Decreased Time to Viral Suppression After Implementation of Targeted Testing and Immediate Initiation of Treatment of Acute Human Immunodeficiency Virus Infection Among Men Who Have Sex With Men in Amsterdam

Maartje Dijkstra,1,2 Martijn S. van Rooijen,1 Mariska M. Hillebregt,3 Ard van Sighem,3 Colette Smit,3 Arjan Hogewoning,1,2 Udi Davidovich,1,2 Titia Heijman,1 Elske Hoornenborg,1 Peter Reiss,2,3,4,5 Marc van der Valk,2 Maria Prins,1,2 Jan M. Prins,2 Maarten F. Schim van der Loeff,1,2 and Godelieve J. de Bree2; for the HIV Transmission Elimination Amsterdam (H-TEAM) Initiative

Background. Men who have sex with men (MSM) with acute human immunodeficiency virus (HIV) infection (AHI) are a key source of new infections. To curb transmission, we implemented a strategy for rapid AHI diagnosis and immediate initiation of combination antiretroviral therapy (cART) in Amsterdam MSM. We assessed its effectiveness in diagnosing AHI and decreasing the time to viral suppression.

Methods. We included 63,278 HIV testing visits in 2008–2017, during which 1,013 MSM were diagnosed. Standard of care (SOC) included HIV diagnosis confirmation in <1 week and cART initiation in <1 month. The AHI strategy comprised same-visit diagnosis confirmation and immediate cART. Time from diagnosis to viral suppression was assessed for 3 cART initiation periods: (1) 2008–2011: cART initiation if CD4 < 500 cells/μL (SOC); (2) January 2012–July 2015: cART initiation if CD4 < 500 cells/μL, or if AHI or early HIV infection (SOC); and (3a) August 2015–June 2017: universal cART initiation (SOC) or (3b) August 2015–June 2017 (the AHI strategy).

Results. Before implementation of the AHI strategy, the proportion of AHI among HIV diagnoses was 0.6% (5/876); after implementation this was 11.0% (15/137). Median time (in days) to viral suppression during periods 1, 2, 3a, and 3b was 584 (interquartile range [IQR], 267–1065), 230 (IQR, 132–480), 95 (IQR, 63–136), and 55 (IQR, 31–72), respectively (P < .001).

Conclusions. Implementing the AHI strategy was successful in diagnosing AHI and significantly decreasing the time between HIV diagnosis and viral suppression.

Keywords. acute HIV infection; men who have sex with men; viral suppression; targeted testing; same-day start.
Several studies in countries with limited healthcare access have shown that early cART initiation improves retention in care and viral suppression rates [11–24]. However, the majority of these studies included people diagnosed with established HIV infection [12–15, 17–19]. The studies that focus specifically on immediate cART initiation among MSM with AH are scarce [16, 21–24], and some lack comparison groups not offered immediate cART. None of these studies provided AH diagnosis at the point of care, and they did not focus on mobilizing MSM for AH testing.

To the best of our knowledge, there are no studies on the feasibility and effectiveness of a combined strategy to increase awareness of AH and to offer targeted testing and point-of-care diagnosis linked to same-visit referral and immediate cART initiation. It remains unclear whether such a strategy would be of additional value in countries like the Netherlands with universal healthcare. We implemented a strategy for rapid diagnosis of AH in MSM using point-of-care HIV RNA testing at the Amsterdam sexually transmitted infection (STI) clinic as of August 2015. This was linked to immediate cART initiation, along with a media campaign to increase awareness of AH among MSM [25]. Amsterdam has 1 large public STI clinic, which performs > 50 000 annual consultations and accounts for approximately 46% of new HIV diagnoses among MSM in Amsterdam (van Sighem, personal communication). The objective of this study was to assess the feasibility and effectiveness of a strategy in diagnosing AH and decreasing the time to viral suppression in Amsterdam, and historically relating this to changes in the time between diagnosis, cART initiation, and viral suppression during prior calendar periods reflective of cART initiation guidelines.

METHODS

Standard Testing

The standard HIV testing policy was as follows: From January 2008 through April 2014, MSM were tested with a rapid antibody test (Alere Determine HIV 1/2, Alere Inc), and a combined Ag/Ab test if AH was clinically suspected (through April 2013: AxSYM, Abbott Laboratories; from May 2013: LIAISON XL Murex, Diasorin). From May 2014, rapid antibody and Ag/Ab tests were used. Positive or indeterminate samples were confirmed with line immunoassay (Inno-Lia HIV 1/II Score; Fujirebio). Rapid antibody results were delivered at the same visit, and Ag/Ab results within 1 week. MSM with positive or indeterminate test results returned to the STI clinic 1 week after their initial visit for confirmation with a rapid test, were subsequently referred to an HIV treatment center and had an intake at an HIV treatment center within 5 business days.

