European AIDS Clinical Society

Second meeting on Standards of Care, Brussels, 16-17 November 2016

Report

The European AIDS Clinical Society (EACS) organised this second meeting on the Standard of HIV Care in Europe.

EACS is a not-for-profit organisation whose mission is to promote excellence in standards of care, research and education in HIV infection and related co-infections, and to actively engage in the formulation of public health policy, with the aim of reducing HIV disease burden across Europe.

Aims of the meeting

EACS held this second meeting:

- to see how to improve, standardise and monitor the quality of HIV care in the European region
- to specifically discuss guidelines for monitoring retention in care and for TB treatment and care
- to monitor adherence to guidelines for treatment initiation and treatment monitoring and outcome
- to review the contribution of EACS' own guidelines to this process
- to see how the function and remit of the EACS guidelines could be extended from clinical care standards to broader quality-of-care standards
- to discuss working in partnership with other agencies to improve the standard of care in the European region.

Introduction and themes

The meeting was introduced by Manuel Battegay, president of EACS (until end of 2016), who explained EACS's different activities to improve the standard of care across Europe.

He said that the model that doctors apply to treating HIV, and the purpose and structure of clinical HIV guidelines, may have to change now that universal treatment upon diagnosis is the clinical consensus.[1][2] Physicians may have to acknowledge that guidelines needed to address a stronger perspective of implementation. "We have to get more political about this" was how he summed it up.

Guidelines still had an important role to play in setting down the clinical standards that should be expected in HIV care, Battegay added, but in themselves would not necessarily change national practice if reasons of cost or prioritisation prevented their adoption. For instance, Battegay showed, nine European countries, including some surprising ones like Ireland and Norway, still had guidelines saying that ART should only be started when the

[1] WHO Guidelines: http://www.who.int/hiv/pub/arv/arv-2016/en/ .
[2] EACS Guidelines: http://www.eacsociety.org/guidelines/eacs-guidelines/eacs-guidelines.html

CD4 count had fallen below 350 cells/mm^3, and Latvia had only recently raised its threshold for starting treatment from 200 cells/mm^3.[3]

Battegay explained that in an era of 'test-and-treat, "getting to zero" and the UNAIDS 90-90-90 target, which seeks to have 72.9% of everyone with HIV virally undetectable by 2020 and 85.7% by 2030, HIV treatment has to move from an individualised patient-care model, like cancer treatment, additionally towards a public health model, like vaccination or TB treatment.[4]

This implied that a professional body like EACS had to ally itself to other organisations and issue guidelines in collaboration with health agencies like the World Health Organization (WHO) and surveillance ones like the European Centre for Disease Control (ECDC).

If the focus shifts from care to the standard of care, that means that public health, equality of access, and quality of life outcomes must be added to the clinical evidence base.

It also means that guidelines can more easily be used as a standard against which to measure clinical practice. A main theme that emerged at the meeting was the part physicians can play as a profession in broadening guidelines to standards, and what data and alliances are needed to do this.

Former WHO HIV chief outlines barriers to ending the epidemic

In a wide-ranging scene-setting presentation, Kevin De Cock, former director of HIV for the World Health Organization, said that the difficulty of bringing the HIV epidemic "down to zero" should not be underestimated.

Dr De Cock now heads the US Centers for Disease Control's HIV programme in Kenya. He included issues ranging from climate change to the political future of Africa as factors that would influence and challenge future progress not only in HIV care, but global healthcare generally.

Dr De Cock had some criticism of the '90/90/90' target's influence in how people viewed the possibility of ending the HIV epidemic.

He warned against a too-literal interpretation of getting HIV infection "down to zero" by 2030. He said he preferred the definition offered by Hillary Clinton after the Democratic National Convention in 2016.[5] This was that virtually no child should be born with HIV; that teenagers and young adults everywhere would be at "significantly lower risk" of becoming infected than they are today; and that all people with HIV should have access to treatment to prevent illness and onward transmission.

"This could result in almost no deaths from AIDS: that at least," de Cock said, "is achievable by 2030."

