Viral suppression after 12 months of antiretroviral therapy in low- and middle-income countries: a systematic review

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Objective To establish estimates of viral suppression in low- and middle-income countries (LMICs) in patients who received antiretroviral therapy (ART) for human immunodeficiency virus (HIV) infection.

Methods Data on viral suppression after 12 months of ART in LMICs were collected from articles published in 2003 to 2011 and from abstracts of conferences held between 2009 and 2011. Pooled proportions for on-treatment and intention-to-treat populations were used as summary estimates. Random-effects models were used for heterogeneous groups of studies ($I^2 > 75\%$).

Findings Overall, 49 studies covering 48 cohorts and 30 016 individuals met the inclusion criteria. With thresholds for suppression between 300 and 500 copies of viral ribonucleic acid (RNA) per ml of plasma, 84.3% (95% confidence interval, CI: 80.4–87.9) of the pooled on-treatment population and 70.5% (95% CI: 65.2–75.6) of the intention-to-treat population showed suppression. Use of different viral RNA thresholds changed the proportions showing suppression: to 84% and 76% of the on-treatment population with thresholds set above 300 and at or below 200 RNA copies per ml, respectively, and to 78%, 71% and 63% of the intention-to-treat population at thresholds set at 1000, 300 to 500, and 200 or fewer copies per ml, respectively.

Conclusion The pooled estimates of viral suppression recorded after 12 months of ART in LMICs provide benchmarks that other ART programmes can use to set realistic goals and perform predictive modelling. Evidence from this review suggests that the current international target – i.e. viral suppression in > 70% of the intention-to-treat population, with a threshold of 1000 copies per ml – should be revised upwards.

Abstracts in عربي, 中文, Français, Русский and Español at the end of each article.

Introduction

At the end of 2011, over 8 million people in low- and middle-income countries (LMICs) were receiving antiretroviral therapy (ART).[1] The guidelines of the World Health Organization (WHO) for the treatment of human immunodeficiency virus (HIV) infection recommend that, where possible, the viral loads of individuals receiving ART be measured every 6 months to detect viral replication and confirm treatment failure whenever it occurs.[2] Although viral load tests are currently too costly for routine use in many LMICs, the potential for increased access to such tests exists as costs decrease and countries prioritize this method of patient monitoring.[3]

WHO's guidelines for the treatment of HIV infection recommend that a viral load of > 5000 copies of viral ribonucleic acid (RNA) per ml be taken as indicative of virological failure.[2] According to WHO's strategy for the surveillance and monitoring of HIV drug resistance in LMICs, a viral load of < 1000 RNA copies per ml should be taken as evidence of viral suppression.[4] Guidelines for the treatment of HIV infection in high-income countries stipulate that a viral load of < 50 RNA copies per ml – or a load below the limit of detection of the most sensitive assay available – be taken as evidence of viral suppression,[5–7] and that a load of ≥ 50 RNA copies per ml,[5,7] or one of ≥ 200 viral RNA copies per ml confirmed by repeat testing,[6] be used as evidence of virological failure or rebound.

The proportion of a study cohort showing viral suppression is calculated as the number of patients with viral suppression divided either by the number of patients in the study cohort who began ART (i.e. the intention-to-treat population), or by the number of patients in the cohort who are alive and on treatment (i.e. the on-treatment population). On-treatment analyses reflect the effectiveness of ART for those receiving antiretroviral drugs. Intention-to-treat analyses, which use a denominator that includes individuals who die or are lost to follow-up during the study period, reflect factors at the individual or programme level that influence the risk of death and disengagement from care. Relatively high mortality in the first 6 to 12 months of ART and substantial loss to follow-up, both of which have been widely reported in LMICs, can therefore influence estimates of viral suppression based on intention to treat.[8,9]

Summary estimates of viral suppression (as measured, for example, 12 months after ART initiation) are needed to guide ART programme managers on the normative levels of population-level viral suppression and to define desirable levels of clinic and programme performance. Such estimates are also useful when creating and improving mathematical models of the different strategies that might be followed to provide ART in LMICs. Recent reviews of virological outcomes have focused on sub-Saharan Africa and levels of acquired resistance to antiretroviral drugs.[10,11] Across LMICs, summary estimates of viral suppression based on different HIV-RNA thresholds are lacking. The objective of this systematic review was to establish estimates, based on different viral RNA thresholds, of the percentages of the intention-to-treat and on-treatment populations in LMICs that show viral suppression 12 months after ART initiation.

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Methods

Study selection

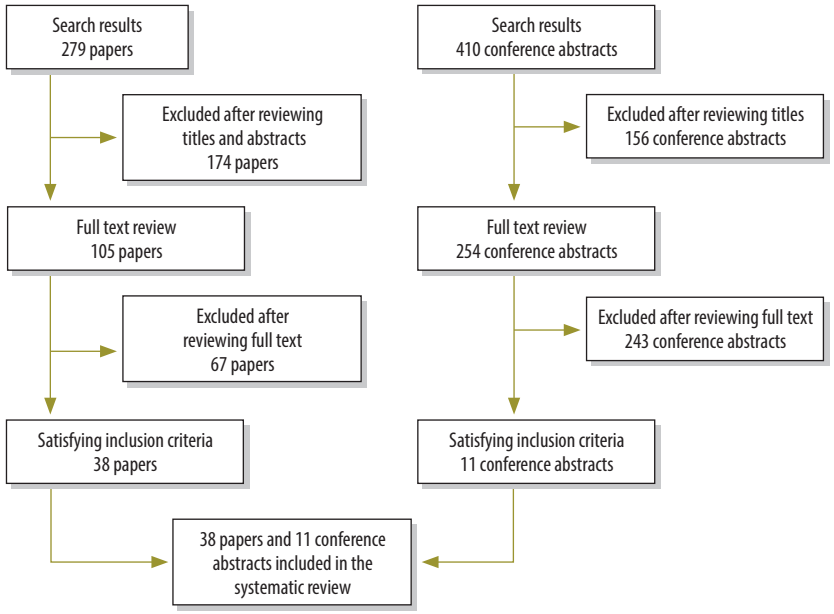
We included publications ("papers") or conference abstracts that reported the proportion of individuals in a study cohort from an LMIC for whom a virological outcome after 12 months of ART was reported, either as a primary or a secondary finding. If only the median duration of follow-up was reported for a study, that study was included in the review provided the median duration was between 9 and 15 months. Any definition of viral suppression (or failure) reporting a proportion of patients below (or above) a defined viral RNA threshold was accepted. If the threshold was not reported, the relevant authors were contacted and asked for details of the threshold that they had used. A study was excluded if (i) the threshold used could not be determined; (ii) only changes in viral RNA loads from the baseline values were reported; (iii) most of the patients were less than 13 years old; (iv) patients received only one or two antiretroviral drugs; or (v) the study was not from an LMIC. All the studies included in the review were published in English and were either clinical trials or cross-sectional or cohort in design.