Staging of Infection

In line with prior publications, we defined AH as Fiebig stages I–II, early HIV infection as Fiebig stages III–V, and acute or early HIV infection (AEHI) as Fiebig stages I–V (Supplementary Table 1) [6, 26–28].

Standard cART Initiation

We considered 3 historical standard of care (SOC) cART initiation periods: (1) In 2008–2011, Dutch guidelines recommended to initiate cART if CD4 < 500 cells/μL; (2) in 2012–2014, cART initiation was recommended if CD4 < 500 cells/μL or irrespective of CD4 count in case of AEHI; and (3) since 2015, guidelines recommend cART initiation as soon as HIV genotype results are available, irrespective of CD4 count or stage of infection, and first-line treatment with integrase strand transfer inhibitor (INSTI)–based regimens [29].

AHI Search and Treat-to-Suppression Strategy

In August 2015, we launched a media campaign promoting an online intervention specifically designed to increase AH detection and immediately treat individuals with AH (ie, “AHI search and treat-to-suppression strategy” or in short, the “AHI strategy”). The online intervention aimed to increase awareness for AH among Amsterdam MSM, help them self-identify AH symptoms, and increase their behavioral motivation to test [25]. This included a dedicated website (www.hebikhiv.nl/en) with a self-administered screening tool based on a pragmatic AH risk score [30]. MSM who reported condomless anal intercourse in the previous 3 months and AH symptoms could download a referral letter to the AH strategy. Next to this online referral, MSM could also be referred by their general practitioner or during routine STI screening at the STI clinic; eligibility was assessed with the pragmatic AH risk score at health providers’ discretion [30]. Although the campaign was specifically designed for the AH strategy, wider dissemination took place, and MSM in SOC and health providers likely have also been exposed to the campaign part of the strategy.

The AH strategy’s testing procedures included simultaneous rapid antibody (Alere Determine HIV 1/2, Alere Inc), Ag/Ab (LIAISON XL Murex, Diasorin), and qualitative point-of-care HIV RNA testing (GeneXpert, Cepheid), and same-visit delivery of results. MSM identified with AEHI were immediately referred to an HIV treatment center to initiate cART within 24 hours. To summarize, SOC procedures included diagnosis confirmation within 1 week and referral to an HIV treatment center within 5 days of confirmed diagnosis, and cART initiation varied per period (within 1 month of referral for period 3, 2015–2017). AH strategy procedures included same-visit confirmation of diagnosis, same-day referral to an HIV treatment center, and immediate cART initiation.

Data Linkage

The STI clinic and HIV treatment centers have separate databases. To assess time to viral suppression, we aimed to link records from the STI clinic to medical records from HIV treatment centers, retrieved from the ongoing AIDS Therapy Evaluation in the Netherlands (ATHENA) National HIV cohort [31]. Clinical
data in the ATHENA cohort are collected prospectively and encompass data of 98% of all people living with HIV in care in the Netherlands. A trusted third party (ZorgTTP, Utrecht) conducted the linkage based on date of birth and postal code. The Medical Ethics Committee of Amsterdam University Medical Center approved this study (W17_248 number 17.290).

**Statistical Analyses**

We assessed AHI as a proportion of HIV testing visits yielding a diagnosis of AHI (AHI yield), and as the proportion of AHI among all HIV diagnoses in MSM at the STI clinic, before (January 2008–July 2015) and after (August 2015–June 2017) implementation of the AHI strategy. The latter period was further stratified by testing policy: MSM diagnosed via standard testing vs the AHI strategy.

Time from diagnosis to viral suppression was defined as the number of days between the first STI clinic visit with a positive or indeterminate test result and the first HIV treatment center visit with a viral load < 50 copies/mL. Follow-up HIV treatment center visits were included up to 2 January 2018; data were censored on that date, or on the last HIV treatment center visit date if MSM were lost to follow-up (LTFU). Virological failure was defined as 2 consecutive measures of a plasma viral load ≥ 200 copies/mL within 6 months after viral suppression [32].

