

Pure-AMC

Is reaching 90/90/90 enough to end AIDS? Lessons from Amsterdam

on behalf of the HIV Transmission Elimination Amsterdam (H-TEAM) Initiative; HIV Transmission Elimination Amsterdam (H-TEAM) Initiative; de Bree, Godelieve J.; van Sighem, Ard; Zuilhof, Wim; van Bergen, Jan E. A. M.; Prins, Maria; Heidenrijk, Michiel; van der Valk, Marc; Brokx, Pieter; Reiss, Peter Published in:

Current opinion in HIV and AIDS

DOI: 10.1097/COH.000000000000586

Published: 01/11/2019

Citation for pulished version (APA):

on behalf of the HIV Transmission Elimination Amsterdam (H-TEAM) Initiative, HIV Transmission Elimination Amsterdam (H-TEAM) Initiative, de Bree, G. J., van Sighem, A., Zuilhof, W., van Bergen, J. E. A. M., Prins, M., Heidenrijk, M., van der Valk, M., Brokx, P., & Reiss, P. (2019). Is reaching 90/90/90 enough to end AIDS? Lessons from Amsterdam. *Current opinion in HIV and AIDS*, *14*(6), 455-463. https://doi.org/10.1097/COH.0000000000586

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
 You may not further distribute the material or use it for any profit-making activity or commercial gain
 You may freely distribute the URL identifying the publication in the public portal ?

Take down policy If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.



Is reaching 90/90/90 enough to end AIDS? Lessons from Amsterdam

Godelieve J. de Bree^a, Ard van Sighem^c, Wim Zuilhof^d Jan E.A.M. van Bergen^e, Maria Prins^f, Michiel Heidenrijk^g Marc van der Valk^a, Pieter Brokx^h, and Peter Reiss^{a,b,c}, on behalf of the HIV Transmission Elimination AMsterdam (H-TEAM) Initiative

Purpose of review

Although cities present opportunities for infectious pathogens such as HIV to spread, public health infrastructure within these cities also provides opportunities to design effective approaches to eliminate transmission of these pathogens. The HIV Transmission Elimination AMsterdam (H-TEAM) Initiative, a consortium of relevant stakeholders involved in HIV prevention and care, designed an integrated approach to curb the HIV epidemic in Amsterdam, including providing preexposure prophylaxis (PrEP), increasing awareness of acute HIV infection, offering same-day test and treat, and improving indicator disease-driven HIV testing.

Recent findings

In 2013, approximately 230 people in Amsterdam were newly diagnosed with HIV, largely belonging to one of two key affected populations, namely MSM and people with a migration background. Since the start of H-TEAM in 2014, a decrease in new diagnoses was observed (130 in 2017), with an increasing proportion of MSM who had been diagnosed with a recent infection.

Summary

The H-TEAM shows that a city-based concerted effort is feasible. However, major challenges remain, such as reducing the number of late HIV diagnoses, and identifying and providing appropriate services to a diminishing group of individuals who are likely the source of transmission.

Keywords

Amsterdam, epidemic, HIV

INTRODUCTION THE POTENTIAL OF CITY-CENTERED APPROACHES TO END THE HIV EPIDEMIC (MAX 2500>2495)

Worldwide, around eight million people living with HIV live in urban areas (http://www.unaids.org/en/ resources/documents/2014/thecitiesreport), where social, economic and structural factors drive inequality in access to health services, thereby contributing to the propagation of an HIV epidemic in a city. At the same time, cities often have strong prevention and care infrastructures that could be used to curb the ongoing transmission of the virus. In addition, various interventions are currently available that individually target each of the potential drivers of HIV transmission. These interventions range from protection from infection through preexposure prophylaxis (PrEP), testing for, and diagnosis of, early HIV infection, and institution of immediate treatment to achieve rapid viral suppression, that in turn prevents ongoing viral transmission. The potential of such interventions in containing HIV epidemics in urban areas has been demonstrated in San Francisco and British Columbia. For example, in San Francisco, a reduction in

^aDivision of Infectious Diseases, Department of Internal Medicine, Amsterdam Infection and Immunity Institute, ^bDepartment of Global Health, Amsterdam Institute for Global Health and Development, Amsterdam University Medical Centers, University of Amsterdam, ^cStichting HIV Monitoring, ^dSoa Aids Nederland, ^eDepartment of General Practice, Amsterdam University Medical Centers, University of Amsterdam, ^fDe-Department of Infectious Diseases, Public Health Service of Amsterdam, ^gAmsterdam Health Technology Institute and ^hDutch Association of People Living With HIV, Amsterdam, The Netherlands

Correspondence to Peter Reiss, Division of Infectious Diseases, Department of Internal Medicine, Amsterdam Infection and Immunity Institute, Amsterdam University Medical Centers, University of Amsterdam, Amsterdam, The Netherlands. Tel: +31 20 5664172; e-mail: p.reiss@amsterdamumc.nl