De Cock put the struggle against HIV into the context of the much longer and broader struggle for global health generally. This had made remarkable progress. For instance, 12.7 million children under five died in 1990; in 2015 it was six million, despite population increases.[6] Infant mortality had declined in Kenya from 7.4% a year to 3.9% during the same period.[7] An even better method of direct improvements in healthcare was maternal mortality

[3] ECDC. Evidence brief: HIV and treatment. Stockholm: ECDC; 2015. For 2016, preliminary unpublished ECDC data.
[4] See http://www.unaids.org/en/resources/909090
[5] See https://www.hillaryclinton.com/briefing/factsheets/2016/08/02/an-aids-free-generation-is-within-our-reach-hillary-clintons-plan-to-tackle-hiv-and-aids-together/
[6] United Nations Inter-agency Group for Child Mortality Estimation (UN IGME), as published in UNICEF: Committing to Child Survival: A promise renewed-Progress report 2015, UNICEF, New York 2015.
[7] Kenya Demographic Health Survey 2014: Key Indicators (2015)

in childbirth: in Kenya, this had declined from 0.38 per 100 live births a year in 1990 to 0.21 now.

HIV acted as an amplifier of progress towards global health in many ways. Indeed, before 2000 "global health" was not commonly used as a term to describe an area of work – "tropical medicine" was still used before then, with its focus on specific treatment for specific maladies.[8] It was the fight for antiretrovirals (ARVs) for Africa and the programmes set up to provide them, such as the US PEPFAR programme and the Global Fund, that had helped to turn global medicine into a public heath endeavour.[9]

There were some indicators, however, that further progress against HIV and its associated diseases might face a more difficult path ahead. Tuberculosis, for instance, had not declined by as much as other diseases. In 2000, there had been 2.3 million deaths from TB, 25% of them in people with HIV; in 2015, this was 1.7 million (a 26% decline), 29% in people with HIV.[10]

De Cock commented that the target of having 90% of all people with HIV diagnosed was proving frustratingly difficult to reach in some countries.

Testing rates vary across Europe. In central Europe, they are low; in western Europe, the rate of *regular* testing among high-risk populations needs to be improved. In eastern Europe, where there is more of a culture of institutional testing as part of healthcare, even high testing rates might not lead to high diagnosis rates if it is the most stigmatised and high risk people who are likely to avoid testing.[11]

De Cock gave an example from Kenya that showed that high numbers of people tested does not necessarily translate into high rates of diagnosis if testing is untargeted. In Kenya, between 2014 and 2015, there had been 6.5 million HIV tests in a country of 44 million people. Three per cent of people tested had HIV. This is half the national prevalence rate. And yet it is estimated that 28% of people with HIV in Kenya, and 48% in the highest-prevalence county, are not in care, which largely means undiagnosed.[12] Testing programmes in high-prevalence counties are not detecting a higher proportion of undiagnosed people than in low-prevalence ones; rather the reverse.

Testing programmes need to be redesigned to focus on testing the populations most likely to have HIV, de Cock said. In Kenya, as elsewhere, the highest yield of positive tests was in people diagnosed with TB, where 18% turned out to have undiagnosed HIV;[13]

Yet still only 50% of people diagnosed with TB worldwide get an HIV test and it is estimated that only 10% of people with HIV worldwide without existing TB diagnosis or symptoms have been screened for TB. [14]

Other than in people with TB, the highest detection rate of positive HIV results came from programmes that tested all people admitted as hospital inmates: in PEPFAR countries, the HIV rate was about 4.6%. In contrast, out-patient, mobile and home testing programmes had lower rates (between 1.5% and 3%). Out-patient testing was still by far the most common

[8] See for instance Lucas, Adetokunbo: It was the Best of Times--: From Local to Global Health. Bookbuilders, Editions Africa, 2010.
[9] De Cock KM et al.. Emerg Infect Dis. 2013 Aug; 19(8): 1192–1197.
[10] WHO. Global TB report 2016. See http://www.who.int/tb/publications/global_report/en/
[11] ECDC/WHO: Europe HIV/AIDS Surveillance Report 2015. See http://ecdc.europa.eu/en/publications/Publications/HIV-AIDS-surveillance-Europe-2015.pdf
[12] NACC&NASCOP, 2014 HIV Estimates
[13] PEPFAR Kenya APR 2015 Analysis.
[14] WHO. TB/HIV Facts 2015. http://www.who.int/hiv/topics/tb/tbhiv_facts_2015/en/

setting for testing so yielded the biggest absolute number of positive results.[15] However, de Cock argued that false-positive and false-negative tests may become an increasing problem in a situation where most of the chronically-infected had been diagnosed.[16] [17]