We assessed time from diagnosis to intake at an HIV treatment center, cART initiation, and viral suppression for the following periods: (1) 2008–2011: cART if CD4 < 500 cells/μL; (2) 2012–July 2015: cART if CD4 < 500 cells/μL or if AEHI; and (3a) August 2015–June 2017: universal cART in SOC, or (3b) August 2015–June 2017: the AHI strategy. We estimated median time-to-event with the Kaplan-Meier method, and compared periods with the log-rank test. Two-sided p values < .05 were considered statistically significant. Analyses were performed using Stata software (version 15.1; StataCorp).

**RESULTS**

**Trends in AHI Diagnosis Over Time**

Between 2008 and 2017, 19,728 MSM without prior known HIV infection visited the STI clinic, and during 63,278 visits, 1013 MSM were diagnosed. The AHI yield per visit was 0.01% (5/47,008) before and 0.09% (15/16,270) after implementation of the AHI strategy (Table 1). When we stratified for testing policy during the period 2015–2017, AHI yield was 0.03% (5/16,021) via standard testing and 4.0% (10/249) via the AHI strategy. The proportion of AHI among HIV diagnoses was 0.6% (5/876) before and 11.0% (15/137) after implementation of the AHI strategy. Stratified for testing policy (2015–2017), this was 4.2% (5/118) via standard testing and 52.6% (10/19) via the AHI strategy. After implementation of the AHI strategy, AEHI yield decreased; however, the proportion of AEHI among HIV diagnoses increased. Fiebig stages are displayed in Figure 1; referral source and test results of MSM in the AHI strategy are shown in Supplementary Figure 1. Of the 127 MSM who had been referred through the campaign’s online referral, none were diagnosed with AHI, 1 with early HIV infection, and 1 with established HIV infection. Characteristics of MSM diagnosed with HIV in 2015–2017 are shown in Supplementary Table 2. Median time from STI clinic visit to delivery of confirmed HIV diagnosis was 6.9 (interquartile range [IQR], 5.9–7.1) days in the standard testing setting and 3.5 (IQR, 1.7–3.8) hours in the AHI strategy; this did not differ by infection stage.

**Data Linkage**

Of the 1013 STI clinic records of diagnosed MSM (2008–2017), a subset could be linked to records of HIV treatment centers and were used to assess time to viral suppression: 66.1% in period 1 (2008–2011), 65.8% in period 2 (2012–2015), 61.0% in period 3a (2015–2017; SOC), and 79.0% in 3b (2015–2017; AHI strategy) (Table 2). Compared with MSM with unlinked records, median age was higher among MSM with linked records (36 [IQR, 30–43] years vs 31 [IQR, 26–39] years), and a higher proportion of MSM were born in the Netherlands (48.6% vs 28.6%). Of the 348 records that could not be linked, 31.9% contained an invalid or no postal code, and 0.3% an invalid date of birth.

**Time to Viral Suppression**

Median time between diagnosis and intake at an HIV treatment center was similar in the first 2 periods (14 and 13 days, respectively), decreased to 9 days in period 3a (SOC), and was reduced to 1 day in the AHI strategy (Table 2). LTFU before cART initiation was similar in SOC (2.2%–6.9%) and 0% in the AHI strategy among MSM with linked records. Median time from diagnosis to cART initiation was 439 days, 99 days, 29 days, and 1 day in periods 1, 2, 3a, and 3b, respectively (Figure 2). Median time from diagnosis to viral suppression was 584 (IQR, 267–1065) days in period 1; 230 (IQR, 132–480) days in period 2; 95 (IQR, 63–136) days in period 3a; and 55 (IQR, 31–72) days in 3b (the AHI strategy).

As MSM with AEHI may have initiated cART earlier than MSM with established infection, we created separate Kaplan-Meier graphs for MSM with AEHI and those with established infection. These indicate that the time from diagnosis to viral suppression decreased from period 1 to period 3a for MSM with AEHI and also for those with established infection (Supplementary Figure 2). Median time from cART initiation to viral suppression was 125, 91, 59, and 54 days in periods 1, 2, 3a, and 3b, respectively. As there was no standardized study visit schedule for viral load measurements, we assessed median interval between the cART initiation visit and the follow-up viral load measurements until viral suppression was achieved. This decreased from 125 days in period 1 to 54 days in period 3b, which may explain the observed decline in time from cART...
initiation to viral suppression. All MSM achieved viral suppression at the first follow-up visit after cART initiation. In a subgroup analysis of MSM with similar intervals between viral load measurements (ie, a median of ≤ 60 days), the median time from diagnosis to viral suppression was 799, 129, 63, and 34 days in periods 1, 2, 3a, and 3b, respectively (P < .0001; Figure 2C).

