Lessons from the field

Ensuring uninterrupted supplies of antiretroviral drugs in resource-poor settings: an example from Malawi

Anthony D Harries,[a] Erik J Schouten,[b] Simon D Makombe,[a] Edwin Libamba,[a] Henry N Neufville,[c] Eliab Some,[c] Godfrey Kadewere[d] & Douglas Lungu[e]

Problem Drug procurement and distribution practices are weak in many resource-poor countries, and are a major reason for lack of access to medicines. With many countries scaling up antiretroviral therapy (ART), it is vital to avoid interrupted drug supplies, which would lead to drug resistance and treatment failure.

Approach Malawi has adapted a model, based on that adopted by the country's Tuberculosis Control Programme, to allow rational ART drug forecasting.

Local setting The model includes a focus on one standardized first-line ART regimen; a "push system" and "ceilings" for first-line ART drugs for facilities; use of starter pack and continuation pack kits; quarterly monitoring of patient outcomes and ART drug stocks at facility level; provision of a three-month buffer stock of ART drugs at facility level; and use of a procurement and distribution system outside central medical stores.

Lessons learned The focus on a single first-line regimen, "ceilings" for first-line ART drugs and quarterly data collections to calculate drug needs (for new and follow-up patients, respectively), as well as the use of an independent procurement facility, allow drug orders to be made 6–9 months ahead. These measures have so far ensured that there have been no ART drug stock-outs in the country.

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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

Chloramphenicol and penicillin out of stock. For anyone working in sub-Saharan Africa, receiving this statement from central medical stores or facility-level pharmacies never comes as a surprise. A major cause of lack of medicines in Africa is weak procurement and distribution practices,[1] and this is of major concern with many countries now scaling up antiretroviral therapy (ART) to thousands of patients.[2] ART drug stock-outs are being documented, and various African facilities[3,4] have identified the single greatest logistic challenge to ART scale-up being that of maintaining drug supplies. Stock-outs mean unplanned treatment interruptions, which in turn cause drug resistance and treatment failure. Such adverse events have already been documented from ART clinics in sub-Saharan Africa.[5]

Prevention is better than cure. One of the cornerstones of the "DOTS" tuberculosis (TB) control strategy is a regular, secure supply of anti-TB drugs.[6] Well-run national TB programmes, including the programme in Malawi, have a structured system of drug forecasting and do not experience drug stock-outs. Similar principles should be applied to ART. First-line ART in many African countries consists of a generic fixed-dose triple-drug combination, usually taken as a single tablet twice a day.[7] Resistance to first-line therapy means switching to a more complicated, expensive, toxic and less effective second-line regimen, and as far as possible this must be avoided. The Ministry of Health in Malawi has therefore worked with key partners, such as the United Nations Children's Fund (UNICEF), to develop an ART procurement model that allows rational drug forecasting and uninterrupted drug supplies. We describe this model and the lessons learned.

Key principles of ART procurement and delivery in Malawi

Scale-up using one standardized first-line ART regimen

The Ministry of Health selected a fixed-dose generic combination of stavudine (d4T), lamivudine (3TC) and nevirapine (NVP) as the national first-line regimen, and this is the only regimen used by most facilities in scaling up ART.[8,9]

[a] Clinical HIV Unit, Ministry of Health, PO Box 30377, Lilongwe, Malawi. Correspondence to Dr Harries (email: adharries@malawi.net).
[b] Ministry of Health, Lilongwe, Malawi.
[c] UNICEF, Malawi Country Office, Lilongwe, Malawi.
[d] Department of Health Technical Services, Ministry of Health, Lilongwe, Malawi.
[e] Department of Clinical Services, Ministry of Health, Lilongwe, Malawi.

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Alternative first-line regimens are offered in case of side-effects and/or specific contraindications, and a second-line regimen in case of treatment failure. Because of limited experience in estimating demand for, and in the use of, these drugs, orders are made only for central hospitals and two large district hospitals. A system for other facilities to access these drugs has been developed and is in operation.

A "push system" and "ceilings" for first-line ART drugs

From June 2005, there were 60 government and mission health facilities delivering first-line ART. Each facility is designated as a low burden (starting 25 new patients per month, $n = 30$), medium burden (starting 50 new patients per month, $n = 25$), high burden (starting 150 new patients per month, $n = 4$) or very high burden unit (starting 250 new patients per month, $n = 1$). This classification is based on number of inpatient beds, area of population served, HIV prevalence rate in the population (if known) and TB case burden (as a proxy for AIDS cases). Drugs are ordered for each facility for six months. Facilities should not recruit more than their expected number of patients, as this will endanger drug availability. During quarterly supervisions conducted by the HIV Unit of the Ministry of Health and its partners, facilities are assessed in terms of patient recruitment, and those doing well are offered the opportunity to raise their ceiling and move from a lower to a higher category status. Using this system, the HIV Unit can calculate the number of new patients needing therapy every six months. With the current classification, 17 100 new patients would start ART in a six-month period, provided facilities worked to full capacity.

