

Malawi's contribution to "3 by 5": achievements and challenges

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Problem Many resource-poor countries have started scaling up antiretroviral therapy (ART). While reports from individual clinics point to successful implementation, there is limited information about progress in government institutions at a national level.

Approach Malawi started national ART scale-up in 2004 using a structured approach. There is a focus on one generic, fixed-dose combination treatment with stavudine, lamivudine and nevirapine. Treatment is delivered free of charge to eligible patients with HIV and there is a standardized system for recruiting patients, monthly follow-up, registration, monitoring and reporting of cases and outcomes. All treatment sites receive quarterly supervision and evaluation.

Local setting In January 2004, there were nine public sector facilities delivering ART to an estimated 4 000 patients. By December 2005, there were 60 public sector facilities providing free ART to 37 840 patients using national standardized systems. Analysis of quarterly cohort treatment outcomes at 12 months showed 80% of patients were alive, 10% dead, 9% lost to follow-up and 1% had stopped treatment.

Lessons learned Achievements were the result of clear national ART guidelines, implementing partners working together, an intensive training schedule focused on clinical officers and nurses, a structured system of accrediting facilities for ART delivery, quarterly supervision and monitoring, and no stock-outs of antiretroviral drugs. The main challenges are to increase the numbers of children, pregnant women and patients with tuberculosis being started on ART, and to avert high early mortality and losses to follow-up. The capacity of the health sector to cope with escalating case loads and to scale up prevention alongside treatment will determine the future success of ART delivery in Malawi.

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Une traduction en français de ce résumé figure à la fin de l'article. Al final del artículo se facilita una traducción al español.

الترجمة العربية لهذه الخلاصة في نهاية النص الكامل لهذه المقالة.

Background

In December 2003, the World Health Organization (WHO) and the joint United Nations Programme on HIV and AIDS (UNAIDS) launched the "3 by 5" initiative, with the goal of having 3 million people on antiretroviral therapy (ART) in developing countries by the end of 2005. By December 2005, an estimated 1.3 million people from low- and middle-income countries had started treatment, with 810 000 of these living in sub-Saharan Africa.¹

Although the 3 by 5 target was not reached, it has been a remarkable effort, particularly in the challenging working arena of sub-Saharan Africa. Reports

from clinics in Botswana,² Kenya,³ Uganda⁴ and other African countries⁵ have shown that ART can be delivered successfully to HIV-infected eligible patients with excellent clinical and immunological benefit. However, despite these encouraging successes, there is limited information about how ART delivery has fared in the routine government health services of resource-poor African countries.

In Malawi, we embarked on national scale-up of ART through government and mission health facilities in early 2004. With 170 000 HIV-infected patients thought to be in need of ART,⁶ the country set a target to have 80 000

patients on treatment by the end of 2005. This goal was in line with the WHO initiative to place half the patients in need of ART in developing countries on treatment by 2005. We have previously reported on progress made during 2004,⁷ and here we report on Malawi's achievements and the technical challenges faced during the "3 by 5" campaign up to December 2005.

Scale-up methods

Details of ART delivery in Malawi between 2004 and 2005 have been described elsewhere.⁸ A standardized structured approach was used for treatment, details of which are shown in Box 1.

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With the shortage of doctors in Malawi, paramedical clinical officers and medical assistants and nurses were trained to manage and deliver ART. The HIV Unit of the Ministry of Health and selected partners developed a 5-day training module and a certification of competence linked to a formal examination, and successful participants then undertook a 2-week practical clinical attachment at one of the experienced ART sites. The HIV Unit and the same selected partners implemented the training by mid-2004. By the end of 2005, 1138 health care workers in the public sector including 118 doctors, 384 clinical officers, 23 medical assistants and 613 nurses had been trained and certified in ART management.

Sixty facilities in the public health sector were selected for ART scale-up between 2004 and 2005, with each site being accredited by the HIV Unit of the Ministry of Health before being allowed to deliver ART. At the beginning of 2004, nine public health facilities were delivering ART using their own systems and treatments. By July 2005 there were 60 facilities, all of which were delivering ART using national standardized systems.

