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*In Memory: Dr Mags Portman*

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## h-tb

### HIV TREATMENT BULLETIN

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## EDITORIAL

**This issue of HTB includes a range of short articles and reports in the relative lull before the upcoming CROI conference being held this year in Seattle in the first week of March.**

We also lead with a tribute to the inspirational Dr Mags Portman whose passion, energy and kindness will be remembered by all who knew her, including by activists at i-Base where she was a co-author to the UK Guide to PrEP.

Conference reports in this issue are from the International Drug Resistance Workshop in Johannesburg, focusing on drug resistance in low- and middle-income countries.

BHIVA has published two major sets of updated guidelines - on pregnancy and on TB/HIV coinfection.

And we review a paper from the long-running MACS cohort that reports an association between smoking marijuana and lung complications in HIV positive men that was independent of smoking cigarettes.

Although our next issue will bring reports from CROI, this conference will publish webcasts in virtual real-time and we will also publish early reports ahead of press online.

### SUPPLEMENTS

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

Please continue to order these free resources.



### i-Base 2019 appeal

This year we are continuing a funding appeal to help i-Base continue to provide free publications and services.

Your help has been inspiring – and we hope this support will continue during 2019. If 1000 people support us with £5 a month we will be on course to meet our funding shortfall.

All help is appreciated.

<http://i-base.info/i-base-appeal-we-need-your-help>

## IN MEMORY

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### Dr Mags Portman: pioneer activist for sexual health

**It is with great sadness that we have to report the death of the much-loved sexual health pioneer and community activist Dr Mags Portman.**

Mags had immense energy and enthusiasm for everything that she became involved with. Most recently this included linking with community activists to demand access to PrEP.

Mags initially trained as a GP in Glasgow, qualifying in 2003, where she also worked at the Steve Retson Project that specialised in services for gay and bisexual men. After working briefly as a GP in Leeds, Mags retrained to become a specialist in sexual health, while continuing to support community projects including Leeds Skyline and Yorkshire MESMAC.

By 2014, Mags was working as a consultant at both the Royal London and Homerton Hospitals in East London, where involvement in the PROUD study started a new focus as a PrEP activist. From September 2015, Mags was working at the Mortimer Market Centre, where she expanded services to be one of the first NHS services to provide monitoring for people accessing PrEP online.

It was for her many diverse activities related to PrEP, that in April 2018, at the Joint BHIVA/BASHH conference in Edinburgh, Mags was awarded the BASHH Outstanding Achievement Award, where hundreds of delegates showed their appreciation with a standing ovation at the ceremony awards.

Her generosity as a friend also included the decision to write openly about her two-year struggle after being diagnosed with an aggressive form of mesothelioma. This slowly documented the painstaking experiences of a doctor accessing NHS care as a patient, always with insights into the importance of her family and friends.

Mags died on 6 February 2019, in her hometown of Leeds. Our thoughts are with her husband Martin and their two children. She was 44.

Mags made such a lasting impression on everyone who was lucky enough to know her that she will always be remembered as an inspirational example of how to lead life to the best.



Dr Mags Portman

Tributes from her friends and colleagues remembered Mags as an exceptional, talented, passionate and committed doctor who touched everyone with her compassion and kindness.

*Simon Collins, HIV i-Base*

**Messages of farewell or in celebration of Mags' life are being collected by friend and colleague, PrEP activist Greg Owen and can be sent to:**

***thankyoumags@outlook.com***

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3. Mags Portman Blog. NotDoingThingsByHalf.  
<https://notdoingthingsbyhalf.wordpress.com>
4. Remembering Dr Mags Portman – an exceptional, talented, passionate, committed sexual health physician. (12 February 2019).  
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5. Greg Owen blog. (6 February 2019).  
<https://gregowenblog.wordpress.com>

## CONFERENCE REPORTS

### 27th International Workshop on HIV Drug Resistance and Treatment Strategies

22–23 October 2018, Johannesburg

#### Introduction

**The resistance workshop focuses specifically on the growing issue of resistance to antiretrovirals, especially in low- and middle-income countries (LMICs).**

It comprises two days of invited plenary presentations and abstract-driven oral and poster sessions followed by a half-day workshop.

The scientific committee is especially interested in research and topics from LMICs and the 2018 workshop (as well as the previous one) was appropriately held in Johannesburg, with The Southern African HIV Clinicians Society as secretariat. This arrangement continues with the 2019 resistance workshop to be held in October.

Topics at the 2018 workshop included, the clinical implications of resistance in LMICs, the dolutegravir dilemma (much discussion on the risk/benefits of potential safety signal vs increasing NNRTI resistance), new generation sequencing, and new and long acting drugs.