**DISCUSSION**

The implementation of a strategy for rapid AHI diagnosis in MSM linked to immediate cART initiation proved feasible at the Amsterdam STI clinic, and was temporally associated with a higher AHI yield and a significant reduction in the time from HIV diagnosis to viral suppression, in relation to SOC. The increase in AHI diagnoses may have resulted from increased awareness of AHI among MSM and healthcare providers, as well as more frequent testing among MSM. This assumption is supported by recent citywide data from MSM entering HIV care in Amsterdam, showing an increase in the proportion of MSM with a negative HIV test in the 6 months before diagnosis (as a proxy for early infection): from 18% in 2010–2015 to 34% in 2016, and 27% in 2017 [1]. In the AHI strategy, 53% of MSM diagnosed with HIV had AHI, and 89% had AEHI. The recommendation for universal use of cART dramatically decreased time from diagnosis to viral suppression: from 584 days in 2008–2011 to 95 days in 2015–2017. The interventions of the AHI strategy decreased the time from diagnosis to viral suppression even further to 55 days.

The addition of the point-of-care HIV RNA test resulted in 2 MSM diagnosed with Fiebig stage I, who otherwise would not have been diagnosed. More importantly, it ensured same-visit results and confirmation of an indeterminate Ag/Ab test result (Fiebig II), as described by others [33].

### Table 1. Human Immunodeficiency Virus (HIV) Diagnoses and Fiebig Stages Among 63,278 HIV Testing Visits of 19,728 Unique Men Who Have Sex With Men at the Amsterdam Sexually Transmitted Infection Clinic, Before and After Implementation of the Acute HIV Infection Search and Treat-to-Suppression Strategy

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<tbody>
<tr>
<td><strong>Diagnostic strategy</strong></td>
<td></td>
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<tr>
<td>Point-of-care RNA test</td>
<td>No</td>
<td>If eligible*</td>
<td>No</td>
<td>If eligible*</td>
</tr>
<tr>
<td>Fourth-generation Ag/Ab test</td>
<td>If symptoms of AHI*</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Rapid antibody test</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Visits, No.</td>
<td>47,008</td>
<td>16,270</td>
<td>16,021</td>
<td>249</td>
</tr>
<tr>
<td>Diagnosed with HIV, no.</td>
<td>876</td>
<td>137</td>
<td>118</td>
<td>19</td>
</tr>
<tr>
<td>HIV yieldd</td>
<td>1.9%</td>
<td>0.8%</td>
<td>0.7%</td>
<td>76%</td>
</tr>
<tr>
<td>Diagnosed with AHI,* no.</td>
<td>5</td>
<td>15</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>AHI yieldd</td>
<td>0.01%</td>
<td>0.09%</td>
<td>0.03%</td>
<td>4.0%</td>
</tr>
<tr>
<td>Proportion of AHI among diagnosed with HIV</td>
<td>0.6%</td>
<td>11.0%</td>
<td>4.2%</td>
<td>52.6%</td>
</tr>
<tr>
<td>Diagnosed with AEHI, no.</td>
<td>237</td>
<td>52</td>
<td>35</td>
<td>17</td>
</tr>
<tr>
<td>AEHI yieldd</td>
<td>0.5%</td>
<td>0.3%</td>
<td>0.2%</td>
<td>6.8%</td>
</tr>
<tr>
<td>Proportion of AEHI among diagnosed with HIV</td>
<td>27.1%</td>
<td>38.0%</td>
<td>29.7%</td>
<td>89.5%</td>
</tr>
<tr>
<td><strong>Fiebig stage, No.</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>NA</td>
<td>2</td>
<td>NA</td>
<td>2</td>
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<tr>
<td>II</td>
<td>5</td>
<td>13</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>III</td>
<td>22</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>IV</td>
<td>9</td>
<td>6</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>V</td>
<td>19</td>
<td>4</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>VI</td>
<td>182</td>
<td>27</td>
<td>24</td>
<td>3</td>
</tr>
<tr>
<td>VII</td>
<td>639</td>
<td>85</td>
<td>83</td>
<td>2</td>
</tr>
</tbody>
</table>

**Abbreviations:** AEHI, acute or early human immunodeficiency virus infection; AHI, acute human immunodeficiency virus infection; Ag/Ab, antigen/antibody test; HIV, human immunodeficiency virus; NA, not assessed.

*Eligibility was assessed using a pragmatic AHI risk score.

*Defined as Fiebig stages I–II.

*Visits with a new HIV diagnosis as a proportion of all visits.

