Implications of adopting new WHO guidelines for antiretroviral therapy initiation in Ethiopia

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Objective To assess the implications of implementing the World Health Organization (WHO) 2010 guidelines for antiretroviral therapy (ART) initiation in adults and adolescents with human immunodeficiency virus (HIV) infection, which recommend initiating ART at a CD4+ T lymphocyte (CD4+) threshold of \leq 350 cells/mm³ instead of \leq 200 cells/mm³, which was the earlier threshold.

Methods Between April and May 2010, CD4+ test results were collected for all HIV-infected patients recorded in the pre-ART and ART registers of 19 high-patient-load health centres in Addis Ababa, Ethiopia, and the regions of Amhara, Oromia, SNNPR (Southern Nations, Nationalities and People's Region) and Tigray. At 12 centres patient records were independently reviewed to assess data accuracy. To estimate the total number of patients who would need ART at health centres if Ethiopia adopted the new WHO guidelines, the number of patients needing ART based on current guidelines were added to the number of asymptomatic patients enrolled in pre-ART with a CD4+ count > 200 but \leq 350 cells/mm³

Findings Adoption of the new WHO guidelines would increase the total number of patients on ART in the 19 health centres in Ethiopia by about 30%: from 3583 to 4640.

Conclusion The shift in the CD4+ threshold for ART initiation will substantially increase the demand for ART in Ethiopia. Since under the current systems only 60% of Ethiopia's patients in need of ART are receiving the medications, scaling up ART programmes to accommodate the increased demand for drugs will not be possible unless government funding and support increase concurrently.

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

Introduction

In 2010, the World Health Organization (WHO) issued new guidelines for the initiation of antiretroviral therapy (ART) in adults and adolescents with human immunodeficiency virus (HIV) infection. The guidelines cover a range of issues associated with ART, including initiation of the regimen at an earlier stage of infection, updated first- and second-line drug regimens and improved criteria for switching antiretrovirals.1 This paper focuses on the CD4+ T-lymphocyte (CD4+) count used as the clinical threshold for initiating ART, which has been shifted to ≤350 cells/mm3 from the former standard, \leq 200 cells /mm³.

Studies and modelling exercises suggest that HIV-related mortality could be reduced by 20% between 2010 and 2015 by raising the CD4+ cell threshold required for initiating ART. Another possible benefit would be reduced HIV transmission between couples and from mother to child. An increase in the CD4+ threshold and hence in the demand for treatment entails certain risks, however: a rise in treatment costs as high as 57%; the displacement of patients in urgent need of ART; longer exposure to ART, resulting in unknown side-effects and in the development of resistance mechanisms. WHO has declared that in making these revisions, a high value, over and above cost and feasibility, was placed on avoiding death, disease progression and HIV transmission. However, implementing these guidelines is not always possible in the countries where ART is most needed.

Some studies on the feasibility of implementing WHO guidelines in resource-constrained settings have been conducted, and many of them have shown that in such settings health system constraints make it difficult to roll out the new WHO guidelines.^{2,3} According to one model-based analysis that projected clinical and economic outcomes in a South African HIV-infected cohort, initiation of ART in patients with a CD4+ count of \leq 350 cells/mm³ provides the greatest short- and long-term survival advantage and is also highly cost-effective.² Other studies that have explored how health system constraints impeded the roll-out of the 2006 WHO guidelines count among the barriers ART stock-outs, lack of capability for performing CD4+ counts and human resource shortages. The same factors are obviously applicable to the new 2010 guidelines.4,5

If countries are to adopt the new WHO guidelines, the health system will have to be equipped to conduct more HIV tests and CD4+ counts and health-care services will have to become capable of absorbing higher patient case-loads. A study using Cameroon, Kenya, Viet Nam and Zambia as examples demonstrated that the change in the CD4+ threshold for initiating ART would increase the number of patients requiring ART not only in the immediate future, but also in the long term.4

Context in Ethiopia

While the overall prevalence of HIV infection in Ethiopia, which is currently 2.1%, remains relatively low, the country is home to an estimated 1.1 million HIV-positive people.^{6,7} Ethiopia's epidemic of HIV infection is marked by pockets of high prevalence in urban areas and among women. In 2009, the prevalence of HIV infection was 7.7% in urban areas (versus 0.9% in rural areas) and 2.8% among females (versus 1.8% among males).8 Less than one third of Ethiopia's HIV-positive patients are currently enrolled in comprehensive care and support services. Of those among them who need ART, only 62%

