MEETING REPORT

Women Against Viruses in Europe (WAVE) educational workshop

25th October 2017

16th European AIDS Conference

MiCo Milano Congressi

Piazzale Carlo Magno, 1, 20149 Milano MI, Italy

Contents

Executive summary

The third WAVE workshop was held on Wednesday the 25th of October 2017 in Milan, Italy as part of the annual European AIDS Clinical Society (EACS) congress.

The aim of the meeting was to inform the audience and stimulate discussion about barriers to care for women living with HIV (WLWH). Our speakers came from across and outside Europe, with differing experiences of HIV care for WLWH and preventing HIV in women at risk.

The workshop was broken down into three sessions discussing personal experiences followed by the role of integrase inhibitors in women, models of care in HIV positive women in Europe and clinical cases for pre exposure prophylaxis (PrEP) in women respectively. There was a high degree of audience participation with the use of voting devices making the three sessions of the workshop more interactive but also highly engaging.

Several key points were identified. Firstly, there are many facets to care for WLWH, however there are still prominent barriers in care across all European countries. Secondly, there is a deficit in research in WLWH care and more cooperative research between European countries is needed. Thirdly, PrEP availability and education for patients and healthcare professionals should be increased across Europe. Finally the WAVE committee was repeated highlighted as a platform to address these issues and improve healthcare outcomes for HIV positive women in Europe.

WAVE 2017 Award

Prof. Anna Maria Geretti, the former Chair of WAVE, was given the WAVE award 2017 for her outstanding contribution to promoting the welfare of HIV-positive women in Europe.

Introduction

This report summarises the key outputs from the WAVE workshop held on Wednesday 25th October in Milan, Italy, as part of the biennial European AIDS Clinical Society (EACS) congress.

The aim of this meeting was to discuss:

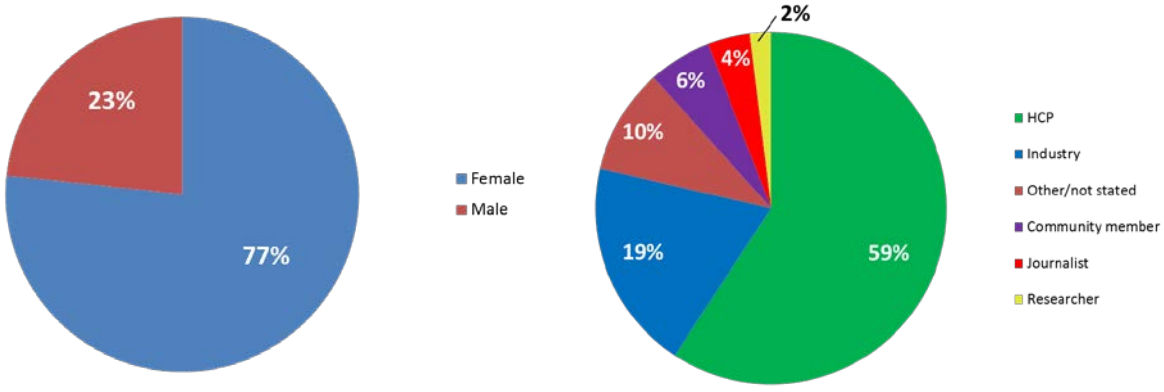
- The lack of clinical trial data regarding antiretroviral therapy (ART) in women
- Current models of care and the barriers to care for women living with HIV (WLWH) in Europe
- Encourage inter-European exchange of knowledge and encourage future collaborative research projects

The workshop was organised into a series of three sessions, each focusing on different models of care for WLWH:

1. The role of integrase inhibiters in WLWH care
2. Different models of care for WLWH in Europe
3. The use of PrEP in HIV prevention, focusing on real patient care.

Each session was set up to have individual speaker presentations followed by discussion, with a strong emphasis on audience participation and debate using keypads to answer pre-set questions.

The venue accommodated 160 people and was at full capacity for the duration of the workshop. A sample of 103 delegates from 29 countries was used to give insight into attendee demographics. This analysis demonstrated that over three quarters of the attendees were women and over half were healthcare providers (HCPs).