Search strategy

We searched for relevant articles published between 1 January 2003 and 31 May 2011 through Ovid MEDLINE. Online databases containing the abstracts of presentations made at the International AIDS Society Conferences held in 2009–2010 and at the Conferences on Retroviruses and Opportunistic Infections held in 2009–2011 were also searched.[12,13]

Our search strategy combined the relevant medical subject headings (MeSH) with additional search terms to identify those studies that reported virological outcomes for HIV-infected participants receiving ART. We used other MeSH and search terms to identify studies from LMICs in which outcomes after 12 months of ART were investigated. When more than one article reported data from the same cohort of patients and used the same viral RNA threshold, only the article that contained the most detailed information was selected. Fig. 1 summarizes the search strategy and study selection process. The study protocol provides further details.[14]

Fig. 1. **Search strategy and study selection used in the systematic review**



Note: We excluded duplicate reports, studies on subjects not receiving antiretroviral therapy, studies with patients younger than 13 years or not infected with human immunodeficiency virus or not living in a low- or middle-income country, and reports that provided insufficient information.

The following data were abstracted from each study: first author, year of publication, study country or countries, health-care setting (i.e. public sector, private sector or nongovernmental organization), whether the study patients had to pay for their ART, dates the patients were observed, number of study sites, number of patients receiving ART, baseline demographics (i.e. age, gender, CD4+ T-lymphocyte count and clinical stage), ART regimen, whether patients were ART-naive at baseline, study definition of virological outcome, and the proportion of patients meeting that definition 12 months after initiating ART. When available, the percentages of subjects who died, transferred out, stopped ART or were lost to follow-up were also abstracted. Whether the proportion of the study cohort reported to have viral suppression was based on an on-treatment or intention-to treat analysis was noted. If intention-to-treat values had not been reported, they were calculated from the raw data (when available). In these calculations, the number of patients who had died or been lost to follow-up at the time of the estimation of virological outcome and, when available, the number that had stopped ART were included in the denominator. Patients who transferred out of the study cohort were excluded from the denominator, consistent with the indicators of retention in care recommended by WHO and the United States President's Emergency Plan for AIDS Relief (PEPFAR).[15–18] If only the fraction of patients showing virological failure was reported, we calculated from this figure the proportion with viral suppression.

Data analysis

Proportions (%) of patients meeting the study definition of viral suppression were derived from text, tables or, if they could be accurately determined or estimated in this manner, from published graphs. Summary estimates were determined and categorized as on-treatment or intention-to-treat values. We assessed heterogeneity among proportions by calculating the I^2 statistic. If heterogeneity was high ($I^2 > 75\%$), we pooled proportions using the Freeman–Tukey method with a random-effects model and DerSimonian–Laird weights.[19,20] When possible, we determined summary estimates of viral suppression using different threshold ranges for viral RNA: ≥ 1000, 300–500 and/or ≤ 200 copies per ml. Additionally, we calculated summary estimates separately for studies in which one or two viral load tests were used per patient to define virological outcomes. We performed subgroup analyses to examine the influence of the

year of ART initiation and of the time taken to publish the research findings (i.e. the "time-lag bias") on the summary estimates for the on-treatment populations. Year of ART initiation was defined as the median year of ART initiation and reported as pre-2004, 2004–2005 or post-2005. The time from the median year of ART initiation until publication was categorized as ≤ 3, 4 or ≥ 5 years. Analyses were conducted using Excel (Microsoft, Redmond, United States of America) and version 2.7.9 of the StatsDirect software package (StatsDirect, Altrincham, United Kingdom of Great Britain and Northern Ireland).

Results

Overall, 49 studies (38 papers[21–58] and 11 conference abstracts[59–69]), together comprising 48 cohorts and 30 016 individuals, were identified for inclusion (Fig. 1). Details of the cohorts from the papers and conference abstracts are presented in Table 1 and Table 2 (available at: http://www.who.int/bulletin/volumes/90/5/12-112946), respectively. Two reports[29,52] described outcomes from the same cohort but made use of two different thresholds to define viral suppression. A further seven reports[26,27,43,44,47,53,55] described outcomes using two or more thresholds of viral suppression. The data from another two papers[24,25] were combined to obtain an estimate of viral suppression in a single cohort. The 48 cohorts in the systematic review comprised 43 single-country cohorts – 37 from sub-Saharan Africa, 3 from Asia and 3 from Latin America or the Caribbean – and 5 multi-country cohorts (of which 4 were from sub-Saharan Africa).

All but one study[68] used a single viral load measurement per patient to define the virological outcome. The ART regimens used were reported for 39 of the studies. In each of 35 (90%) and 29 (74%) of these studies, at least 50% and 95% of the patients, respectively, had received a regimen based on a non-nucleoside reverse-transcriptase inhibitor (NNRTI). Most of the patients in another three studies – a clinical trial studying the efficacy of boosted protease-inhibitor regimens[26] and two studies from regions with high prevalences of HIV-2 infection[35,45] – had received regimens based on a protease inhibitor.

Summary estimates from on-treatment and intention-to-treat analyses are presented – for those studies in which outcomes were defined using a single viral load measurement– in Table 3 and Fig. 2. As high levels of heterogeneity were observed ($I^2 > 90\%$), all summary estimates and 95% confidence intervals (CI) were calculated using a random-effects model.

The summary estimate of the proportion of patients showing viral suppression, for all viral load thresholds in 43 on-treatment analyses, was 84.0% (95% CI: 81.3–86.6; $n = 26\,599$). For the nine cohorts in which viral suppression was defined as < 1000 viral RNA copies per ml, 83.5% (95% CI: 77.8–88.4; $n = 3192$) of the combined on-treatment populations showed suppression. Thresholds ranging from 300 to 500 copies per ml were used for 32

Table 3. **Summary estimates of the proportions achieving viral suppression after 12 months of antiretroviral therapy in low- and middle-income countries**

Type of analysis and viral load threshold	No. of cohorts[a]	No. of patients starting ART	Patients (%) with viral suppression	
			Range	Pooled (95% CI)[b]
On-treatment				
On-treatment, all thresholds[c]	43	26 599	49–97	84.0 (81.3–86.6)
1000 copies/ml	9	3192	74–94	83.5 (77.8–88.4)[d]
300–500 copies/ml	32	25 708	62–97	84.3 (80.4–87.9)
≤ 200 copies/ml	9	2167	49–93	76.1 (66.8–84.3)
Intention-to-treat				
Intention-to-treat, all thresholds[c]	27	13 134	50–92	71.2 (66.5–75.7)
1000 copies/ml	4	1201	69–87	77.5 (67.6–86.1)
300–500 copies/ml	21	11 528	51–92	70.5 (65.2–75.6)
≤ 200 copies/ml	6	1654	46–77	62.9 (51.2–73.8)

ART, antiretroviral therapy; CI, confidence interval.