Curr Opin HIV AIDS 2019, 14:000-000 DOI:10.1097/COH.0000000000000586

1746-630X Copyright $\ensuremath{\mathbb{C}}$ 2019 Wolters Kluwer Health, Inc. All rights reserved.

www.co-hivandaids.com

KEY POINTS

- Despite having achieved and in fact surpassed the UNAIDS 90–90–90 goals, Amsterdam still faces a significant number of individuals who enter care at a late stage of infection.
- Our experience with the H-TEAM Initiative shows that a city-based combination prevention approach, involving all relevant stakeholders, offers novel opportunities by which to further curb the HIV epidemic in Amsterdam.
- The demonstration study on PrEP for MSM at high risk of HIV infection shows that offering PrEP assists in reaching out to a subgroup of MSM at very high risk of infection and, at least over the short term, does not lead to a significant increase in sexually transmitted infections.
- Early recognition, testing and immediate linkage to care for same day start of treatment of acute HIV infection is feasible and has potentially contributed to an increase in the proportion of early HIV diagnosis among MSM.

mean viral load and community viral load (defined as the sum of the most recent viral loads of all HIVpositive individuals in a community in the city) was accompanied by a decrease in new HIV diagnoses. This decline in new diagnoses correlated with increased combination antiretroviral therapy (cART) coverage and changes in regulation regarding HIV testing [1,2]. Moreover, over a 15-year period (1996-2009) in British Columbia, community viral load decreased as cART coverage increased [3]. Furthermore, in San Francisco, the early introduction of PrEP as an effective measure to prevent new infections among individuals at high risk for HIV infection, together with a roll out of testing coupled with immediate initiation of cART, has contributed to a further decline in new HIV diagnoses [4]. These studies indicate that a tailored and comprehensive combination intervention approach, in which prevention and treatment are combined with city-specific strategies to remove structural barriers for access to services, are potentially most successful to significantly reduce incident HIV infections [5].

SITUATION IN 2013-2014 AGAINST THE BACKGROUND OF STANDARD PREVENTION AND CARE AT THE TIME

In 2013–2014, the Netherlands faced around 1000 new HIV diagnoses each year [6]. Twenty-two percentage of these new HIV diagnoses occurred within the Amsterdam area (data National Institute for



FIGURE 1. Trend in new HIV diagnoses in Amsterdam and the Netherlands. Number of new diagnoses in the Netherlands and Amsterdam since 2002 (data Stichting HIV Monitoring). *Source:* van Sighem AI, Boender TS, Wit FWNM, *et al.* Monitoring report 2018. HIV infection in the Netherlands. Amsterdam: Stichting HIV Monitoring; 2018. Available online at www.hiv-monitoring.nl.

Public Health and the Environment). Today, an estimated 6000 individuals living with HIV reside in Amsterdam, with MSM being the largest key affected population (78% of new diagnoses). Of the remaining 22%, the majority is heterosexual with a migration background. Most likely due to the very early introduction and high coverage of harm reduction strategies in Amsterdam in the early years of the HIV epidemic, the proportion of individuals acquiring HIV through injection drug use has become extremely small (<1%). The number of new diagnoses in Amsterdam in 2013 was around 230 (Fig. 1). Several HIV test and treat strategies were in place at the time, including the introduction of opt-out testing for HIV at the large Amsterdam sexually transmitted infection (STI) clinic (introduced in 2007 [7]) and online test facilities for MSM (Man tot Man Testlab) (introduced in 2009), and the recommendation to already start cART during early HIV infection in 2012. However, despite all these 'standard' prevention and care measures, a rapid decline in new diagnoses was not yet being achieved. Of all people living with HIV in Amsterdam, an estimated 5% remained unaware of their infection in 2017 (Stichting HIV Monitoring, Amsterdam, The Netherlands). Within this group of individuals, MSM, especially those who have an acute or recent HIV infection, are particularly likely to be the main source of ongoing transmission [8]. At the same time, in 2017, an average of around 32% of newly diagnosed individuals presented for care

with a late stage of infection (i.e. with a $CD4^+$ cell count below 350 cells/ml or with an AIDS-defining illness). Although such late presentation is more common in women and men other than MSM (41%), the group of late presenters is quite diverse and also includes a substantial proportion of MSM (30%). In addition to MSM who are unaware of experiencing an acute infection, late presenting MSM may also be importantly contributing to ongoing transmission of HIV. It is therefore critical to obtain more granular insight into the characteristics of specific late presenter subgroups. Such insights would facilitate identification of those who contribute most importantly to onward HIV transmission and thereby enable improved and novel testing interventions. These considerations were the rationale behind the HIV Transmission Elimination AMsterdam (H-TEAM) Initiative that aims to deploy a city-based combination intervention strategy focused on all factors that maintain the epidemic. To accomplish these aims H-TEAM (www.hteam.nl) brought together all relevant stakeholders from public health, civil society, key affected communities, general practitioners (GPs) and HIV-treating physicians in Amsterdam, with the aim of designing and implementing a multidisciplinary and integrated approach. In the present article, we describe changes in the HIV epidemic in Amsterdam over time, covering the period of 2 years (2013–2014) before the start of the H-TEAM Initiative in 2015, until 2017. In addition, we briefly summarize the introduction of different interventions concerning prevention, testing and treatment uptake and how they may relate to observed trends in new diagnoses and stage of infection at time of diagnosis.