A pre-packed kit system with "starter packs" and "continuation packs"

The development of a starter pack and continuation pack kit simplifies drug procurement.[9] The kit composition is shown in Fig. 1. In its first six-month period, a low burden facility needs two starter pack kits (one for each quarter) and three continuation pack kits (one for the first three months and two for the next three months for those placed on treatment in the first quarter and those starting treatment in the second quarter). Likewise, a medium burden unit needs four starter pack and six continuation pack kits, while a high burden unit needs 12 starter pack and 18 continuation pack kits.

Fig. 1. **Pre-packed kits of starter packs and continuation packs**

Starter pack kit (based on low burden unit starting 25 new patients on ART per month for three months)
Provides drugs for 75 new patients starting ART for 14 days 150 tins of ART 60 tins of d4T-30 mg/ 3TC (15 tablets – one extra tablet as buffer) 15 tins of d4T-40 mg/ 3TC (15 tablets – one extra tablet as buffer) 60 tins of d4T-30 mg/ 3TC/ NVP (15 tablets – one extra tablet as buffer) 15 tins of d4T-40 mg/ 3TC/ NVP (15 tablets – one extra tablet as buffer)

Continuation pack kit (based on low burden unit keeping 75 patients on treatment for three months)
Provides drugs for 75 patients to continue on ART for three months, and receive drugs every month 225 tins of ART 180 tins of d4T-30 mg/ 3TC/ NVP (60 tablets) 45 tins of d4T-40 mg/ 3TC/ NVP (60 tablets)

ART = antiretroviral therapy; d4T = stavudine; 3TC = lamivudine; NVP = nevirapine.
Note: ART drugs are provided as d4T-30 mg or d4T-40 mg, 3TC-150 mg and NVP-200 mg. The use of d4T-30 mg or d4T-40 mg depends on the patient's weight: those weighing less than 60 kg receive d4T-30 mg and those weighing 60 kg or more receive d4T-40 mg. Based on previous experience it was estimated that 80% of patients would weigh less than 60 kg and 20% would weigh 60 kg or more.

Quarterly monitoring of patient treatment outcomes and ART drug stocks

Patients' outcomes are followed on a monthly basis, using ART patient master cards.[9,10] During quarterly site supervisions, data are collected from each facility on the number of patients alive and on therapy at a set moment in time. This is the number who will need continuation therapy, which has to be added to the number of new patients starting treatment. An ART drug stock check is also made in the pharmacy to record the number of different bottles of first-line, alternative first-line and second-line therapy on the shelves.

Buffer stocks of first-line ART

Buffer stocks are important to guard against unforeseen events. Each facility is given a three-month buffer stock, the mechanism being that the six-month drug orders come in three months early on a regular basis.

Forecasting first-line ART drug requirements for each facility

An example of how to forecast first-line ART drug needs at a low burden facility is provided in Table 1. This drug order was prepared in early October 2005 for the period July to December 2006, with the arrival of drugs planned three months early in April 2006. For new patients starting ART between July and December 2006, the calculations are straightforward: two starter pack and three continuation pack kits. The calculation of drugs needed for six months for patients already on ART and predicted to be alive in July 2006 is shown in the table. Several calculations and assumptions are required which include: number of patients alive and on ART in October 2005; number of new patients starting ART between October 2005 and July 2006; estimated number of patients who will die, default, stop treatment or transfer-out during this period (based on quarterly monitoring reports);[9,10] drugs arriving in country for the facility between October 2005 and July 2006; and drug stocks in October 2005.