WAVE committee updates

Dr Justyna D. Kowalska gave an update on changes in the WAVE committee members and actions to be planned for 2018.

Committee leavers:

- Prof. Anna Maria Geretti (WAVE Chair)
- Ms. Adrienne Seed (WAVE S.C. Member and WAVE logo designer)

Actions for 2018:

- To have more regular face to face scientific committee meetings
- To attend more co-meetings: Regional meeting in 2018 (SoC)
    - Glasgow 2018
- Activating WAVE members to
    - Create working committees in key areas
    - invitations to be send out by e-mail to WAVE members
- New forms of action
- Short-course clinical exchange program for WAVE (application will be on EACS website)
- WAVE endorsement and support for research aiming to improve the health and wellbeing of WLWH
- WAVE award (to be presented at each annual EACS conference)

WAVE survey 2017 results:

Dr Karoline Aebi-Popp presented the results of WAVE survey


Survey.pptx

A link to the survey is available on the EACS website, on the WAVE webpage.

Session 1: Personal story and the role of integrase inhibitors in HIV-positive women

Chairs: Karoline Aebi-Popp (Switzerland); Justyna Kowalska (Poland); Ben Collins (UK)

The first session of the workshop opened with a presentation from Justyna Kopeć who described her experiences and emotional journey over the past 20 years. This was followed by a review of clinical trials investigating antiretrovral therapy (ART) and treatment in women from Sharon Walmsley.

20 years with HIV: The longest relationship I had

Justyna Kopeć, Poland

Justyna Kopeć presented insights from her experience of being diagnosed with HIV in Poland in 1997 (aged 23) through to achieving an undetectable viral load (VL) in the present day. A story-telling document was also provided as a handout.

Justyna presented with multiple indicators of HIV infection, but HIV was not considered as a cause due to social attitudes in the 1990s suggesting that she was not in a high-risk group. Poor relationships with gynaecologists also contributed to her delayed HIV diagnosis.

Following eventual diagnosis in 1997, Justyna began a drug regimen of antibacterial and antifungal drugs along with new anti-HIV drugs, such as zidovudine (known as AZT), but often experienced debilitating side effects.

However, her relationship with her HIV clinical team was good, and she was able to access newer antiviral drugs as they became available. As is common in people living with HIV, Justyna also suffered from depression. She managed to overcome this, and on a life-changing trips to the Himalayas, where she was able to reclaim her independence and conquer her fear of being remote from the HIV clinic. Currently she has an extremely positive outlook on life, life partner and an undetectable VL; however, her mental health is still monitored.

Justyna's insights into being an HIV-positive woman demonstrate the social stigma still attached to HIV infection, and highlight the mental health pressures associated with living with HIV.

The role of integrase inhibitors in WLWH

Sharon Walmsley, Canada

Sharon Walmsley is a professor of medicine at University of Toronto Department of Medicine and director of clinical research at the Immunodeficiency Clinic, Toronto Hospital. She is an expert in ART, with over 30 years' experience in the field, and has interests in maximising drug efficacy and reducing toxicity. She is also a strong advocate for reducing stigma, fear and depressing in WLWH.

Sharon opened by stating the need for more analysis by gender in ART trials. Most pivotal HIV trials are in men who have sex with men (MSM) and the results of these trials are extrapolated to women. Female participation in HIV studies is currently less than 20%, with one recent study having only 4% of women participants. Broadly

speaking, there have been no significant differences in ART efficacy between men and women in these trials, but there may be differences in tolerance and adherence. Two women-only trials have been conducted, the WAVES and ARIA studies, which have demonstrated that a drug combination can be superior in women**.**

In younger women, consideration should be given to potential interactions of ART with contraception and the safety of antiretrovirals in pregnancy. Currently, some aspects of guidelines on ART in pregnant women are based on expert opinion where data are lacking; furthermore, many countries do not have active pregnancy reporting systems to track HIV-positive pregnant women and births. Use of raltegravir is advised in late pregnancy presenters, where the clinician's aim is to reduce VL to undetectable at delivery to minimise baby transmission risk. Two recent clinical trials in Brazil and Thailand have demonstrated rapid reduction in VL using raltegravir, providing strong data for guidance on how quickly VL can be suppressed close to birth. The drug elvitagravir (boosted with cobicistat) is not advised for use during pregnancy due to evidence that elvitegravir does not cross the placenta well and, therefore, have reduces ART exposure to the foetus *in utero.*

In older WLWH, co-morbidity and the menopause are important considerations. Early menopause, immunosuppression and socioeconomic factors can lead to osteoporosis or fracture, with fracture rate being higher in HIV-positive women compared with HIV-negative women of a similar age. Tenofovir has been linked to possible changes in bone mineral density; therefore, menopause should be a time to reconsider ART treatment in women.