*Visits with an AHI diagnosis as a proportion of all visits.

*Defined as Fiebig stages I–V.

*Visits with an AEHI diagnosis as a proportion of all visits.

*Until May 2013, the AxSYM Ag/Ab test was used, and no distinction between Fiebig stage II and III could be made; from May 2013 onward, the LIAISON Ag/Ab test was used, allowing for distinction between Fiebig stages II and III.
Table 2. Time to Intake at a Human Immunodeficiency Virus (HIV) Treatment Center, Combination Antiretroviral Therapy Initiation, and Viral Suppression for 665 Men Who Have Sex With Men Diagnosed With HIV at the Amsterdam Sexually Transmitted Infection (STI) Clinic of Whom Records From the STI Clinic Were Successfully Linked With Records From HIV Clinics, January 2008–June 2017

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>(1) Standard&lt;sup&gt;a&lt;/sup&gt;</th>
<th>(2) Standard&lt;sup&gt;b&lt;/sup&gt;</th>
<th>(3a) Standard&lt;sup&gt;M&lt;/sup&gt;</th>
<th>(3b) AHI Strategy&lt;sup&gt;g&lt;/sup&gt;</th>
<th>Overall&lt;sup&gt;b&lt;/sup&gt;</th>
<th>(3a) vs (3b)&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>cART initiation policy&lt;sup&gt;d&lt;/sup&gt;</td>
<td>CD4 count &lt; 500&lt;sup&gt;e&lt;/sup&gt;</td>
<td>CD4 count &lt; 500&lt;sup&gt;e&lt;/sup&gt; or AEHI</td>
<td>Universal</td>
<td>Immediate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>STI clinic record linked with HIV treatment center record&lt;sup&gt;f&lt;/sup&gt;</td>
<td>355 (66.1%)</td>
<td>223 (65.8%)</td>
<td>72 (61.0%)</td>
<td>15 (79.0%)</td>
<td>.80&lt;sup&gt;g&lt;/sup&gt;</td>
<td>.13&lt;sup&gt;h&lt;/sup&gt;</td>
</tr>
<tr>
<td>Baseline viral load (log&lt;sub&gt;10&lt;/sub&gt; copies/mL)&lt;sup&gt;i&lt;/sup&gt;</td>
<td>4.6 (4.0–5.1)</td>
<td>4.7 (4.0–5.1)</td>
<td>4.7 (4.1–5.2)</td>
<td>6.0 (4.7–7.0)</td>
<td>.0034</td>
<td>.0019</td>
</tr>
<tr>
<td>Baseline CD4 count (cells/μL)&lt;sup&gt;j&lt;/sup&gt;</td>
<td>455 (330–600)</td>
<td>520 (390–700)</td>
<td>480 (400–600)</td>
<td>480 (380–520)</td>
<td>.0021</td>
<td>.63</td>
</tr>
<tr>
<td>Baseline CD4 nadir (cells/μL)&lt;sup&gt;k&lt;/sup&gt;</td>
<td>330 (260–410)</td>
<td>440 (310–570)</td>
<td>478 (400–600)</td>
<td>480 (380–520)</td>
<td>.0001</td>
<td>.79</td>
</tr>
<tr>
<td>Lost to follow-up before cART initiation&lt;sup&gt;l&lt;/sup&gt;</td>
<td>16 (4.5%)</td>
<td>5 (2.2%)</td>
<td>5 (6.9%)</td>
<td>0 (0%)</td>
<td>.77&lt;sup&gt;g&lt;/sup&gt;</td>
<td>.29&lt;sup&gt;h&lt;/sup&gt;</td>
</tr>
<tr>
<td>Initial cART regimen&lt;sup&gt;n&lt;/sup&gt;</td>
<td>NNRTI use</td>
<td>225 (70.5%)</td>
<td>71 (33.2%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td></td>
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<tr>
<td>PI use</td>
<td>52 (16.3%)</td>
<td>33 (15.4%)</td>
<td>1 (6.9%)</td>
<td>0 (0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>INSTI use</td>
<td>42 (13.2%)</td>
<td>106 (49.5%)</td>
<td>49 (75.6%)</td>
<td>3 (20.0%)</td>
<td></td>
<td></td>
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<tr>
<td>INSTI + PI use&lt;sup&gt;o&lt;/sup&gt;</td>
