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EDITORIAL

Welcome to the second HTB for 2018.

For those readers rubbing your eyes, yes, this is part of the re-launched HTB schedule.

Faster, shorter, more frequent - yet just as cutting edge...

This issue includes a special report on the PHE UK incidence data, PrEP news with an update from the IMPACT study, and reviews on key papers related to cure research. And another chance to learn about the Miami macaque case if you missed this when it was published ahead of print in December.

And a victory for HIV positive people who have been asking doctors and researchers to use alternatives to the term “HIV-infected”: the latest US HIV guidelines have now adopted better, friendlier and less stigmatising language.

i-Base presented research on the impact of medical language at the IAS conference in 2010, [1] contributing to the changes in BHIVA guidelines from 2012 and EACS guidelines from 2013.

As with the US CDC endorsement of the U=U campaign, the weight from the change in the US guidelines is important.

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SPECIAL REPORT

HIV in the UK 2017: reports and data online

Simon Collins, HIV i-Base

Two important new reports from Public Health England (PHE) review the latest data on key aspects of HIV diagnoses, testing and care across the UK. [1, 2]

Both are essential reading, as are the surveillance tables for 2016 that are the basis for the reports that are also published online. [3]

Similar EU surveillance data was also published by the European Centre for Disease Prevention and Control (ECDC), giving comparative demographic breakdowns by country. [4]

Introduction

The 2017 UK HIV surveillance report is notable for reporting the most significant drop in HIV incidence for over a decade: fewer people were diagnosed HIV positive, even though more people were tested. This was not part of a steady decline but was driven by a rapid drop in new diagnoses in gay men.

In response, this year the main report has been restructured to emphasise the potential to end the HIV epidemic in the UK rather than just presenting a summary of the surveillance data.

This is organised into three main sections (plus appendices tables):

1. HIV diagnosis and transmission, AIDS and HIV-related mortality
2. Towards elimination of HIV transmission, AIDS and HIV-related mortality
3. Living with diagnosed HIV

Throughout, there is an emphasis on the importance of new approaches that are likely to explain the drop in incidence.

- More frequent HIV testing as part of routine sexual health.
- Earlier linkage to care reduces the period when people are unaware of their HIV status,
- Earlier use of HIV treatment (ART) for those who are diagnosed HIV positive.
- Greater awareness and use of PrEP by HIV negative gay and bisexual men.

Summary of new HIV diagnoses

The big news is that new diagnoses last year fell by 16% - against a background of consistently high incidence from 2000 to 2015 – with approximately 6000 new diagnoses reported each year.

The HIV testing report (only for England) notes that more than one million tests were carried out in 2016 (approximately half in antenatal care), with 100,000 tests in gay and bisexual men.

However, although overall estimated numbers of people living with HIV (both in care and undiagnosed) steadily increased from 2000 to 2013, this total has changed little or fallen in the last few years (from 107,000 in 2013 to 102,000 in 2016). This is only partly accounted for by having fewer people who are undiagnosed. See Table 1.

In 2016, a total of 5164 people were diagnosed HIV positive, 931 fewer than 2015. The largest change was a 22% drop among gay and bisexual men, with 2810 new diagnoses in 2016 compared to 3570 in 2015. Reductions were also reported for heterosexually acquired HIV,

Although this decrease was driven by significant drops at five highest incidence clinics in London, similar percentage reductions reported in all regions of the UK, were likely driven by centres in other cities with high HIV expertise, following a similar shift to earlier testing and ART.

Also, although the report places a heavy emphasis on the reductions in gay men diagnosed in London - rightly because of numbers of diagnoses at very high incidence clinics - these declines occurred in every region in the UK. The impressive 29% reduction in London was relatively modest in percentage terms, compared to

drops of 61% in Wales, 43% in Northern Ireland, 34% in the East Midlands and 33% in Scotland. (See Table 2).

The breakdowns by gender, age, route of transmission and geographical region show that diagnoses in heterosexual men and women also fell, partly related to different patterns of migrations. Approximately half of heterosexually acquired HIV occurred in the UK and half outside the UK.

Approximately 2% of HIV diagnoses were related to injecting drug use - roughly constant each year.

Of the 41 children diagnosed HIV positive, only five were born in the UK and only two were born in 2016.

Late diagnosis - still a considerable problem

Late diagnosis, defined as having a CD4 <350 cells/mm^3, is still a significant concern, perhaps more so than is reported.