Results

In early 2004, an estimated 4000 patients had started on ART in the public health sector. By the end of 2005, the number of patients cumulatively started on ART was 37 840, which was 47% of the national target. Characteristics and outcomes of patients started on ART are shown in Table 1. ART was given to 6680 patients with active or previous tuberculosis, who as a result were staged in WHO clinical stage III or stage IV (18% of those placed on ART), and 336 HIV-positive pregnant women through Prevention of Mother to Child Transmission programmes (1% of those placed on ART).

For reporting purposes, cohorts of patients are grouped by quarters of the calendar year, allowing 6-month and 12-month cohort outcome analyses to be performed. For example, all patients registered in a cohort from January to March 2005 could have their outcomes assessed on 30 September 2005, and these data were included in the 6-month outcome analysis (although we do recognize that this method includes patient outcomes 6–9 months after starting ART). This same cohort at a later time

Table 1. Characteristics and outcomes of 37 840 patients starting antiretroviral treatment in Malawi, 2004 – 2005

| Characteristic | Number (%) ^a |
|--|-------------------------|
| Male | 1 4819 (39%) |
| Female | 2 3021 (61%) |
| Adults (age ≥13 years) | 3 5841 (95%) |
| Children (age ≤12 years) | 1999 (5%) |
| Occupation recorded | 26 172 (69%) |
| Housewife | 5 895 (23%) |
| Farmer | 6 035 (23%) |
| Small-scale business employee | 3 669 (14%) |
| Army or police force employee | 559 (2%) |
| Teacher | 1 127 (4%) |
| Health care worker | 616 (2%) |
| Other | 8 271 (31%) |
| Occupation not recorded | 11 668 (31%) |
| Reason for starting ART ^b | |
| Stage III ^c | 24 712 (65%) |
| Stage IV ^c | 9 232 (24%) |
| Stage I or II ^c with CD4 count < 200/mm ³ | 3 896 (10%) |
| Outcome | |
| Alive and on ART at the initial ART registration site ^b | 28 110 (74%) |
| On first line regimen | 27 066 (96%) |
| On alternative first line regimen due to side-effects | 983 (3%) |
| On second line regimen due to treatment failure | 61 (<1%) |
| Able to walk at home unaided ^d | 26 846 (96%) |
| Able to do productive work ^d | 25 964 (93%) |
| Significant side-effects present in December 2005 ^e | 1 159 (5%) |
| Drug adherence >95% measured by pill counts ^f | 19 254 (91%) |
| Transferred out to another ART registration site | 2 466 (7%) |
| Dead | 3 923 (10%) |
| Died in month 1 | 1 439 (37%) |
| Died in month 2 | 897 (23%) |
| Died in month 3 | 438 (11%) |
| Died in month 4 or later | 1 149 (29%) |
| Lost to follow-up (not seen at the clinic for > 3 months) | 3 047 (8%) |
| Permanently stopped ART ^b | 294 (1%) |

^a Percentages may not add to 100 because of rounding.

^b ART, antiretroviral therapy.

^c WHO clinical staging system for HIV.

^d Data known for 27894 patients

^e Data known for 25151 patients.

^f Data Known for 21101 patients.

could also have their outcomes assessed on 31 March 2006, with these data being included in the 12-month outcome analysis.

During each of the supervisory and monitoring visits in 2005 and 2006, data from all cohorts of patients at the ART facilities were included in 6-month and 12-month outcome analyses: these were combined to give results which are shown in Fig.1. Outcomes at 6 months and 12 months were similar, indicating that most deaths in a young programme such as Malawi's occur in the early months of ART.

Discussion

Achievements

The Malawian example that we describe shows that using a simple, structured approach to ART delivery, government health sectors can deliver treatment to large numbers of patients fairly quickly with good outcomes. A few facilities in Malawi are supported by international organizations, such as Médecins sans Frontières, but in most facilities local health care workers are the sole providers of ART. Although the national target for numbers of people on ART

was not reached, there has been general satisfaction to date with the achievement in ART scale-up, especially given that trained health care personnel, monitoring tools and systems of drug procurement and distribution were not in place at the beginning of 2004.

