new STI outbreaks. It has also further destablised clinics economically by losing more than £600,000 in income due to displaced commissioned services. The limited funding promised for delivering vaccines has neither arrived or expected to cover the actual cost of these services.

This is another example of how fragmenting national health responses leads to poorer care.

Monkeypox is an exceptional and unpredicted crisis that in the responsibility of the NHS, including for vaccination. The response however is being met by sexual health clinics that are funded and commissioned by local authorities.

The second letter is a plea to commissioners and providers not to withdraw funding. It includes further details on the impact of MPX on commissioned services. Examples include that more than 90% of sexual health services have been affected and the more than 50% of PrEP clinics have suffered reductions of 25% in services.

Both letters are published in full in the online edition of HTB and are hyperlinked in the PDF version of HTB.

For further information, please contact bhiva@bhiva.org. For media enquiries, please contact Jo Josh at jo@commsbiz.com or +44 (0)7306 391875.

References
1. Joint letters on monkeypox crisis. (6 October 2022). https://www.bhiva.org/joint-letters-on-monkeypox
2. Joint letter to DHSC and UKHSA. Monkeypox – impact of unfunded monkeypox (MPX) activity on sexual health and HIV. (6 October 2022). https://www.bhiva.org/file/633eed1de62e2/Joint-letter-to-DHSC-and-UKHSA.pdf (PDF)
3. Joint letter to commissioners and providers. Displacement of Sexual Health and Sexual and Reproductive Health Activity by Monkeypox (MPX). (6 October 2022). https://www.bhiva.org/file/633eed194a554/Joint-letter-to-commissioners-and-providers.pdf (PDF)

Joint letter to DHSC and UKHSA. Monkeypox – impact of unfunded monkeypox (MPX) activity on sexual health and HIV.

To: Dr Jeanelle de Gruchy, Deputy Chief Medical Officer, Office of Health Improvement and Disparities Department of Health and Social Care.

Dame Jenny Harries, Chief Executive UK Health Security Agency.

Steve Russell, National Director of Vaccination and Screening, NHS England/Improvement

cc.
Susan Hopkins Chief Medical Adviser, UK Health Security Agency.

Partner Agencies in the roundtable of Friday 23 September 2022.

Matthew Taylor, Chief Executive, NHS Confederation

Dear Colleagues

Monkeypox – impact of unfunded monkeypox (MPX) activity on sexual health and HIV

This letter is jointly sent, further to the meeting on 23 September 2022. Together our organisations provide, commission and represent the professionals leading the services which are the front-line for assessment, response and care of those experiencing the highest burden of preventable morbidity in the current outbreak.

As you know, the meeting on 23 September 2022 agreed we need to reconvene because we did not have sufficient time to consider the issues we raised. We are writing

1. To summarise our position.
2. To offer our further evidence of impact.
3. To appraise you of concerns raised by providers and commissioners with us in the last few days.
4. To ask for a further urgent meeting to resolve these issues.

Level of displacement of activity

We have made clear in repeated fora that unfunded monkeypox clinical assessment and treatment activity in sexual health clinics has been displacing routine sexual health testing, assessment, treatment and other clinical activity. We have stated clearly that this represents 25-30% of activity displacement in many clinics across the country. You will recall that BASHH provided evidence from clinics that this was the case.

We now have further evidence that this is the case. Activity data collated by Commissioners from Provider Trusts has established that in those areas most impacted by MPX displacement of routine sexual health activity is running at 30%. We are happy to supply this to you.

We have had repeated requests from government for verification of our statements. In our view we have provided this on more than one occasion, without result. At this juncture, we feel it right to point out that government does have access to data which would confirm the situation we now find ourselves in.

It would, we suggest, be a relatively straightforward task to collate positive for MPX (using GUMCAD and other data

sources), and then use this as the basis of a cost and resource assessment for cases, linked to the costings work which BASHH undertook and which was shared with you some time ago. That would at least provide a basis from operational data.

Impact of the displacement and Situation coming to light during the week beginning 26 September 2022

It has become clear during this week from provider data submitted to commissioners as part of routine activity monitoring that a number of providers have seen a drop in core work in sexual health activity of 30% over several months because of the work they have been undertaking to vaccinate for MPX and assess and treat presentations, along with associated cleaning and the need to have suspected and confirmed MPX cases properly separated from other service users to prevent spread of infection. Ongoing advice and support for pain management, other symptom management and the significant emotional consequences of MPX are also part of this burden.