So although the report describes a 45% decrease in late diagnoses compared to 2007, which might sound impressive, this approach to comparing percentages doesn't adjust for the higher numbers of people who were diagnosed in 2007.

Using the total diagnosed for each year as a denominator, the figures for late diagnosis have changed little and remain worryingly high.

In 2016, 42% (2159/5164) of people diagnosed HIV positive still had CD4 counts <350 – very little change from the 50% (3930/7777) in 2007. So rather than a 45% reduction, this data could therefore be presented as an 8% reduction over seven years - or worse still, given this is a key performance indicator, only reducing late diagnoses by just over 1% a year.

Here the demographic breakdowns are very useful to inform programmes that might have a great impact.

Younger people were less likely to be diagnosed late (31% of those aged 15-24, compared to 57% of those aged 50-64 and 63% aged >65 years old. Regional differences were also significantly different with London at the lowest rate (36%) with other regions varying between 42% to 47%.

While overall mortality for people diagnosed promptly has now normalised to the general population (1.22 vs 1.39 per 1000, respectively) rates are more than 20 times higher (26.1/1000) for those diagnosed late.

Overall, while the results are groundbreaking, they only take us back to 2010 levels, we still have a long way to go. (see Table 1).

Table 1: UK HIV surveillance data 2007-2016

Data year	Total +ve*	Undiagnosed*	In care*	New dx	New dx MSM	Change in MSM dx.
2016	102,300	10,400	92,000	5164	2810	– 22 %
2015	101,200	13,500	89,200	6286	3570	+ 6 %
2014	103,700	18,100	85,200	6200	3360	+ 4 %
2013	107,800	26,100	81,500	5973	3230	+ 1 %
2012	98,400	21,900	77,300	6204	3180	+ 7 %
2011	96,000	22,600	73,600	6146	2010	+ 3%
2010	91,500	22,200	69,900	6319	2860	+ 3%
2009	86,500	22,200	64,900	6583	2850	0 %
2008	83,000	22,400	60,800	7156	2800	0 %
2007	77,400	21,700	56,000	7277	2850	+ 5%

Key: dx - diagnosed; MSM - gay and bisexual men;

* rounded to nearest 100

Source: Public Health England, UK HIV surveillance data (2017)

Table 2: Regional declines in new diagnoses in gay and bisexual men

	2015	2016	% change
London overall	1555	1096	– 29%
Five high incidence London clinics	1034	672	– 35%
Other London clinics	520	424	– 16%
East Midlands	110	73	– 34%
West Midlands	192	145	– 24%
South East	259	233	– 10%
South West	145	110	– 24%
Wales	85	33	– 61%
N. Ireland	61	35	– 43%
Scotland	131	90	– 33%

Source: Public Health England, UK HIV surveillance data (2017)

Living with HIV

The third section of the report highlights the generally excellent level of care available to HIV positive people who are diagnosed: approximately 96% are on ART and 97% of those on ART have undetectable viral load.

With median age of 46 the report highlights that more than one-third (38%) are now older than 50.

Demographic breakdown by ethnicity includes that 14% of gay and bisexual men were from black and minority ethnic (BAME) groups and among heterosexuals, 58% were black African and 25% were white.

Summary data are also included on TB coinfection (2015 data) and transmitted drug resistance (7.5% mainly to a single class, with rates stable since 2005),

Next year, the experiences of HIV positive people in these reports will also be included. In 2018, for the first time, the report will include results from a cross-sectional survey of approximately 4,400 demographically representative people receiving care.

C O M M E N T

The annual UK surveillance reports are amongst the most timely and comprehensive national datasets and they have tracked patterns in HIV incidence and mortality since the 1980s. The more recent testing reports is an essential new development.

While the UK reports are essential summaries, on a few generally small points the narrative doesn't necessarily correlate with the data.

One is the way some percentages are used to compare results from different years (including the late diagnoses example above), rather than using the number of people diagnosed each year as the denominator.

Another is to report the drop in diagnoses in gay and bisexual men as having occurred "for the first time in over thirty years". Annual diagnoses have sometimes gone down (though only modestly) and the extent of the drop this year is really significant.

The challenges for subsequent years are whether this improved signal can continue or whether the combination of frequent testing, early ART and PrEP simply reduced transmission to the people at highest risk - who were easiest to reach but being seen at large urban clinics who had responded quickly to incorporate new services.