There have been several factors responsible for the successes in ART delivery in Malawi. The most important are: clear national ART guidelines, with an emphasis on the system of registration, monitoring and recording of results; agreement by all implementing partners to work with the Ministry of Health and use national standardized systems; an intensive training schedule focused on clinical officers and nurses learning the ART guidelines; a structured system of accrediting ART sites before they are permitted to deliver treatment to patients; quarterly supervision and monitoring of all ART delivery sites by the HIV Unit of the Ministry of Health and its partners; and an ART procurement and distribution system that was associated with no stock-outs of antiretroviral drugs. ART facilities vary in their quality and some do not perform as well as they should. However, regular and structured supervision ensures that a basic standard is always maintained and that data are always collected.

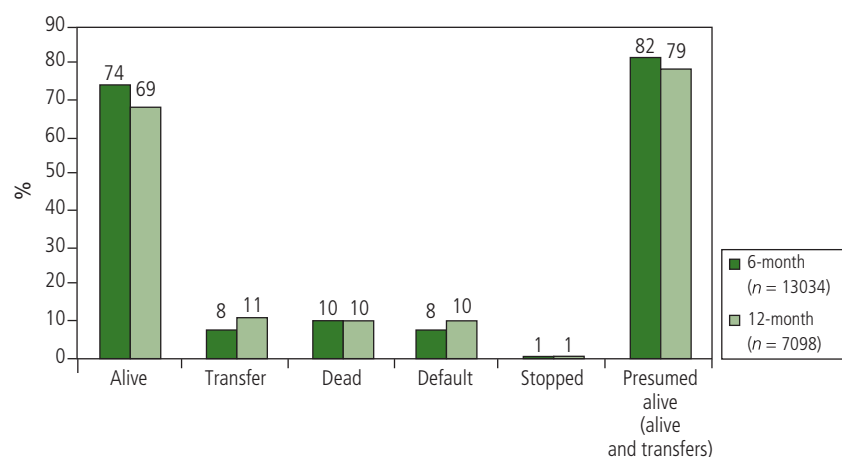
Challenges

There have been several challenges in the scaling-up of ART delivery. Children, HIV-positive pregnant women and patients with tuberculosis were, and still are, under-represented in treatment populations. The new revised 2006 WHO Paediatric Guidelines,⁹ and Malawi's revised ART Guidelines,¹⁰ which emphasize the importance of ART for children and recommend prioritizing CD4-lymphocyte counts in HIV-infected pregnant women, should increase the number of children and pregnant women accessing ART. Tuberculosis remains a difficult problem as a result of drug-drug interactions between rifampicin and non-nucleoside reverse transcriptase inhibitors¹¹ and the fact that in Malawi ART is usually distributed from hospital clinics, whereas delivery of anti-tuberculosis treatment

Box 1. Standardized approach for delivery of antiretroviral treatment in Malawi

- A focus on one generic, fixed-dose combination treatment with stavudine, lamivudine and nevirapine. Treatment is delivered free of charge to eligible HIV-positive patients.
- The initiation of treatment at antiretroviral treatment clinics that included: patient referral from HIV testing sites for clinical staging; attendance of the patient and a guardian at a group counselling session where the principles of ART are described; re-attendance about 1 week later for individual counselling with the clinician and the start of treatment. The process from clinical staging to the start of ART takes on average about 2 weeks.
- Monthly follow-up of patients, with usually only clinical criteria (for example, weight gain) and the presence or absence of side effects being used to judge treatment progress.
- Use of a standardized system for registration, monitoring and reporting of cases and outcomes.
- Quarterly supervision and evaluation of all antiretroviral treatment sites.

Fig. 1. Six-month and 12-month outcomes for patients started on antiretroviral treatment in Malawi, 2004 – 2005



is decentralized and is done from health centres.¹²

There is a high early death rate in patients starting ART, similar to that reported from other low-income countries.¹³ This finding is related to patients presenting with advanced HIV disease, tuberculosis, bacterial infections, malignancy and immune reconstitution syndrome.¹⁴ An aggressive approach to the diagnosis of tuberculosis before initiating ART and concomitant broad-spectrum antibiotic prophylaxis targeted at common serious bacterial infections may be two ways to reduce this problem of early deaths. The number of cases lost to follow-up is also of concern, and operational research is needed to identify the true outcomes of these patients to establish a more complete data set for analysis.

Other challenges to ART scale-up include equitable access to ART sites especially for patients in rural areas, the capacity of the health sector to absorb the extra demands of ART delivery without compromising other aspects of general health care, and the scaling-up of prevention efforts alongside treatment.¹⁵ ■

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Competing interests: none declared.