In some cases, this displacement in financial terms means a potential loss of income to clinics of over £600,000 per quarter. This level of loss of income risks destabilising clinics, with loss of staff and, as some providers have warned us, the potential exit from the market of some providers. This situation is, we hope you would agree, potentially very serious because it would have long term consequences for access to and availability of sexual health services and consequences for peoples' health. Vaccination funding at £15 per capita has yet to reach any clinics, does not meet clinic expenditure on vaccination or enable providers to recover costs of vaccination and work displacement. Loss of income to some providers risks destabilising the provider financially and operationally and may result in some sexual health services declining to manage MPX as it is not commissioned activity.

Displacement of routine sexual health activity by MPX activity has serious consequences for the health of our population:

1. People are already finding it difficult or impossible to get appointments for assessment and treatment, with the result that infections persist, people develop complications either requiring costly admission to hospital or chronic morbidity may become more unwell, and infections spread. We have already indicated that we are aware of outbreaks of STIs in several areas associated with this.
2. The risk of people developing treatment resistant infections grows if people cannot access treatment services.
3. The risk that people will not get treated, become asymptomatic and believe the infection has gone, means people may have persistent infections which worsen and present with serious morbidity later on, in addition to spreading infection.
4. If people cannot access Pre-exposure prophylaxis for HIV or post-exposure prophylaxis the risk of new HIV infections is increased.
5. The risk that people present to Accident and Emergency services with pain or symptoms increases.
6. Women are unable to access contraceptive services. Reduced access to contraceptive services has multiple impacts:

(i) Reduced access to contraceptive services, particularly long-acting reversible contraception (LARC) will worsen the health, financial, societal and psychological costs of unplanned pregnancies, including further cost to the NHS and other agencies.

(ii) Reduced access to experts in complex contraception means that the most high risk women with comorbidities are unlikely to be able to access effective contraception or preconception care. We are aware that reduced access to complex LARC removals is already discouraging women from using these methods to present for care.

Displacement from contraceptive services may mean people are diverted back to General Practice for contraception. As you know, the General Medical Services contract still places a duty on primary care to provide contraception. Sexual Health Services may need to divert people back to primary care if displacement from monkeypox continues, further increasing pressure on the NHS.

In addition to existing poorer health for individuals as a result of displacement and lack of access, provider collapse or market exit would exacerbate significantly both harm to individuals and populations and concomitant rise in cost as people are displaced to Accident and Emergency or Primary Care. This potentially compromises the duty of the Secretary of State to provide a comprehensive health service pursuant to the NHS Act 1966, of which sexual health services remain a part, and in so being compromised the Secretary of State is placed in a situation where residents may seek remedy before the courts through judicial review.

It is possible to prevent this situation

Sexual health clinics are the right place for gay and bisexual men and men who have sex with men to be assessed, treated and cared for. This fact has been well established in previous meetings. But we need to be able to both continue sexual health service provision and to ensure suspected and actual MPX cases in GBMSM are assessed, treated and cared for through these services.

We have been very clear that the exceptional nature of this epidemic, the transmission routes and its impacts are an unfunded burden which should not be borne by the Public Health Grant or by sexual health clinics. This needs funding centrally to reduce risk of serious further impact on the NHS by market exit or provider collapse, to help eliminate the epidemic locally and to prevent the sexual health of the population from worsening. We believe, as has been stated in the *Consensus Statement* , that this funding would be less than the cost of not funding services, and that doing nothing is justifiable neither on economic nor on public health grounds.

We look forward to discussing with you urgently the need for funding to address these issues and to resolving this together. There are limited levers open to us temporarily to act to prevent provider collapse or market exit, but these have consequences for non MPX sexual health activity and performance which are not recoverable. We need a solution which recognises equitably the impact of this novel epidemic on our GBMSM populations.

As a starting point, our understanding is that NHS England has responsibility for the supply and distribution to NHS Trusts of vaccine and commissioning of services to deliver vaccination programmes. The responsibility of local commissioners is to commission the overall SRH and GUM service. That does not include MPX activity which is not in scope as part of national commissioning. Services will rightly expect reimbursement for their activity on monkeypox. We believe this should come from national sources, and that is a matter for discussion between all of us. The situation now risks provider collapse or market exit. This must be addressed urgently.