An optimistic signal comes from the similar percentage reductions that were reported from all regions of the UK. A pessimistic response comes from the lack of central government investment in health care, especially sexual health, such that some clinics (anecdotally)

are being told by health providers to cap the number of HIV tests, even if this limit is reached early in the year.

Another is that the long-awaited PrEP IMPACT study in England, might only have a limited effect on HIV incidence if it primarily enrolls those who were previously buying PrEP online.

Clearly HIV services, together with all other areas of health, need to resist policies that progressively destabilise and dismantle the NHS.

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TRANSMISSION AND PREVENTION

Update on PrEP IMPACT study - January 2018

Simon Collins, HIV i-Base

In the 12 weeks since the first sites opened, the PrEP IMPACT study has enrolled more than 3,200 participants. More than 65 of the planned 200 clinic sites across England are also now running. [1]

This early demand has meant that places have quickly become filled in many sites. Of the 10,000 places, approximately one-third were initially held back from clinics. This, together with reallocation from any under-used sites will be managed with input from community advisors involved in the study.

This is making it difficult for many people trying to enrol. For example, by November 2017, the Dean Street clinic in Soho had already used its allocation of 1700 places, but the IMPACT study website still doesn't have this information in January 2018. [2]

The allowance for 1,000 places to be ring-fenced for populations that have less awareness of PrEP is not affected by the reallocation. The ring-fencing is to prioritise access for women, transgender men and women and African people at high risk of HIV. Updated enrollment data for these groups has not been released by the study team, but community-led programmes that will highlight PrEP in these communities are planned for 2018.

Since this article was first posted online, the IMPACT website has been updated to include enrollment status of sites separately for gay men and other populations. As of 22 January 2018, several London clinics still have places for both categories.

https://www.prepimpacttrial.org.uk

An easier to use map developed by the community organisation Forum-link provides the same information in an easier format. This uses a country map with colour-coded pins for recruitment status. Importantly, it also includes contact details for each sites and information about rough allocation numbers.

http://forum-link.org/where-prep

C O M M E N T

The high demand for access to PrEP was always expected to help the study rapidly enrol, especially among gay and bisexual men. Strategically for the as yet missed goal of open NHS access, rapid enrolment is the strong point of this exercise.

The delay in updating the study website in real time however is making it difficult for many people to find an active site. The official website is not a strong point.

The next enrollment from the study team is planned following the management board meeting in February.

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PrEP use can reduce HIV stigma in gay communities

Simon Collins, HIV i-Base

A study published ahead of print in the Journal of AIDS reports how earlier prejudice against people who use PrEP has largely been overcome among users of social media hook-up apps in four large US cities.

The study also found that people who used PrEP (approximately 11% of participants) were not prejudiced against potential partners who were HIV positive. This was in contrast to non-PrEP users who rated social media profiles of people who were HIV positive as significantly less attractive and desirable than HIV-negative or PrEP profiles.

Results were from an online survey in 2015 completed by almost 700 HIV negative gay and bisexual men in New York, Washington, Miami and Atlanta. In this population, there was no evidence of stigma when interacting with race, but that profiles disclosing recreational drug use received significantly lower ratings across all five outcomes (attractiveness, desirability, trust, likely to use a condom and riskiness of sex).

Although observational data are vulnerable to confounding (ie people using PrEP might have been less prejudiced beforehand) it is likely that the positive results reported are likely underestimated given the wider acceptance of PrEP since 2015.

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European HIV/AIDS report (2017)

ECDC and WHO

In 2016, approximately 160,000 people were diagnosed HIV positive in the 53 WHO defined countires in the European region. Of these, just under 30,000 were from the European Union and European Economic Area (EU/EEA) and 103,000 were from Russia.

Executive summary

For the first time in a number of years, several countries reported a decline in new HIV diagnoses, even after adjusting for reporting delay.

However, similar to recent years, the highest proportion of HIV diagnoses (40%) was reported to be in men who have sex with men (MSM).

While the data in this year's report indicate alarming rates and increases in new diagnoses in some parts of eastern and central Europe over the last decade, at the same time there has been a tendency towards stabilising or even decreasing rates in some EU/EEA countries.