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are receiving it, despite unprecedented government efforts in the past four years to rapidly scale up comprehensive care for patients with HIV infection and acquired immunodeficiency syndrome (AIDS) throughout the country.9

In response to the HIV/AIDS epidemic, the Government of Ethiopia made drastic policy shifts that set a precedent in sub-Saharan Africa. Comprehensive HIV/AIDS services, including ART, were made widely available free of charge to the country's population of nearly 80 million people. To ensure the availability of these services, the government decentralized HIV patient care, which it transferred from physicians in hospitals to mid-level healthcare workers in health centres. Nurses and health officers in health centres are also supported by the work of community health workers administering community-based and home-based care.

Unlike its neighbouring countries, Ethiopia has a good supply of ART drugs. The unmet need for ART in Ethiopia is caused not by a shortage of drugs, but by health system constraints. Many health centres do not have the equipment for conducting CD4+ counts and yet lack a vehicle for transporting samples quickly and safely to the nearest hospital having the required machine. Furthermore, hospitals are putting caps on the number of health centre samples processed. The health system also lacks mechanisms for tracking pre-ART patients. Plans are under way to introduce pre-ART registers and develop a routine appointment system to prevent losses to follow-up among these patients. Because of all these constraints, in Ethiopia some HIV-positive patients are started on ART on the basis of clinical staging without performing a CD4+ count, as a result of which some patients begin treatment when the count is already \leq 200 cells/mm³.

If Ethiopia adopts the new WHO guidelines, ART will have to be initiated not solely on the basis of patients' clinical staging, but early on in the course of HIV infection. To meet the new guidelines, Ethiopia will have to address current system constraints as well as ensure the availability of enough financial resources to provide ART for the influx of newly-eligible patients. To assess the implications of adopting the new guidelines, the Government of Ethiopia asked the HIV/AIDS Care and Support Program (HCSP), funded

by the United States Agency for International Development, to conduct a study that would provide an estimate of the increase in patient case-load that this policy change would bring about.

Methods

CD4+ cell test results recorded on pre-ART and ART registers were collected from all pre-ART and ART patients at 19 high-patient-load health centres in Addis Ababa, capital of Ethiopia, and the regions of Amhara, Oromia, SNNPR (Southern Nations, Nationalities and People's Region) and Tigray between April and May 2010. The 19 health centres are part of a network of 350 ART health centres supported by the HCSP, Ethiopia's main partner in decentralizing HIV/AIDS treatment to primary-health-care facilities. These 19 health centres offer a large representative sample of patients on ART in health centres in Ethiopia; they probably cover as many as 50% of all such patients.

At the 12 most accessible centres, patient records were independently reviewed after one month to assess data accuracy. Patients included adults as well as children aged 6 years or older. The Ethiopian national ART guidelines recommend testing children aged 6 years and older and prescribing ART according to the same criteria as for adults. To estimate the total number of patients who would need ART at health centres if Ethiopia adopted the new WHO guidelines, the number of patients needing ART based on current guidelines (CD4+ count ≤ 200 cells/mm³ and symptomatic, stages III or IV) were added to the number of asymptomatic patients enrolled in pre-ART with a CD4+ count > 200 but \leq 350 cells/mm³. In Ethiopia, CD4+ counts are performed with a fluorescence-activated cell sorter.

Results

A total of 9824 HIV-positive patients (male: 3283; female: 6533; sex unknown: 8) were enrolled in care and support in the 19 study health centres at the time of data collection. Among them were 5066 pre-ART patients (male: 1613; female: 3446; sex unknown: 7). The remaining 4758 patients (48.4%) were on ART (male: 1670; female: 3087; sex unknown: 1). The age of the patients was 31.7 years on average and ranged from 6 to 88 years. CD4+ test results were

recorded for 79.6% of patients who had ever enrolled in pre-ART and for 79.0% of all patients receiving ART.