The only way definitively to establish HIV prevalence and its contribution to mortality is to test everyone, or at least a completely random sample. One way to do this ethically is by testing the deceased. De Cock gave some very interesting data from a study in which every cadaver arriving at two mortuaries in Nairobi was tested for HIV.[18] Although HIV prevalence in both Nairobi and Kenya generally is 6%, 20% of all the deceased tested HIV-positive, and 30% of females. A quarter of those ages 25-44 tested HIV-positive but even in those over 45, 15% were positive, and the proportion of deaths due to HIV was also 15%. This is despite an estimated 70% of all people with HIV in Nairobi being on antiretroviral therapy. HIV is therefore still responsible for a disproportionate number of deaths, even in some settings where ART coverage is good.

Regarding the 'second 90', retention in care, this differs hugely between countries, from excellent in places with 'one stop shop' HIV services to poor in countries where people may have to seek care in different places or have some care needs unsupported.

Some studies such as the ANRS 12249 study show that testing people and then just expecting HIV-positive ones to turn up at clinics for treatment does not always work.[19] There was no doubt that same-day prescribing – letting people walk out of the clinic with their antiretrovirals the day they are diagnosed – encouraged better retention and adherence, as did single-pill regimens.[20] Ensuring good retention did not have to mean offering more intensive support to all patients. It did, however, mean offering a stable programme, and a place to call if things went wrong.

Models of care in which newly-diagnosed patients and ones starting ART receive monthly or even weekly appointments while people who have been on stable ART for more than two years received full checkups only every six months are already being adopted in Kenya and indeed high-income countries by default, but should be fitted into a differentiated care model, as advocated by WHO guidelines.[21] [22] This should not only consider the frequency of appointments but also *Where* people were seen (Hospital? Community clinic? Home?) by *Whom* (doctor? Nurse? Pharmacist? Peer adherence support worker?) and with *What* (Psychosocial assessment? Peer adherence support? Drug level monitoring?).

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[15] These findings have been replicated in European settings. See, for instance Health Protection Agency: *Time to test for HIV: Expanded healthcare and community HIV testing in England.* 2010. See http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1287145497243.

[16] Pant Pai N et al. Head-to-head comparison of accuracy of a rapid point-of-care HIV test with oral versus whole-blood specimens: a systematic review and meta-analysis. Lancet Infectious Diseases 12: 373-380, 2012.

[17] Garcia-Prats AJ et al. *False negative post-18 month confirmatory HIV tests in HIV DNA PCR positive children: a retrospective analysis from Lesotho*. Advance online edition AIDS 26, doi: 10.1097/QAD.0b013e32835705bf, 2012.

[18] Othieno J. *Authorities launch HIV tests on bodies in mortuaries*. Nairobi Standard, July 2016. Read more at: https://www.standardmedia.co.ke/health/article/2000208958/authorities-launch-hiv-tests-on-bodies-in-mortuaries.

[19] Dabis F et al. *The impact of universal test and treat on HIV incidence in a rural South African population: ANRS 12249 TasP trial, 2012-2016.* 21st International AIDS Conference, Durban, abstract FRAC0105LB, 2016.

[20] Koenig S et al. *Same-day HIV testing and antiretroviral therapy initiation results in higher rates of treatment initiation and retention in care.* 21st International AIDS Conference, Durban, abstract WEAE0202, 2016.

[21] WHO HIV treatment guidelines 2016, page 239.

[22] CHAI Kenya. *Cross-sectional Assessment of ART prescription practices*, 2016

The mention of clinical monitoring brings us to the third 90 - viral suppression. Here there is one very clear barrier to overcome – the continued unavailability of regular viral load testing.[23]

Even in Europe, Serbia is one example of a country that does not offer routine viral load testing. Viral load test availability meant nothing if it was irregular, unrecorded, or led to no change in regimen in cases of virological failure, de Cock said. Kenya had relatively high rates of viral load testing in Africa but factors like the high cost of 2nd- and 3rd-line regimens conspired with the lack of clear clinical guidelines to a situation in which people still stayed on failing regimens for too long, resulting in widespread drug resistance.[24]

People with HIV, he added, were still too often subjected to inconsistent, individualised care regimens, partly because of the range of antiretroviral (ARV) drugs available.