Trends by transmission mode, for example, show that the number of HIV diagnoses among MSM in the EU/EEA decreased slightly in 2016 and the number of heterosexually acquired cases has decreased steadily over the last decade.

Moreover, in the EU/EEA, the number of AIDS cases, and the number of AIDS-related deaths, has consistently declined since the mid-1990s.

Source and links

European Centre for Disease Prevention and Control (ECDC). HIV/AIDS surveillance in Europe 2017 - 2016 data. (28 November 2017).

https://ecdc.europa.eu/en/publications-data/hivaids-surveillance-europe-2017-2016-data

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BASIC SCIENCE & CURE RESEARCH

Additional remission cases published: but eradication needs 10,000-fold reduction in viral reservoir

Richard Jefferys, TAG

Two recent case reports of temporary HIV remission, first presented at the CROI 2017 and IAS 2017 conferences, have been published in the open access journal *PLoS Medicine.*

Tim Henrich and colleagues from UCSF report on an adult male diagnosed with HIV and started on ART unusually early, due to acquiring the infection during a short window between a screening visit for a pre-exposure prophylaxis (PrEP) demonstration project and the day on which Truvada PrEP was initiated. Truvada was switched to ART with four active drugs (adding darunavir/ritonavir and raltegravir) as soon as the test result confirming the HIV diagnosis became available. The time from infection to PrEP initiation was estimated to be 10 days, and ART was begun seven days later. As first reported by Hiroyu Hatano at CROI in 2014, HIV rapidly became undetectable by multiple assays, including measures of the viral reservoir. [1]

ART was eventually interrupted and the individual did not experience an HIV viral load rebound until 225 days afterwards (at 36 copies/mL, that rose to 59,805 copies/mL six days later). Henrich's talk at the IAS 2017 conference is available on youtube [2] and was covered on the blog in a report from the meeting. [3]

The new paper adds information on analyses of possible predictors of the viral load rebound, noting that expression of CD30 (a lymphoma tumor marker and member of the tumor necrosis factor super-receptor family) increased on the surface of both CD4 and CD8 T cells months before the HIV viral load rebound occurred. [4]

A similar increase in CD30 expression was observed in one of the Boston patients, who experienced a very similar period of HIV remission resulting from a stem cell transplant procedure for cancer. [5]

As mentioned on the blog previously, Henrich's research group has a longstanding interest in CD30 as a possible biomarker of the HIV reservoir and is continuing to pursue investigations in this area. [6]

The paper also describes results obtained using a relatively new approach to HIV reservoir measurement, the murine virus outgrowth assay (mVOA). The mVOA involves transferring large numbers of sampled CD4 T cells into multiple immunodeficient mice and monitoring for evidence of the emergence of HIV RNA (the methodology is described in detail in a recent open access review by Kelly Metcalf Pate and Joel Blankson in the open access journal Retrovirology). [7]

After 18 months on ART (prior to the interruption), approximately 530 million CD4 T cells were sampled from the individual and divided among ten mice. One of the mice displayed a low HIV RNA level of 201 copies/mL in plasma after receiving an anti-CD3 antibody to activate the T cells, around five weeks after the transfer. Efforts to genetically sequence the virus in order to confirm the finding were unsuccessful however.

In discussing the mVOA result, the authors note that it may have represented the only evidence that HIV was still present, and go on to write: "our study suggests that sampling of hundreds of millions of PBMCs may, at times, be more sensitive than tissue-based studies for the detection of residual HIV infection since a much larger number of cells can be interrogated. Further studies comparing mVOAs with traditional ex vivo co-culture assays utilising rigorous positive and negative controls are certainly warranted."

The researchers also provide information on a second individual diagnosed under similar circumstances – between screening for a PrEP demonstration project and starting Truvada. The timing was slightly later, with HIV infection estimated to have been acquired approximately 12 days before starting Truvada PrEP, and the switch to ART occurring after another 12 days. ART has not been interrupted in this study participant, and HIV RNA was more readily detected in the mVOA, with three of eight

mice displaying viral loads of 1,000, 5,000, and 11,000 copies/mL, respectively (from a total of 50 million CD4 T cells transferred into each mouse).

A key takeaway highlighted in the paper is that PrEP programmes represent an opportunity to catch individuals at the very earliest stages of HIV infection and study the impact of rapid ART initiation. The authors recommend that PrEP programs conduct HIV RNA testing before starting PrEP, as well as prior to restarting if there is an interruption, and immediately switch to a full ART regimen if an individual is found to be infected.