Session 2: Workshop on models of care for HIV-positive women in Europe

Chairs: Karoline Aebi-Popp (Switzerland); Cristina Mussini (Italy); Annette Piecha (Germany); Kristina Thorsteinsson (Denmark)

The second session focused on the different models of care for HIV-positive women across Europe. European countries were divided into West, Central or East Europe with an expert from each region giving an oversight to the models of care from the countries within each region.

West Europe

Annette Haberl, Germany

Countries: Austria, Denmark, Germany, Poland, Portugal, Spain, Switzerland and the UK

Dr Annette Harberl is a leading medical doctor in HIV Germany with 20 years' experience in the field. She is a member of the "adult antiretroviral therapy" and "HIV therapy in pregnancy" guideline groups as well as a board member of the German AIDS Society (DAIG) and a member of the national AIDS Advisory Board (NAB). In addition, Dr Haberl has been scientific director and organizer of the annual German symposium "HIV and Pregnancy" since 2000.

Dr Haberl surveyed clinical experts in HIV for each of the eight countries composing the West Europe region on 12 topics relating to WLWH care (Please see Table 1 in the Appendix results). The proportion of women in people living with HIV ranged from 18% to 29. All countries except Switzerland had gynaecologists onsite at HIV clinics; however, the UK was the only country to have women-only HIV clinics. The HIV clinicians who were surveyed identified key areas for improvement, including addressing HIV stigma in Denmark, retention of care in Switzerland and PrEP equality for women in the UK. Dr Haberl also described studies in care for HIV-positive women that are being conducted across West European countries but highlighted an imbalance in research activities between the different countries. More cooperation across countries is required in the future and WAVE could be a platform to achieve this.

- The Supporting Women with HIV Information Network (SWIFT) that brings together community representatives, HIV clinicians and academic researchers to collaborate and support research in women with HIV was highlighted as being unique in the UK
- German University Clinic in Frankfurt that cares for over 1,500 patients. The clinic has an interdisciplinary team of gynaecologists, obstetricians and paediatric doctors with women's care integrated into the outpatient clinic. Despite limited funding the clinic is able to perform some sex and gender-specific research. Peer support is also provided onsite that has a focus on patient education through the "Helpinghand programme", which supports patients from foreign countries (largely sub Saharan Africa) to educate newly diagnosed patients about living with HIV in the community

Central Europe

Cristiana Oprea, Romania

Countries: Albania, Bosnia and Herzegovina, Bulgaria, Croatia, Czech Republic, Hungary, Macedonia, Montenegro, Poland, Romania, Serbia, Slovenia, Slovakia and Turkey

Dr Cristiana Oprea is an HIV specialist and head of HIV at Victor Babes Clinical Hospital for Infectious and Tropical Diseases, Bucharest. She has over 25 years of clinical and research experience working with HIV as well as being a regional representative of the EACS committee and is a member of the governing body.

Similarly to West Europe, Dr Oprea surveyed clinical experts in HIV for each of the 14 countries composing the Central Europe region on 12 topics (Please see table 2 in the appendix for results). Central European countries had greater variation in population and gross domestic product per capita, and HIV burden compared with

Western Europe. There was also a range of political attitudes and religious beliefs. These differences were identified as contributing to the different HIV rates amongst women and as barriers to care. A high percentage of late presentation (greater than 60% of newly diagnosed cases) was reported in Macedonia, Hungary, Romania, Bulgaria and Slovenia. Romania was noted as a country with a particularly high HIV burden (relative to population size) having 22,000 registered cases. Approximately 60% of these cases are F1 subtype of Angolan origin and can be attributed to nosocomial transmission by contaminated needles or blood transfusions in the late 1980s.