PREVENTION OF NEW INFECTIONS: THE IMPLEMENTATION AND EVALUATION OF PREEXPOSURE PROPHYLAXIS IN AMSTERDAM

PrEP is currently recommended for individuals at substantial risk for HIV infection, namely MSM, transgender persons and heterosexual serodiscordant couples at substantial risk for HIV [9]. After the efficacy of PrEP had been demonstrated in large clinical trials [10–12], it remained unclear how PrEP would preferably be used in practice (that is daily or event-driven), how it would affect sexual risk-taking behavior, and whether longer term PrEP use would change the incidence of STIs. Therefore, in 2015, the Amsterdam PrEP demonstration project (AMPrEP) was initiated to study the uptake, acceptability and usability of the choice between daily or event-driven PrEP for MSM and transgender persons (n = 367) at high risk of acquiring HIV infection. The majority of

individuals (73%) chose daily PrEP, and the baseline analysis showed a remarkably high prevalence of common STIs (17%) and an unexpectedly high prevalence of hepatitis C virus (HCV) (4.8% compared with 1% among HIV-negative MSM not on PrEP visiting the STI clinic in Amsterdam) [13–16]. Very similar to what was observed in the PROUD [11] and Ipergay studies [12], these data suggest that offering PrEP assists in reaching MSM at particularly high risk for HIV infection. An ongoing concern is whether offering PrEP may induce risk compensation and could result in an increase in STI incidence. In the AMPrEP study, the number of condomless anal sex acts with casual partners increased, but the STI incidence did not increase statistically significantly during the first 24 months after enrollment [17[•]]. We did observe one case of incident wild-type HIV infection in an individual with a very high frequency of receptive condomless anal intercourse, in spite of adequate and sustained adherence to PrEP [18]. The initial results of the AMPrEP study, together with those from other PrEP studies and the ongoing international experience with PrEP, importantly informed the advice issued by the Dutch National Health Council to the Ministry of Health to support the implementation of PrEP in the Netherlands. The high STI prevalence in the population likely to access PrEP underscores the need for careful implementation, with regular screening for STIs, including for HIV and HCV. The expected increase in PrEP uptake in the near future will hopefully result in a steeper reduction in incident HIV infection among MSM than has been observed in previous years.

PREVENTION OF NEW INFECTIONS: IMMEDIATE 'TEST AND TREAT' FOR ACUTE HIV INFECTION

As indicated previously, individuals with acute HIV infection (AHI), who are generally characterized by having very high viral load levels, have a particularly high likelihood of transmitting HIV [19–21]. According to a recent study on HIV transmission that combined viral phylogenetics and detailed clinical and demographic data, 70% of all forward transmissions in MSM in the Netherlands were estimated to have occurred during the early stage of infection (defined as 3 months post infection) [8]. The challenge, however, is that AHI may easily be missed because individuals are unaware of their infection. This is primarily due to a lack of knowledge of AHI and its symptoms, and/or failure to recognize or link symptoms to recent risk behavior [22,23]. Other factors contributing to this unawareness of infection include an underestimation of one"s own risk

1746-630X Copyright © 2019 Wolters Kluwer Health, Inc. All rights reserved.

www.co-hivandaids.com 3



FIGURE 2. Increase in proportion of recent HIV diagnoses. Proportion of all newly diagnosed MSM (blue), other men (red) and women (gray) in Amsterdam with documented evidence of recent HIV infection. A recent infection is defined as a known negative HIV test within the 6 months preceding diagnosis. *Source:* van Sighem AI, Boender TS, Wit FWNM, *et al.* Monitoring report 2018. HIV infection in the Netherlands. Amsterdam: Stichting HIV Monitoring; 2018. Available online at www.hiv-monitoring.nl.

behavior and lack of awareness regarding the benefits of early treatment initiation during AHI [19,24]. The clinical importance of early cART initiation became evident from recent studies which revealed that starting cART during the acute phase of infection improved prognosis [24-26]. These insights prompted us to design a specific acute HIV diagnostic pathway to which people can self-refer through an online AHI awareness tool (www.hebikhiv.nl) or be referred by their GP or the general STI clinic in Amsterdam. Using a symptom recognition score, adopted to fit the characteristics of individuals with AHI [27], which is obtained through the website symptom checker tool, together with point of care HIV RNA testing, we have tested 431 individuals since August 2015 (data until March 2019). Of these individuals, 25 turned out to have AHI (5.8%) and four had chronic HIV infection. All these individuals were referred to a treatment center in Amsterdam for same day start of cART [28]. These data resemble those from a similar approach in San Francisco [29], both demonstrating that targeted screening for AHI and immediate referral for start of treatment is feasible. We evaluated the effectiveness of the



FIGURE 3. Continuum of care for the total estimated HIV-positive population in Amsterdam by the end of 2017. The percentages at the top of the bars are calculated relative to the number living with HIV, while percentages at the bottom correspond to UNAIDS' 90–90–90 targets. Individuals were considered to be retained in care if they had at least one HIV RNA or CD4⁺ cell count measurement or a clinic visit in 2017. Viral suppression was defined as a most recent HIV RNA measurement in 2017 below 200 copies/ml.