The second paper is by Nathan Cummins and colleagues [8] and features a case of temporary HIV remission that was presented as a poster at CROI 2017. [9]

Similar to the Boston patients, the individual in question underwent a stem cell transplant for the treatment of a cancer (acute lymphoblastic leukaemia) and measures of the HIV reservoir subsequently declined to undetectable levels while ART was maintained.

Permission was ultimately obtained to conduct an analytical treatment interruption, which took place at day 784 post-transplant. Viral load remained undetectable for 288 days, at which point a rebound to 60 copies/mL was detected. Five days later the level had risen to 1,640 copies/mL and ART was restarted. Genetic sequencing of the rebounding virus indicated it emerged from a source that was not detected in blood samples prior to transplantation, and the authors write that it "may have originated from sanctuary tissue sites harboring archived viral species seeded during the extensive HIV-1 disease process preceding the patient's oncologic history."

The report adds to the evidence that stem cell transplantation can significantly reduce the size of the HIV reservoir, but the researchers note that the estimated decline was approximately 200-fold at most, considerably short of the 10,000-fold reduction that mathematical modelling studies have indicated may be needed to prevent HIV rebound for a lifetime. [10]

Source

Jefferys R. TAG Basics Science Blog (05 December 2017)

http://tagbasicscienceproject.typepad.com

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Update on AAV vectors as delivery vehicles for bNAbs: Ron Desrosiers and the Miami macaque

Richard Jefferys, TAG

The idea of using adeno-associated virus (AAV) as a vehicle to deliver genes encoding anti-HIV broadly neutralising antibodies (bNAbs) has been around for some time, and has been covered a number of times previously on the blog (see posts from May 2009 and January 2013). [1, 2]

The approach was first developed by Phil Johnson as a possible way of circumventing the challenges associated with inducing broadly neutralising antibodies using traditional vaccines. AAVs primarily take up residence in muscle tissue and can act as a factory for producing proteins encoded by genes inserted into the AAV genome. At the opening lecture of the 8th HIV Persistence Workshop in Miami, the researcher Ron Desrosiers presented an update on efforts to deliver bNAbs with AAV, including the intriguing tale of a macaque in which the method appeared to have a profound therapeutic effect. [3]

Many years ago Desrosiers, then at the New England Primate Research Center, collaborated with Phil Johnson on the first study to demonstrate that anti-SIV antibodies delivered by AAV could protect macaques against a highly pathogenic SIV challenge. [4] Desrosiers has since moved to the University of Miami and is now exploring the potential of AAV to deliver the more recently discovered potent bNAbs.

At the workshop, Desrosiers described a preliminary study in which four macaques were infected with a SHIV AD8 challenge virus and, 86 weeks later, given three AAV vectors encoding the bNAbs 10E8, 3BNC117 and 10-1074, respectively. Because they originated in humans, the bNAbs were modified to make them compatible with rhesus macaque antibodies (rhesusised, to use Desrosiers term). No antiretroviral therapies were employed in the experiment.

Evaluations of bNAb levels after AAV administration produced disappointing results: 10E8 was very low or undetectable in all cases, 3BNC117 was delivered successfully in just one out of four animals and 10-1074 achieved significant levels in three out of four. As Desrosiers and colleagues explained in a paper published in Molecular Therapy last year, the problem was caused by the generation of antibodies against the AAV-encoded bNAbs (anti-antibody responses). This problem was also seen in SIV prevention experiments. [5]

There was a more encouraging finding, however. One macaque developed sustained levels of both 3BNC117 and 10-1074, and this was associated with a persistent decline in SHIV AD8 viral load to undetectable levels – below 15 copies/mL in 26 samples taken over a 24-month period (viral load analyses were conducted by Jeff Lifson at the National Cancer Institute). Virus reservoirs also became undetectable: 62 weeks after AAV administration, no SHIV AD8 could be recovered from 180 million peripheral blood mononuclear cells (PBMC) using a quantitative virus outgrowth assay (QVOA).