We look forward to meeting.

Yours sincerely

Jim McManus President, Association of Directors of Public Health.
James Woolgar, Chair, English HIV and Sexual Health Commissioners' Group.
Claire Dewsnap, President, British Association of Sexual Health and HIV.
Laura Waters, President, British HIV Association.
Janet Barter, President, Faculty of Sexual and Reproductive Health.

Joint letter to commissioners and providers. Displacement of Sexual Health and Sexual and Reproductive Health Activity by Monkeypox (MPX)

6 October 2022

Dear Colleagues

Displacement of Sexual Health and Sexual and Reproductive Health Activity by Monkeypox (MPX)

We are writing jointly to you as a result of the displacement of sexual health (SH) and sexual and reproductive health (SRH) activity by MPX activity in clinics and its potentially serious impact on both the sustainability of SH and SRH services and the health of our populations.

As you know, the performance data for SH services in a range of clinics nationally has shown that on average, 25% to 30% of SH tariff activity has been displaced by currently unfunded MPX activity. As a result, in several areas the volume of usual contracted SH activity, including out-of-area activity, is down. This is evidenced by

1. BASHH Monkeypox Survey

(i) Reduced access and delivery of STI screening on 90% of Sexual health services.

(ii) Reduced PrEP delivery by at least 25% in more than 50% of services.

2. FSRH member Survey

(i) Increased waiting times and delays to contraception including basic contraception.

(ii) Clinical time spent delivering SRH has been reduced impacting on women and girls.

(iii) Some services have stopped delivery of some types of SRH care altogether.

(iv) Workforce shortages have been exacerbated by MPX.

(v) Occupational Health vaccines and other vaccines such as HPV and Hep B not being prioritised which risks outbreaks and infections.

English HIV & SH commissioners are also undertaking surveys and gathering intelligence from members and will share that in due course.

We are writing to request that you do not withdraw funding from services at the current time, nor otherwise exert contractual penalties for this exceptional displacement, while we continue to press for specific funding for this unfunded burden. There are several reasons for this:

1. MPX activity is exceptional and should be funded by national government.
2. Withdrawal of funding from some providers risks destabilising the provider financially and operationally.
3. Destabilising services could have serious enduring impacts, including collapse of provision or withdrawal of providers from the market, with consequent worsening of SH and SRH provision and outcomes for service users and worsening of health inequalities.
4. Any reduction in provision of SH and SRH services risks:

(i) Reduced access to HIV pre-exposure prophylaxis potentially leading to avoidable HIV infections

(ii) Outbreaks of STIs, increased STI transmission, increased burden on acute medical services and long-term consequences of untreated infection.

(iii) Reduced access to contraceptive services, particularly long-acting reversible contraception (LARC), the most effective methods, and the consequent financial, societal and psychological costs of unplanned pregnancies.

(iv) Reduced access to experts in complex contraception means that the most high risk women with comorbidities are unlikely to be able to access effective contraception or preconception care. We are aware that reduced access to complex LARC removals is discouraging women from using these methods going forward

We do not make this request lightly. After repeated advocacy with government and with NHS England/Improvement, we are still at the stage of these national agencies repeatedly requesting evidence while this burden on services remains unfunded. We continue to press them for MPX funding and have repeatedly advised them that the exceptional nature of this epidemic, the transmission routes of MPX and its impact should not be considered as routine sexual health expenditure. This request for you to honour contract value is done by exception to prevent a real risk of serious system destabilisation.

During the COVID pandemic, many local commissioners accepted that contracted sexual health activity and KPIs had not been met. We ask you to consider the current MPX situation – without creating a precedent – one of similar severity and to act **not to withdraw funding**. We recommend that you should consult your Borough/District/County/City legal teams and would suggest that local authorities have powers in place which would enable you to take this exceptional course of action as commissioners.

Our goal is to enable SH and SRH services to return as soon as possible to a situation where activity is not displaced, and where MPX activity is properly funded. In the meantime, we ask you to use your powers to continue funding clinics as per currently contracted values, and to honour payments, while we continue to push for funding.

The English HIV and Sexual Health Commissioners Group Executive and networks will be inviting you to discuss this further shortly. Meanwhile, we have one further request, which is that you share with us your data on the impact of MPX on SH and SRH service activity so that we can continue to map the ongoing impact of this to government.