"If you have TB, you will get the same drug regimens whether you are in Los Angeles or Malawi," he said. "But physicians like to fiddle, and people get dozens of different regimens. Such 'centrifugal prescribing' does not help to establish equity of treatment." He added that such variety often went in the face of clear scientific evidence.

It was agreed that a more 'normative' set of guidelines, adapted to the continent, are badly needed in Europe.

Commenting, Dorthe Raben, Director of Research Coordination at CHIP and Co-ordinator of the OptTEST programme,[25] warned that the adoption of guidelines based on public health as well as clinical necessities could be misused by politicians and funders to adopt a restrictive, minimal set of guidelines purely based on epidemiological needs rather than the needs of individuals.

She urged better communication and more joint working between physicians' organisations like EACS with the ECDC and with national surveillance organisations, with national health ministries, and with WHO Europe, to ensure that the type of expanded, quality-of-life-based guidelines proposed would result in a genuine improvement in standards of care and a more integrated approach to achieving them.

A culture of quality

Marco Vitoria from the World Health Organization contributed an in-depth look at what "quality of care" really meant.

"What has quality of care not become part of the culture of medicine?" he asked. "We need a culture of quality". He then partly answered his own question by talking about the complexity of the idea. "Quality" is a multidimensional concept that has to include and synthesise the viewpoints of doctors, patients and healthcare funders.[26] It has to be able to supply measurable benchmarks against which improvements and deteriorations in care can be measured, especially in conditions of expansion, scale-up and task shifting.

And, while it is certainly about "access to high quality commodities and diagnostics", it is potentially about being able to measure so many other variables. These include laboratory performance; patient tracking and retention; treatment coverage; nutrition and food insufficiency; proportion virally suppressed; transmitted and acquired drug resistance; psychosocial variables ranging from financial situation to mental health; and, last but not least, the proportion of people reporting discrimination of stigma.

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[23] See Lecher S et al. *Progress with scale-up of HIV viral load monitoring – seven sub-Saharan African countries, January 2015-June 2016*. MMWR 65 (47): 1332-5, 2016. (View full text here).

[24] Brooks K et al. *Treatment failure and drug resistance in HIV-positive patients on tenofovir-based first-line antiretroviral therapy in western Kenya.* JIAS 19(1):20798. See full text here.

[25] http://www.opttest.eu/

[26] WHO. Quality of care: a Process for Making Strategic Choices in Health Systems. 2006. See https://www.who.int/management/quality/assurance/QualityCare_B.Def.pdf

Revisiting the 2014 Standard of Care Workshop

Antonella d'Arminio Monforte of the University of Milan recapped the previous workshop EACS held on standards of care, 0n 25-26 November 2014 in Rome.[27] [28]

The meeting was attended by members of EATG, WHO, UNAIDS and the European Commission as well as EACS. It aimed:

- To establish a complete picture of HIV and hepatitis care, so as to identify critical areas of intervention;
- To identify challenges in screening monitoring and diagnosis of people with HIV and hepatitis C or hepatitis B;
- To develop recommendations for integrating the latest scientific results to improve the quality of life of people with HIV and hepatitis in Europe.

It discussed the epidemiology of HIV in the European region, including late presentation; overcoming barriers to effective HIV testing and screening; improving access to ARV treatment (ART); improving retention in, and quality of, care; and more effective and better integration of tuberculosis and hepatitis B and C coinfections within HIV care.

The meeting identified that there had been little positive change in the European HIV epidemic in the previous decade, and since the 2014 meeting, this situation has largely remained the same, with subtle shifts within a largely unchanged overall picture of incidence. There are continued rises in HIV diagnoses in gay men in central Europe and some countries in western Europe (though with early signs of a fall in a few others), and HIV is threatening to become a generalised heterosexual epidemic in parts of the east, attendant on poor and patchy treatment access.[29]

In 2010, 76% of all new HIV diagnoses in the region occurred in Eastern Europe: in 2015, this was virtually the same (73%).

In 2010, three countries (Estonia, Russia, and Ukraine) reported more than 20 new HIV diagnoses per 100,000 inhabitants in the previous year. In 2015, Belarus and Moldova had also reported more than 20 infections per 100,000, and rates in some other countries such as Georgia, Latvia, Malta and Cyprus are increasing, though rates are declining in Ukraine and Estonia.