4 www.co-hivandaids.com

Volume 14 • Number 00 • Month 2019



FIGURE 4. Decreasing number of new diagnoses in Amsterdam. The trend in new diagnoses is depicted against the different prevention and treatment interventions over the years 2002 until 2017. The *y* axis shows the number of new diagnoses among MSM in Amsterdam. *Source:* Stichting HIV Monitoring, Amsterdam, The Netherlands.

Amsterdam AHI trajectory by comparing the time between diagnosis and viral suppression for MSM diagnosed through this pathway and for those diagnosed through the routine testing facility at the STI clinic. For all MSM diagnosed with HIV (chronic as well as acute infection) at the STI clinic in Amsterdam, the median time between diagnosis and achieving viral suppression on treatment decreased from 228 days (median) [interrquartile range (IQR) 129-435] in the period 2012-2015 to 95 days (median) in 2015-2017 (IQR 63-136). In comparison, MSM who were diagnosed through the AHI trajectory between 2015 and 2017 (n = 19) achieved an undetectable viral load a median of 55 (IQR 31-74) days after diagnosis [28]. Finally, potentially following implementation of this approach, a sharp increase was observed in the proportion of MSM in Amsterdam diagnosed with HIV with evidence of recent infection (Fig. 2).

FINE-TUNING OUR INSIGHT INTO THE HIV EPIDEMIC ACROSS THE CITY: TARGETING INTERVENTIONS TO REDUCE LATE PRESENTATION FOR CARE

Immediate test and treat is critical in reducing onward transmission [30,31]. Recently, the final results of the PARTNER study confirmed the absence of a risk of linked transmission in serodiscordant gay couples in whom the seropositive partner was on suppressive ART [32^{•••}]. These data provided the final scientific grounds for the 2016 Prevention Access Campaign 'U=U' statement [33] and will hopefully also contribute to a reduction in HIV-associated stigma and criminalization. In Amsterdam, the policy of test and treat was implemented city-wide in 2016 and the city almost reached the UNAIDS 95– 95–95 goals in 2017 (Fig. 3). Nonetheless, despite the decline in new HIV diagnoses in Amsterdam over the past years (from 230 in 2013 to 130 in

Copyright © 2019 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited.

2017) (Fig. 4), one of the remaining challenges is to reduce the proportion of individuals who are diagnosed at a late stage of infection. Recent numbers show that around 32% of all newly diagnosed individuals in Amsterdam are diagnosed at a late stage [6]. Of the total number of individuals diagnosed late in 2017 (n = 51), 35 were MSM and 12 were non-MSM born abroad. To tackle this issue of late diagnosis, we are currently developing multiple simultaneous strategies to gain more detailed insight into the distribution of late presenters across the city and improve targeted testing practices. This approach involves the application of geospatial information system mapping that uses postal code level data on new HIV diagnoses and late presentation. Such data can be combined with sociodemographic data and data regarding other relevant health issues (e.g. data regarding cardiovascular comorbidity), thereby providing further insight into which areas in the city may be prioritized for improved targeted testing for HIV combined with other health prevention efforts. In addition, the approach involves efforts to improve testing based on HIV indicator diseases in both general practices and hospitals. In the Netherlands, the GP provides primary care and therefore the general practice setting provides an especially important opportunity to further expand testing, including for migrants from HIV endemic countries [34]. GPs in the Netherlands perform an estimated 50-70% of STI consultations and diagnose roughly one-third of HIV infections [35]. However, recent data show that GPs may overlook opportunities to test for HIV, including opportunities within the MSM population [35,36]. For example, a recent study among individuals newly diagnosed with HIV showed that in the 5 years prior to HIV diagnosis, 60% had visited their GP with an HIV indicator illness without the visit resulting in an HIV test being carried out [37,38]. Therefore, to improve testing and recognition of a possible HIV infection, specific training sessions for GPs that include direct personalized feedback on HIV tests requested, have been developed and rolled out as part of the H-TEAM effort.

Since 2015, 21% of new HIV diagnoses in Amsterdam have been made in hospital, 73% of which involved late presenters [6]. Several studies have demonstrated that, despite European guideline recommendations, testing for HIV in the presence of an HIV indicator disease is still not routine practice in hospitals, and, as such, opportunities for earlier diagnoses are frequently missed [39,40]. To clarify the extent to which this also occurs in Amsterdam hospitals, we are currently undertaking a study to analyze compliance with such HIV indicator disease-based testing guidelines in Amsterdam hospitals.