<http://www.hivresistance2018.co.za>

The programme is online at:

<http://www.hivresistance2018.co.za/wp-content/uploads/2018/11/HIVDR-2018-programme-web.pdf> (PDF)

Some, but not all, of the presentations can be found at:

<http://www.hivresistance2018.co.za/programme>

Articles in this issue of HTB include:

- Drug resistance in low- and middle-income countries

### Drug resistance in low- and middle-income countries

Polly Clayden, HIV i-Base

**Several studies presented at the 27th International Workshop on HIV Drug Resistance and Treatment Strategies described rates of HIV drug resistance in low- and middle-income countries (LMICs).**

#### High rates of pretreatment drug resistance in women

NNRTI pretreatment drug resistance was nearly twice as high in women compared to men in a pooled analysis, conducted by WHO, in LMICs in Africa, South America and South East Asia. [1]

These findings were based on analyses of data from 11 nationally representative surveys: Cameroon, Namibia, Uganda, Zimbabwe, Argentina, Brazil, Colombia, Guatemala, Mexico, Nicaragua and Myanmar. The surveys were performed during 2014–2017 and included 4275 people starting first-line ART – as reported in the WHO HIVDR report 2017.

Women comprised 38% of the survey population with higher proportions in sub-Saharan Africa: 56.7–65.4%.

Eight of 11 countries had NNRTI pretreatment drug resistance prevalence estimates exceeding 10% in women compared to 5 of 11 for men: 12.2% (95% CI 9.1 to 16.3) vs 6.3% (95% CI 5.0 to 8.1),  $p < 0.0001$ , in women and men respectively.

Prevalence of NRTI pretreatment drug resistance was greater than 10% in women in 2/11 countries (Nicaragua and Mexico) and less than 10% in men in all countries. Prevalence of PI pretreatment drug resistance was less than 5% overall in all countries.

The authors concluded that this survey suggests the urgent need for alternative non-NNRTI regimen for women and reinforces the need for routine nationally representative pretreatment drug resistance surveys.

#### Drug resistance mutations and virologic failure in women on efavirenz-based ART following PROMISE study

Pre-efavirenz-ART drug resistance was detected in approximately 16% of women and viral failure in approximately 18% of women, who participated in PROMISE 1077BF and subsequently started efavirenz-based ART for their own health. [2]

PROMISE compared a PMTCT strategy (AZT and single-dose nevirapine plus a 1–2 week postpartum tail of tenofovir and emtricitabine) to PI-based ART in women not indicated for treatment for their own health ( $< 350$  cells/mm<sup>3</sup>) at the time the study was conducted. Antenatal ART resulted in significantly lower rates of early HIV transmission than the PMTCT strategy.

The resistance study, conducted in Kenya, was designed to assess whether pre-efavirenz-ART drug resistance in PROMISE participants who subsequently started efavirenz-based ART was associated with viral failure.

Pre-efavirenz-ART drug resistance was found in 209/1316 women: 15.9% (95% CI 13.9 to 18%).

Viral failure was found in 233/1316 women (95% CI 15.7 to 19.9%).

There was no difference in rates of viral failure by 6–12 months in women who were previously randomised to ART or PMTCT strategies.

Pre-efavirenz-ART drug resistance to multiple drug classes ( $\geq 1$  NRTI and  $\geq 1$  NNRTI) was associated with increased viral failure (7/8 women),  $p < 0.0001$ .

### High prevalence of pretreatment drug resistance associated with poor treatment outcomes in South Africa

The ITREMA study, conducted at a rural clinical site in Limpopo, found pretreatment drug resistance prevalence of 13% in this population. [3] Pretreatment drug resistance was significantly associated with poor treatment outcomes. This association was mainly driven by dual NNRTI and NRTI resistance.

ITREMA is an open-label randomised controlled study in adults either starting first-line or stable on first-line ART. The intervention arm includes intensive viral load monitoring, drug levels and resistance testing. The control arm has viral load monitoring according to South African guidelines.

At time of analysis, 501 participants were recruited. A total of 207 were enrolled while starting first-line ART: 60.4% women; 96.6% received tenofovir/emtricitabine/efavirenz (TDF/FTC/EFV); overall 6.3% (13/207) reported prior ART [46.2% [6/13] TDF/FTC/EFV].

Pretreatment samples were available and sequencing successful for 194/207 and 12.9% (25) had pretreatment drug resistance: 19/25 NNRTI and 6/25 NNRTI + NRTI.

At week 48, dual class pretreatment drug resistance was strongly associated with viral load  $>1000$  copies/mL and treatment failure: aOR 2.56 (95% CI 2.00 to 3.27).