<td>0 (0%)</td>
<td>4 (1.9%)</td>
<td>14 (21.9%)</td>
<td>12 (80.0%)</td>
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<td></td>
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<tr>
<td>cART initiation after diagnosis&lt;sup&gt;q&lt;/sup&gt;</td>
<td>Same-day</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>2 (13.3%)</td>
<td>&lt;.0001&lt;sup&gt;g&lt;/sup&gt;</td>
</tr>
<tr>
<td>After 1 day</td>
<td>0 (0%)</td>
<td>1 (0.5%)</td>
<td>1 (1.5%)</td>
<td>7 (46.7%)</td>
<td></td>
<td></td>
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<tr>
<td>From 2 through 7 days</td>
<td>1 (0.3%)</td>
<td>4 (1.8%)</td>
<td>11 (15.9%)</td>
<td>5 (33.3%)</td>
<td></td>
<td></td>
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<tr>
<td>Lost to follow-up before viral suppression&lt;sup&gt;r&lt;/sup&gt;</td>
<td>5 (1.5%)</td>
<td>3 (1.4%)</td>
<td>2 (3.0%)</td>
<td>0 (0%)</td>
<td>.95&lt;sup&gt;g&lt;/sup&gt;</td>
<td>.498&lt;sup&gt;h&lt;/sup&gt;</td>
</tr>
<tr>
<td>Virological failure&lt;sup&gt;s&lt;/sup&gt;</td>
<td>7 (2.3%)</td>
<td>2 (1.0%)</td>
<td>1 (2.4%)</td>
<td>0 (0%)</td>
<td>.45&lt;sup&gt;g&lt;/sup&gt;</td>
<td>.57&lt;sup&gt;h&lt;/sup&gt;</td>
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<tr>
<td>Days from diagnosis to:</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Intake at HIV clinic&lt;sup&gt;t&lt;/sup&gt;</td>
<td>14 (9–21)</td>
<td>13 (9–17)</td>
<td>9 (6–14)</td>
<td>1 (0–2)</td>
<td>&lt;.0001&lt;sup&gt;g&lt;/sup&gt;</td>
<td>&lt;.0001&lt;sup&gt;h&lt;/sup&gt;</td>
</tr>
<tr>
<td>cART initiation&lt;sup&gt;u&lt;/sup&gt;</td>
<td>439 (102–899)</td>
<td>99 (43–339)</td>
<td>29 (15–43)</td>
<td>1 (1–3)</td>
<td>&lt;.0001&lt;sup&gt;g&lt;/sup&gt;</td>
<td>&lt;.0001&lt;sup&gt;h&lt;/sup&gt;</td>
</tr>
<tr>
<td>Viral suppression&lt;sup&gt;v&lt;/sup&gt;</td>
<td>584 (267–1065)</td>
<td>230 (132–480)</td>
<td>95 (63–136)</td>
<td>55 (31–72)</td>
<td>&lt;.0001&lt;sup&gt;g&lt;/sup&gt;</td>
<td>.007&lt;sup&gt;h&lt;/sup&gt;</td>
</tr>
<tr>
<td>Days from cART initiation to&lt;sup&gt;u&lt;/sup&gt;:</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Viral suppression&lt;sup&gt;v&lt;/sup&gt;</td>
<td>125 (77–172)</td>
<td>91 (39–152)</td>
<td>59 (28–97)</td>
<td>54 (28–66)</td>
<td>&lt;.0001&lt;sup&gt;g&lt;/sup&gt;</td>
<td>.18&lt;sup&gt;h&lt;/sup&gt;</td>
</tr>
<tr>
<td>Days between viral load measurements&lt;sup&gt;w&lt;/sup&gt;</td>
<td>125 (78–172)</td>
<td>91 (39–152)</td>
<td>59 (28–97)</td>
<td>54 (28–66)</td>
<td>.0001&lt;sup&gt;g&lt;/sup&gt;</td>
<td>30&lt;sup&gt;h&lt;/sup&gt;</td>
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Abbreviations: AEHI, acute or early human immunodeficiency virus infection; AHI, acute human immunodeficiency virus infection; cART, combination antiretroviral therapy; HIV, human immunodeficiency virus infection; INSTI, integrase strand transfer inhibitor; MSM, men who have sex with men; NNRTI, nonnucleoside reverse-transcriptase inhibitor; PI, protease inhibitor; STI, sexually transmitted infection.