Multiple barriers to care were identified in this region, including:

- Social (stigma, fear of discrimination, meeting people they know, shame and fear) and geographical (distance to HIV clinic)
- Economical (lack of health insurance, lack of money to travel large distances, childcare availability while travelling)
- Educational barriers (lack of knowledge in community of HIV, personal education level)
- Loss of follow up, partially due to emigration to West Europe, and a lack of integrated HIV and gynaecological care were also identified

East Europe

Inga Latysheva

Countries: Russia, Ukraine, Armenia, Belarus

Dr Inga Latysheva is deputy head at the Republican Clinical Hospital of Infectious Diseases in St Petersburg, Russia where she helps coordinate 25 regional HIV centres across Russia to provide HIV diagnosis and treatment access across the country. She is an expert in care for HIV positive pregnant women, women in childbirth and children.

Dr Latysheva opened her presentation by describing that the HIV epidemic started later in this region compared with the rest of Europe. Transmission in this region is largely accounted for by injecting drug users and heterosexual contacts, with women accounting for approximately half of the HIV-positive population in East Europe (highest concentration in young women in Ukraine and Russia). Vertical transmission from WLWH women remains a concern in this region, especially in Russia and Ukraine (with more than 1,600 deliveries in HIV-positive women per year in Ukraine). However, Russia is currently working towards eliminating mother-to-child transmission and 80% of pregnant women receiving ART in Russia have undetectable VL at birth.

- There is a strong focus on early testing in East Europe with an annual growing number of people being tested(in 2016, more than 20% of the total population were tested for HIV in Russia. Early detection was very frequent in women during pregnancy; however, late presentation was higher in women older than 40 years (50%)
- Russia employs modern approaches to HIV testing, including integrated care at different medical centres, (such as tuberculosis clinics, antenatal clinics, sexually transmitted infection [STI] clinics, prisons and injecting drug clinics). HIV testing has been decentralised and accelerated, especially during HIV testing campaigns that have occurred twice a year for the past 2 years. During these campaigns more than 1 million individuals were tested for HIV. Russia also has a federal institution for reporting HIV and the management of complicated cases

Session 3: PrEP in women – clinical cases

Chairs: Margaret Johnson (UK); Justyna Kowalska (Poland); Jean-Michel Molina (France); Magdalena Ankiersztejn-Bartczak (Poland)

The final session of the workshop focused on the use of PrEP in clinical cases from three regions of Europe (Armenia, Ukraine and the UK). Audience participation was encouraged in this session, with the use of set questions and key pads for answering. In general, answers to the questions were very varied, highlighting both the difference in treatment expectation and the availability of PrEP in these countries.

Case 1: Armenia – HIV exposure during pregnancy

Tatevik Balayan, Armenia

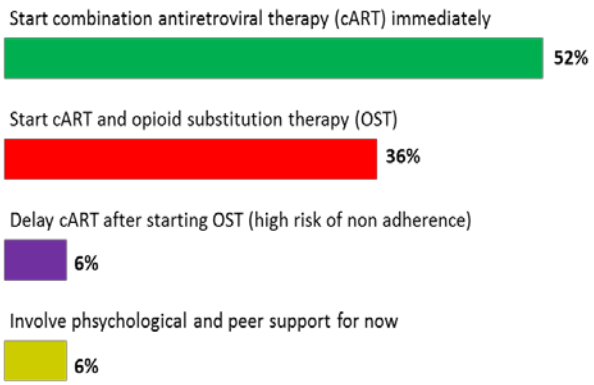
Dr Tatevik Balayan is an epidemiologist at the National Centre for Disease Control and Prevention of the Republic of Armenia where she contributes to development of national guidelines and protocols on prevention, diagnosis and treatment of HIV in Armenia.