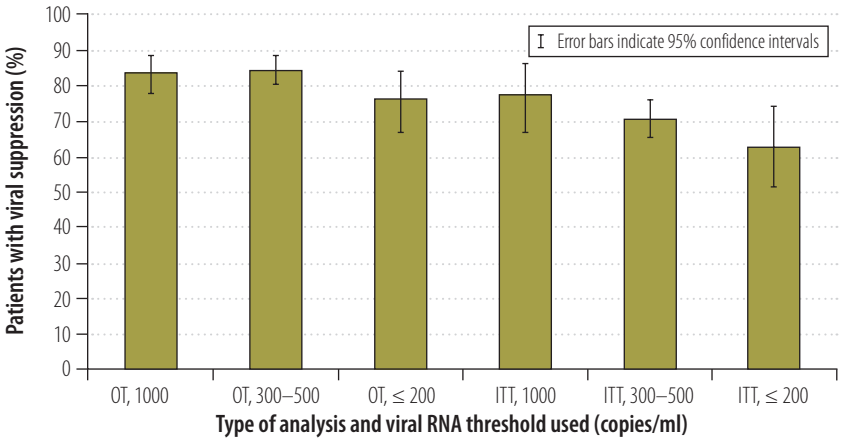
[a] Only includes data from studies in which suppression was detected by one viral load test per patient.

[b] Pooled proportions and CIs were calculated using the Freeman–Tukey method in a random effects model.

[c] When two different thresholds were applied in the study of one cohort, the data for the threshold that was closer to 1000 copies/ml was used.

[d] These values changed to 84.2 (79.1–88.7) when we included in the calculations the data for the study in which two viral load measurements were used, per patient, to define viral suppression (i.e. Scarsi et al.[68] [$n = 2366$]).

Fig. 2. **Viral suppression after 12 months of antiretroviral therapy in low- and middle-income countries**



ITT, intention-to-treat; OT, on-treatment; RNA, ribonucleic acid.

Note: The data shown summarizes OT or ITT analyses in which viral suppression was defined by a viral load – measured as copies of human immunodeficiency virus ribonucleic acid (HIV-RNA) per ml of plasma – that fell below a threshold value.

cohorts (a threshold of 400 copies per ml was used for 27 cohorts) and 84.3% (95% CI: 80.4–87.9; $n = 25\,708$) of the combined on-treatment populations of these 32 cohorts showed suppression. The reported outcomes for nine and six cohorts were based on thresholds set at or below 200 and at or below 50 viral RNA copies per ml, respectively. When thresholds set at or below 200 copies per ml were used, 76.1% (95% CI: 66.8–84.3; $n = 2167$) of the combined on-treatment populations showed suppression.

The summary estimate of viral suppression for all 27 cohorts ($n = 13\,134$) in intention-to-treat analyses was 71.2% (95% CI: 66.5–75.7). The corresponding value for the four analyses in which a threshold of 1000 copies per ml was used was 77.5% (95% CI: 67.6–86.1; $n = 1201$). In intention-to-treat analyses of the data from 21 and 19 cohorts, thresholds of 300–500 and 400 copies per ml, respectively, were used. With thresholds that ranged from 300 to 500 copies per ml, 70.5% (95% CI: 65.2–75.6; $n = 11\,528$) of the combined intention-to-treat populations showed viral suppression. Six studies reported the results of intention-to treat analyses based on thresholds set at or below 200 copies per ml – four studies used a threshold set at or below 50 copies per ml – and these produced a summary estimate for the frequency of viral suppression of 62.9% (95% CI: 51.2–73.8; $n = 1654$).

To investigate possible sources of heterogeneity, we performed subgroup analyses exploring the median time of ART initiation and the potential bias introduced by the time taken to publish results: the I^2 values for the subgroups considered were all > 90%. When the median year of ART initiation was pre-2004, 2004–2005 and post-2005, the on-treatment estimates of suppression after 12 months of ART were 80.9% (95% CI: 73.0–87.7), 84.1% (95% CI: 78.3–89.2) and 84.3% (95% CI: 80.0–88.2), respectively. The corresponding values for delays of ≤ 3, 4 and ≥ 5 years between the median year of ART initiation and the year of the publication of results were similar: 83.3% (95% CI: 78.0–88.0), 84.0% (95% CI: 78.7–88.6) and 83.0% (95% CI: 76.9–88.3), respectively.

Discussion

This is the first systematic review to quantify population-level viral suppression 12 months after ART initiation in LMICs, and to stratify estimates by viral RNA thresholds in on-treatment and intention-to-treat analyses. Over 70% of the cohorts included in the review were investigated using thresholds ranging from 300 to 500 viral RNA copies per ml and, after 12 months of ART, viral suppression was noted in 84% (on-treatment) or 71% of patients (intention-to-treat). These summary estimates compare favourably with outcomes reported in high-income countries after 12 months of NNRTI-based ART, such as the 58–73% viral suppression seen in intention-to-treat analyses in early clinical trials and in a meta-analysis at thresholds set from 400 to 500 viral RNA copies per ml.[70–72] Observational data from Canada, the United Kingdom and the United States of America also indicate similar frequencies of viral suppression after 12 months of ART. For example, when a viral load threshold of 50 copies per ml was used, 82% of an on-treatment population investigated in the United Kingdom showed viral suppression.[73] In Canada and the United States, in on-treatment analyses based on suppression thresholds between 500 and 1000 copies per ml, 60–63% of individuals initiating ART when they had CD4+ T-lymphocyte counts of < 200 cells per µl were found to have attained viral suppression 12 months later.[74,75]

As anticipated, summary estimates for viral suppression were found to be higher in the on-treatment analyses than in the intention-to-treat analyses and to increase as the viral RNA thresholds used to define suppression increased. Individuals who are lost to follow-up in studies on the efficacy of ART – and included in intention-to-treat analyses but excluded from on-treatment analyses – are defined as not having achieved viral suppression. In addition, as the viral load thresholds for suppression are increased, increasing numbers of patients with low-level viraemia are categorized as cases of viral suppression.

We found no evidence of studies in LMICs that had used viral load thresholds of 10 000 or 5000 copies per ml – as recommended in the ART guidelines published by WHO in 2006[2] and 2010,[76] respectively – to define viral suppression. The reasons for this are unclear. Investigators in LMICs may simply have preferred to use the lower thresholds supported either by the national ART guidelines used in the country where the study was performed or by guidelines not specifically intended for use in a public health model of care.[5–7] They may also have wished to use thresholds based on the lower limit of sensitivity of the viral load assay that they had available.

Only one study[68] reported the frequency of viral suppression based on two viral load measurements per patient. In this case, use of a second test increased the percentage of patients showing viral suppression. A second test is particularly likely to increase the percentage of patients who are virologically suppressed if an intervention to improve adherence to ART occurs after an initial detectable viral load, in a strategy that is recommended by WHO[2] and already followed in several LMICs.[33,77,78] Given that the overwhelming majority of reported outcomes are based on a single viral load measurement per patient, efforts to understand and summarize virological outcomes in LMICs should also be based on a single test result for each patient.

As far as possible, this review used intention-to-treat estimates of viral suppression that, as recommended in the relevant international guidelines,[15–18] excluded individuals who transferred out of the included studies. Individuals were reported to have transferred out of only six cohorts included in the review and, in each case, such individuals were excluded from the intention-to-treat estimate of viral suppression.[21,24,25,38,46,48,49] However, only two of the reports included in the review specifically stated that no patient had transferred out.[44,53] For the other 19 cohorts with intention-to-treat estimates of viral suppression, no data on transfers out were presented. This lack of data left it unclear whether any patients had transferred out and, if so, whether such patients had been incorporated in the denominator used in the final analyses. If any patients who did transfer out were unreported and still included in the denominators used in the final analyses, the intention-to-treat summary estimates generated in this review may be too low.