<sup>a</sup>Proportion (%) or median (interquartile range).
<sup>b</sup>Kruskal-Wallis rank test, unless stated otherwise.
<sup>c</sup>Wilcoxon rank-sum test, unless stated otherwise.
<sup>d</sup>In routine strategies, cART was initiated as per national treatment guidelines; men who have sex with men (MSM) diagnosed in the AHI strategy were offered cART within 24 hours of diagnosis.
<sup>e</sup>In cells per microliter.
<sup>f</sup>Proportion of diagnosed MSM at Amsterdam STI clinic.
<sup>g</sup>Nonparametric trend test.
<sup>h</sup>χ² test.
<sup>i</sup>Two missing values.
Immediate cART initiation has been shown to decrease time to viral suppression in different settings with limited to moderate access to healthcare [11–24], including for people with AHI. The Rapid ART Program Initiative for HIV Diagnoses (RAPID) intervention in San Francisco decreased time from diagnosis to viral suppression from 170 to 65 days [22]. This included, among other interventions, accelerated insurance approval and 5-day cART starter packs. A study among MSM in London showed that cART initiation after a median of 20 days of diagnosis resulted in 99% being virally suppressed at 24 weeks [24]. In San Diego, MSM with AHI initiated cART slightly later after diagnosis than MSM with established infection (14 vs 9 days, respectively), because AHI diagnosis was not provided at the point of care [21], but there were no significant differences in median time from diagnosis to viral suppression (12 weeks in both groups). Our study suggests that, even in the Dutch context, where health insurance is mandatory and includes coverage of cART, the interventions of the AHI strategy could have potential additional value in preventing onward transmission. In our experience, the accelerated confirmation of diagnosis and linkage to care were the most valuable and...
Although none of the MSM with linked records were LTFU in the AHI strategy, a small but worrisome proportion (4%) of MSM in SOC were LTFU before cART initiation. This needs careful attention in HIV elimination programming.

This study has some limitations. First, MSM tested in SOC and the AHI strategy may not have been independent groups, as wider dissemination of the campaign may have reached both groups. The campaign referrals yielded no direct AHI diagnoses, which warrants critical evaluation of the benefits of the campaign. It could be hypothesized that the campaign increased general awareness of AHI among MSM and healthcare providers, which should be assessed in future studies. Furthermore, one of the referral sources of the AHI strategy was the STI clinic itself. This has overestimated the difference in AHI yield when we compared standard testing with the AHI strategy in 2015–2017, as MSM with Fiebig stage II would otherwise have been diagnosed via routine testing. However, the high AHI yield (4%) in the AHI strategy suggests that MSM with high risk of AHI were rightly targeted. Second, we were unable to link 35% of STI clinic records to HIV treatment center records. These records were excluded from the analyses of time to viral suppression. The proportion of record linkages was similar across all years; therefore, we expect that limited bias was introduced. A possible explanation for failure to link could be that the STI clinic allows anonymous free-of-charge consultations for MSM residing in Amsterdam. Thirty-two percent of MSM with unlinked records submitted an invalid postal code; other MSM might have moved or submitted a valid postal code which was not theirs, as they did not want to be traceable or lived outside the region. Since Amsterdam has exceeded the Joint United Nations Programme on HIV/AIDS (UNAIDS) 90-90-90 targets [34], we expect that the majority of MSM with unlinked records are in care, but we were unable to confirm this due to privacy regulations. Third, median time between viral load measurements decreased over time, which may partly explain the decreased time from cART initiation to viral suppression, but not the decreased time from diagnosis to cART initiation. Due to the differences in viral load measurement intervals, we were unable to assess the potential effect of treatment regimen on the time from cART initiation to viral suppression. As INSTI-based regimens decrease the time to viral suppression compared with other cART regimens [21, 35], we expect that the introduction of INSTI-based regimens has also contributed to the decreased time from cART initiation to viral suppression observed in this study.

CONCLUSIONS

We found that targeted testing for AHI is feasible and resulted in a high AHI yield and uptake of immediate cART. Changes in HIV treatment guidelines over time, increased testing rates, and awareness of AHI among MSM, along with the combined interventions of the AHI strategy, decreased the time between HIV diagnosis to combination antiretroviral therapy (cART) initiation and viral suppression, respectively, among men who have sex with men (MSM) diagnosed with HIV at the Amsterdam sexually transmitted infection clinic, stratified by cART initiation period, January 2008–June 2017. A. Estimated time from HIV diagnosis to cART initiation. B. Estimated time from HIV diagnosis to viral suppression. C. Estimated time from diagnosis to viral suppression among MSM with a median of ≤ 60 days between viral load measurements. Stratification for all panels was done by cART initiation period, based on the Dutch HIV treatment guidelines: (1) standard of care (cART if CD4 count < 500 cells/μL, January 2008–December 2011); (2) standard of care (cART if CD4 count < 500 cells/μL or if in acute or early HIV infection [AEHI], January 2012–July 2015); and (3) standard of care (universal cART, January 2015–June 2017) or (3b) acute HIV infection (AHI) strategy (immediate cART, January 2015–June 2017). The black hashes represent censored MSM.
infection, subsequent diagnosis, and viral suppression. Future studies should assess the impact of early diagnosis and immediate cART initiation on HIV incidence in Amsterdam, as well as experiences of MSM with immediate cART initiation, long-term retention in care, and cost-effectiveness.