In 2010, 43% of new infections in Eastern Europe were reported as due to injecting drug use, compared to 4% in Western Europe. Since then, this proportion has fallen considerably, but has been matched by an increase in the proportion of new infections ascribed to sex between men and women.

In central Europe, very low rates of testing (in Poland, 0.62% of the adult population has been tested for HIV, and in Serbia 0.71%) mean that a high proportion of people with HIV remain undiagnosed and that diagnosis rates may have little relationship to ongoing incidence. Generally, though, longitudinal cohort data show little change in late presentation over the past decade.

The 2014 meeting identified that low rates of testing were also a problem in several other European countries such as Greece, and could be improved in most countries. Provider-initiated testing and counselling strategies need to be expanded in different settings: genitourinary medicine clinics, TB clinics, drug dependence clinics and antenatal care. There needed to be an expansion of community-based testing for men who have sex with men

[27] See http://www.eacsociety.org/conferences/eacs-partnerships/standard-of-care-2014.html

[28] Report at Mussini C European AIDS Clinical Society Standard of Care meeting on HIV and related coinfections: The Rome Statements. HIV Medicine 17(6):445-52. 2016.

[29] ECDC/WHO: Europe HIV/AIDS Surveillance Report 2015. See reference 11 above.

(MSM) and people who inject drugs (PIDs). There also needed to be an expansion of indicator-condition guided HIV testing.

Key recommendations from discussion workshops on testing at the 2014 meeting included:

- Guidance on testing should form part of EACS' portfolio of clinical guidance;
- Health care providers should be encouraged to ask patients for more information about their HIV testing history;
- More information is needed about successful models of community HIV testing, to be resourced at national level;
- Demand-side, supply-side and structural barriers should be addressed via mass media campaigns that aimed at reducing stigma around HIV testing and diagnosis;
    - through normalisation of testing
    - though making verbal rather than written informed consent standard,
    - by providing brief post-test information as standard rather than assuming risk-reduction counselling is needed in all cases;
- The continued barriers to community testing programmes within Europe needed to be addressed.

Key to the least point was developing more partnerships between community-based organisations and health care providers, and developing local models of provision and information that suit the local community. Examples include no-appointment STI checkup systems as developed by clinics such as Dean St in the UK[30] or the European Checkpoints,[31] or via local pharmacies in rural Spain.[32]

The 2014 meeting found that the situation of ART access in Eastern Europe was unacceptable. In coverage in Russia as reported by WHO in its 2010 report was 20-34%, 30% in Kazakhstan, 45% in Belarus and 47% in Ukraine (on a first-line regimen based on nelfinavir).[33] Only Russia has reported ART stock outs in the past two years.[34] [35] Even for those on ART, lack of awareness of HIV and of treatment and limited availability of treatment for financial reasons and ones of criminalisation and exclusion were contributing to very low rates of viral suppression.

In central Europe, ART coverage was better, above 60% in most countries and 69% in Romania. However newer agents and single-tablet regimens were unavailable in most countries and stockouts were reported from Albania, Macedonia, Serbia and some regions of Romania.

In the high-income countries of western Europe prescribers of full-cost, brand-name ART were facing growing budgetary pressures in many European settings to limit overall expenditure on ART and to consider the costs of individual agents.[36] The introduction of generic antiretrovirals upon the expiry of patents between 2014 and 2018 is likely to force further consideration of costs when prescribing.

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[30] http://dean.st

[31] See https://en.wikipedia.org/wiki/Checkpoint_(rapid_HIV_testing_facility)

[32] Fernández-Balbuena S et al. *Widening the access to HIV testing: the contribution of three in-pharmacy testing programmes in Spain.* PLoS ONE 10(8): e0134631. doi: 10.1371/journal.pone.0134631. 2015.

[33] WHO. Towards Universal Access: Scaling up priority HIV/AIDS interventions in the health sector: progress report 2010.

[34] Parfitt T. *Russia's drug-supply system leaves HIV patients wanting.* The Lancet Volume 377, No. 9763, p369–370, 29 January 2011.

[35] ITPC Russia. ARV treatment procurement and provision in Russia - ITPCru.