Résumé**La contribution du Malawi à l'initiative « trois millions d'ici 2005 » : résultats obtenus et défis à relever**

Problématique De nombreux pays pauvres en ressources ont entamé l'extension du traitement antirétroviral (ART). Si les informations provenant des différents établissements font état d'une mise en œuvre satisfaisante, les données restent limitées quant aux progrès accomplis par les services publics au niveau national.

Démarche Le Malawi a commencé l'extension du traitement antirétroviral au niveau national en 2004 au moyen d'une approche structurée utilisant principalement une association fixe de type générique, associant stavudine, lamivudine et névirapine. Le traitement est fourni gratuitement aux sujets porteurs du VIH et remplissant les critères d'inclusion et un système normalisé est appliqué pour le recrutement des malades, le suivi mensuel, l'enregistrement et la surveillance, ainsi que pour la notification des cas et des issues du traitement. Une supervision et une évaluation trimestrielles sont assurées dans tous les centres de traitement.

Situation locale En janvier 2004, un traitement antirétroviral était fourni à quelque 4000 malades dans neuf centres relevant du secteur public. En décembre 2005, 60 de ces centres délivraient gratuitement des antirétroviraux à 37 840 malades par l'intermédiaire de systèmes nationaux normalisés. L'analyse des résultats trimestriels

du traitement pour les cohortes a montré qu'au bout de 12 mois 80 % des sujets étaient en vie, 10 % étaient décédés, alors qu'on avait perdu la trace de 9 % d'entre eux et qu'on enregistrait 1 % d'abandons du traitement.

Enseignements tirés Les résultats ont pu être obtenus grâce à des directives nationales claires sur le traitement antirétroviral, à la collaboration entre les partenaires chargés de la mise en œuvre, à une formation intensive des cliniciens et des infirmières, à un système structuré d'accréditation des centres appelés à délivrer le traitement, à une supervision et une surveillance trimestrielles, ainsi qu'à un approvisionnement continu en antirétroviraux. Les principaux défis consistent à améliorer le nombre - limité au demeurant - d'enfants, de femmes enceintes et de malades souffrant de la tuberculose et entamant un traitement ARV et à réduire la forte mortalité précoce et le nombre de sujets perdus de vue. L'aptitude du secteur de la santé à faire face au nombre sans cesse plus élevé de cas et à étendre les activités de prévention en plus du traitement est aussi une source de préoccupations. C'est la capacité à relever ces défis qui conditionnera le succès du traitement antirétroviral au Malawi.

Resumen**La contribución de Malawi a la iniciativa «tres millones para 2005»: logros y retos**

Problema Muchos países con escasos recursos han iniciado una expansión del tratamiento antirretrovírico (TAR). Aunque los informes de algunas clínicas señalan el éxito de la iniciativa, hay escasa información sobre los progresos realizados en las instituciones gubernamentales a nivel nacional.

Estrategia Malawi comenzó en 2004 la expansión nacional del TAR con una estrategia estructurada, centrada en el tratamiento con un genérico consistente en la combinación de estavudina, lamivudina y nevirapina a dosis fijas. El tratamiento es ofrecido gratuitamente a los pacientes infectados por VIH que cumplen los criterios, y hay un sistema normalizado de reclutamiento de los pacientes, seguimiento mensual, registro, y monitorización y notificación de los casos y los resultados. Todos los lugares donde se dispensa el tratamiento son supervisados y evaluados trimestralmente.

Entorno local En enero de 2004 había nueve centros del sector público que proporcionaban TAR a unos 4 000 pacientes. En diciembre de 2005 había 60 centros del sector público que proporcionaban TAR gratuito a 37 840 pacientes en el marco de

los sistemas nacionales normalizados. El análisis de los resultados trimestrales del tratamiento de las cohortes a los 12 meses reveló que el 80% de los pacientes estaban vivos y el 10% muertos, mientras que en el 9% se había interrumpido el seguimiento y en el 1% se había detenido el tratamiento.