The authors noted recent or current undisclosed ART use in a subset of participants and suggest that efforts to uncover previous exposure are indicated in clinical practice.

### High levels of viral load suppression in Malawi but emerging drug resistance among those with virological failure

A prospective study of 921 people starting NNRTI-based regimens between October 2009 and December 2013 at 10 sentinel ART sites in Malawi found approximately 85% of participants in follow up had undetectable viral load at 24 and 36 months. [4]

But, loss to follow up was very high in this study: 33.7% and 50.6% overall at 24 and 36 months. Smaller proportions of participants transferred out, stopped ART, had regimen substitutions or suspected or confirmed TB. At 36 months, only 340 (36.9%) were documented to be on ART.

There was a very high prevalence of dual NNRTI/NRTI resistance among people with detectable viral load at follow up. M184V accounted for most NRTI resistance; NNRTI resistance was

largely due to K103N or Y181C. Almost all participants with drug resistance had adequate nevirapine drug levels.

### Drug resistance in adults failing protease inhibitor-based ART in KwaZulu-Natal

A retrospective analysis ART resistance among adults not responding to second-line PI-based ART in Kwazulu-Natal found increasing triple class resistance in this population.

A total of 166 patient records (87 men and 79 women) were assessed. Over half (55.4%) were receiving AZT, 3TC and lopinavir/r. Other regimens included abacavir, tenofovir, emtricitabine and atazanavir/r. The majority of patients received a PI plus two NRTIs; 8 patients received lopinavir/r with three NRTIs.

Of the group, 35.5% had major PI resistance mutations; 30% had three or more major PI mutations; 28.9% had 154V; 25% had V82A; 22.7% had M46I; 11.4% had L76V; 6% had 184V; 5.4% had M46L and 2.4% other PI mutations.

Most frequent NRTI mutations were TAMs. Respectively 68% and 65% remained susceptible to AZT and tenofovir. Over 50% had high level resistance to first generation NNRTIs.

The authors noted increasing frequency of PI resistance: 35.5% reported in this study compared with 6.7% reported in 2009–2010. And increasing triple-class resistance in patients with second-line failure

There were relatively low levels darunavir, etravirine, AZT and tenofovir resistance observed in patients with ART failure which they suggest might warrant use of these antiretrovirals in third-line regimens.

They recommended continued surveillance of drug resistance levels in LMICs to guide management of patients on ART. [5]

## C O M M E N T

**Several other presentations at the workshop told similar stories.**

**Atypical resistance patterns at time of first-line failure were shown in a study conducted in Uganda and South Africa, suggesting previous undisclosed ART use, increasing transmitted drug resistance or different resistance patterns in non-sub type B viruses to those usually seen in subtype B. [6]**

**Another Ugandan study suggested a majority of successful treatment outcomes in about 87% of people after 48 months but high prevalence of drug resistance in those with viral failure. [7]**

**But a study from Cameroon showed decreasing rates of drug resistance among patients failing first-line ART from 2016, which the authors suggested could be explained by earlier detection of virological failure following the introduction of**

## Test and Treat and perhaps the availability of newer drugs and regimens. [8]

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All references are to the programme and abstracts of the 27th International Workshop on HIV Drug Resistance and Treatment Strategies. 22–23 October 2018. Johannesburg, South Africa unless otherwise stated.

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## TREATMENT GUIDELINES

### UK BHIVA pregnancy guidelines (2018)

#### Polly Clayden, HIV i-Base

**There have been some changes in recommendations in the 2018 BHIVA pregnancy guidelines. The particular focus areas are psychosocial, infant feeding, neonatal and postnatal management as well as a few updates on use of specific antiretrovirals in pregnant women living with HIV.**

The new guidelines include updated prevalence data showing that very low vertical HIV transmission rates continue in the UK and Ireland: an estimated 0.27% in 2012–2014.

During this period, 85% of deliveries were to women who became pregnant when they already knew their HIV status. About half of the women were having a second or subsequent child since they were diagnosed.

Almost all women received ART during pregnancy, and the proportion conceiving on ART increased from 40% in 2007–2011 to 60% in 2012–2014.

The proportion of vaginal deliveries also increased: from 37% to 46%. But emergency caesarean section rates are still high: around 20–25% of deliveries.

The proportion of pregnancies in women over 40 rose from 2% in 2000–2004 to 9% in 2010–2014. And a growing number of pregnant women have vertically acquired HIV.

The main changes in recommendations for the management of HIV in pregnancy and postpartum are as follows:

#### Psychosocial care

The section on psychosocial care of women living with HIV during and after pregnancy has been expanded and moved to the beginning of the guidelines to reflect its importance.