The summary estimates presented in this systematic review are important for target-setting and benchmarking. They provide guidance to ART clinics and programmes on the mean rates of viral suppression achieved in LMICs (normative referencing). The managers of ART programmes may define adequate levels of programme performance as those that lead to levels of

viral suppression that match or exceed the summary estimates (criterion referencing).[79] A combination of normative and criterion referencing methods, incorporating the data summarized in this review, may be used to categorize poor, intermediate and optimal levels of performance. In its strategy for the surveillance and monitoring of resistance to antiretrovirals, WHO recommends that ART treatment sites achieve viral suppression (as indicated by a viral load of < 1000 copies per ml) in at least 70% of the intention-to-treat population after 12 months of ART.[80] Although data from this review are limited, this target should probably be increased since, in the four reviewed studies that used the same viral load threshold ($n = 1201$), 78% of the intention-to-treat population achieved suppression. Although detectable viral RNA after ART does not prove the presence of resistance to antiretrovirals, individuals who are virologically suppressed on ART have no effective drug resistance. Detectable viral RNA in populations receiving ART is often associated with suboptimal adherence to ART, which is predictive of the emergence of drug-resistant strains of the virus.[65]

The estimates presented in this review may not be truly representative, despite being mean or normative levels of viral suppression. For example, ART programmes or clinics that evaluated and reported viral loads may have greater resources and better clinical outcomes than those where viral loads were not evaluated and/or where virological outcomes were not reported. Additionally, in settings where viral loads were evaluated but where poor virological outcomes were observed, researchers may have chosen not to disseminate the results, and this may have led to publication bias. The summary estimates may therefore overestimate the mean frequency of viral suppression in the broader population receiving ART in LMICs. In addition, high levels of statistical heterogeneity ($I^2 > 90\%$) were observed during the review. Analyses that focused on year of ART initiation and the delays between the recording and publishing of results revealed persistent heterogeneity but no major differences in the proportions achieving viral suppression between the subgroups considered. These findings suggest that other, unidentified factors are potentially contributing to the between-study variation seen in the proportions of viral suppression. Despite these limitations, the systematic method used to identify studies and the statistical methods used to generate summary estimates allow for a reliable estimate of viral suppression rates based on the data available from LMICs. Another potential limitation of the present review is that most of the data investigated came from studies that used thresholds between 300 and 500 copies per ml. Relatively few results from studies based on thresholds set at 1000 or at or below 200 viral RNA copies per ml were available. In the on-treatment analyses, the summary estimate of suppression seen with a threshold of 1000 copies per ml was similar to that seen with thresholds in the range of 300 to 500 copies per ml. However, only nine cohorts were included in the calculation of viral suppression at the high threshold ($n = 3192$), whereas 32 cohorts ($n = 25\,708$) were included in the calculation at the lower thresholds. The summary estimates established at 1000 copies per ml may have been too underpowered to demonstrate a difference with the estimates established at thresholds between 300 and 500 copies per ml.

In conclusion, this is the first systematic review of viral-suppression rates from LMICs after 12 months of ART. It includes summary estimates, at multiple HIV RNA thresholds, based on both on-treatment and intention-to-treat analyses. At the most commonly reported viral RNA thresholds (i.e. 300–500 copies per ml), approximately 71% of the patients in the intention-to-treat analyses and 84% of those in the on-treatment analyses had attained viral suppression 12 months after ART initiation. These proportions compare favourably with outcomes observed in high-income countries and represent a substantial achievement for LMICs, where ART is generally provided under great resource constraints.

The data reported in this review have important public health implications. Researchers and managers of ART programmes in LMICs could use these results to support mathematical models of the effects of ART and set rates of viral suppression as performance targets. Use of these targets would help identify those ART clinics with suboptimal performance that would most benefit from focused interventions to improve service delivery and patient outcomes. ■

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ملخص

الكبت الفيروسي بعد 12 شهراً من العلاج بمضادات الفيروسات القهقرية في البلدان المنخفضة الدخل والبلدان المتوسطة الدخل: استعراض منهجي

الغرض تقييم تواتر الكبت الفيروسي في البلدان المنخفضة الدخل والبلدان المتوسطة الدخل لدى المرضى الذين تلقوا العلاج بمضادات الفيروسات القهقرية لعلاج الإصابة بعدوى فيروس العوز المناعي البشري.

الطريقة تم جمع البيانات حول الكبت الفيروسي بعد 12 شهراً من العلاج بمضادات الفيروسات القهقرية في البلدان المنخفضة الدخل والبلدان المتوسطة الدخل من المقالات التي تم نشرها من عام 2003 إلى عام 2011، ومن ملخصات المؤتمرات التي عقدت من عام 2009 إلى عام 2011. وتم استخدام النسب المجمعة للمجموعات السكانية الخاضعة للعلاج والمجموعات

السكانية التي تنوي تلقي العلاج كتقديرات موجزة. وتم استخدام نماذج التأثيرات العشوائية لفئات الدراسات التي تتسم بالتغايرية (I^2 > 75٪).

النتائج إجمالاً، توافرت معايير الإدراج في 49 دراسة شملت 48 مجموعة و30016 فرداً. وفي حين تراوحت عتبات الكبت بين 300 و500 نسخة من الحمض الريبي النووي الفيروسي (RNA) لكل ملي لتر من البلازما، أظهرت نسبة 84.3 ٪ (فاصل الثقة 95 ٪، فاصل الثقة: من 80.4 إلى 87.9) من المجموعة السكانية المجمعة الخاضعة للعلاج و70.5 ٪ (فاصل الثقة 95 ٪، فاصل الثقة: من 65.2 إلى 75.6) من المجموعة السكانية التي تنوي تلقي العلاج وجود كبت. وغيّر استخدام عتبات الحمض الريبي النووي الفيروسي المختلفة النسب التي أظهرت كبتاً: إلى 84 ٪ و76 ٪ من المجموعة السكانية الخاضعة للعلاج بالعتبات المحددة فوق 300 وعند 200 نسخة حمض ريبي نووي فيروسي أو دونه لكل ملي لتر، على التوالي، وإلى 78 ٪ و71 ٪ و63 ٪ من المجموعة السكانية التي تنوي تلقي العلاج عند العتبات المحددة عند 1000 و300 نسخة حمض ريبي نووي فيروسي إلى 500 و200 نسخة حمض ريبي لنووي فيروسي أو عدد أقل عن ذلك من النسخ لكل ملي لتر، على التوالي.

الاستنتاج تشير التقديرات المجمعة للكبت الفيروسي التي تم تسجيلها بعد 12 شهراً من العلاج بمضادات الفيروسات القهقرية في البلدان المنخفضة الدخل والبلدان المتوسطة الدخل على أنه يمكن استخدام برامج العلاج بمضادات الفيروسات القهقرية الأخرى لتحديد المرامي التي تتسم بالواقعية وتنفيذ النمذجة التنبؤية. وتشير البيّنات المأخوذة من هذا الاستعراض إلى أنه ينبغي تنقيح المرمى الدولي الراهن – أي الكبت الفيروسي لدى أكثر من 70 ٪ من المجموعة السكانية التي تنوي تلقي العلاج التي تصل عتبتها إلى 1000 نسخة لكل ملي لتر بشكل تصاعدي.