CONCLUSION

To date, our collective experience with the H-TEAM Initiative shows that a city-centered effort, addressing multiple aspects across the HIV prevention and care continuum, is a feasible approach and may contribute to optimize epidemic control. In the context of an epidemic that has reached a phase in which only a relatively limited number of new annual diagnoses occurs, the most important insight is that HIV transmission likely continues to occur in communities at risk within the small geography of a city. These communities are potentially heterogeneous and apparently insufficiently manage to access existing medical and public health services. Key remaining challenges include identifying and reaching out to the relatively small group of individuals who are not accessing testing in a timely manner, which include those who continue to sustain onward transmission. Within such a context continuing to only provide services according to existing city and nationwide policies proves to be an insufficient and too blunt of a tool. Making use of more granular demographic, socioeconomic, behavioral and additional data, and close collaboration with each relevant affected community, will be essential when designing novel ways of ensuring access to the optimal mix of services for all of those remaining in need.

Acknowledgements

We thank Catriona Ester for critically reviewing the article.

H-*TEAM Steering Committee: J.E.A.M.v.B.*^{4,5,6}, *G.J.d.B.*^{1,2}, *F. Deug*⁶, *M.H.*¹, *M.P.*^{2,3}, *P.R.*^{1,7} (*Chair*), *M.v.d.V.*².

H-TEAM Core Project Group: J.E.A.M.v.B.^{4,5,6}, G.J.d.B.^{1,2} (Chair), P.B.⁸, U. Davidovich³, S.E. Geerlings², E. Hoornenborg³, A. Oomen⁶, A.v.S.⁷, W.Z.⁶.

*H-TEAM Project Management: M.L. Groot Bruinderink*¹, *N. Schat*¹.

H-TEAM Additional Collaborators: R.C.A. Achterbergh³, M. van Agtmael²⁴, J. Ananworanich²², D. Van de Beek¹⁷, G.E.L. van den Berk¹¹, D. Bezemer⁷, A. van Bijnen⁶, W.L. Blok¹¹, S. Bogers², M. Bomers²⁴, C.A.B. Boucher¹³, W. Brokking²⁶, D. Burger²⁰, K. Brinkman¹¹, N. Brinkman³², M. de Bruin¹², S. Bruisten³, L. Coyer³, R. van Crevel²⁹, C.G. Daans^{3,34}, T. Derckx⁸, M. Dijkstra³, Y.T. van Duijnhoven³, A. van Eeden²⁶, L. Elsenburg²⁶, M.A.M. van den Elshout³, C. Ester⁷, E. Ersan³, P.E.V. Felipa³, T.B.H. Geijtenbeek¹⁸, J. van Gool³, A. Goorhuis², M. Groot²⁶, C.A. Hankins¹, A. Heijnen^{30,31}, M.M.J. Hillebregt⁷, A. Hogewoning³, M. Hommenga³, J.W. Hovius², Y. Janssen³², K. de Jong³, V. Jongen³, N.A. Kootstra¹⁹, R.A. Koup²¹, F.P. Kroon¹⁶, T.J.W. van de Laar^{35,36}, F. Lauw³⁷, M.M. van Leeuwen³, K. Lettinga²⁷, I. Linde³, D.S.E. Loomans³, T.

Volume 14 • Number 00 • Month 2019

Copyright © 2019 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited.

Mouhebati⁶, B.J. Mulder³, J. Mulder²⁵, F.J. Nellen², A. Nijsters⁶, H. Nobel², P. Oostvogel³, E.L.M. Op de Coul⁵, E. Peters²⁴, I.S. Peters³, T. van der Poll², O. Ratmann²⁸, C. Rokx¹⁴, M.S. van Rooijen³, M.F. Schim van der Loeff^{3,10}, W.E.M. Schoute¹¹, G.J. Sonder³, J. Veenstra²⁷, A. Verbon¹⁴, H.J. de Vries^{3,9,10}, S. Vrouenraets²⁷, M. van Vugt², W.J. Wiersinga², F.W. Wit^{2,7}, S. Zaheri⁷, P. Zantkuijl⁶, M.C. van Zelm²³, A. Żakowicz³³, H.M.L. Zimmermann³.