Enseñanzas Los logros se debieron a la existencia de directrices nacionales claras sobre el TAR, al trabajo en colaboración con los asociados, a un plan intensivo de formación centrado en los ayudantes clínicos y las enfermeras, a un sistema estructurado de acreditación de los centros dispensadores de TAR, a la supervisión y monitorización trimestrales, y al hecho de que nunca se agotaran las existencias de antirretrovíricos. Los principales retos consisten en aumentar el número de niños, embarazadas y pacientes tuberculosos que reciben TAR, y evitar la elevada mortalidad inicial y las interrupciones del seguimiento. La capacidad del sector de la salud para hacer frente al aumento del número de casos y la ampliación de la prevención a la par del tratamiento serán determinantes del éxito futuro del TAR en Malawi.

ملخص**مساهمة ملاوي في مبادرة 3 في 5: الإنجازات والتحديات**

المستحقين للمعالجة، كما أن هنالك نظاماً موحداً لتعيين المرضى، وللمتابعة الشهرية، وللتسجيل ولرصد الحالات والتبليغ عنها وعن النتائج. ويتم الإشراف والتقييم على جميع المواقع دورياً كل ثلاثة أشهر.

الموقع المحلي: في كانون الثاني/يناير 2004 كان هنالك تسعة مرافق تابعة للقطاع العام تقدم المعالجة بمضادات الفيروسات القهقرية لنحو 4 آلاف مريض. وبحلول كانون الأول/ديسمبر 2005. ازداد عدد تلك المرافق في القطاع العام إلى 60 مرفقاً تقدم المعالجة المجانية لنحو 37840 مريضاً باستخدام النظم الوطنية القياسية للمعالجة. وبين تحليل نتائج معالجة

المشكلة: بدأ العديد من البلدان الفقيرة الموارد في توسيع نطاق المعالجة بالأدوية المضادة للفيروسات القهقرية. وفي حين تشير التقارير الواردة من عيادات خاصة إلى نجاح هذه المساعي، إلا أن هنالك نقصاً في المعلومات المتعلقة بالتقدم المحرز في المؤسسات الحكومية على المستوى الوطني.

الأسلوب: بدأت ملاوي في توسيع نطاق المعالجة على المستوى الوطني في عام 2004 باتباع أسلوب منهجي. وتركزت المعالجة على استخدام دواء جنيس (غير محدد الملكية) واحد، وهو توليفة ثابتة الجرعة تتكوّن من الستافودين، واللاميفودين، والنفيرابين. وتقدم المعالجة مجاناً للمصابين بفيروس الإيدز

وللإشراف على تلك المرافق كل ثلاثة أشهر، وإلى عدم نفاذ مخزون أدوية المعالجة. وتتمثل التحديات الرئيسية في زيادة عدد الأطفال والحوامل ومرضى السل الذين يحصلون على المعالجة، وارتفاع معدل الوفيات المبكرة، وعدم المتابعة، وفي تحسين قدرة القطاع الصحي على التغلب على الأعباء المرضية المتصاعدة، وكيفية النهوض بأنشطة الوقاية إلى جانب المعالجة. إن قدرتنا على مواجهة هذه التحديات سوف تقرر مدى النجاح المستقبلي لتقديم المعالجة بمضادات الفيروسات القهقرية في ملاوي.

المرضى، الذي أجري كل ثلاثة أشهر، أنه بعد 12 شهراً كان 80% من المرضى لا يزالون على قيد الحياة، فيما مات 10% منهم، و9% فُقدوا من المتابعة، و1% أوقفوا المعالجة.

الدروس المستفادة: تُعزى الإنجازات التي تحققت إلى وجود دلائل إرشادية وطنية واضحة للمعالجة بمضادات الفيروسات القهقرية، وإلى تعاون الشركاء، وإلى وجود برنامج مكثف للتدريب يركّز على الأطباء والممرضات، وإلى وجود نظام منهجي لاعتماد مرافق إيتاء المعالجة المضادة للفيروسات القهقرية.