摘要

中低收入国家抗逆转录病毒治疗12 个月后病毒抑制:系统评价

目的 估计中低收入国家(LMIC)接受艾滋病病毒(HIV)感染抗逆转录病毒治疗(ART)的患者的病毒抑制率。

方法 从2003 至2011 年发表的文章以及2009 至2011 年之间举行的会议摘要中收集中低收入国家患者在接受ART 的12 个月之后的病毒抑制数据。使用治疗和意向治疗人群的集合比例作为汇总估计值。对研究(I^2 >75%)的异质群体使用随机效应模型。

结果 总体而言,涉及48 个群组和30016 名个人的49 项研究符合纳入标准。在抑制阈值为每毫升血浆病毒核糖核酸(RNA)拷贝数为300 至500 时,84.3%(95% 置信区间,CI:80.4 – 87.9)的集合治疗人群和70.5%(95% CI:65.2 – 75.6)的意向治疗人群显示抑制。使用不同的病毒RNA阈值则显示抑制的比例有所变化:阈值为高于每毫升RNA拷贝数300 以上和200 以下的治疗人群,抑制率分别变为84% 和76%;阈值为每毫升拷贝数1000、300-500 和200 或更少时,意向治疗人群抑制率分别变为78%、71%和63%。

结论 中低收入国家ART治疗12 个月后记录的集合病毒抑制估计可供其他ART计划用来设定现实的目标,并进行预测建模。此评价的证据表明,目前的国际目标(也就是以每毫升拷贝数1000 为阈值,达到70%以上意向治疗人群中的病毒抑制)应向上修正。

Résumé

Suppression virale après 12 mois de traitement antirétroviral dans les pays à revenu faible et intermédiaire: bilan systématique

Objectif Estimer la suppression virale dans les pays à revenu faible et intermédiaire (PRFI) chez des patients ayant reçu un traitement antirétroviral (TAR) contre l'infection due au virus de l'immunodéficience humaine (VIH).

Méthodes Des données sur la suppression virale après 12 mois de TAR dans les PRFI ont été recueillies à partir d'articles publiés entre 2003 et 2011 et de comptes rendus de conférences qui ont eu lieu entre 2009 et 2011. Comme estimations sommaires, on a utilisé des proportions globales pour les populations en cours de traitement et ayant l'intention d'être traitées. On a utilisé des modèles d'effets aléatoires pour les groupes d'études hétérogènes (I^2 > 75%).

Résultats Dans l'ensemble, 49 études couvrant 48 cohortes et 30 016 individus respectaient les critères d'inclusion. Avec des seuils de suppression allant de 300 à 500 copies d'acide ribonucléique (ARN) viral par ml de plasma, 84,3% (intervalle de confiance de 95%, IC: 80, 4–87,9) de la population en cours traitement analysée et 70,5% (95% IC: 65,2–75,6) de la population ayant l'intention d'être traitée indiquaient une suppression. L'utilisation de différents seuils d'ARN viral changeait les proportions montrant la suppression: à 84% et 76% de la population en cours de traitement avec des seuils fixés respectivement à plus de 300 et à 200 copies ou moins d'ARN par ml, et à 78%, 71% et 63% de la population ayant l'intention d'être traitée à des seuils fixés respectivement à 1 000, 300 à 500, et à 200 copies ou moins par ml.

Conclusion Les estimations globales de la suppression virale enregistrées après 12 mois de TAR dans les PRFI indiquent que d'autres programmes de TAR peuvent être utilisés pour définir des objectifs réalistes et pour créer une modélisation prédictive. Les conclusions de cette étude suggèrent que l'objectif international actuel – la suppression virale chez plus de 70% des personnes qui ont l'intention de se soigner, avec un seuil de 1 000 copies par ml – devrait être revu à la hausse.

Резюме

Вирусная суппрессия после 12 месяцев антиретровирусной терапии в странах с низким и средним уровнем дохода: систематический обзор

Цель Оценка частоты вирусной супрессии в странах с низким и средним уровнем дохода (СНСД) у пациентов, которые прошли антиретровирусную терапию (АРТ) против инфекции вируса иммунодефицита человека (ВИЧ).

Методы Данные о вирусной супрессии через 12 месяцев после начала АРТ в СНСД были собраны из статей, опубликованных в

период с 2003 по 2011 годы и тезисов докладов на конференциях, состоявшихся в период с 2009 по 2011 годы. В качестве сводных данных использовались совокупные пропорции людей, прошедших лечение и начавших лечение. Модели со случайными эффектами были использованы для гетерогенных групп исследований (I^2 > 75%).

Результаты В целом, 49 исследований, охватывающих 48 когорт и 30 016 лиц, были признаны соответствующим критериям включения. С порогами супрессии от 300 до 500 копий вирусной рибонуклеиновой кислоты (РНК) на мл плазмы, 84,3% (95% доверительный интервал, ДИ: 80,4-87,9) от совокупной выборки людей, прошедших лечение, и 70,5% (95% ДИ: 65,2-75,6) людей, начавших лечение, проявили признаки супрессии. Использование других порогов содержания вирусных РНК изменило пропорции тех, у кого проявлялись признаки супрессии: до 84% и 76% людей, прошедших лечение, с порогами, установленными выше 300, и на уровне или ниже уровня 200 копий РНК на 1 мл, соответственно, и до 78%, 71% и 63 % от людей, начавших лечение, с порогами, установленными на уровне 1000, от 300 до 500 и 200 или меньшим количеством копий на 1 мл, соответственно.

Вывод Совокупная оценка вирусной супрессии, зафиксированной после 12 месяцев проведения АРТ в СНСД, показывает, что для постановки реалистичных целей и прогнозного моделирования можно использовать другие программы АРТ. Данные из этого обзора позволяют сделать вывод о необходимости пересмотра в сторону увеличения текущих международных целевых показателей, предусматривающих вирусную супрессию у 70% людей, начавших лечение, с порогом 1000 копий на 1 мл.

Resumen

Supresión viral tras 12 meses de terapia con antiretrovirales en países de renta baja y media: una revisión sistemática

Objetivo Calcular la supresión viral en países de renta baja y media (PRBM) en pacientes que recibieron terapia con antiretrovirales (TAR) para tratar la infección por el virus de inmunodeficiencia humana (VIH).

Métodos Se recabaron datos sobre la supresión viral tras 12 meses de TAR basados en artículos publicados entre 2003 y 2011, así como en resúmenes de conferencias que tuvieron lugar entre 2009 y 2011. Se emplearon proporciones combinadas entre poblaciones en tratamiento y con intención de tratar como estimaciones globales. Se usaron modelos de efectos aleatorios para grupos de estudio heterogéneos (I^2 > 75%).