Yours sincerely

Jim McManus President, Association of Directors of Public Health.
James Woolgar, Chair, English HIV and Sexual Health Commissioners' Group.
Claire Dewsnap, President, British Association of Sexual Health and HIV.
Laura Waters, President, British HIV Association.
Janet Barter, President, Faculty of Sexual and Reproductive Health.

HIV COMPLICATIONS

Reduced HAND prevalence in large cross-sectional cohort study

Kirk Taylor, HIV i-Base

A study evaluated the prevalence of HAND (HIV-associated neurocognitive disorders) in a large cross-sectional cohort (n=1424). HAND prevalence decreased from 39% to 18% across a 12-year period from 2009 to 2020.

Lower prevalence of HAND was associated with INSTI-containing regimens, being HCV negative, younger age and CD4 count <350 cells/mm^3. Whilst complainers experienced a higher rate (38%) of HAND, 15% of those that were non-complainers also met HAND criteria.

HAND prevalence was assessed in HIV positive participants (n=1,424) in a retrospective observational cross-sectional cohort study. Each participant had undergone at least one neuropsychological assessment (NPA) as indicated for clinical (e.g. suspected or increased risk of neurocognitive impairment (NCI)) or research purposes. This study reported the outcomes for the first NPA only. Results are presented for NPAs conducted between 2009 to 2011 (n=244), 2012 to 2014 (n=414), 2015 to 2017 (n=292) or 2018 to 2020 (n=474).

NCI was assessed using the three-question screening test to assess memory, reasoning, and attention, as recommended by EACS guidelines. Participants with positive screening tests were classified as "complaining" and those that were negative were "not-complaining". NCI included a comprehensive array of 12 tests to explore 5 areas of cognition and HAND was classified using Frascati's criteria (HIV-associated dementia (HAD), mild or asymptomatic).

HAND prevalence was 24% (n=327) across the study population, which was split between asymptomatic (17%), mild (6%) and HAD (1%). Considering complainers and non-complainers HAND prevalence as 38% and 15%, respectively.

Over time HAND prevalence decreased from 39% for the earliest group (2009 to 2011) to 18% for the most recent group (2018 to 2020) p>0.001. Rates declined for both groups but was only significant for complainers. The proportion of asymptomatic diagnoses remained stable, whilst mild diagnoses declined over time. HAD prevalence did not change over time.

Potential HAND risk factors were calculated from pooled data from complainers and non-complainers. Increasing age by 10 years (AOR: 1.01, 95%CI: 1.00 to 1.18) and being HCV positive (AOR: 1.37, 95%CI: 1.02 to 1.85) increased the chance of HAND. CD4 counts >350 cells/mm^3 were associated with lower risk of HAND (AOR: 0.66, 95%CI: 0.46 to 0.95). Reduced incidence of HAND was detected for INSTI-containing ART (AOR: 0.65, 95% CI: 0.47 to 0.99) and dual therapy (AOR: 0.54, 95% CI: 0.34 to 0.87), relative to NNRTI-containing regimens. It is not clear whether reduced HAND incidence on INSTI-containing regimens is due to positive effect of the drug or better virologic control in these people.

Participants were HIV positive, predominantly men (81%) with a median age of 49 years (IQR: 41 to 55). 19% of participants had viral load >50 copies/mL. Median CD4 counts were lower for those in the complaining group (512 cells/mm^3, IQR: 297 to 526) compared to the non-complaining group (605 cells/mm^3, IQR: 433 to 790). The most used ART regimen was NRTI+NNRTI (41%), followed by NRTI+PI (21%), NRTI+INSTI (16%) and dual therapy (9%). There were significantly more people on BIC in the complaining group (n=135) compared to the non-complaining group (n=10), p<0.001.

References

Mastrorosa I et al. Declining prevalence of HIV-associated neurocognitive disorders in more recent years and associated factors, in a large cohort of ART-treated HIV-infected individuals. Clinical Infectious Diseases, ciac658. (19 August 2022).

https://doi.org/10.1093/cid/ciac658

DRUG RESISTANCE

Update to IAS-USA drug resistance tables

The IAS-USA 2022 Update of the Drug Resistance Mutations in HIV-1 is now available in early e-publication.

The 2022 edition cover the following drugs.