The need for antenatal HIV care to be delivered by a multi-disciplinary team is emphasised. The guidelines also recommend that women are assessed for antenatal and postnatal depression at booking, 4–6 weeks postpartum and 3–4 months postpartum, following NICE guidance.

#### Infant feeding

The guidelines continue to stress that in the UK and other high-income settings, the safest way to feed infants born to women with HIV is with formula milk, as there is a small on-going risk of exposure to HIV with breastfeeding.

ART significantly reduces, but does not completely eliminate, the risk of vertical transmission through breastfeeding. U=U applies

only to sexual transmission, and there are currently insufficient data to apply this to breastfeeding.

Women should receive appropriate support from their multi-disciplinary team, including peer support, psychological and practical support, as well as financial support for formula feeding.

Women who formula feed their infants should be offered cabergoline to suppress lactation.

But the updated advice also includes new data on breastfeeding and the emotional impact of not breastfeeding on women.

Women who are fully suppressed on ART and choose to breastfeed should be advised of the small on-going risk of HIV transmission and supported in their decision. The woman and her infant should be reviewed monthly in clinic for viral load testing during breastfeeding and two months after stopping.

### Treat all

All women (including elite controllers) are recommended to start (or continue) and remain on lifelong ART.

New data are included on tenofovir DF, raltegravir, rilpivirine, dolutegravir, elvitegravir and cobicistat.

Abacavir/lamivudine or tenofovir DF/emtricitabine with efavirenz or atazanavir/r are recommended for women starting ART in pregnancy. Dolutegravir is recommended after eight weeks' gestation.

It is recommended that women conceiving on effective ART should continue with this. Exceptions that require modification are: non-standard regimens, for example protease inhibitor monotherapy; regimens like darunavir/cobicistat and elvitegravir/cobicistat that have shown lower pharmacokinetics in pregnancy, or where there is no pharmacokinetic data such as raltegravir 1200 mg once daily.

A woman who conceives on dolutegravir should see her doctor as soon as possible to discuss current evidence on neural tube defects.

### Infant post-exposure prophylaxis (PEP)

The length of infant PEP has been stratified according to risk of transmission being very low, low or high risk by maternal viral load and ART. Two weeks of zidovudine monotherapy is recommended if the following criteria are met: a woman has been on ART for longer than 10 weeks; and has two documented viral loads <50 copies/mL during pregnancy at least four weeks apart; and viral load <50 copies/mL at or after 36 weeks.

### Hepatitis

Information has been added on tenofovir alafenamide for hepatitis B and on direct-acting agents for hepatitis C.

### Postpartum

A new section has been added on the postpartum management of women living with HIV. This includes recommendations on

contraception, continuing and/or modifying ART after delivery as well as assessment of their mental health needs postpartum.

## C O M M E N T

**The writing group aim to next revise these guidelines by 2021.**

**The writing group will meet at least once a year to consider new information and will issue revisions or updates in reaction to clinically important and relevant data should it become available.**

#### Reference

BHIVA. BHIVA guidelines on the management of HIV in pregnancy and postpartum 2018.

<https://www.bhiva.org/pregnancy-guidelines>

## BHIVA guidelines for adult TB/HIV coinfection (2018)

**Simon Collins, HIV i-Base**

**The latest BHIVA adult TB guidelines are now online.**

They have been fully revised from the 2011 version using the modified GRADE system to evaluate evidence.

The guidelines make recommendations for diagnosing and treating all TB related complications

These are broadly similar for HIV positive adults as for HIV negative adults. However, the complexity of TB and HIV infection makes it essential to involve specialists in HIV, respiratory and/or infectious diseases.

Additional recommendations including timing and choice of ART.

The guidelines are designed be used in conjunction with:

- NICE. Tuberculosis. ([www.nice.org.uk/guidance/ng33](http://www.nice.org.uk/guidance/ng33))
- BHIVA guidelines for the treatment of HIV-1-positive adults with antiretroviral therapy (2015).
- WHO 2016 guidelines for the treatment of drug-resistant TB.

#### Reference

BHIVA. BHIVA guidelines on the management of HIV in pregnancy and postpartum 2018.

<https://www.bhiva.org/TB-guidelines>

## SIDE EFFECTS & COMPLICATIONS

### Regular marijuana smoking linked to lung disease in HIV positive but not HIV negative men

Simon Collins, HIV i-Base

**A new analysis from the US MACS cohort reports independent links between smoking marijuana and lung disease in HIV positive men. The results adjusted for cigarette smoking. [1]**

MACS is a long-running observational cohort that has collected data on more than 7000 men from four US cities since 1984. Participants have been recruited in four different time periods. This analysis included 1352 HIV positive men >30 years old and the same number of HIV negative controls matched by age and race - contributing 53,000 patient years of follow-up between 1996 and 2014.