Of the patients for whom CD4+ data were available, 3583 met the current national guidelines for ART initiation (Table 1). Under the new WHO guidelines, the number of patients who would need ART would also include the 1057 asymptomatic patients with a CD4+ $count > 200 \text{ but} \le 350 \text{ cells/mm}^3$. All else being equal, adoption of the new guidelines would increase the total number of ART patients at the 19 study health centres from 3583 to 4640, and 23% of the patients with HIV (infection) not currently receiving ART would have to start receiving it. This would correspond to a 30% increase in the total load of patients on ART.

A subset of patient records at the 12 most accessible health centres were independently verified one month after data collection. At four such health centres, 298 records were verified for staging. Of these, 8 (2.7%) records showed data errors. Data on patients with a CD4+ count of < 50 cells/mm³ were verified for all patients at eight health centres and for a random sample of 58 of 247 patients (24%) at the other four health centres. Of these patient records, 4.6% contained patient CD4+ counts that differed by more than 5% from the reported counts. If, for instance, the reported CD4+ count was 300 cells/ mm3 and the recorded count was 400 cells/mm³, the difference between the two was 25%, a value above the 5% difference considered acceptable. Data on CD4+ counts ranging from 50 to 900 cells/mm3 were verified for 88 of 425 (21%) patients at one health centre; 2.3% of these records were found to contain CD4+ counts that deviated by more than 5% from the original data. Lastly, CD4+ counts > 900 cells/mm³ were verified for all patients at eight health centres and for 21 of 24 patients (88%) at the four additional health centres. The proportion of records showing a difference in CD4+ data of more than 5% was 3.1%. Overall, 5.3% of patient records were verified for data accuracy and 3.8% of these records deviated by more than 5% from the data collected originally.

Discussion

Following its new recommendations for ART initiation, WHO supported a study in Malawi to assess the feasibility

Current guidelines New WHO guidelines No. of pre-ART patients No. of patients on ART No. of patients Percentage of pa-Per cent increase eligible for ART tients not eligible in total no. of pawith a CD4+ count with a CD4+ count with a CD4+ count \leq 200 under new WHO for ART under previtients on ART > 200 but ≤ 350 cells/ > 350 cells/mm 3 , cells/mm³, symptomatic guidelines ous guidelines [(D-C)/C]asymptomatic (stages III, IV) mm3, asymptomatic [A+C=D][A/D] [A] [B] [C] 1057 1445 3583 4640 23 30

Table 1. CD4+ T-lymphocyte (CD4+) profile of patients with human immunodeficiency virus (HIV) before starting antiretroviral therapy (pre ART) or while on ART, 19 health centres, Ethiopia, May 2010

WHO, World Health Organization.

of adopting the new guidelines. The results of this rapid assessment in Malawi indicate that if the country adopts the new guidelines calling for ART initiation at a higher CD4+ count, it will have to rely on clinical staging primarily, since most ART facilities in Malawi do not have access to CD4+ counters. Data from several sites in Malawi suggest that patient case-loads could increase by as much as 40%, and this would result in waiting lists at ART sites. In its final recommendation, the report reiterated that without large injections of resources, guideline implementation could have crippling effects on the health system.¹⁰ Despite this, Malawi has moved to adopt the new guidelines and is aggressively working to address various challenges involving finances, infrastructure, supply-chain management and health worker shortage.

Ethiopia is rapidly expanding comprehensive HIV services to health centres. This relieves hospitals of a large patient load and makes services available to many more HIV-positive people in the country. Despite the current national guidelines on ART initiation, a substantial number of patients with HIV infection who need ART are not accessing it yet. Our study has shown, based on the number currently enrolled in ART, that by adopting the new WHO guidelines,

the load of patients needing ART would be 30% higher than at present, although the treatment coverage of such patients would not increase accordingly. If the distributions of CD4+ counts found at health centres resemble those seen among the many HIV-positive patients who need ART but are not receiving it, this percentage remains valid, even if the current unmet need for ART is met.

Within health centres, our data verification showed that the study result is a valid and realistic estimate of the additional ART patient case-load that Ethiopia's health centres may anticipate after the new WHO guidelines for ART initiation are implemented.

Implications

A 30% increase in ART patient case-load has important financial and logistical implications for Ethiopia. The average cost of treating a patient with a first-line antiretroviral drug is currently estimated at 190 United States dollars (US\$) per year. 11 If Ethiopia adopts the new WHO guidelines for ART initiation, it will need around US\$ 127 million per year, as opposed to the annual sum of US\$ 97.6 million it needs at present. Furthermore, the feasibility of adopting the new WHO guidelines in Ethiopia will have to be weighed against the limited absorptive

capacity of Ethiopia's health-care system and service providers.