Resultados En líneas generales, 49 estudios que incluían 48 cohortes y 30 016 individuos cumplieron los criterios de inclusión. El 84,3% (intervalo de confianza del 95%, IC: 80,4–87,9) del conjunto de la población en tratamiento y el 70,5% (IC del 95%: 65,2–75,6) de la población con intención de tratar mostraron supresión con umbrales para la supresión de entre 300 y 500 copias de ácido ribonucleico viral (RNA) por ml de plasma. El empleo de diferentes umbrales virales RNA cambió las proporciones que indican supresión: al 84% y 76% de la población en tratamiento con umbrales superiores a 300 y a o por debajo de 200 copias de RNA por ml, respectivamente, y a 78%, 71% y 63% de la población con intención de tratar con umbrales fijados en 1000, 300 a 500 y 200 o menos copias por ml, respectivamente.

Conclusión Las estimaciones combinadas de supresión viral que se registraron tras 12 meses de TAR en PRBM establecen que pueden emplearse otros programas TAR para establecer objetivos realistas y realizar modelos de predicción. Las constataciones de esta revisión sugieren que el objetivo internacional en la actualidad – es decir, la supresión viral en > 70% de la población con intención de tratar, con un umbral de 1000 copias por ml – debe revisarse al alza.

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Table 1. **Study cohorts included in the systematic review and described in journal articles on viral suppression after 12 months of antiretroviral therapy in low- and middle-income countries**

Study	Country/ site	Type of care	Patient paid for ART?	Dates observed	No. of sites	*n*[a]	Study design	Baseline features[b]	ART regimen[c]	Time on ART[d]	Viral suppression		Percentage of patients			
											Definition (HIV RNA copies/ml)	Percentage meeting definition and type of analysis	Died	LTFU	Stopped ART	TFO
Bussman et al.[33] (2009)	Botswana (Gaborone)	Public	No	Started 2002–2004, followed to Apr. 2006	5	650	RCT	33; 31; 199; 34% III and 9% IV	NNRTI	12 months	< 400	92 (OT; *n* = 586), 86 (ITT; *n* = 624)	3.4	2.4	NR	NR
Bourgeois et al.[31] (2005)	Cameroon (Yaoundé)	Public, NGO	Partially	Started Jan. 2001–Apr. 2003	1	109	Cohort	36; 34; 150; 54% III and 20% IV	NNRTI	12 months	< 400	97.3 (OT; *n* = 75), 86.9 (ITT; *n* = 84)	NR	NR	NR	NR
Seyler et al.[57] (2003)	Côte d'Ivoire (Abidjan)	Public	Partially	Mar. 1999–Aug. 2002	> 1	101	Cohort	36; 38; 135; 48% III and 39% IV	NNRTI	12 months	< 200	51 (OT; *n* = 29)	NR	NR	NR	NR
Ferradini et al.[37] (2006)	Malawi (Chiradzulu)	Public, NGO	No	Jan.–Apr. 2004	1	398	Cross section	34; 31; 114; 58% III and 24% IV	99% NNRTI, 98% naive	9.5 months (median)	< 1000	87 (OT; *n* = 397)	NR	NR	NR	NR
Laurent et al.[45] (2005)	Senegal	Public	Partially (free in trial)	Started Aug. 1998–Apr. 2001	NR	176	Cohort (*n* = 80 in trial)	38; 48; 144; NR	47% NNRTI, 43% PI, 92% naive	12 months	< 500	77 (OT; *n* = 143), 63 (ITT; *n* = 176)	NR	NR	NR	NR
Gandhi et al.[39] (2009)	South Africa (Msinga)	Public, partner	No	Started Oct. 2003–Jan. 2006	1	119	Cohort	34 (mean); 44; 79; NR	NNRTI	12 months	< 400	94 (OT; *n* = 98), 78 (ITT; *n* = 118)	11	5.9	NR	NR
Wouters et al.[24,25] (2008–09)	South Africa (Free State)	Public	No	NR	> 1	268	Cohort	38 (mean); 33; 109 (mean); NR	NR	12 months (median)	< 400	85 (OT; *n* = 232), 78 (ITT; *n* = 254)	5.6	2.2	NR	5.2
Ahoua et al.[21] (2009)	Uganda (Arua)	Public, NGO	No	Started Sept. 2004–Jul. 2005	1	229	Cohort and cross section	37; 34; 100; 18% III/IV	NNRTI, 98% naive	12 months	< 1000	89 (OT; *n* = 229), 69 (ITT; *n* = 297)	5.0	17.0	1.0	5.0
Mujugira et al.[49] (2009)	Botswana (Gaborone)	Public	No	Started Feb–Mar. 2002	1	349	Cohort	35; 41; 22; NR	NNRTI	9 months	< 400	60 (ITT; *n* = 349)	22	13.5	NR	1.1
Fielding et al.[38] (2008)	South Africa	Private (work)	No	Started before 2004, followed to Mar. 2006	39	1760	Cohort	41; 97; 156; 73% III/IV	NNRTI	12 months	< 400	72 (OT; *n* = 953), 51 (ITT; *n* = 1328)	9.9	11.4 (or stopped)	See LTFU	12.1
Keiser et al.[22] (2008)	South Africa (Khayelitsha Gugulethu)	Public	No	Started 2001–2006	13	2348	Cohort	33; 29; 80; 91% III/IV	99.6% NNRTI	10.8 months (median)	< 500	96 (OT; *n* = 1788), 81 (ITT; *n* = 2128)	11[e]	3.5	NR	NR
Bisson et al.[29] (2008)	Sub-Saharan Africa (9 countries)	Private (work)	Insured	Started Dec. 2000–Feb. 2003	> 1	872	Cohort	NR (55% < 35 years old); 37; 165; NR	NNRTI	12 months	< 1000	74 (OT; *n* = 872)	NR	NR	NR	NR
Nachega et al.[52] (2009)	Sub-Saharan Africa (9 countries)	Private (work)	Insured	Started Jan. 1999-Aug. 2006	> 1	7776	Cohort	37; 38; 146; NR	97% NNRTI, 3% PI	12 months	< 400	62 (OT; *n* = 3192)	NR	NR	NR	NR