Use of a parallel procurement and distribution system for ART

A World Bank assessment of the government central medical stores in 2002 strongly advised, for various reasons, that another institution be used for procurement of HIV/AIDS and ART drugs with funding from the Global Fund to Fight AIDS, Tuberculosis and Malaria. UNICEF was chosen and is responsible

Table1. **Forecasting first-line antiretroviral therapy (ART) drug requirements**

Patients alive and needing ART by 1 July 2006	**Number of patients**
A. Patients alive and on ART at end of September 2005 (156) and predicted to be alive and on ART by 1 July 2006 — assuming a 10% attrition rate over this period	140
B. New patients starting ART between October 2005 and June 2006 (225) and predicted to be alive and on ART by 1 July 2006 — assuming a 10% attrition rate over this period	203
Patients alive and needing ART by 1 July 2006 (A+B)	**343**
Bottles (60 tablets) of d4T-3TC-NVP in stock by 1 July 2006	**Number of bottles**
Bottles of d4T-3TC-NVP consumed by patients in category A	1260
Bottles of d4T-3TC-NVP consumed by patients in category B	1012
C. Total bottles of d4T-3TC-NVP consumed by patients in categories A and B by 1 July 2006	2272
Bottles of d4T-3TC-NVP in stock at end of September 2005	1730
Bottles of d4T-3TC-NVP arriving in October–November 2005	2000
D. Total bottles of d4T-3TC-NVP in stock or arriving before next drug order in April 2006	3730
Bottles of d4T-3TC-NVP in stock by 1 July 2006 (D-C)	**1458**
Bottles (60 tablets) of d4T-3TC-NVP to procure July–Dec 2006	**Number of bottles**
E. Bottles of d4T-3TC-NVP for 343 patients for 6 months — assuming no attrition during this period	2058
F. Bottles of d4T-3TC-NVP already in stock on 1 July 2006	1458
Bottles of d4T-3TC-NVP to procure July–Dec 2006 (E-F)	**600**

d4T = stavudine; 3TC = lamivudine; NVP = nevirapine.
Note: This is an example of a drug procurement order, put together in October 2005, for a low burden unit. This six-month order was for continuation drugs for patients predicted to be alive and on ART on 1 July 2006, and translated into three continuation pack kits.

for procuring and distributing ART drugs in Malawi. WHO pre-qualified drugs are procured mainly from CIPLA, India, packaged into the quantities determined for each facility, shipped to Malawi and immediately distributed to the facilities.

Box 1. **Lessons learned**

- A focus on a single first-line regimen simplifies the process of drug ordering.
- The use of "ceilings" for first-line ART drugs and quarterly data on patient outcomes and drug stocks allow rational calculations of ART drug needs for new and follow-up patients, respectively.
- The use of another procurement agency, if the government facility is judged to be weak, allows ART scale-up to proceed with confidence.

Evaluation and lessons learned

This drug procurement model has worked well so far. Drug stocks are monitored during quarterly site supervisions, and there have been no drug stock-outs as of 30 June 2006. There have been three important lessons learned in this process (Box 1). First, a focus on a single first-line regimen, rather than having several different regimens to choose from, simplifies the process of drug ordering, particularly as patient numbers continue to increase. Second, using "ceilings" for first-line ART drugs and obtaining quarterly data on patient outcomes and drug stocks provide a rational basis for calculating ART drug needs for new and follow-up patients, respectively. Quarterly supervisions also allow site-specific distribution problems to be tackled, and drugs can be moved between facilities that under-perform or over-perform. Third, once government procurement facilities had been judged to be weak, taking the decision to use another procurement agency has allowed scale-up to proceed smoothly, although eventually ways will have to be found to integrate drug supplies back into national procurement systems. Time will tell whether Malawi's model will cope with increasing numbers of ART facilities and patients starting treatment. ■

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Résumé

Garantir un approvisionnement ininterrompu en médicaments antirétroviraux dans un pays à ressources limitées : exemple du Malawi

Problème Dans beaucoup de pays à ressources limitées, il n'existe guère de procédures d'achat et de distribution des médicaments solidement organisées, ce qui est l'une des raisons majeures du manque d'accès aux médicaments. De nombreux pays ayant entrepris d'étendre l'application des traitements antirétroviraux (ART), il importe d'éviter toute interruption de l'approvisionnement en médicaments, susceptible d'entraîner l'apparition d'une résistance médicamenteuse et des échecs thérapeutiques.

Démarche suivie Le Malawi a adapté le modèle utilisé par le Programme national de lutte contre la tuberculose pour prévoir les besoins nationaux en antirétroviraux.

Contexte local Ce modèle fait appel à un schéma thérapeutique ART de première intention unique et standardisé, à un système de type «pulsion» et à des «plafonds» pour les médicaments antirétroviraux de première intention destinés aux établissements de santé ; à l'association d'un kit de mise en route du traitement et de kits pour phase d'entretien, à un suivi sur trois mois des résultats obtenus chez les patients et des stocks d'antirétroviraux au niveau des établissements, au maintien d'un stock tampon pour 3 mois dans les établissements, ainsi qu'à un système d'achat et de distribution indépendant des magasins centraux de médicaments.