¹Department of Global Health, Amsterdam UMC – Location AMC, Amsterdam Institute for Global Health and Development, Amsterdam, The Netherlands

²Division of Infectious Diseases, Department of Internal Medicine, Amsterdam UMC – Location AMC, Amsterdam, The Netherlands

³Department of Infectious Diseases, Public Health Service of Amsterdam, Amsterdam, The Netherlands

⁴Department of General Practice, Amsterdam UMC – Location AMC, University of Amsterdam, Amsterdam, The Netherlands

⁵Epidemiology and Surveillance Unit, Center for Infectious Disease Control, National Institute of Public Health and the Environment, Bilthoven, The Netherlands

⁶Soa Aids Nederland, Amsterdam, The Netherlands

⁷Stichting HIV Monitoring, Amsterdam, The Netherlands

⁸Dutch Association of PLHIV, Amsterdam, The Netherlands

⁹Department of Dermatology, Amsterdam UMC – Location AMC, University of Amsterdam, Amsterdam, The Netherlands

¹⁰Center for Infection and Immunology, Amsterdam (CINIMA), Amsterdam UMC – Location AMC, University of Amsterdam, Amsterdam, The Netherlands

¹¹Department of Internal Medicine, OLVG – Location East, Amsterdam, The Netherlands

¹²Aberdeen Health Psychology Group, Institute of Applied Health Sciences, University of Aberdeen, Aberdeen, UK

¹³Department of Viroscience, Erasmus Medical Center Rotterdam, Rotterdam, The Netherlands

¹⁴Department of Internal Medicine and Infectious Diseases, Erasmus Medical Center, Rotterdam, The Netherlands

¹⁶Department of Infectious Diseases, Leiden University Medical Center, Leiden, The Netherlands

¹⁷Department of Neurology, Center of Infection and Immunity Amsterdam (CINIMA), Amsterdam UMC – Location AMC, Amsterdam, The Netherlands

¹⁸Laboratory of Experimental Immunology, Amsterdam UMC – Location AMC, Amsterdam, The Netherlands

¹⁹Laboratory for Viral Immune Pathogenesis, Amsterdam UMC – Location AMC, Amsterdam, The Netherlands ²⁰Department of Pharmacy, Radboud University Nijmegen Medical Center, Nijmegen, The Netherlands ²¹Immunology Laboratory, Vaccine Research Center,

²¹*Immunology Laboratory, Vaccine Research Center, NIAID, National Institutes of Health, Bethesda, Maryland, USA*

²²US Military HIV Research Program and the Henry M. Jackson Foundation for the Advancement of Military Medicine, Bethesda, Maryland, USA

²³Department of Virology, Erasmus Medical Center, Rotterdam, The Netherlands

²⁴Department of Internal Medicine, Amsterdam UMC – Location VUMC, Amsterdam, The Netherlands

²⁵Department of Internal Medicine, Slotervaart Hospital (Former), Amsterdam, The Netherlands

²⁶DC Klinieken, Amsterdam, The Netherlands

²⁷Department of Internal Medicine, OLVG – Location West, Amsterdam, The Netherlands

²⁸School of Public Health, Faculty of Medicine, Imperial College London, London, UK

²⁹Department of Internal Medicine, Radboud University Nijmegen Medical Center, Nijmegen, The Netherlands

³⁰Sexology Center Amsterdam, Amsterdam, The Netherlands

³¹GP Practice Heijnen & de Meij, Amsterdam, The Netherlands

³²Elaa, Amsterdam, The Netherlands

³³*AIDS Healthcare Foundation, Amsterdam, The Netherlands*

³⁴Center of Expertise on Gender Dysphoria, Amsterdam UMC – Location VUMC, Amsterdam, The Netherlands ³⁵Department of Medical Microbiology, OLVG, Amsterdam, The Netherlands

³⁶Department of Donor Medicine Research, Laboratory of Blood–Borne Infections, Sanquin Research, Amsterdam, The Netherlands

³⁷Department of Internal Medicine, Medical Center Jan van Goyen, Amsterdam, The Netherlands

Financial support and sponsorship

The H-TEAM Initiative is being supported by Aids Fonds (grant number: 2013169), Stichting AmsterdamDiner Foundation, Bristol-Myers Squibb International Corp. (study number: AI424-541), Gilead Sciences Europe Ltd (grant number: PA-HIV-PREP-16-0024), Gilead Sciences (protocol numbers: CO-NL-276-4222, CO-US-276-1712), Janssen Pharmaceutica (reference number: PHNL/JAN/0714/0005b/1912fde), M.A.C. AIDS Fund, ViiV Healthcare (PO numbers: 3000268822, 3000747780) and ZonMw (grant number: 522002003).

Conflicts of interest

G.J.d.B. has received grants through her institution from Bristol-Meyer Squibbs and Mac Aids Fund; honoraria to her Institution for scientific advisory board participations for Gilead Sciences and speaker fees from

1746-630X Copyright $\ensuremath{\mathbb{C}}$ 2019 Wolters Kluwer Health, Inc. All rights reserved.

