# Perspectives

**Limited access to drugs for resistant tuberculosis: a call to action**

**Sabine Bélard**¹,²,³,⁴, Saskia Janssen¹,²,³, Kara K. Osbak¹,², Ayola A. Adegnika¹,³, Magloire Ondounda⁵, Martin P. Grobusch¹,²,³

¹Centre de Recherches Médicales de Lambaréné (CERMEL), Lambaréné BP118, Gabon
²Division of Internal Medicine, Centre of Tropical Medicine and Travel Medicine, Academic Medical Centre, University of Amsterdam, Amsterdam 1100 DD, The Netherlands
³Institute of Tropical Medicine, University of Tübingen, Tübingen 72074, Germany
⁴Department of Pediatric Pneumology and Immunology, Charité-Universitätsmedizin Berlin, Berlin 10117, Germany
⁵Hôpital d’Instruction des Armées OBO, Libreville BP 20404, Gabon

Address correspondence to Martin P. Grobusch, Department of Infectious Diseases, Division of Internal Medicine, Center of Tropical Medicine and Travel Medicine, Amsterdam Medical Center, University of Amsterdam, Meibergdreef 9, PO Box 22660, Amsterdam 1100 DD, The Netherlands. E-mail: m.p.grobusch@amc.uva.nl

**ABSTRACT**

Although the rate of new tuberculosis (TB) cases has been falling worldwide, progress toward the targets for diagnosis and treatment of drug-resistant TB is far off-track. In countries with no reliable TB surveillance system, setbacks and progression of TB control is barely reflected and little is known on the situation in the field. Interviews with health professionals in Gabon revealed limited access to first- and second-line TB drugs and important deficiencies in basic TB control. National and international action needs to be taken to meet the global TB control targets.

**Keywords** accessibility, Africa, Gabon, tuberculosis treatment, drug-resistance

**Background**

Universal access to high-quality care for all people with tuberculosis (TB) is central to proper epidemic control for this airborne disease. For TB patients in some countries highly affected by the TB/HIV pandemic, this still appears to be an empty promise.¹

Gabon is a Central African country with an estimated annual TB incidence of 428 cases per 100 000 population² and a HIV prevalence of ~4%.³ Diagnosis and treatment of TB are entirely covered by the National TB Program (NTP) whereby TB care is principally free of charge.

Given the high estimated TB burden in Gabon, which is paralleled by a lack of systematic epidemiological data, a TB research facility was opened at the ‘Centre de Recherches Médicales de Lambaréné’, based at the Albert Schweitzer Hospital, Lambaréné. The initial phase of research activities concentrated on data collection related to clinical and microbiological TB epidemiology. First retrospective analyses of clinical data revealed a high TB and HIV/TB burden and a disconcertingly poor TB control in terms of low treatment completion rates.⁴–⁶ Currently, prospective observational studies are ongoing to provide further insight into local TB epidemiology, including microbiological resistance patterns. Alarmingly, patients reported repeated drug stock-outs of first-line TB medication. In addition, drugs against resistant *Mycobacterium tuberculosis* are neither provided by the NTP, nor readily available in the country.

The context of repeatedly interrupted drug supply of first-line antituberculous drugs at the public TB clinics, together with the unavailability of second-line TB drugs through the NTP prompted us to conduct interviews with local health officials in order to better understand the current situation as a prerequisite for health care improvement.

© The Author 2014. Published by Oxford University Press on behalf of Faculty of Public Health. All rights reserved. For permissions, please e-mail: journals.permissions@oup.com.
Methods

During 2012 and 2013, semi-structured interviews with drug shop vendors (n = 3; drug shops are locally called ‘depos pharmaceutiques’) and were operated without a trained pharmacist), pharmacists (n = 3), TB clinic nurses (n = 2) and medical doctors including infectious disease experts in the field (n = 5) were conducted in Mouila, Lambaréné and Libreville, Gabon. In Lambaréné, capital of the province of Moyen-Ogooué, interviews in all pharmacies and drug shops were performed; in Mouila, capital of the province Ngounié, and in Libreville, the country’s capital, interviews were performed in the leading pharmacy. Topics of the interviews covered the general perception of the national TB burden, the performance of local TB management including diagnosis and treatment, drug availability and procurement, drug stock-outs and prices of first- and second-line TB drugs.

Results

First-line TB drugs

All drug shop vendors and pharmacists reported that in periods of drug stock-outs at the public TB clinics, up to 10 patients per week presented to pharmacies in Mouila and Lambaréné, whereas up to 50 patients per day presented to the main pharmacy in the capital, Libreville. Most often the stock-outs only affected certain components of the first-line combination therapy, yet sometimes the complete TB treatment package was unavailable for purchase.

All pharmacies and all but one drug shop had TB drugs for sale. Altogether the available single drugs or combination drugs traded were as follows: Rifater® [rifampicine/isoniazid/pyrazamid (RHZ)], Rifinah® (RH), Rifadine® (R), Rifadine suspension® (R), Rimifon® (H), Pirilene® (Z), Myambutol® [ethambutol (E)], Dexambutol® (E) and streptomycin (S). The cheapest four drug initiation phase regimen (RHZE) costs 72 770 CFA (€111) per month, whereas the cheapest two drug continuation phase regime (RH) costs 46 300 CFA (€71) per month (Table 1). Although the gross national income per capita is relatively high in Gabon (10 650 USD per capita in 2013), important inequalities exist, as illustrated by the high poverty headcount (32.7% living below the national poverty line in 2013), important inequalities exist, as illustrated by the high poverty headcount (32.7% living below the national poverty line in 2013). It is well known that TB causes the highest burden among the poorest; therefore, also the poorest population will be mostly affected by the consequences of drug stock-outs. If patients could not pay the whole prescription, they were given parts of the drug regimen they could afford. Pharmacies and drug shops outside the capital reported difficulties in obtaining TB drugs because pharmacies in Libreville being stocked first. Consequently, during stock-outs, patients have been forced to travel to the capital to buy their drugs or were left without access to treatment, regardless of drug affordability.