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Study	Country/ site	Type of care	Patient paid for ART?	Dates observed	No. of sites	*n*[a]	Study design	Baseline features[b]	ART regimen[c]	Time on ART[d]	Viral suppression		Percentage of patients			
											Definition (HIV RNA copies/ml)	Percentage meeting definition and type of analysis	Died	LTFU	Stopped ART	TFO
Garrido et al.[40] (2008)	Angola	NR	NR	NR	1	294	Cross section	36; 28; 144; NR	89% NNRTI, 80% naive	12.6 months (median)	< 1000	74 (OT; *n* = 294)	NR	NR	NR	NR
Vanni et al.[58] (2007)	Brazil (Ribeira Porto)	Public	No	Jan. 2002–Dec. 2003	1	126	Cohort	37; 69; NR; NR	60% NNRTI, 40% PI	12 months	< 400	65 (ITT; *n* = 126)	NR	NR	NR	NR
Ndembi et al.[53] (2010)	Uganda (Kampala, Entebbe)	Public (trial)	No	Started Jan.–Oct. 2004	2	600	RCT	37; 28; 99; 55% III and 18% IV	NNRTI (in one arm)	48 weeks	< 50	77 (ITT; *n* = 300)	4.2	2.0	1.0	NR[f]
As above	–	–	–	–	–	–	–	–	–	48 weeks	< 1000	87 (ITT; *n* = 300)	4.2	2.0	1.0	NR[f]
Ananworanich et al.[26] (2008)	Thailand	Public (trial)	No	Started after 2001	7	272	RCT	34 (mean); 39; NR; NR (28% CDC category B and 2% category C)	PI	48 weeks	< 400	96 (OT; *n* = 164), 79 (ITT; *n* = 129)	NR	6.0	NR	NR
As above	–	–	–	–	–	–	–	–	–	48 weeks	< 50	93 (OT; *n* = 164), 69 (ITT; *n* = 129)	NR	6.0	NR	NR
Bussman et al.[32] (2008)	Botswana (Gaborone)	Public	No	Started Jan.–Aug. 2002	1	633	Cohort	35; 40; 67, 43% III and 38% IV	NNRTI	12 months	< 400	91 (OT; *n* = 467), 67 (ITT; *n* = 633)	17.3	8.9	NR	NR
Kouanfack et al.[43] (2009)	Cameroon (Yaoundé)	Public	Partially	Enrolment Nov. 2006–Oct. 2007	1	249	Cross section	NR (all 35–40 years); 29; NR; NR	99% NNRTI	12 months	< 500	78 (OT; *n* = 249)	NA	NA	NA	NA
As above	–	–	–	–	–	–	–	–	–	12 months	< 1000	84 (OT; *n* = 249)	NA	NA	NA	NA
Djomand et al.[35] (2003)	Côte d'Ivoire (Abidjan)	Public, partners	Partially	Started Aug. 1998–May 2000	6	276	Cohort	35; 50; 182; NR	80% PI, 19% NNRTI	12 months	< 200	50 (ITT; *n* = 276)	NR	NR	NR	NR
Sarna et al.[56] (2008)	Kenya (Mombasa)	Public (2 sites), private	No	Started Sept. 2003–Nov. 2004	3	137	RCT	37; 36; 96–106; NR	NNRTI	12 months	< 400	82 (OT; *n* = 137)	NR	NR	NR	NR
Landman et al.[44] (2009)	Senegal (Dakar)	Public, partner	No	Started Jun.–Dec. 2004	1	40	Clinical trial	38 (mean); 40; 111; NR (93% CDC category B/C)	NNRTI	12 months	< 400	94 (OT; *n* = 35), 83 (ITT; *n* = 40)	7.5	5	NR[f]	NR[f]
As above	–	–	–	–	–	–	–	–	–	12 months	< 50	83 (OT; *n* = 35), 73 (ITT; *n* = 40)	7.5	5	NR[f]	NR[f]
Barth et al.[27] (2008)	South Africa (Ndlovu)	NGO	No	Started Sept. 2003–Apr. 2006	1	609	Cohort	35; 29; 67, 62% III and 17% IV	NNRTI	12 months	< 400	83 (OT; *n* = 407), 55 (ITT; *n* = 609)	19	15	NR	NR

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Study	Country/ site	Type of care	Patient paid for ART?	Dates observed	No. of sites	*n*[a]	Study design	Baseline features[b]	ART regimen[c]	Time on ART[d]	Viral suppression		Percentage of patients			
											Definition (HIV RNA copies/ml)	Percentage meeting definition and type of analysis	Died	LTFU	Stopped ART	TFO
As above	–	–	–	–	–	–	–	–	–	–	< 50	70 (OT; *n* = 407), 46 (ITT; *n* = 609)	19	15	NR	NR
Orrell et al.[23] (2003)	South Africa (Cape Town)	Public	No	Started Jan. 1996–May 2001	> 1	289	Clinical trial	33 (mean); 57; 197–268 (mean); < 49% III/IV	42% PI, 33% NNRT, 10% 3NRTI	12 months	< 400	66 (OT; *n* = 242), 58 (ITT; *n* = 278)	See LTFU	16.2 (or died or stopped)	See LTFU	NR
Bedelu et al.[28] (2007)	South Africa (Lusikisiki)	Public, NGO	No	Started Jan. 2005, followed to Jul. 2006	1	430	Cohort	NR	NR	12 months (median)	< 400	78 (OT; *n* = 41)	13.5	19.3	NR	NR
As above	–	Public, NGO	No	Started Jan. 2005, followed to Jul. 2006	12	595	Cohort	NR	NR	12 months (median)	< 400	90 (OT; *n* = 296)	16.8	2.2	NR	NR
Nachega et al.[51] (2010)	South Africa (Western Cape)	Public	No	Feb 2005–Jul 2008	1	274	RCT	36; 42; 98; 45% III and 46% IV	NNRTI	13 months	< 400	90 (OT; *n* = 213), 71 (ITT; *n* = 272)	NR	NR	NR	NR
Ramadhani et al.[55] (2007)	United Republic of Tanzania (Kilimanjaro)	Public	Partially	Jun.–Aug. 2008	1	150	Cross section	41; 37; 114; NR	NNRTI	12 months (median)	< 400	68 (OT; *n* = 150)	NA	NA	NA	NA
As above	–	–	–	–	–	–	–	–	–	12 months (median)	< 1000	77 (OT; *n* = 150)	NA	NA	NA	NA
Kamya et al.[42] (2007)	Uganda (Makerere, Ulago)	Public	No	Started Apr. 2004–Jun. 2005	1	526	Cohort	37 (mean); 31; 99; 54% III and 34% IV	NNRTI	12 months	< 400	87 (OT; *n* = 454), 75 (ITT; *n* = 526)	12.5	NR	NR	NR
Charles et al.[34] (2008)	Haiti	NGO	No	Started Mar. 2003–Dec. 2005	1	146	Cohort	NR; 34; 129; 40% II/III and 49% IV	78% NNRTI	12 months	< 50	49 (OT; *n* = 79)	NR	NR	NR	NR
Blacher et al.[30] (2010)	Kenya, Zambia	Public	No	Started May 2005–Jan. 2007	3	661	Clinical trial	32; 100; NR; 49% III and 8% IV	NNRTI, 59% naive	12 months	< 400	87 (OT; *n* = 563), 74 (ITT; *n* = 661)	NR	NR	NR	NR
Fatti et al.[36] (2010)	South Africa (Cape, KZN, Mpumalanga)	Public, NGO	No	Started Dec. 2004–Dec. 2007	59	29 203	Cohort	34; 32; 114; 76% III/IV	NNRTI	12 months	< 400	87 (OT; *n* = 6725)	6.3	NR	NR	NR
Hegazi et al.[41] (2010)	Gambia	Public	No	Started Oct. 2005–Jan. 2007	1	147	Cohort	36; 39; NR; NR	75% NNRTI, 25% PI	12 months	< 100	79 (OT; *n* = 75)	NR	NR	NR	NR
Lester et al.[46] (2010)	Kenya (Nairobi, Kajiado)	Public	No	Started May 2007–Oct. 2008	3	538	RCT	37; 35; 161–168; 38% III and 4% IV	NNRTI	12 months	< 400	71 (OT; *n* = 402), 53 (ITT; *n* = 533)	10.2	8.2	NR	0.9