References

- World Health Organization and UNAIDS. *Progress on global access to HIV antiretroviral therapy. a report on "3 by 5" and beyond*. Geneva: WHO; 2006.
- Wester CW, Kim S, Bussmann H, Avalos A, Ndwapu N, Peter TF, et al. Initial response to highly active antiretroviral therapy in HIV-1C-infected adults in a public sector treatment program in Botswana. *J Acquir Immune Defic Syndr* 2005;40:336-43.
- Wools-Kaloustian K, Kimaiyo S, Diero L, Siika A, Sidle J, Yiannoutsos CT, et al. Viability and effectiveness of large-scale HIV treatment initiatives in sub-Saharan Africa: experience from Western Kenya. *AIDS* 2006;20:41-8.
- Spacek LA, Shihab HM, Kanya MR, Mwesigire D, Ronald A, Mayanja H, et al. Response to antiretroviral therapy in HIV-infected patients attending a public, urban clinic in Kampala, Uganda. *Clin Infect Dis* 2006;42:252-9.
- Ivers LC, Kendrick D, Doucette K. Efficacy of antiretroviral therapy programs in resource-poor settings: a meta-analysis of the published literature. *Clin Infect Dis* 2005;41:217-24.
- National AIDS Commission. *National estimates of HIV/AIDS in Malawi*. Lilongwe, Malawi: National AIDS Commission; 2003.
- Libamba E, Makombe S, Mhango E, de Ascurra Teck O, Limbambala E, Schouten EJ, et al. Supervision, monitoring and evaluation of nationwide scale-up of antiretroviral therapy in Malawi. *Bull World Health Organ* 2006; 84:320-6.
- Libamba E, Makombe S, Harries AD, Chimzizi R, Salaniponi FM, Schouten EJ, et al. Scaling up antiretroviral therapy in Africa: learning from tuberculosis control programmes; the case of Malawi. *Int J Tuberc Lung Dis* 2005; 9:1062-71.
- World Health Organization. *Antiretroviral therapy of HIV infection in infants and children in resource-limited settings, towards universal access: recommendations for a public health approach (2006 revision)*. Geneva: World Health Organization; 2006.
- Malawian Ministry of Health. *Treatment of AIDS: guidelines for the use of antiretroviral therapy in Malawi*. Second edition. Lilongwe: Malawian Ministry of Health; 2006.
- Kwara A, Flanigan TP, Carter EJ. Highly active antiretroviral therapy (HAART) in adults with tuberculosis: current status. *Int J Tuberc Lung Dis* 2005;9:248-57.
- Zachariah R, Teck R, Ascurra O, Gomani P, Manzi M, Humblet P, et al. Can we get more HIV-positive tuberculosis patients on antiretroviral treatment in a rural district of Malawi? *Int J Tuberc Lung Dis* 2005;9:238-47.
- The Antiretroviral Therapy in Lower-Income Countries (ART-LINC) Collaboration and ART Cohort Collaboration (ART-CC) groups. Mortality of HIV-1-infected patients in the first year of antiretroviral therapy: comparison between low-income and high-income countries. *Lancet* 2006;367:817-24.
- Lawn SD, Myer L, Orrell C, Bekker L-G, Wood R. Early mortality among adults accessing a community-based antiretroviral service in South Africa: implications for programme design. *AIDS* 2005;19:2141-8.
- Van Damme W, Kober K, Laga M. The real challenges for scaling up ART in sub-Saharan Africa. *AIDS* 2006;20:653-6.

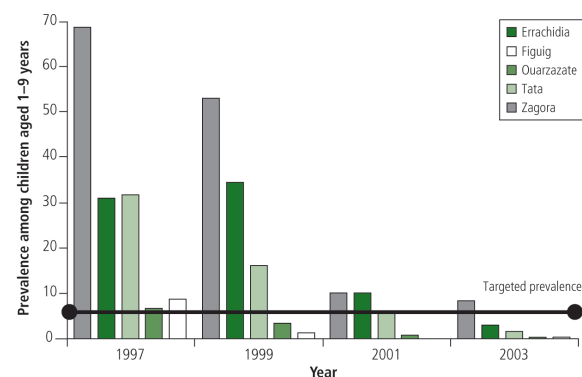
Corrigenda

In Vol. 84, issue number 12, 2006, page 980, the first sentence in the second paragraph under "Overweight and obesity" should read as follows:

"We calculated the percentage of males and females who were overweight and obese in each quintile over time [data not shown]."

In Vol. 84, issue number 8, 2006, page 615, Figure 3 should be:

Fig. 3. Impact of 7 years of the SAFE strategy on prevalence of grade TF^a trachoma in children aged 1–9 years in five endemic provinces in Morocco



Source: National coordinator of the Moroccan National Eye Care Programme.

^a Prevalence of >10% trachomatous inflammation, follicular.

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