Overall, 363 HIV positive and 244 HIV negative participants reported one or more years smoking marijuana daily/weekly (median 4.0/4.5 years daily/weekly). Regular use of heroin or cocaine use was an exclusion criteria for this study.

Incident lung diseases in the analysis included influenza or viral pneumonia, bacterial pneumonia, other pneumonia, acute bronchitis, tuberculosis, COPD or emphysema, pulmonary hypertension, other non-infectious diagnoses, other lung disease and lung cancers.

Baseline characteristics included approximate median age 43 (IQR 38 to 49), 65% white and 21% black.

Over a median of 10.5 years follow-up, there were 1630 incident cases of lung disease. HIV positive people had an increased risk of both infectious lung disease (33.2% vs. 21.5%) and non-infectious lung disease (20.6% vs. 17.2%) compared to HIV negative controls. Regular marijuana use (smoking daily or weekly) was reported by 27% of positive vs 18% of negative groups.

Heavy or binge alcohol use during follow-up was also more common among regular marijuana smokers (37% vs 23%). Among HIV positive participants, there were no differences in CD4 count, viral load, or ART use linked to marijuana smoking.

Independent of tobacco smoking and other risks, regular recent marijuana smoking was associated with increased risks of infectious lung diagnoses and chronic bronchitis only in HIV positive people (hazard ratio: 1.43 [95%CI: 1.09 to 1.86], and 1.54 [95%CI: 1.11 to 2.13], respectively). These risks were additive in participants smoking both marijuana and tobacco.

Influenza and viral pneumonia and other pneumonias were among diagnoses occurring more frequently in marijuana smokers: in approximately 23% compared to 16% in non-smokers.

Each 10 days/month smoking marijuana was associated with a 6% increased risk of infectious lung disease. This was most strongly predicted by having a CD4 count <200 cells/mm<sup>3</sup> but the associations remained strong in analyses restricted to higher CD4 counts. Smoking cigarettes (≥0.5 vs 0 packs/day) was strongly associated with increased risk of infectious pulmonary diagnoses (HR

1.48 [95% CI: 1.14 to 1.93], p = 0.0037), but not with lower use <0.5 vs 0 packs/day (likely due to lower numbers in this group).

Of note, only tobacco smoking (not marijuana) was associated with infectious pulmonary diagnoses in HIV negative participants.

Similar associations were also reported for non-infectious chronic bronchitis, including cumulative estimates of marijuana and cigarette smoking over the previous ten years.

Multivariate analysis also reported a calendar effect, with a reduced risk for participants enrolled from 2001 to 2014 compared to earlier participants (1996 to 2000): for example for infectious lung disease: OR 0.63 (95%CI: 0.48 to 0.82), p=0.0006.

The researchers concluded that their findings support previous reports of higher incidence of lung infections in HIV positive people and that they provide new evidence that HIV may make people more vulnerable to complications from marijuana use.

The mechanisms suggested for HIV-specific factors included lung immune cell depletion and dysfunction, persistent immune activation, systemic inflammation, respiratory microbiome alterations, and oxidative stress many of which are likely to be more significant in advanced HIV, or with long periods of delayed/deferred use of ART.

Senior author, Dr Dana Gabuzda summarised the clinical importance of these results: "The most important thing an HIV positive person can do for their health is suppress their viral load by taking their ART medication. The next most important thing is not smoking cigarettes. Our study suggests that marijuana smoke can cause similar problems if there is long-term heavy exposure."

## COMMENT

**This is the first study to report different effects of marijuana smoking depending on HIV status and is important for completeness of smoking data to be able to show this is independent of tobacco use.**

**This study links long-term regular marijuana smoking to serious medical problems.**

**The safest alternative to smoking is probably adding marijuana to food (cakes, brownies etc) although dosing is more difficult to predict. Pharmacokinetics with oral administration include longer time to absorption and also longer therapeutic effect.**

**Discussion papers on vaping marijuana raise concerns about toxins release from the vape process and generally conclude there is too little evidence to comment on safety. [2, 3]**

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## TREATMENT ACCESS

### Civil society organisations push for a target of \$18 billion for the Global Fund's sixth replenishment

David Garmaise, for GFO

**Organisations representing civil society have renewed their call for a more ambitious target for the Global Fund's sixth replenishment.**

On the occasion of the preparatory meeting for the replenishment, held on 7–8 February 2019 in New Delhi, India, the Global Fund Advocates Network (GFAN), communities and civil society called for a “bold” replenishment target of \$18 billion. This is \$4 billion higher than the \$14 billion target announced by the Global Fund on 11 January. At that time, several civil society organisations (CSOs) said that the target was not sufficiently ambitious. [1]

The call for an \$18 billion target was contained in a statement from Communities and Civil Society. [2]

In an accompanying statement, GFAN stated that the \$14 billion target represents “a maintenance level of funding” and would not allow for programs to be scaled up to put countries on track to reach the 2030 targets for the three diseases. [3]

The \$14 billion target is just \$1 billion (or 8%) higher than the \$13 billion target for the last replenishment in 2016.