- Cabotegravir, fostemsavir and ibalizumab are all now included. The capsid inhibitor lenacapavir (GS 6207) has been added to the Figure 2.
- A new section on recently approved drugs.
- Several changes were made to the bars of the integrase strand transfer inhibitors (InSTIs) cabotegravir and dolutegravir, the protease inhibitors atazanavir and lopinavir, and the nonnucleoside analogue reverse transcriptase (NNRTI) inhibitor doravirine.
- The user notes for tenofovir have been modified as recent clinical data suggest that the K65R plus M184V mutational profile is of less clinical relevance if tenofovir with either lamivudine or emtricitabine is prescribed in combination with a boosted protease inhibitor or one of the second generation InSTIs bictegravir or dolutegravir.
- Antiretroviral drugs that are no longer recommended are listed at the bottom of the drug class and are shaded in gray. Their user notes are retained for historical significance.

This article will be published in Issue 30, Volume 4, of *Topics in Antiviral Medicine*.

https://www.iasusa.org/tam/september-october-2022

https://www.iasusa.org/wp-content/uploads/2022/09/30-4-muta.pdf (PDF)

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: cutt.ly/xZUgx14
- Link to programme: HIV from A to Z
- https://i-base.info/htb/wp-content/uploads/2022/10/Webinar-HIV-from-A-to-Z-Program.pdf

MEETINGS

BHIVA General Medicine Course 2022

Friday 11 November 2022; 8.30–17.00

National Council for Voluntary Organisations (NCVO), London N1

The BHIVA General Medicine Course is an opportunity for HIV/GU physicians to hear what's new in the ever-changing world of medicine.

The programme centres around recent updates and advice on various specialities to help clinicians in the management of people living with HIV in an inpatient and outpatient setting.

Delegates will attend four out of six 60-minute workshops and will receive handouts for all workshops and attend the summary of learning points at the end of the day.

The course is open to BHIVA members and non-members and includes the following groups of people:

Consultants Staff grade and associate specialists

Speciality trainees within 12 months of CCT

BHIVA members: £180 Non-members: £240

CPD credits at the rate of one per course hour.

https://www.bhiva.org/General-Medicine-Course-2022

Future meetings and webinars 2022/23

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)

Webcasts from meetings (YouTube listing)

2022

HIV Glasgow 2022

23 – 26 October 2022, Glasgow and hybrid

https://www.hivglasgow.org

BHIVA Autumn Conference 2022

Friday 25 November 2022, London

https://www.bhiva.org/HIVEventDiary

2023

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

19–22 February, 2023, Seattle

https://www.croiconference.org

12th IAS Conference on HIV Science (IAS 2023)

23–26 July 2023, Brisbane, Australia and virtually

https://www.iasociety.org

19th European AIDS Conference (EACS 2023)

18-21 October 2023, Warsaw, Poland

https://www.eacsociety.org

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

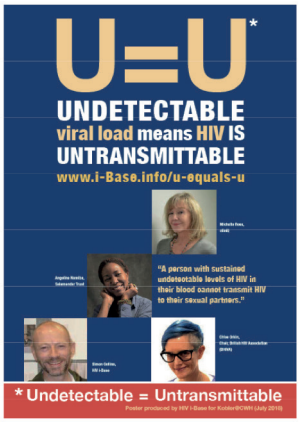
i-Base has produced a new series of posters, postcards and leaflets to help raise awareness about U=U in clincs.

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

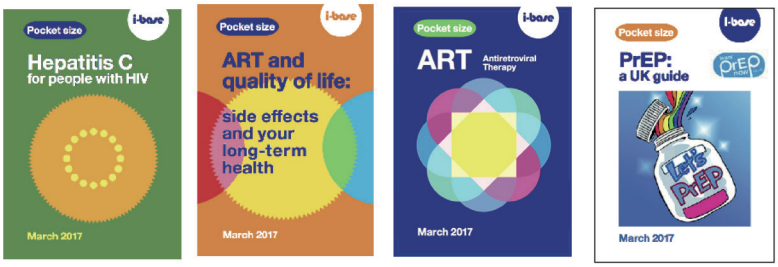


Customise U=U posters for your clinic

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

HTB is a not-for-profit community publication that aims to provide a review of the most important medical advances related to clinical management of HIV and its related conditions as well as access to treatments. Comments to articles are compiled from consultant, author and editorial responses.

HIV i-Base receives unconditional educational grants from charitable trusts, individual donors and pharmaceutical companies. All editorial policies are strictly independent of funding sources.

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- **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:

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