This shift in the CD4+ threshold for ART initiation will only increase the demand for ART. With the systems currently in place, only 60% of eligible patients are receiving ART. Without concurrent increases in funding and governmental support, it will not be possible to scale up ART programmes to accommodate the increased patient demand in Ethiopia. These increased costs are not currently affordable for the Ethiopian Government, which has decided to continue to observe the 2006 ART guidelines. While the 2010 revision is sound in principle and value, resources in Ethiopia are not enough to absorb the ensuing increased demand for existing services.

Other resource-poor countries that have elected to implement the new WHO guidelines may face similar challenges and could benefit from an effort to estimate how much the change in policy would increase the load of patients needing ART. The results may prove useful for resource analysis and planning and for determining the feasibility of adopting the new WHO guidelines on ART initiation and the country's readiness to do so. ■

الآثار المترتبة على اعتهاد المبادئ التوجيهية الجديدة لمنظمة الصحة العالمية لبدء العلاج بمضادات الفيروسات القهقرية في

 ≤ 200 خلية لكل ميليمتر مكعب، والتي كانت العتبة السابقة. الطريقة في الفترة من نيسان/ إبريل إلى أيار/ مايو 2010، تم جمع الطريقة في الفترة من نيسان/ إبريل إلى أيار/ مايو 2010، تم جمع نتائج اختبارات خلايا +CD4 الخاصة بجميع المرضى المصابين بعدوى فيروس العوز المناعي البشري المسجلة في سجلات ما قبل العلاج بمضادات الفيروسات القهقرية وسجلات العلاج بمضادات الفيروسات القهقرية الخاصة بتسعة عشر مركزاً صحياً

عني... الغرض تقييم الآثار المترتبة على تنفيذ المبادئ التوجيهية لمنظمة الصحة العالمية لعام 2010 لبدء العلاج بمضادات الفيروسات القهقرية (ART) لدى البالغين والمراهقين المصابين بعدوى فيروس العوز المناعى البشري (HIV)، التي توصى ببدء العلاج يوو عن ... بمضادات الفيروسات القهقرية عند بلوغ عتبة الخلايا اللمفاوية التائية +CD4 معدل ≤ 350 خلية لكل ميليمتر مكعب بدلاً من

النتائج سيؤدي اعتهاد المبادئ التوجيهية الجديدة لمنظمة الصحة العالمية إلى ويادة العدد الإجمالي للمرضى الخاضعين للعلاج يمضادات الفيروسات القهقرية في المراكز الصحية في إثيوبيا البالغ عددها 19 مركزاً بنسبة 30 ٪ تقريباً: من 3583 مريضاً إلى 4640

الاستنتاج سيؤدي التغير في عتبة خلايا +CD4 لبدء العلاج بمضادات الفيروسات القهقرية إلى زيادة الطلب على العلاج بمضادات الفتروسات القهقرية في إثيوبيا بشكل كبير. ونظراً لحصول 60 ٪ فقط من المرضى الإثيوبيين المحتاجين للعلاج بمضادات الفيروسات القهقرية على الأدوية في ظل النظم الحالية، فلن يتسنى تعزيز برامج العلاج بمضادات الفيروسات القهقرية عمل يستعي - ريز . ريخ الله على الأدوية ما لم تكن ثمة زيادة في التمويل والدعم الحكوميين في آن واحد.

من المراكز كثيفة المرضى في أديس أبابا بإثيوبيا وأقاليم أمهرة وأُوروميا وSNNPR (إقليم قوميات وشعوب وأجناس الجنوب) وتيغراي. وفي 12 مركزاً، تم استعراض سجلات المرضى بشكل مستقل بغية تقييم دقة البيانات. ولتقدير العدد الإجمالي للمرضى الذين سيحتاجون إلى العلاج بمضادات الفيروسات القهقرية في المراكز الصحية في حالة اعتباد إثيوبيا للمبادئ التوجيهية الجديدة لمنظّمة الصحة العالمية، تم إضافة عدد المرضى المحتاجين إلى العلاج بمضادات الفروسات القهقرية استناداً إلى المبادئ التوجيهية الحالية إلى عدد المرضى الذين لا تظهر عليهم أعراض المرض المسجلين في سجلات ما قبل العلاج بمضادات الفيروسات القهقرية الذين يزيد لديهم عدد خلايا +CD4 على 200 خلية لكل ميليمتر مكعب ولكنه ≤ 350 خلية لكل ميليمتر مكعب.