GFAN and other CSOs also expressed concerns about some of the projections and estimates in the Global Fund's investment case.

(A summary of the investment case was released on 11 January; the full document was published on the Global Fund website at the time of the preparatory meeting.) [4, 5]

The CSOs said they were concerned that total projected resources from all sources for the grant implementation period 2021-2023 – \$83.0 billion – was \$18 billion shy of the \$101 billion that the Investment Case estimates is required to fight the three diseases.

The CSOs said they were also concerned that the \$46 billion projected for domestic funding for 2021-2023 represents a 48% increase compared to the \$31.1 billion from domestic funding for the current period (2018-2020). The CSOs also noted that the majority of the projected \$17 billion increase in total funding – from \$66 billion in 2018-2020 to \$83 billion in 2021-2023 – is expected to come from domestic funding.

The CSOs questioned whether these expectations for domestic funding were realistic. “Many low-income countries continue

to require international assistance for health to supplement low levels of resources budgeted for health,” the CSOs stated.

“With only 11 years left to reach the Sustainable Development Goals (SDGs),” the CSOs said, “it is time to step up our efforts. 2019 marks a crucial milestone in the fight against AIDS, TB and malaria, which calls for bold action.”

Bold action against the three diseases, the CSOs affirmed, means adopting bold fund-raising targets.

Representatives from the communities and civil society constituencies reiterated the concerns about the \$14 billion target at the preparatory meeting in New Delhi and they expressed the hope that the Fund will be able to raise more than \$14 billion. Participants from other constituencies did not raise similar concerns.

In a related development, Ireland has announced that for the sixth replenishment it will increase its contribution by 50% (to €45 million from the €30 million it pledged for the fifth replenishment). The announcement was made at the African Leadership Meeting in Addis Ababa on February 9. The first country to pledge for the sixth replenishment, however, was Luxembourg, which announced a commitment of €9 million, up 11% from its fifth replenishment pledge.

Source:

Global Fund Observer (GFO) **Issue 350**. (13 February 2019).

<http://www.aidspace.org/node/4854>

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1. Step up or slip back? The case for investing \$14 billion for the Global Fund's sixth replenishment. GFO Issue 349 30 January 2019. [http://www.aidspace.org/gfo\\_article/step-or-slip-back-case-investing-14-billion-global-fund's-sixth-replenishment](http://www.aidspace.org/gfo_article/step-or-slip-back-case-investing-14-billion-global-fund's-sixth-replenishment)
2. Global Fund Advocacy Network (GFAN). Communities and civil society statement on the investment case for the sixth replenishment of the Global Fund to Fight AIDS, Tuberculosis and Malaria. (7 February 2019). [http://www.aidspace.org/sites/default/files/GFAN\\_Communities-and-CS-statement-on-IC-for6thReplen.pdf](http://www.aidspace.org/sites/default/files/GFAN_Communities-and-CS-statement-on-IC-for6thReplen.pdf) (PDF)
3. GFAN. Investment case for Global Fund sixth Replenishment. Advocacy Briefing. (January 2019). <http://www.aidspace.org/sites/default/files/GFAN-Advocacy-Briefing-Investment-Case-A.pdf> (PDF)
4. Global Fund. Investment Case Summary. sixth replenishment 2019. [https://www.theglobalfund.org/media/8174/publication\\_sixthreplenishmentinvestmentcase\\_summary\\_en.pdf?u=636838287180000000](https://www.theglobalfund.org/media/8174/publication_sixthreplenishmentinvestmentcase_summary_en.pdf?u=636838287180000000)
5. Global Fund. Investment Case Report. Sixth replenishment 2019. [https://www.theglobalfund.org/media/8279/publication\\_sixthreplenishmentinvestmentcase\\_report\\_en.pdf?u=636852020830000000](https://www.theglobalfund.org/media/8279/publication_sixthreplenishmentinvestmentcase_report_en.pdf?u=636852020830000000)

## TRANSMISSION & PREVENTION

### Arabic translation of U=U factsheet

An Arabic translation of an i-Base factsheet about U=U is now available online.