Supplementary Data
Supplementary materials are available at Clinical Infectious Diseases online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copublished and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes
Author contributions. M. D., M. S. R., M. M. H., M. F. S. L., and G. J. B. designed the study, M. D., A. H., T. H., U. D., E. H., M. P., J. M. P., P. R., M. F. S. L., and G. J. B. contributed to design of the acute human immunodeficiency virus (HIV) infection strategy; M. D., A. H., T. H., E. H., and G. J. B. had oversight in data collection and procedures at the sexually transmitted infection (STI) clinic. M. M. H., A. S., C. S., P. R., and M. V. had oversight in data collection and procedures at the ATHENA cohort. M. D., M. S. R., M. M. H., A. S., and C. S. conducted data cleaning. M. D. conducted the statistical analyses and drafted the manuscript. All authors critically reviewed and revised the manuscript and approved the final version for publication.

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APPENDIX
HIV Transmission Elimination Amsterdam (H-TEAM). Members are listed in alphabetical order.

H-TEAM Steering Committee. J. E. A. M. van Bergen,1,2,3 P. Brokx,4 F. Deug,4 M. Heidenrijk,4 M. Prins,6,7 P. Reiss,5,8 (chair) M. van der Valk.9

H-TEAM Core Project Group. J. E. A. M. van Bergen,1,2,3 G. J. de Bree,7 (chair) P. Brokx,5 U. Davidovich,6 S. E. Geerlings,7 E. Hoornenborg,6 A. Oomen,7 A. van Sighem,1 W. Zuilhof.5

H-TEAM Project Management. N. Schat.5


1Soa Aids Nederland, Amsterdam, the Netherlands; 2Department of General Practice, Amsterdam UMC – location AMC, University of Amsterdam, Amsterdam, the Netherlands; 3Epidemiology and Surveillance Unit, Center for Infectious Disease Control, National Institute of Public Health and the Environment, the Netherlands; 4Dutch Association of PLHIV, Amsterdam, the Netherlands; 5Department of Global Health, Amsterdam UMC – location AMC, Amsterdam UMC, Amsterdam, the Netherlands; 6Department of Internal Medicine, Division of Infectious Diseases, Amsterdam UMC – location AMC, Amsterdam, the Netherlands; 7Stichting HIV Monitoring, Amsterdam, the Netherlands; 8Department of Internal Medicine, Amsterdam UMC – location VUMC, Amsterdam, the Netherlands; 9US Military HIV Research Program and the Henry M. Jackson Foundation for the Advancement of Military Medicine, Bethesda, United States; 10Center of Infection and Immunity Amsterdam (CINIMA), Department of Neurology, Amsterdam UMC – location AMC, Amsterdam, the Netherlands; 11Department of internal medicine, Onze Lieve Vrouwe Gasthuis – location East, Amsterdam, the Netherlands; 12Department of viro-science, Erasmus Medical Center Rotterdam, Rotterdam, the Netherlands; 13DC Klinieken, Amsterdam, the Netherlands; 14Department of Pharmacy, Radboud University Nijmegen Medical Center, Nijmegen, the Netherlands; 15Primary Care Amsterdam and Almere (Elaa), Amsterdam, the Netherlands; 16Aberdeen Health Psychology Group, Institute of Applied Health Sciences, University of Aberdeen, Aberdeen, United Kingdom; 17Department of Internal Medicine, Radboud University Nijmegen Medical Center, Nijmegen, the Netherlands; 18Center of Expertise on Gender Dysphoria, Amsterdam UMC – location VUMC, Amsterdam, the Netherlands; 19Laboratory of Experimental Immunology, Amsterdam UMC – location AMC Amsterdam, Amsterdam, the Netherlands; 20Sexology Center Amsterdam, Amsterdam, the Netherlands; 21GP practice Heijn & de Meij, Amsterdam, the Netherlands; 22Laboratory for Viral Immune Pathogenesis, Amsterdam

Immediate Treatment of Acute HIV • CID 2021;72 (1 June) • 1959

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