[36] Foreman C et al. *Maintaining cost-effective access to antiretroviral drug therapy through a collaborative approach to drug procurement, consensus treatment guidelines and regular audit: the experience of London HIV commissioners and providers.* Sexually transmitted infections 88(2):112-5 · March 2012.

Strategies for improvement of care in Eastern Europe were discussed, and it was concluded that EACS and other professional groups have an important role, especially in fostering greater engagement with other healthcare professionals in the region.

Political and policy dialogue will also be essential, especially when it comes to providing services for people who inject drugs and MSM, where the climate is hostile to harm-reduction approaches to HIV treatment provision and to prevention. Countries that may be close to some Eastern European countries in political culture (e.g. China, Vietnam) have adopted harm reduction policies in recent years.[37] [38] What can be learnt from these policy shifts?

In terms of implementation of better practice in infection control in TB and HIV, rapid TB diagnostic and drug susceptibility tests needed to be more available; there should be adequate empiric TB treatment and subsequent TB re-treatment and unlimited availability of all TB drugs and of shorter regimens. Due to methadone's interaction with rifampicin, use of buprenorphine or forms of OST other than methadone should be available.

In terms of HCV co-infection, the burning issue in 2014 was the need for support from clinical societies on advocacy against unacceptably high drug prices. More research was urgently needed to characterise which patients are at highest risk of decompensation. And more data were needed on the non-hepatic complications of hepatitis C in coinfected patients.

Better data is crucial

There was a consensus at the 2016 meeting that many national surveillance systems would have to improve to provide enough data for even minimal rating against standards of care. Justyna Kowalska from the Hospital for Infectious Diseases at the Medical University of Warsaw, presented the outcomes of an EACS meeting for physicians held in February 2016 in Warsaw.[39]

The "Euroguidelines in Central and Eastern Europe" Conference (ECEE) brought together over 60 participants from 15 countries: Albania, Armenia, Belarus, Croatia, the Czech Republic, Estonia, Georgia, Hungary, Lithuania, Moldova, Poland, Romania, Russia, Serbia, Slovakia and Turkey.

Key areas of Euroguidelines were presented by invited speakers; country representatives presented national data and topics specific for central and eastern Europe were presented by lecturers from the region including HIV in PIDs, children & adolescents, and women.

Kowalska said that a major issue emerging from this meeting was the necessity for better surveillance prior to achieving improvements in standards of care. There were major and often unacknowledged differences in epidemics between countries.

Half the countries at the meeting had surveillance systems based on totally anonymous rather than anonymised, name-based reporting. This meant that even the current prevalence of HIV was often not capturable by surveillance; that information on transmission mode often missing; that there was little or no data on linkage and suppression rates; and that only AIDS-related rather than non-AIDS deaths were reported. Many doctors not tied to major centres did not report on HIV positive patients in their care. As a result, data from

[37] Reid G, Aitken C. *Advocacy for harm reduction in China: a new era dawns.* Int J Drug Policy. 2009 Jul;20(4):365-70.

[38] Reid G, Higgs P. *Vietnam moves forward with harm reduction: an assessment of progress.* Glob Public Health. 2011;6(2):168-80.

[39] Report at http://www.eacsociety.org/conferences/eacs-partnerships/ecee-conference-2016.html

regional/national cohorts often gave better insight but these were often restricted by publication policies.

For these reasons, some countries like Croatia with small epidemics had located HIV care in just one centre.

Progress had been made on CD4 thresholds. In his presentation, Manuel Battegay showed that in 2014, one country in the CEE region (Latvia) still had a CD4 count threshold of 200 cells/mm^3 for starting therapy, 19 had a threshold of 350 cells/mm^3, five a threshold of 500 cells/mm^3 and only one (Romania) with no threshold. By 2016 this had changed to none with a CD4 threshold of 200, six with a threshold of 350, nine with a threshold of 500 and eleven with no threshold.[40]

Kowalska added, however, that 15/26 CEE countries (58%) still had some CD4 threshold for treatment in their national guidelines, whereas only 8/24 (33%) of western European countries still did.

More importantly, there were significant limitations in first line choice of ART, not all ARVs were available, there was delayed registration of TB, HCV and other co-morbidities and in most participating countries there were difficulties in access to laboratory capacity and well-trained staff to do CD4, viral load, tropism, and resistance tests. Resistance testing is rarely routine despite the SPREAD study finding a regional prevalence for transmitted drug resistance of 8.3%.[41] Crucially, as has already been discussed, viral load testing is *not* routine in many countries and in Serbia is not available at all, even at diagnosis.[42] TB and MDR-TB are specific problems in the region yet TB services are poorly aligned with HIV services and the structural drivers of TB, especially poverty and poor housing, are rarely addressed in clinical settings.