摘要

在埃塞俄比亚采用新的世界卫生组织启动抗逆转录病毒疗法的指导方针的影响

目的 评估在感染艾滋病病毒 (HIV) 的成年人和青少年 当中实施世界卫生组织 (WHO) 启动抗逆转录病毒疗法 (ART) 2010 指导方针的影响,新指导方针建议在 CD4+ T淋巴球 (CD4+) 阈值 ≤ 350 个/mm³ 时启动 ART 治疗, 而不是早先的≤ 200 个/ mm³ 的阈值。

方法 在 2010 年 4 月和 5 月间, 收集埃塞俄比亚亚的斯 亚贝巴以及阿姆哈拉、奥罗莫州、SNNPR(南方各族州) 和提格雷等地区的 19 个高病人负担卫生中心的预 ART 和 ART 登记中记录的所有 HIV 感染患者的 CD4+ 检测结果。 在12个中心,病例经过独立评审以评估数据准确性。为 了估计在埃塞俄比亚采用新 WHO 指导方针情况下需要在

卫生中心接受 ART 治疗的病人数量,将基于当前指导方针 需要ART治疗的病人数量与其CD4+数>200但≤350个/ mm³ 并在预 ART 中登记的无症状病人数量相加。

结果 采用新的 WHO 指导方针会使埃塞俄比亚 19 个卫生 中心 ART 治疗病人的总数增加约 30%: 从 3583 人增加 至 4640 人。

结论 启动 ART 的 CD4+ 阈值的改变将大量增加埃塞俄比 亚对 ART 的需求。因为在目前的系统中,埃塞俄比亚需 要 ART 治疗的患者仅有 60% 正在接受药物治疗, 所以政 府需要投入资金,同时增加支持,才有可能扩大 ART 规 划, 适应不断增加的药物需求。

Résumé

Implications de l'adoption de nouvelles directives de l'OMS pour le lancement du traitement antirétroviral en Éthiopie

Objectif Évaluer les implications de la mise en œuvre des directives 2010 de l'Organisation mondiale de la Santé (OMS) relatives au lancement du traitement antirétroviral (TAR) chez les adultes et adolescents infectés par le virus d'immunodéficience humaine (VIH), qui recommandent de débuter le TAR à un seuil de lymphocytes T CD4+ (CD4+) \leq à 350 cellules/mm³ au lieu de \leq 200 cellules/mm³, qui était l'ancien seuil.

Méthodes Entre avril et mai 2010, les résultats de tests de CD4+ ont été recueillis chez tous les patients infectés par le VIH, enregistrés dans les registres pré-ART et ART de 19 centres de santé comptant un grand nombre de patients, à Addis-Abeba, en Éthiopie, et dans les régions d'Amhara, d'Oromia, la SNNPR (Région des nations, nationalités et peuples du Sud) et le Tigray. Dans 12 centres, les dossiers des patients ont été examinés de manière indépendante afin d'évaluer l'exactitude des données. Pour estimer le nombre total de patients nécessitant un TAR dans les centres de santé si l'Éthiopie adoptait les nouvelles directives de l'OMS, le nombre de patients nécessitant un TAR sur la base des directives actuelles a été ajouté au nombre de patients asymptomatiques inscrits dans le pré-TAR avec un nombre des CD4+ > 200 cellules/mm³, mais \leq 350 cellules/mm³.

Résultats L'adoption des nouvelles directives de l'OMS augmenterait d'environ 30% le nombre total de patients sous TAR dans les 19 centres de santé en Éthiopie, le faisant passer de de 3 583 à 4 640.

Conclusion Le changement du seuil de CD4+ au lancement du TAR augmentera considérablement la demande de TAR en Éthiopie. Étant donné que seuls 60% des patients éthiopiens nécessitant un TAR reçoivent leurs médicaments, dans le cadre des systèmes actuels, la mise à niveau des programmes de TAR pour répondre à la demande accrue de médicaments ne sera pas possible, à moins d'un financement gouvernemental et d'un accroissement simultané de l'aide.