Diagnosis of and treatment for drug-resistant TB

According to national TB guidelines, patients with suspected resistant TB should be referred to the national reference hospital, however, national diagnostic or treatment algorithms for multi-drug-resistant TB (MDR-TB) do not exist. The diagnosis of resistant TB is based solely on history and clinical grounds as only smear microscopy is available. Patients referred for resistant TB may be treated with first-line antituberculous drugs including streptomycin. All doctors and nurses interviewed knew numerous patients in need of second-line drugs who were left without any treatment in the field.

Table 1 Availability and prices of tuberculosis drugs in the private sector, Gabon.

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Cheapest price per month* CFA (euro)</th>
</tr>
</thead>
<tbody>
<tr>
<td>First-line TB drugs (available in drug shops and/or pharmacies)</td>
<td></td>
</tr>
<tr>
<td>RHZE</td>
<td>72 770 (111)</td>
</tr>
<tr>
<td>Streptomycin</td>
<td>15 655 (23)</td>
</tr>
<tr>
<td>Second-line TB drugs (available in drug shops and/or pharmacies)</td>
<td></td>
</tr>
<tr>
<td>Levofloxacin (1000 mg/d)</td>
<td>62 000 (94)</td>
</tr>
<tr>
<td>Ofloxacin (800 mg/d)</td>
<td>68 200 (104)</td>
</tr>
<tr>
<td>Imipenem (2 g/d)</td>
<td>1 178 000 (1798)</td>
</tr>
<tr>
<td>Clarithromycin (1 g/d)</td>
<td>62 000 (95)</td>
</tr>
<tr>
<td>Ciprofloxacin (1 g/d)</td>
<td>54 250 (83)</td>
</tr>
<tr>
<td>Amoxicilline/clavulanate 3 g/d</td>
<td>116 925 (180)</td>
</tr>
<tr>
<td>Amikacin</td>
<td>Price unavailable</td>
</tr>
</tbody>
</table>

*Prices were calculated for an adult patient of 70 kg.

**RHZE is not available as fixed dose combination, price pieced together.

**Drugs fall under the regulations for hospital use only.
the only second-line/third-line drugs in stock (Table 1). Linezolid, ethionamide, cycloserine, moxifloxacin and kanamycin could be ordered from overseas if the hospital’s pharmacists ordered the drug following the regulations for medications reserved for hospital use only (Table 1). Ordered drugs would be shipped with maritime freight, and taxes would be added when passing customs. Pharmacists with this import expertise were often unavailable in the hospitals. Capreomycin, para-aminosalicylic acid, clofazimine, terizidine, prothionamide and thiacetazone were inaccessible for pharmacists (Table 1). As the newly introduced national medical insurance does not cover any TB-related costs and the NTP does not provide second-line TB drugs, patients are forced to cover the full costs for second-line treatment, including hospitalization and consultation fees summing up to several thousands of euros.

**Discussion**

Although the rate of new TB cases has been falling worldwide for about a decade, the African WHO region is not on track to achieve the mortality and prevalence targets set for 2015 and worldwide progress toward the targets for diagnosis and treatment of MDR-TB is far off-track. The important deficiencies in TB control revealed are not only translating into high morbidity and mortality of TB patients. Limited availability of first-line TB drugs lead to spread of TB and emergence of MDR-TB. Unavailability of diagnostics and drugs for MDR-TB leads to increased transmission of resistant strains in families, communities and hospital wards. MDR-TB and extensively drug-resistant tuberculosis (XDR-TB) have been reported from Gabon, and 2.5 and 10% of new and retreatment cases are estimated to be MDR-TB, yet there is a general absence of accessible diagnostic and management means to identify and treat resistant TB.

Reducing drug shortages is only one of the challenges in the quest for improved patients’ access to TB care. Gaps within health system capacity to deliver care beyond continuous provision of free TB medication need to be closed; these include strengthening and integrating decentralized TB/HIV clinics, improve counseling, diagnostics and retention in care and develop reliable TB surveillance and systematic data collection.

However, the situation in Gabon as analyzed in detail here, with the purpose of facilitating appropriate, target-oriented action to amend the situation, only exemplifies a problem that is not confined to the Central African region. Extrapolating from this concrete example, this is a call for national and international action to widely increase TB diagnostic capacities across the areas still most in need and to reinforce public health structures to optimize the functioning of TB control programs. Commitment is needed to improve effective pharmaceutical management of first-line and second-line TB drugs. Furthermore, novel MDR-TB drugs such as bedaquiline or delamanid ought to be carefully integrated into TB programs as not to spoil their efficacy.

**Acknowledgement**

We thank all interview partners for their participation.

**Funding**

No specific funding was obtained for this study. SB was funded by a PANACEA EDCTP grant, Project ID 1P2007.32011.013.

**References**