Kowalska added that an additional brake on changing from pure clinical practice guidelines was that in Poland the national guidelines were actually used as a teaching aid and students examined against them. Finally, especially with generic antiretrovirals (ARVs) already available in some of eastern Europe and soon arrive significantly in the west, guidelines could not ignore the issues of cost-effectiveness and cost per patient: “Maybe we also need a $90/$90/$90 cascade”, she said, referring to costings for the three main measures of diagnosis, retention in care, and viral suppression.

She added that physicians were in an advantaged position to complement and critique surveillance data such as that compiled by the ECDC. “Physicians are in a unique position to know what’s going on at ground level,” she said. “Whether it’s primary care physicians seeing HIV in their patients, or HIV physicians seeing poor retention, treatment shortages, poor adherence and viral suppression in their patients. Because of this EACS could be in a good position to add precision to ECDC’s surveillance figures. It is not possible to discuss continuity of care without physicians.”

What clinical standards do we need?

Two workshops at the meeting formulated the minimum data needed to establish a set of clinical standards. The first looked at guideline harmonisation across Europe and the minimum standard of data needed. Andrea Antonori of Italy and Nina Friis Møller of

[40] ECDC. Evidence brief: HIV and treatment. Stockholm: ECDC; 2015. For 2016, preliminary unpublished ECDC data.

[41] Hofstra LM et al. *Transmission of HIV Drug Resistance and the Predicted Effect on Current First-line Regimens in Europe.*

[42] See JUSTRI. Third meeting on HIV in South-eastern Europe and Middle East-North Africa. 2011. http://www.justri.org/malta/full-report-malta.pdf

Denmark said that if EACS' aim was to be *the* European HIV guidelines they would have to reform their evidence base, as they do not use the GRADE system for evaluating the strength of evidence, unlike the British BHIVA guidelines and the Netherlands ones. This would include minimal expectations of appropriate regimens, monitoring and outcomes including viral suppression.

One fairly radical suggestion was that regular CD4 monitoring could be dropped completely as long as there were regular viral load tests. CD4 counts would only be done on diagnosis, in patients not on ART, in cases of virological failure, and when patients were on immunosuppressive e.g. cancer) chemotherapy.

This step might not be possible in eastern/central Europe. Viral load monitoring is irregular in some countries and in Serbia is not done at all, a situation all delegates agreed needed redressing.

"To conform to guidelines, you *have* to provide access to proper care and diagnostics," commented Antinori and Møller. "Where does EACS' responsibility start and end in this? It implies a more political role."

Mapping shortages and loss to follow-up

From this arose an idea that EACS should start a project that would enable members to report on drug and diagnostic shortages, issues of retention, prevalence and eligibility for care of migrants, use of generics versus single-tablet regimens, and so on.

Retention in care was the subject of a workshop by itself. One problem is defining what retention in care actually is, and how to measure it, given that stable patients in long term care may only be having two appointments a year and even less frequent monitoring.

One draft definition is that the patient has no attendances within a given period that is significantly larger than either the usual monitoring frequency or the treatment refill period. A simpler one suggested at the meeting by Kevin de Cock was that of the proportion of patients failing to appear within a certain number of weeks after a missed appointment. He urged that "test and immediate treat" (i.e. patients walk out of the clinic with their first ART prescription the day they are diagnosed) should be adopted throughout Europe as it had been in parts of Africa.[43] [44]

If we can identify "loss to follow-up" (LTFU) patients, can we develop strategies suitable for summary in a set of guidelines that can usually restore linkage to care and prevent LTFU in future? One issue is how to find them. Some studies have found that text messages work best because the one thing highly mobile patients keep in their mobile phone number; in other situations this might be regarded as intrusive.[45] One course of action is to (discreetly) ask other services about them: another is to search for attendances at STI and indeed other clinics; if names-based HIV reporting is there to look for evidence of HIV re-tests; to monitor attendances at TB, antenatal and mental health clinics; to make enquiries to see if they are known at local community organisations and centres; and to check for incarcerations with prisons and migrant detention centres.