Several additional experiments were conducted in an attempt to ascertain if a cure of the challenge virus might have been achieved. Cells from an entire lymph node sampled after 74 weeks were transferred into an uninfected macaque, without causing SHIV AD8 infection. A follow up five weeks later, in which approximately 140 million cells derived from an extracted cluster of lymph nodes were transferred, also failed to establish SHIV AD8 infection. Desrosiers presented these results earlier this year in a talk that is available on Youtube (thanks to @DanWilliamsVisa for sharing this). [6]

In the workshop lecture, Desrosiers reported that 87 weeks after AAV was given, SHIV AD8 was finally recovered at very low levels on three occasions by QVOA, with the frequency of infected cells estimated to be ~1 in 50 million PBMC (depleted of CD8 cells). While this ends hopes that the virus may have been entirely eradicated, Desrosiers noted that the animal—dubbed the Miami macaque by some of his colleagues—might legitimately be described as functionally cured, although he acknowledged the major caveat: it is just one case.

Desrosiers's research group is now focussed on circumventing the problem of anti-bNAb antibodies. The AAV variant used in studies to date has been AAV1, and he showed evidence that AAV8 appears less prone to inducing anti-antibodies. This may be because AAV8 is tropic for the liver, a site in the body where immune responses against vector-encoded bNAbs are less likely to be induced (a phenomenon known as the "liver tolerance effect"). [7]

Experiments in which AAV8 administration was followed later by AAV1 have suggested the combination might further reduce anti-antibody levels; in essence a type of "prime-boost" in which the booster is enhancing immunological tolerance rather than enhancing immune responses. An additional strategy involves including a piece of genetic code in the AAV vector that is designed to shut down antigen presentation by cells (e.g. dendritic cells) that might otherwise promote the development of anti-antibodies.

Plans are now underway to conduct a study in which 12 macaques infected with SHIV AD8 will be divided into two groups and receive either AAV8 vectors encoding 3BNC117 and 10-1074 (possibly with an AAV1 boost) or antiretroviral therapy.

There is one ongoing trial of an AAV1 vector encoding a bNAb (PG9) in humans, launched several years ago by a collaboration involving Phil Johnson and the International AIDS Vaccine Initiative (IAVI). The trial population is HIV-negative men. Results were initially due in January 2016 and have been eagerly anticipated. In his presentation at the Persistence Workshop, Desrosiers stated that he recently attended a meeting at the Gates Foundation at which preliminary data were presented and obtained permission to disclose them. [8]

According to his description, what the results revealed is that the anti-antibody problem is not limited to macaques: nine trial participants that were analysed did not have detectable PG9 levels, but seven out of the nine had readily detectable anti-PG9 antibodies. There may be subtleties to the findings that could not be conveyed in a brief aside, but it sounds like the promise of the AAV approach – both in the preventive and therapeutic contexts – will only be realised if a means to avoid anti-antibodies can be developed.

Source

Jefferys R. TAG Basics Science Blog (14 December 2017)

http://tagbasicscienceproject.typepad.com

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GUIDELINES

UK guidelines on TB/HIV co-infection: online for comment to 9 February

Simon Collins, HIV i-Base

These guidelines update the BHIVA 2011 edition.

They are designed to provide a clinical framework applicable to adults in the UK co-infected with HIV and TB.

The risk of developing TB is more than 25 times greater in HIV positive compared to negative individuals. HIV doctors therefore need to be aware of TB in symptomatic individuals, especially those who have lived in TB-endemic parts of the world.

As the investigation and treatment of both TB and HIV infection is complex, it is essential to involve specialists in HIV, respiratory and/or infectious diseases.

The consultation is open until Friday 9 February 2018.

www.bhiva.org/TB-guidelines-consultation.aspx

US HIV guidelines updated: dropping the term "HIV-infected" (October 2017)

Simon Collins, HIV i-Base

The main US HIV treatment guidelines (HHS) were updated in October 2017. [1]

All changes are highlight in yellow in the PDF version of the quidelines.

Main changes include:

Using person-first language

- Removing the offensive term "HIV-infected" when referring to HIV positive people and adopting more affirmative person-based language throughout.

  This is a way of reducing stigma and showing respect for individuals who are living with HIV by focussing on the person instead of the disease.

  Although this might seem a small point to many health professionals, similar changes were adopted by BHIVA from 2012 and by EACS from 2013.

Starting ART

- The classifications for initial therapy have been changed from Recommended, Alternative, and Other to:

  Recommended for most people and

  Recommended in certain situations.