Case overview

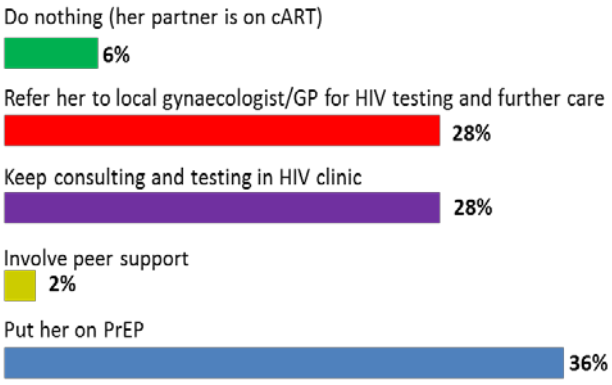
- Ania and Konrad are a heterosexual couple
- Ania is 12 weeks pregnant and is HIV negative
- Her partner, Konrad, has a history of mixed substance abuse and was diagnosed with HIV and Hepatitis C virus (HCV) in 2009 (CD4+ 904, VL 144)
- Konrad had a single visit to a clinic in 2011 where he received detox therapy (CD4+ 850, VL 6000), but was lost to follow up until 2015 when he presented in care after detox, displaying addiction to tramadol and alcohol (CD4+331, VL7880)
- Konrad insists on having unprotected sex with Ania

Questions asked to the audience:

1. What should we do with Konrad?



2. What should we do with Ania?



Discussion points

- Konrad was immediately put on OST and cART and had an undetectable HIV VL within 1 month, but continued harmful drinking
- Ania was not prescribed PrEP but had repeated consultations on HIV transmission risk. She was regularly tested as HIV and HCV negative and delivered a healthy baby
- Members from the audience agreed it would have been appropriate to put Ania on PrEP as it is available in Armenia, has a low risk of complications in pregnant women and Konrad may have ART adherence issues due to his alcohol addiction

Case 2: Ukraine – an HIV-positive women who injects drugs

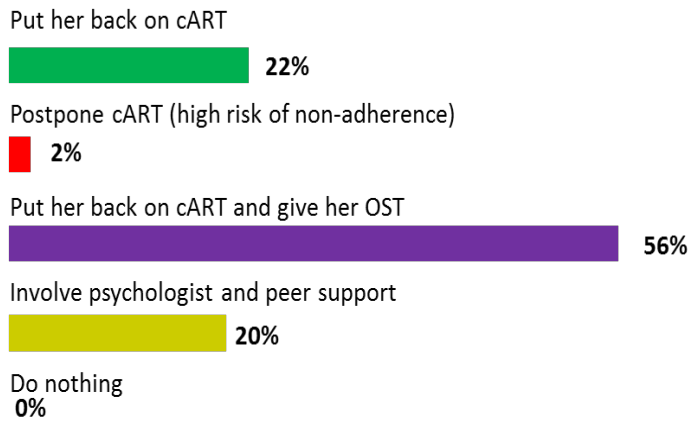
Marta Vasylyev, Ukraine

Case overview

- Olena is a 28-year-old bisexual woman who had HIV and HCV infections diagnosed in 2015 (CD4+ 670, VL 4500), but has poor treatment adherence and was lost to follow up
- She is an active injecting drug user, reporting at least six sexual partners the in the past month, and has previous involvement in the sex industry
- She has a 5-year-old daughter and following her one suicide attempt, is at risk of termination of her parental rights, but is in a stable relationship with HIV-negative partner, Oleg
- Oleg is a 45-year-old male who is HIV-negative but HCV positive. He has a 13-year history of injecting drug use, and is still actively injecting. He suffers from depression but is not attached to a harm reduction programme

Questions asked to the audience:

1. What should we do with Olena?



Discussion points

- Both Olena and Oleg were put on OST and started regular meetings with psychotherapists and social workers. Both individuals received comprehensive counselling on condom use and began HCV treatment
- Olena started cART and had an undetectable HIV VL within 3 months
- It was noted that HIV-positive individuals with undetectable VL should wait for at least 6 months before engaging in unprotected sex and that condom use should be encouraged in this case