<http://i-base.info/uu-factsheet-arabic>

<http://i-base.info/wp-content/uploads/2018/05/Arabic-UU.pdf> (PDF)

لقد حصلنا على نسخة من إرشادات ART العربية بلغة عراقيين سوريف نتاج ع.  
لقد الفرش اضري أيم ان لب-ب-س حف

This might be useful for UK doctors with patients and their partners who speak Arabic as a first language.

Translation thanks to activists at ITPC MENA.

<https://itpcmena.org/language/en/hiv>

## ON THE WEB

### Recent papers from the Swiss HIV Cohort Study newsletter

**The long-running Swiss HIV Cohort Study (SHCS) publishes regular updates in a free monthly email newsletter.**

This includes information and links to recently published papers.

Please subscribe to email newsletter on the SHCS website: It is available in English, French, German and Italian.

<http://www.shcs.ch>

The January edition includes four recent papers.

#### Cessation of cigarette smoking and cancer in HIV

An analysis by Shepherd et al from the D:A:D study showing that the overall risk of cancer in HIV positive people who stop smoking, including for some smoking-related cancers, returns to levels seen in non-smokers 1-2 years after quitting. During the first year, the risks for these outcomes were approximately 60% and 200% higher, respectively.

The risk of lung cancer however, not only remained considerably elevated during the first year after quitting (approximately 20-fold compared to never smokers), but continued to be 8-fold higher over the next five years.

These results, just published in *Clinical Infectious Diseases*, emphasise the huge impact on better health that stopping smoking can have for HIV positive people.

#### The epidemiology of adolescents living with perinatally acquired HIV

A paper by Slogrove et al from the Collaborative Initiative for Paediatric HIV Education and Research (CIPHER) collaboration, published in *PLoS Medicine* (with free open access), describing the experiences of 38,000 HIV positive children who became positive during pregnancy, at birth or from breastfeeding.

This is an international study combining results from 12 cohort studies from 1982 - 2014 looking at characteristics after 10 years as children entered into adolescence.

In addition to describing the characteristics in each cohort, the analysis compared differences in important clinical outcomes by geographic region.

Compared to children in low- or middle-income countries, children in high-income countries started treatment at a younger age, had higher CD4%, less impaired growth and lower mortality.

Loss to follow-up during the study was lowest in South America and the Caribbean and highest in sub-Saharan Africa.

### **Inhibiting natural killer cells in AIDS**

A large international collaboration looking at genetics and HIV, and reporting links between HLA-A expression levels and HIV control. This complex analysis by Ramsuran et al reported independent and significant associations with higher viral load in each ethnicity group and in both acute and chronic infection.

HLA-A expression levels were also independently associated with likelihood of being an HIV controller or non-controller and with CD4 counts in participants with longitudinal data.

This proposed pathway included increased NKG2A- mediated NK (and/or T cell) inhibition, and impaired elimination of HIV-infected target cells, suggesting anti-NKG2A therapy as a potential target in cure-related studies.

### **Comorbidities in people living with HIV**

An analysis by Pelchen-Matthews et al from the EuroSIDA cohort published in the journal AIDS looking at the prevalence of serious comorbidities at two timepoints as the HIV population ages. This involved nearly 10,000 participants from 2006 and nearly 13,000 participants from 2014.

Median age was higher (48 vs 43 years), with higher rates of hypertension (60% vs 47%), diabetes (6.3% vs 5.4%), chronic kidney disease (CKD) (6.9 vs 4.1%) and cardiovascular disease (CVD) (5.9 vs 3.7%), all 2006 vs 2014 respectively.

The higher odds of CKD and CVD in the 2014 cohort was explained in the multivariate analysis by age, comorbidities and other related factors, highlighting the importance of management strategies for the ageing HIV populations in Europe.

## **Fit for the Future: NHS long-term plan explained**

### **The King's Fund**

On 7 January, the NHS long-term plan was published, setting out key ambitions for the health and care service over the next 10 years.

The King's Fund has published an explanatory report, Fit for the Future, that sets out the main commitments in the plan. It provides a view of what they might mean, highlighting the opportunities and challenges for the system as it moves to put the plan into practice.

#### Reference

The King's Fund. NHS long-term plan explained. (23 January 2019).