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Study	Country/ site	Type of care	Patient paid for ART?	Dates observed	No. of sites	*n*[a]	Study design	Baseline features[b]	ART regimen[c]	Time on ART[d]	Viral suppression		Percentage of patients			
											Definition (HIV RNA copies/ml)	Percentage meeting definition and type of analysis	Died	LTFU	Stopped ART	TFO
Lyagoba et al.[47] (2010)	Uganda (Kampala, Entebbe)	Public (trial)	No	Started Jan.–Oct. 2004	2	300	RCT	NR; NR; 108; 51% III and 25% IV	3NRTI	12 months	< 200	71 (OT; *n* = 272), 64 (ITT; *n* = 300)	6.3	NR	NR	NR
As above	–	–	–	–	–	–	–	–	–	–	< 1000	77 (OT; *n* = 272), 69 (ITT; *n* = 300)	6.3	NR	NR	NR
Moore et al.[48] (2010)	Malawi (Blantyre)	Public	No	Started 2005	1	300	Cohort	36 (mean); 39; 157 (mean); 29% IV	NNRTI	12 months	< 400	83 (OT; *n* = 212), 62 (ITT; *n* = 284)	14.3	2.7	5.3	5.3
Mutevedzi et al.[50] (2010)	South Africa (KZN)	Public	No	Started Oct. 2004–Sept. 2007	16	3010	Cohort	34–37; 22; 91–128; NR	NNRTI	12 months	< 25	77 (OT; *n* = 758)	10.9	3.7	NR	1.4
Oyomopito et al.[54] (2010)	Asia (TAHOD)	Mixed	NR	Started after 2000	17	784	Cohort	NR; 75; NR; NR	69% NNRTI, 29% PI, 2% 3NRTI	12 months	< 400	79 (OT; *n* = 204)	NR	NR	NR	NR

3NRTI, triple nucleoside reverse transcriptase inhibitors; ART, antiretroviral therapy; CDC, Centers for Disease Control and Prevention; HIV RNA, human immunodeficiency virus ribonucleic acid; ITT, intention-to-treat; KZN, KwaZulu Natal; LTFU, lost to follow-up; NA, not applicable; NGO, nongovernmental organization; NNRTI, non-nucleoside reverse transcriptase inhibitors; NR, not reported; OT, on-treatment; PI, protease inhibitors; RCT, randomized clinical trial; TAHOD, TREAT Asia HIV Observational Database; TFO, transferred out; WHO, World Health Organization.

[a] Number of patients initiating ART.

[b] The values in this column are median age; percentage of males; median CD4+ T-lymphocyte count (cells per ml); and WHO (or, when indicated, CDC) clinical stage.

[c] All patients were ART-naive at baseline unless indicated otherwise.

[d] When outcomes were recorded.

[e] Estimated from a graph in the published article.

[f] Assumed to be 0%, as other outcomes account for all of the individuals who initiated ART.

Table 2. **Study cohorts included in the systematic review and described in conference abstracts dealing with viral suppression after 12 months of antiretroviral therapy in low- and middle-income countries**

Authors and (conference)	Country/ site	Type of care	Patients paid for ART?	Dates observed	No. of sites	No. of patients[a]	Study design	Baseline features[b]	ART regimen[c]	Time on ART[d]	Virological suppression		Percentage of patients			
											Definition (HIV RNA copies/ml)	Percentage meeting definition and type of analysis	Died	LTFU	Stopped ART	TFO
Chasombat et al.[62] (IAS 2010)	Thailand (4 provinces)	Public	No	Started Feb.–Sept. 2006	6	304	Cohort	38; 54; 56; NR	NNRTI	12 months	< 1000	94.1 (OT; *n* = 269), 83.2 (ITT; *n* = 304)	8.9	NR	NR	NR
Crabtree-Ramírez et al.[63] (IAS 2010)	Mexico	Public	No	2001–2007	1	348	Cohort	33; 72; NR; NR	HAART	12 months	< 50	93.3 (OT; *n* = 348)	NR	NR	NR	NR
Scarsi et al.[68] (IAS 2010)	Nigeria (PEPFAR programmes)	NR	No	Jan. 2006–Dec. 2007	NR	5894	Cohort	34.2; 24.8; NR; NR	NNRTI	24 and 48 weeks	< 1000 (at both 24 and 48 weeks)	89.9 (OT; *n* = 2366)	19.6 (or TFO or LTFU)	See "died"	NR	See "died"
Stafford et al.[69] (IAS 2010)	4 African countries	Public	No	NR	NR	737	Cross-section	NR	NNRTI	9–15 months	< 400	88.1 (OT; *n* = 737)	NR	NR	NR	NR
Chang et al.[61] (IAS 2010)	Uganda (Rakai)	NR	No	May 2006–Jun. 2008	15	1338	RCT	NR	NR	48 weeks	< 400	89.4 (OT; *n* = 606)	NR	NR	NR	NR
Calmy et al.[60] (IAS 2010)	ARTLINC	Mixed	No	NR	NR	3020	Cohort	34; 37; 91; NR	NNRTI	12 months	< 500	89 (OT; *n* = 3020)	NR	NR	NR	NR
Messou et al.[65] (CROI 2010)	Côte d'Ivoire	NR	No	Feb. 2006–May 2007	3	1545	Cohort	NR	NNRTI	12 months	< 300	75.0 (OT; *n* = 928)	39.1	NR	NR	NR
Ratsela et al.[66] (CROI 2009)	South Africa (military)	NR	No	2004–2008	6	1771	RCT	NR; NR; 106; NR	PI or NNRTI	12 months	< 400	66 (ITT; *n* = 1771)	NR	NR	NR	NR
Lockman et al.[64] (CROI 2009)	Botswana	NR	No	NR	1	178	RCT	NR; 0; NR; NR	NNRTI	12 months	< 400	92.1 (ITT; *n* = 178)	NR	NR	NR	NR
Bertagnolio et al.[59] (CROI 2011)	Africa (multiple countries)	Public	NR	2002–2010	6	829	Cohort	NR	NR	12 months	< 1000	90 (OT; *n* = 460)	9.2	12.9	0.8	14.5
Reynolds et al.[67] (CROI 2011)	Uganda (Kampala)	NR	NR	2004–2008	1	559	Cohort	NR; NR; 86–96; NR	NR	12 months	< 400	88 (OT; *n* = 441) 69 (ITT; *n* = 559)	NR	NR	NR	NR

ART, antiretroviral therapy; ARTLINC, Antiretroviral Therapy in Lower Income Countries Collaboration; CROI, Conference on Retroviruses and Opportunistic Infections; HAART, highly-active antiretroviral therapy; HIV-RNA, human immunodeficiency virus ribonucleic acid; IAS, International AIDS Society; ITT, intention-to-treat; LTFU, lost to follow-up; NNRTI, non-nucleoside reverse transcriptase inhibitors; NR, not reported; OT, on-treatment; PEPFAR, United States President's Emergency Plan for AIDS Relief; RCT, randomized clinical trial; TFO, transferred out; WHO, World Health Organization.

[a] Number of patients initiating ART.

[b] The values in this column are median age; percentage of males; median CD4+ T-lymphocyte count (cells per ml); and WHO (or, when indicated, CDC) clinical stage.

[c] All patients were ART-naive at baseline unless indicated otherwise.

[d] When outcomes were recorded.