Enseignements tirés Grâce à l'utilisation majoritaire d'un schéma thérapeutique de première intention unique et de «plafonds» pour les ART de première intention, à la collecte trimestrielle de données pour calculer les besoins en médicaments (pour les nouveaux patients et ceux en cours de traitement respectivement) et au recours à une unité d'achat indépendante, il est possible d'établir les commandes de médicaments 6 à 9 mois à l'avance. Ces mesures ont permis jusqu'à présent d'éviter toute rupture de stocks d'antirétroviraux dans le pays.

Resumen

Garantizar el suministro ininterrumpido de antirretrovirales en los entornos con pocos recursos: el ejemplo de Malawi

Problema Las prácticas de adquisición y distribución de los medicamentos son deficientes en muchos países de escasos recursos, y explican en buena parte los problemas de falta de acceso a los fármacos. Paralelamente a la expansión del tratamiento antirretroviral (TAR) llevada a cabo en numerosos países, es fundamental evitar cualquier interrupción del suministro de medicamentos, circunstancia que conduce a la aparición de farmacorresistencia y al fracaso terapéutico.

Métodos Malawi ha adaptado un modelo, basado en el empleado por el Programa de Lucha contra la Tuberculosis del país, que permite hacer proyecciones racionales de las necesidades de antirretrovirales.

Contexto local El modelo incluye la focalización en un régimen normalizado de TAR de primera línea; un «sistema impulsor» y «techos» de medicamentos antirretrovirales de primera línea para los centros asistenciales; el uso de un kit inicial y de kits de mantenimiento; el monitoreo trimestral de la evolución de los pacientes y de las reservas de antirretrovirales en los centros; la provisión de una reserva de estabilización de tres meses de antirretrovirales en los centros; y el uso de un sistema de adquisición y distribución independiente de los almacenes médicos centrales.

Experiencia adquirida La focalización en un solo régimen de primera línea, los «techos» para los antirretrovirales de primera línea y la recogida trimestral de datos para calcular las necesidades de medicamentos (para pacientes nuevos y de seguimiento, respectivamente), así como el recurso a un centro de adquisiciones independiente, permite hacer los pedidos de medicamentos con 6-9 meses de antelación. Gracias a esas medidas, hasta ahora no se ha producido ninguna situación de desabastecimiento de TAR en el país.

ملخص

ضمان الإمدادات المتواصلة من الأدوية المضادة للفيروسات القهقرية في المواقع الفقيرة الموارد: مثال من مالاوي

المشكلة: تعاني ممارسات الشراء والتوزيع من الضعف في الكثير من البلدان الفقيرة الموارد، وهو السبب الرئيسي لفقدان إتاحة الأدوية، ومن الضروري في الكثير من البلدان التي تنهض بالمعالجة المضادة للفيروسات القهقرية تجنب التقطع في إمداد الأدوية، فهو مما يؤدي إلى مقاومة الأدوية وإلى فشل المعالجة.

الأسلوب: عدَّلت مالاوي نموذجاً يتركز على النموذج الذي تبناه البرنامج الوطني لمكافحة السل، للسماح بالتنبؤ بالأدوية الرشيدة المضادة للفيروسات القهقرية.

الموقع المحلي: يشتمل النموذج على التركيز على نظام علاجي معياري واحد للخط الأمامي للأدوية المضادة للفيروسات القهقرية، و«نظام دفع»، و«سقوف» لأدوية الخط الأول المضادة للفيروسات القهقرية، واستخدام عتائد لعبوة البداية وعبوات المداومة، ورصد يدوم ثلاثة شهور للحصائل لدى المرضى وللمخزونات من الأدوية المضادة للفيروسات القهقرية على مستوى المرفق الصحي، وتقديم مخزون احتياطي دارئ يكفي لثلاثة شهور من الأدوية المضادة للفيروسات القهقرية، واستخدام نظام الشراء والتوزيع خارج المخازن الطبية المركزية.

الدروس المستفادة: إن التركيز على نظام وحيد للخط الأول، وسقوف للخط الأول من الأدوية المضادة للفيروسات القهقرية، وجمع المعطيات كل ثلاثة شهور لحساب الاحتياجات من الأدوية لكل من المرضى الجدد ولمتابعة المرضى القدامى، واستخدام مرافق مستقلة للشراء، كل ذلك يسمح بالتعرُّف على طلبات مسبقة للأدوية للأشهر الستة أو التسعة التالية. وتضمن هذه الإجراءات عدم حدوث حالات نفاد للمخازن من الأدوية المضادة للفيروسات القهقرية في البلد.

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