Резюме

Последствия принятия новых рекомендаций ВОЗ по проведению антиретровирусной терапии в

Цель Оценить последствия внедрения рекомендаций Всемирной организации здравоохранения (ВОЗ) по проведению антиретровирусной терапии (АРТ) у взрослых и подростков с вирусом иммунодефицита человека (ВИЧ) (2010 г.), согласно которым рекомендуется проведение АРТ при пороговой величине числа CD4+ Т-лимфоцитов ≤ 350 клеток/куб. мм. вместо ≤ 200 клеток/куб. мм., являвшейся предыдущей пороговой величиной.

Методы В апреле и мае 2010 года был проведен сбор результатов теста на CD4+ у всех ВИЧ-инфицированных пациентов,

зарегистрированных в реестрах предварительной АРТ и АРТ терапии 19 медицинских центров с высоким уровнем поступления больных в Аддис-Абебе, Эфиопии, и районах Амхара, Оромия, Регионе южных наций, народностей и народов (SNNPR) и Тигрее. В 12 центрах истории болезни подверглись независимому изучению для оценки точности данных. Для оценки общего числа пациентов, которым бы потребовалась АРТ в медицинских центрах, если бы в Эфиопии приняли новые рекомендации ВОЗ, число пациентов, нуждающихся в АРТ, исходя из текущих рекомендаций, присоединялось к числу пациентов без выраженных клинических проявлений, зачисленных на предварительную APT с числом CD4+ > 200, но ≤ 350 клеток/ куб. мм.

Результаты Принятие новых рекомендаций ВОЗ увеличило бы общее число пациентов, зачисленных на АРТ в 19 медицинских центрах в Эфиопии, приблизительно на 30%: с 3583 до

Вывод Изменение пороговой величины СD4+ для проведения АРТ значительно увеличит потребность в АРТ в Эфиопии. При настоящей системе медицинского обслуживания только 60% пациентов в Эфиопии, нуждающихся в АРТ, получают медикаменты. Увеличение программ по АРТ для покрытия повышенной потребности в медикаментах будет невозможным, если параллельно не будет увеличиваться бюджетное финансирование и поддержка.

Resumen

Consecuencias de la adopción de las nuevas directrices de la OMS para el inicio de la terapia antirretroviral en Etiopía

Objetivo Evaluar las consecuencias de la implementación de las directrices de la Organización Mundial de la Salud (OMS) de 2010 para el inicio de la terapia antirretroviral (TAR) en adultos y adolescentes infectados por el virus de la inmunodeficiencia humana (VIH), que recomiendan comenzar la TAR con un umbral de linfocitos CD4+ T (CS4+) igual o superior a 350 células/mm³ en lugar del umbral igual o superior a 200 células/mm³ empleado anteriormente.

Métodos Entre abril y mayo de 2010, se recopilaron los resultados de las pruebas de CD4+ de todos los pacientes infectados por el VIH registrados en los archivos pre-TAR y TAR de 19 centros de salud con un volumen alto de pacientes en Addis Abeba, Etiopía y las regiones de Amara, Oromía, SNNPR (Naciones, Nacionalidades y Pueblos del Sur) y Tigray. En 12 centros, se examinaron de manera independiente los archivos de los pacientes para evaluar la exactitud de los datos. Para calcular el número total de pacientes que necesitarían una TAR en los centros de salud si Etiopía adoptara las nuevas directrices de la OMS, se sumó el número de pacientes que necesitan una TAR en base a las directrices actuales al número de pacientes asintomáticos inscritos en la pre-TAR con un recuento de CD4+ superior a 200 pero igual o inferior a 350 células/mm³.

Resultados La adopción de las nuevas directrices de la OMS aumentaría el número total de pacientes en TAR en los 19 centros de salud de Etiopía en torno a un 30%: de 3583 a 4640.

Conclusión El cambio en el umbral de CD4+ para comenzar la TAR aumentará de manera considerable la demanda de TAR en Etiopía. Dado que con los sistemas actuales sólo el 60% de los pacientes en Etiopía que necesitan una TAR recibe la medicación, el aumento de los programas de TAR para satisfacer la demanda mayor de medicamentos no será posible a menos que también aumenten el apoyo y la financiación gubernamental al mismo tiempo.

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