Case 3: UK – three women

Nneka Nwokolo

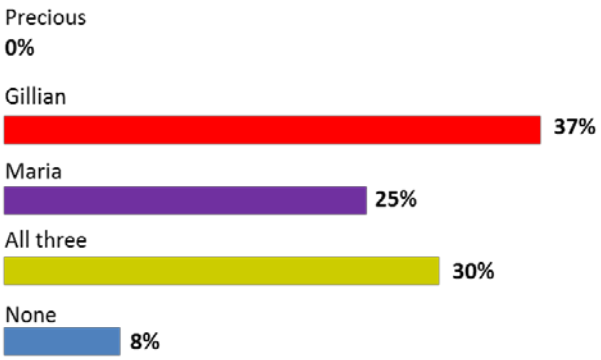
Dr Nneka Nwokolo is a consultant physician in sexual health in HIV medicine at Chelsea and Westminster Hospital (UK). She has published extensively on HIV medicine and her interests include the provision of pre-exposure prophylaxis for the prevention of HIV infection and the management of complex infection and she is the chief UK investigator of the DISCOVERY PrEP study.

Case overviews

- Precious is a 35-year-old Nigerian woman who is married with three children. She tested HIV negative during her last pregnancy but has not been tested since and has never been tested for any other STI. She uses Mirena ISU for contraception and does not use condoms with her husband
- Gillian is a 32-year-old white transsexual woman who has had lower gender reassignment surgery and is receiving hormone treatment with oestrogen gel. She has no regular partner, but has several casual male partners with inconsistent condom use. She tested negative for HIV two years ago at which time she also had an uncomplicated chlamydia diagnosis
- Maria is a 25-year-old white heterosexual woman who has no regular partner and has had six casual partners in the last 6 months. She takes oral contraception pills but rarely uses condoms and has a past history of chlamydia and genital herpes

Questions asked to the audience:

Who do you think would be a candidate for PrEP?



Is Gillian at risk of HIV if she doesn't have anal sex?

Discussion points

- Precious: The highest risk of HIV infection from black African women in the UK will come from their long-term partner, who may be having sexual contact with other women. Black African women may also be unable to negotiate using condoms with their partners, increasing potential risk. **The use of PrEP should therefore be discussed with Precious**
- Gillian: Risk of HIV acquisition in the neovagina is unknown as there have been no studies investigating this patient population to date. The likelihood of epithelial trauma in the neovagina is higher than for the stratified squamous epithelia of vagina and transsexual women are 49 times more likely to be HIV positive than cissexual women. In conjunction with discrimination, poor housing, sex for payment and sexual violence being common in transsexual women, **Gillian is at high risk of HIV infection and the use of PrEP is highly advisable**
- Maria: In the UK, risk of HIV transmission in white females is highly dependent their sexual partners. HIV rates among white heterosexual women remains low (relative to the Black African immigrant population) and **information on sexual partners is required before potentially suggesting use of PrEP**
    - It was noted that HIV transmission risk in white females in the Ukraine is different to the UK. A greater proportion of the population in the Ukraine is HIV positive compared with the UK but is mainly restricted to injecting drug use. In the Ukraine, Maria would be given comprehensive counselling but would not receive PrEP as it is currently unavailable

Closing presentation: HIV serodiscordant couples – is cART enough

Sheena McCormack

Sheena McCormack is a professor of Clinical Epidemiology at Imperial College London and a consultant in HIV medicine who has been coordinating HIV prevention trials in MSM and WLWH since 1994. She has report on the PROUD study, comparing PrEP to no-PrEP. Currently her focus is to ensure that PrEP becomes available to those who need it in the UK and Europe and she continues to work on HIV vaccine trials.

In her talk, Professor McCormack highlighted HPTN052 was an important clinical trial that demonstrated HIV transmission between serodiscordant partners was reduced by 96% and the data give confidence in the statement that undetectable means untransmittable (U=U). This message works well in couples counselling but does not work as a public health strategy. She also highlighted that allowing time for individuals to think about treatment regimens is important and needs to be considered when giving counselling. More work needs to be done to allow more feasible access to testing, care and drugs for prevention and treatment is required along with society to change so that stigma is less of a barrier to care.