- Integrase inhibitor based regimens are recommended as first therapy for most people with HIV. NNRTI- PI-based regimens are recommended in certain clinical situations.
- Longer-term safety data have clarified that TAF has less bone and kidney toxicity but TDF is associated with lower lipid levels.
- Updates have been made throughout the section with new safety and clinical trial data.
- Monotherapy with any single ARV should not be used due to increased risk of virologic failure and drug resistance.
- Dual therapy using lamivudine plus either dolutegravir or boosted darunavir is not recommended, but is an alternative requiring closer monitoring in people who are not able to use other NRTIs.

- Efavirenz is (finally) no longer banned during the first trimester of pregnancy.
- The classifications of ART regimens have been changed from Recommended, Alternative, and Other to:

  (i) Recommended regimens for most people; and

  (ii) Recommended regimens in certain situations. (Specific regimens are listed in Table 6 of the guidelines.)

Virologic Failure

- "Low-level viremia" was defined at <200 copies/mL.
- Several sections were restructured.
- The importance of maintaining HBV treatment in people with hepatitis B virus (HBV)/ HIV coinfection was emphasised.
- Ibalizumab and fostemsavir are included as pipeline compounds for people with mulltiple drug resistance.

Changing treatment

- Discussion of several studies using two-drug maintenance therapy.
- Clinical trial data involving investigational combinations are discussed.

Coinfection with HIV and HBV and/or HCV

- Both sections have been updated to discuss recent reports regarding reactivation of hepatitis B virus (HBV) infection in persons with HBV/hepatitis C virus (HCV) coinfection after starting interferon-free HCV therapy.
- Individuals with chronic HBV infection should receive treatment for HBV with NRTIs that are active against both HIV and HBV before starting HCV therapy.
- For the HCV section, interactions between new HCV direct-acting agents and ARV drugs have been added to Table 12.

Adherence

- The section on adherence has been revised to also include HIV care.
- The importance of doctors working with a multidisciplinary team to understand barriers to care.
- New evidence-based interventions and best practices to improve adherence are summarised.

- In people with adherence problems, dolutegravir and boosted darunavir are mentioned given their high genetic barriers to resistance.

Additional updates have been made to the following sections:

- Laboratory testing
- Acute and recent (early) HIV
- Adverse effects of ART
- Cost considerations and ART
- Appendix tables

C O M M E N T

i-Base presented research on the use of HIV positive compared to HIV infected at the IAS conference in 2010, [1]

This contributed to the changes in BHIVA guidelines from 2012 and EACS guidelines from 2013.

References
1. DHHS guidelines for the use of antiretroviral agents in adults and adolescents living with HIV (October 2017).
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   http://www.abstract-archive.org/Abstract/Share/3331

ON THE WEB

Online resources

Liverpool University PK online videos

A very easy to watch and informative set of training videos from the pharmacology and durg-interaction team at Liverpool University.

- Principles of Drug Absorption
- Principles of Drug Disposition

- Principles of Drug Metabolism and Excretion
- Inter and Intra-variability in PK
- The Basics of Drug Drug Interactions

https://www.hiv-druginteractions.org/educational-videos

FUTURE MEETINGS

Conference listing 2018

The following listing covers some of the most important upcoming HIV-related meetings and workshops.

8th International Workshop of HIV & Women

2 – 3 March 2018, Boston

www.virology-education.com

Conference on Retroviruses and Opportunistic Infections (CROI 2018)

4 – 7 March 2018, Boston

www.croiconference.org

BHIVA 'Best of CROI' Feedback Meetings 2018

Monday 19 March, London

Tuesday 20 March, Birmingham

Wednesday 21 March, Haydock

Tuesday 27 March, Cardiff

Wednesday 28 March, Wakefield

Thursday 29 March, Edinburgh

www.bhiva.org/BestofCROI2018.aspx

4th Joint BHIVA/BASHH Spring Conference

17 – 20 April 2018, Edinburgh

www.bhiva.org

12th INTEREST

29 May – 1 June 2018, Kigali

interestworkshop.org

International Workshop on Clinical Pharmacology of Antiviral Therapy 2018

Tbc May 2018, Washington

www.virology-education.com

22nd International AIDS Conference (AIDS 2018)

23 – 27 July 2018, Amsterdam

www.aids2018.org

International Workshop on HIV & Aging

13 –14 September 2018, New York, USA.

www.virology-education.com

HIV Glasgow 2018

28 – 31 October 2018

www.hivglasgow.org