<https://www.kingsfund.org.uk/publications/nhs-long-term-plan-explained?>

## **FUTURE MEETINGS**

### **Conference listing 2018/19**

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

#### **9th International Workshop on HIV & Women**

2 – 3 March 2019, Seattle

[www.virology-education.com](http://www.virology-education.com)

#### **26th Conference on Retroviruses and Opportunistic Infections (CROI 2019)**

4 – 7 March 2018, Seattle

[www.croiconference.org](http://www.croiconference.org)

#### **25th Annual BHIVA Conference**

2 – 5 April 2019, Bournemouth

[www.bhiva.org](http://www.bhiva.org)

#### **20th International Workshop on Clinical Pharmacology of HIV, Hepatitis & Other Antiviral Drugs**

14 – 16 May 2019, Noordwijk, The Netherlands

[www.virology-education.com](http://www.virology-education.com)

#### **17th European Meeting on HIV & Hepatitis**

22 – 24 May 2019, Rome

[www.virology-education.com](http://www.virology-education.com)

#### **Viruses, vaccines and eradication conference 2019**

Thursday 6 June 2019, London

<http://www.vveconference.com>

#### **11th International Workshop on HIV Pediatrics**

19 – 20 July 2019, Mexico City

[www.virology-education.com](http://www.virology-education.com)

#### **HIV & HBV Cure Forum**

20 – 21 July 2019, Mexico City

<https://www.iasociety.org>

#### **International Workshop on HIV & Transgender People**

July 2019, Mexico City, date TBC

[www.virology-education.com](http://www.virology-education.com)

#### **10th IAS Conference on HIV Science**

21 – 24 July 2019, Mexico City

[www.ias2019.org](http://www.ias2019.org)

#### **4th European Workshop on Healthy Living with HIV**

13 – 14 September 2019, Barcelona

[www.virology-education.com](http://www.virology-education.com)

**10th International Workshop on HIV & Aging**

10 – 11 October 2019 | New York, NY, USA

[www.virology-education.com](http://www.virology-education.com)

**International Workshop on HIV Drug Resistance and Treatment Strategies**

16 – 18 October 2019, Johannesburg

[www.hivresistance2019.co.za](http://www.hivresistance2019.co.za)

**21st Intl Workshop on Comorbidities and Adverse Drug Reactions in HIV**

5 – 6 November 2019, Basel, Switzerland

<https://www.intmedpress.com>

**17th European AIDS Conference**

6 – 9 November 2019, Basel

[www.eacsociety.org](http://www.eacsociety.org)

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## 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 2018)
- HIV & quality of life: side effects & long-term health (Sept 2016)
- Guide to PrEP in the UK (November 2016)
- HIV testing and risks of sexual transmission (June 2016)
- Guide to changing treatment and drug resistance (Dec 2017)
- Guide to HIV, pregnancy & women's health (December 2015)

### Pocket guides

A series of pocket-size concertina folding leaflets that is 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 have produced a new series of posters, postcards and leaflets to help raise awareness about U=U in clinics.

This project was developed with the Kobler Centre in London.

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

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

email: [subscriptions@i-base.org.uk](mailto:subscriptions@i-base.org.uk)

Fax: 0208 616 1250

Other i-Base resources can still be ordered online as usual.

<http://i-base.info/forms/order.php>

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 I would like to make a donation to i-Base - *Please see inside back page*• **HIV Treatment Bulletin (HTB) every two weeks**  **by e-mail**• **Pocket leaflets** - *A7 small concertina-folded leaflets (2017)*

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<b>Pocket ART</b>	<b>quantity</b> _____	<b>Pocket pregnancy</b>	<b>quantity</b> _____
<b>Pocket side effects</b>	<b>quantity</b> _____	<b>PrEP for women</b>	<b>quantity</b> _____

• **Booklets about HIV treatment****ART in pictures: HIV treatment explained** (*August 2018*): 32-page A4 booklet **quantity** \_\_\_\_\_**Guide to hepatitis C coinfection** (*April 2017*): 52-page A5 booklet **quantity** \_\_\_\_\_**UK Guide To PrEP** (*March 2019*): 24-page A5 booklet **quantity** \_\_\_\_\_**Introduction to ART** (*May 2018*): 48-page A5 booklet **quantity** \_\_\_\_\_**HIV and quality of life: guide to side effects and long-term health** (*Sept 2016*): 96-page A5 **quantity** \_\_\_\_\_**Guide to HIV testing and risks of sexual transmission** (*July 2016*): 52-page A5 booklet **quantity** \_\_\_\_\_**Guide to HIV, pregnancy and women's health** (*November 2015*): 52-page A5 booklet **quantity** \_\_\_\_\_**Guide to changing treatment: what if viral load rebounds** (*Jan 2018*): 24-page A5 booklet **quantity** \_\_\_\_\_• **Other resources****U=U resources:****A3 posters** **quantity** \_\_\_\_\_ **A5 leaflets** **quantity** \_\_\_\_\_ **A6 postcards** **quantity** \_\_\_\_\_**HIV Treatment 'Passports'** - Booklets for patients to record their own medical history **quantity** \_\_\_\_\_**Phoneline posters (A4)** **quantity** \_\_\_\_\_

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