Appendix

Models of care questions

West Europe

1. What is the estimated number of people living with HIV in your country? (number of HIV-positive women)
2. What institution is providing this epidemiological data?
3. Is there a national pregnancy registry?
4. Are there cohort studies that focus on, or specially include, women's issues?
5. What about clinical trials on sex and gender-specific issues?
6. Do you have women only clinics?
7. At your site, do you have a gynaecologist working with you?
8. Do women with HIV (or all women) have to pay for contraception?
9. How often is a pap smear recommended for women with HIV?
10. Can your patients get psychosocial support at your site?
11. Do you offer peer support for women with HIV in your clinic?
12. Anything else to add?

Central Europe

1. Total number of HIV patients (2016)
2. Number of HIV positive women
3. New cases diagnosed in women in 2016
4. Number of HIV centres
5. Main routes of HIV acquisition in women
6. Percentage of late presenters in women
7. Dedicated HIV clinics for women
8. Integrated HIV and gynaecological care
9. HIV testing in pregnancy, how often
10. Screening for cervical cancer
11. Barriers to care for HIV positive women

Table 1: WLWH-related information for West Europe

	Austria	Denmark	Germany	France	Italy	Portugal	Spain	Switzerland	UK
PLWH	8,000–9,000	5,000	84,700	153,000	100,000	44,456	130,000	15,200	88,725
WLWH	26%	25%	18%	39%	25–27%	27%	18–20%	25%	29%
Pregnancy registry	No	Yes	Yes	Yes	Yes	Data collection	No	Yes	Yes
Women only clinics	No	No	No	No	No	No	No	No	Yes
Gynaecologist at site	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes
Free access to contraception	No	No (free IUD at one site)	No	Yes	No	Yes (IUD not included)	Specific clinics for contraception	No	Yes
Pap smear interval	Annually	Annually	Annually	Annually	Annually	Annually	'It depends'	Annually	Annually
Psychosocial support at site	Yes	No	Yes	Yes	Yes	psychiatric support available	no specific support	Yes	Yes

IUD, intrauterine device; PLWH, people living with HIV.

Table 2: WLWH-related information for Central Europe

Country	Population (million)	GNI/capita (US $)	Total no. of HIV cases	No. of HIV-positive women	Late presentation	Women-only clinics	Integrated HIV/ gynaecological care	Gynaecologist in HIV clinic	HIV testing in pregnancy	Cervical cancer screening
Albania	2.87	4,250	1,008	286	–	No	No	No	Yes, low rate	No
Bosnia and Herzegovina	3.51	5,030	315	46	–	No	Yes	No	No	Yes (yearly)
Bulgaria	7.12	7,480	2,704	460	50%	No	Yes	No	Yes	Yes (yearly)
Croatia	4.17	12,750	1,433	176	17%	No	No	No	No	Yes
Czech Republic	10.56	18,150	3,087	436	30%	No	Yes	Yes	Yes	Yes (every 1–2 years)
Hungary	9.81	12,970	3,344	343	60%	No	Yes	No	No	Yes (yearly)
Macedonia	2.01	4,834	315	53	66%	No	No (help of NGOs)	No	No	Yes (yearly)
Montenegro	0.62	7,260	144	12	–	No	Yes	No	No	No
Poland	37.9	13,300	21,000	~4,200	60%	No	Yes (some centres)	Yes (some centres)	Yes	Yes (recommended)
Romania	19.9	9,520	22,095	5,971	59%	No	No	Yes (some centres)	Yes	Yes (some centres)
Serbia	7.05	5,540	2,276	560	–	No	No	No	No	No data
Slovenia	2.06	22,250	570	9%	75%	No	Yes	No	No	Yes (every 2–3 years)
Slovak Republic	5.4	17,570	898	92	–	No	No	No	Yes	Yes (yearly)
Turkey	79.5	12,000	14,695	3,203	–	No	No	No	No	Yes (every 1–2 years)

GNI, gross national income; NGO, non-government organisation.

Table 3: WLWH-related information for East Europe

Country	No. of HIV-positive women (2016)	Number of births to HIV-positive women	ART coverage in pregnant women
Azerbaijan	3,100	200	90%
Belarus	16,000	~500	96%
Ukraine	96,000	~3,500	–
Kazakhstan	7,100	~400	89%
Kyrgyzstan	9,700	200	89%
Uzbekistan	9,700	500–1,000	95%
Tajikistan	5,400	500	58%