It was strongly suggested that the next issue of the EACS guidelines include a short section defining retention and suggesting strategies for loss to follow-up.

[43] Hayes R et al. *Reaching 90-90-90? Findings after two years of HTPN 071 (PopART) intervention in Zambia*. Conference on Retroviruses and Opportunistic Infections (CROI 2017), Seattle, abstract 1011, 2017.

[44] Petersen M et al. *SEARCH test and treat study in Uganda and Kenya exceeds the UNAIDS 90-90-90 cascade target by achieving 81% population-level viral suppression after 2 years*. 21st International AIDS Conference, Durban, abstract WEAC0106LB, 2016.

[45] Elul B et al. *A combination intervention strategy for HIV linkage and retention in Mozambique*. Conference on Retroviruses and Opportunistic Infections (CROI 2017), Seattle, abstract 110, 2017.

A third workshop looked specifically at TB. This is firstly because parts of eastern Europe have the highest levels of multi-drug-resistant (MDR) TB anywhere in the world, because HIV and TB co-infection is itself a driver of TB spread and drug resistance, and because HIV cases are being missed to lack of testing in TB patients and vice versa.[46] Only 60% of people diagnosed with HIV in Europe are tested for TB (partly because of assumptions that TB prevalence in gay men in high-income countries will be very low)[47] and globally only 50% of TB patients are tested for HIV (in Europe, 5% turn out to have HIV).[48]

Conclusions

In general, the meeting concluded:

- The EACS guidelines should maintain much of their present shape and follow up with indications for standard of care.
- They should also, however, form part of a broader set of standards of care, in collaboration with agencies such as ECDC and WHO, and that interdisciplinary meetings should happen soon to discuss their shape.
- They should include a definition and simple guide to retention in care.
- A specific agreement should be devised to set out EACS and ECDC's working relationship.
- Measurable standards to include in any new document were:
    - Frequency of CD4 monitoring
    - Viral load monitoring as mandatory and of a given minimum frequency
    - Recommendations for testing in settings likely to yield the highest proportion of diagnoses (including hospital admissions)
    - Testing of all TB patients for HIV and increased testing of HIV patients for TB
    - Proportion late diagnosed
    - Interval between diagnosis and receiving antiretroviral therapy
    - PrEP coverage and uptake/usage.

EACS should start a project that would enable members to report in real time on the above "care deliverables", and especially but not only:

- Drug and diagnostic shortages;
- Difficulties with retention and adherence;
- HIV prevalence and eligibility for care among migrants;
- The use of generics versus single-tablet regimens.

At the same time as a larger set of standards is being formulated, with there being much more unanimity in guidelines, there was now an advantage in issuing specific, easy to read, perhaps graphically-presented fact sheets in a broader variety of languages that could be used by doctors, patients and patient advocates in a variety of settings.

Doctors did have a specific part to play in what should be a much broader and more comprehensive set of standards of care. These should be clear on best practice but sensitive enough to adapt to local conditions.

Mike Youle of London's Royal Free Hospital made the point that especially in the era of comprehensive viral suppression, guideline and standards documents had to be aimed at

[46] Acosta CD et al. Drug-resistant tuberculosis in Eastern Europe: challenges and ways forward. Public Health Action. 2014 Oct 21; 4(Suppl 2): S3–S12.

[47] ECDC. *HIV treatment and care: Monitoring implementation of the Dublin Declaration on Partnership to Fight HIV/AIDS in Europe and Central Asia: 2017 progress report.* See http://ecdc.europa.eu/en/publications/Publications/HIV%20treatment%20and%20care.pdf

[48] WHO. TB/HIV Facts 2015. http://www.who.int/hiv/topics/tb/tbhiv_facts_2015/en/

the whole medical profession. “Otherwise,” he said, “You will still get the phenomenon of surgeons who in some countries refuse to operate on people with HIV and midwives who refuse to deliver babies.”

Germany’s Jürgen Rockstroh summed up the meeting by saying: “We are clinicians and up till now have just been clinicians. But now we need to start working with other specialisms, and with international organisations.”

Reference

The programme and all presentations from the 2016 EACS Standard of Care meeting can be downloaded from http://www.eacsociety.org/conferences/standard-of-care-meeting/standard-of-care-2016.html