www.co-hivandaids.com

Gilead Sciences and Takeda; A.v.S. has received grants from Dutch Ministry of Health, Welfare and Sport, paid to his institution, during the conduct of the study, and grants from European Centre for Disease Prevention and Control, paid to his institution, during the conduct of the study; The ATHENA cohort is managed by Stichting HIV Monitoring and supported by a grant from the Dutch Ministry of Health, Welfare and Sport through the Centre for Infectious Disease Control of the National Institute for Public Health and the Environment; P.R. has received grants through his Institution from Gilead Sciences, Janssen Pharmaceutica, ViiV Healthcare and Merck; honoraria to his Institution for scientific advisory board participation for Gilead Sciences, ViiV Healthcare, Merck and Teva; M.P. – The study drug of the AMPrEP in H-TEAM project was donated by Gilead Sciences. M.P. obtained unrestricted research grants and speaker fees from Gilead Sciences, Roche, Abbvie and MSD; all of which were paid to her institute; M.v.d.V. has received grants through his Institution from Gilead Sciences, Janssen Pharmaceutica, ViiV Healthcare, Merck and Abbvie; honoraria to his Institution for scientific advisory board participation for Gilead Sciences, ViiV Healthcare, Merck, Abbvie, Janssen Pharmaceutica; M.H. has received grants through his Institutions from the City of Amsterdam, EFRO and Gilead Sciences; J.E.A.M.v.B., P.B. and W.Z. have no conflicts reported.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest of outstanding interest
- 1. Das M, Chu PL, Santos G-M, et al. Decreases in community viral load are accompanied by reductions in new HIV infections in San Francisco. PLoS One 2010; 5:e11068.
- 2. https://bridgehiv.org/. San Francisco Getting to Zero 2017.
- 3. Montaner JSG, Lima VD, Barrios R, et al. Association of highly active antiretroviral therapy coverage, population viral load, and yearly new HIV diagnoses in British Columbia, Canada: a population-based study. Lancet 2010: 376:532-539.
- 4. https://www.sfdph.org/dph/files/reports/RptsHIVAIDS/AnnualReport2017-Green-20180904-Web.pdf. San Francisco Department of Public Health 2017 HIV epidemiology annual report. [Accessed June 2019]
- 5. Jones A, Cremin I, Abdullah F, et al. Transformation of HIV from pandemic to low-endemic levels: a public health approach to combination prevention. Lancet 2014; 384:272-279.
- 6. HIV monitoring report 2018 | Stichting HIV Monitoring [Internet]. Available from: https://www.hiv-monitoring.nl/en/resources/monitoring-report-2018. [Cited 13 June 2019].
- 7. Heijman RLJ, Stolte IG, Thiesbrummel HFJ, et al. Opting out increases HIV testing in a large sexually transmitted infections outpatient clinic. Sex Transm Infect 2009; 85:249-255.
- 8. Ratmann O, van Sighem A, Bezemer D, et al. Sources of HIV infection among men having sex with men and implications for prevention. Sci Transl Med 2016: 8:320ra2.
- 9. WHO | Guidance on oral preexposure prophylaxis (PrEP) for serodiscordant couples, men and transgender women who have sex with men at high risk of HIV [Internet]. WHO. 2016. Available from: http://www.who.int/hiv/pub/guidance_prep/en/. [Cited 3 February 2016].
- 10. Grant RM, Lama JR, Anderson PL, et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. N Engl J Med 2010; 363:2587-2599.

- 11. McCormack S, Dunn DT, Desai M, et al. Preexposure prophylaxis to prevent the acquisition of HIV-1 infection (PROUD): effectiveness results from the pilot phase of a pragmatic open-label randomised trial. Lancet 2016; 387:53 - 60
- 12. Molina J-M, Capitant C, Spire B, et al. On-demand preexposure prophylaxis in men at high risk for HIV-1 infection. N Engl J Med 2015; 373: 2237 - 2246
- 13. Hoornenborg E, Achterbergh RCA, Schim van der Loeff MF, et al. MSM starting preexposure prophylaxis are at risk of hepatitis C virus infection. AIDS 2017; 31:1603-1610.
- 14. Hoornenborg E, Coyer L, van Laarhoven A, et al. Change in sexual risk behaviour after 6 months of preexposure prophylaxis use: results from the Amsterdam preexposure prophylaxis demonstration project. AIDS 2018; 32:1527-1532.
- 15. Hoornenborg E, Achterbergh RC, van der Loeff MFS, et al. Men who have sex with men more often chose daily than event-driven use of preexposure prophylaxis: baseline analysis of a demonstration study in Amsterdam, J Int AIDS Soc 2018; 21:e25105.
- 16. Newsum AM, van Rooijen MS, Kroone M, et al. Stable low hepatitis C virus antibody prevalence among HIV-negative men who have sex with men attending the sexually transmitted infection outpatient clinic in Amsterdam, 2007 to 2017. Sex Transm Dis 2018; 45:813-817.
- 17. Hoornenborg E, Coyer L, Achterbergh RCA, et al. Sexual behaviour
- and incidence of HIV and sexually transmitted infections among men who have sex with men using daily and event-driven preexposure prophylaxis in AMPrEP: 2 year results from a demonstration study. Lancet HIV 2019; 6:e447-e455.

In this study, the incidence of sexually transmitted infections (STIs) in the Amsterdam preexposure prophylaxis (PrEP) implementation project was investigated and showed no increase in STIs over 2 years of PrEP usage.

- 18. Hoornenborg E, Prins M, Achterbergh RCA, et al. Acquisition of wild-type HIV-1 infection in a patient on preexposure prophylaxis with high intracellular concentrations of tenofovir diphosphate: a case report. Lancet HIV 2017; 4:e522-e528
- 19. Marks G, Crepaz N, Janssen RS. Estimating sexual transmission of HIV from persons aware and unaware that they are infected with the virus in the USA. AIDS 2006; 20:1447-1450.
- 20. Wawer MJ, Gray RH, Sewankambo NK, et al. Rates of HIV-1 transmission per coital act, by stage of HIV-1 infection, in Rakai, Uganda. J Infect Dis 2005; 191:1403-1409
- 21. Hollingsworth TD, Anderson RM, Fraser C. HIV-1 transmission, by stage of infection. J Infect Dis 2008; 198:687-693.
- Remien RH, Higgins JA, Correale J, et al. Lack of understanding of acute HIV 22. infection among newly-infected persons-implications for prevention and public health: the NIMH Multisite Acute HIV Infection Study: II. AIDS Behav 2009; 13:1046-1053.
- 23. Wood E, Kerr T, Rowell G, et al. Does this adult patient have early HIV infection?: the Rational Clinical Examination systematic review. JAMA 2014; 312:278-285
- 24. Le T, Wright EJ, Smith DM, et al. Enhanced CD4+ T-cell recovery with earlier HIV-1 antiretroviral therapy. N Engl J Med 2013; 368:218–230. 25. Fidler S, Porter K, Ewings F, *et al.*, SPARTAC Trial Investigators. Short-course
- antiretroviral therapy in primary HIV infection. N Engl J Med 2013; 368:207-217.
- 26. Grijsen ML, Steingrover R, Wit FW, et al. No treatment versus 24 or 60 weeks of antiretroviral treatment during primary HIV infection: the randomized Primo-SHM trial. PLoS Med 2012; 9:e1001196.
- 27. Dijkstra M, de Bree GJ, Stolte IG, et al. Development and validation of a risk score to assist screening for acute HIV-1 infection among men who have sex with men. BMC Infect Dis 2017; 17:425.
- 28. Dijkstra M. Targeted screening and immediate start of treatment for acute HIV infection decreases time between HIV diagnosis and viral suppression among MSM at a Sexual Health Clinic in Amsterdam. International AIDS Society Conference on HIV Science 2019, abstract no.
- 29. Pilcher CD, Ospina-Norvell C, Dasgupta A, et al. The effect of same-day observed initiation of antiretroviral therapy on HIV viral load and treatment outcomes in a US public health setting. J Acquir Immune Defic Syndr 2017; 74:44-51.
- 30. Cohen MS, Chen YO, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. N Engl J Med 2011; 365:493-505. 31. Cohen MS, Chen YQ, McCauley M, *et al.* Antiretroviral therapy for the
- prevention of HIV-1 transmission. N Engl J Med 2016; 375:830-839.
- 32. Rodger AJ, Cambiano V, Bruun T, et al. Risk of HIV transmission through condomless sex in serodifferent gay couples with the HIV-positive partner taking suppressive antiretroviral therapy (PARTNER): final results of a multi-

centre, prospective, observational study. Lancet 2019; 393:2428-2438. The PARTNER studied showed that in serodiscordant MSM couples, in whom the HIV-infected partner received combination antiretroviral therapy and had an undetectable viral load, there were no linked transmissions. This study provided the final proof that an undectable viral load equals an untransmittable HIV infection.

Eisinger RW, Dieffenbach CW, Fauci AS. HIV viral load and transmissibility of HIV infection: undetectable equals untransmittable. JAMA 2019; 321:451-452.

Copyright © 2019 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited.

- 35. Trienekens SCM, van den Broek IVF, Donker GA, et al. Consultations for sexually transmitted infections in the general practice in the Netherlands: an opportunity to improve STI/HIV testing. BMJ Open 2013; 3:e003687.
- 36. Joore IK, Arts DL, Kruijer MJ, et al. HIV indicator condition-guided testing to reduce the number of undiagnosed patients and prevent late presentation in a high-prevalence area: a case – control study in primary care. Sex Transm Infect 2015; 91:467–472.
- Joore IK, Reukers DFM, Donker GA, *et al.* Missed opportunities to offer HIV tests to high-risk groups during general practitioners' STI-related consultations: an observational study. BMJ Open 2016; 6:e009194.
- Joore IK, Geerlings SE, Brinkman K, et al. The importance of registration of sexual orientation and recognition of indicator conditions for an adequate HIV risk-assessment. BMC Infect Dis 2017; 17:178.
- Wohlgemut J, Lawes T, Laing RBS. Trends in missed presentations and late HIV diagnosis in a UK teaching hospital: a retrospective comparative cohort study. BMC Infect Dis 2012; 12:72.
- Gullón A, Verdejo J, de Miguel R, et al. Factors associated with late diagnosis of HIV infection and missed opportunities for earlier testing. AIDS Care 2016; 28:1296–1300.