Combining user fees exemption with training and supervision helps to maintain the quality of drug prescriptions in Burkina Faso

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Accepted 20 July 2012

To improve access to health care services, an intervention was implemented in Burkina Faso granting full exemption from user fees. Two further components, staff training and supervision, were added to support the intervention. Our aim in this study was to examine how this tripartite intervention affected the quality of drug prescriptions.

Using a mixed methodology, we first conducted an interrupted time series over 24 months. Nine health centres were studied that had previously undergone a process analysis. A total of 14 956 prescriptions for children 0–4 years old were selected by interval sampling from the visit registries from 1 year before to 1 year after the intervention’s launch. We then interviewed 14 prescribers. We used three World Health Organization (WHO) indicators to assess drug prescription quality. Analysis was carried out using linear regression and logistic regression. The prescribers’ statements underwent content analysis, to understand their perceptions and changes in their practice since the subsidy’s introduction.

One effect of the intervention was a reduced use of injections (odd ratio (OR) = 0.28 [0.17; 0.46]) in cases of acute lower respiratory tract infections (ALRTI) without comorbidity. Another was a reduction in the inappropriate use of antibiotics in malaria without comorbidity (OR = 0.48 [0.33; 0.70]). The average number of drugs prescribed also decreased (coefficient = −0.14 [−0.20; −0.08]) in cases of ALRTI without comorbidity. The prescribers reported that their practices were either maintained or improved.

The user fees exemption programme, combined with health staff training and supervision, did not lead to any deterioration in the quality of drug prescriptions.

Keywords User fees, exemption, intervention, quality, drug prescriptions

KEY MESSAGES

- The intervention, which combined free access to medications, training and supervision, did not produce any deterioration in drug prescription practices.
- These results should encourage health authorities in African countries to implement such interventions in their countries.
Introduction

Many studies in developing countries have shown drug prescription practices to be suboptimal (WHO 2009), seen particularly in the lack of respect for established treatment protocols. Inappropriate prescription practices such as over-prescribing and unnecessarily prescribing antibiotics and injections seem to occur more often when drugs are easily available (Mallet et al. 2001; Cheraghali et al. 2004). Some studies have shown that prescribers tend to make more inappropriate prescriptions when they profit from the sale of drugs (Trap and Hansen 2002) and fewer inappropriate prescriptions when the costs are paid by patients (Holloway 2001). In cases where drugs are available and exempt from payment, two mechanisms can arise. First, in some countries, the prescribing personnel receive bonuses corresponding to a certain percentage of the consultation fees. They also receive benefits based on profits from the sales of drugs to users. There are thus direct financial incentives for prescribing more drugs, and drugs that are of a higher grade and in more expensive therapeutic forms. Second, patients’ demand for certain therapeutic forms such as injections may be heightened by the removal of financial constraints. Prescribers would therefore be more inclined to make inappropriate prescriptions because of this lack of financial constraint.

Consequently, the question arises as to whether user fees exemption interventions could have potentially negative impacts on the quality of drug prescriptions. Similar fears have been expressed by the health authorities of some countries. They worry that these interventions could have a pernicious effect, or more specifically, that allocated resources could be wasted through non-rational use of drugs by prescribers (Meesen 2009; LSHTM 2010; OMS et al. 2010). To date, the literature provides no factual data on the effects of user fees exemption interventions on the quality of drug prescriptions (Ridde and Morestin 2010). Studies on the effects of user fees exemption interventions have looked at quality of care or perception of quality and have not specifically addressed the appropriateness of prescription practices.

The aim of this study was to examine the effects on drug prescription of a tripartite intervention that provided free services to children ages 0–4 years and that incorporated training and supervision of the prescribing health workers. In particular, the analysis attempted to verify whether lifting the financial barrier in a context where drugs are available in a health facility is really likely to lead to a deterioration in the quality of drug prescriptions.

The intervention

In the north-east region of Burkina Faso, in Dori health district, an Non governmental organization (NGO) implemented an intervention targeting children aged 0–4 years. This intervention had three components: (i) free access to medications through the abolition of all user charges for drugs and visits to health care facilities; (ii) training for health professionals on the use of the national Diagnostic and Therapeutic Guidelines (DTG); and (iii) monthly supervision in every health facility (Ridde et al. 2012). Before the intervention, patients admitted to the centre were charged US$0.12 for the consultation. To this administration used the revenues from drug sales to purchase new drugs every month. Each month the health workers received a bonus corresponding to 20% of the consultation fees. The profits from drug sales were applied to the centre’s operations, which included purchasing fuel and repairing the motorcycles of health workers. These were marginal benefits.

The intervention was launched in September 2008 with the agreement of the health authorities. We hypothesized that the concurrent training and supervision activities would protect the quality of prescriptions and counterbalance any potential incentives to over-prescribe or to prescribe in ways that did not respect existing standards.

Method

The study focused on the population of children aged 0–4 years targeted by the intervention (receiving free care). We used a mixed-method design that was primarily quantitative with a nested qualitative component (Creswell and Plano Clark 2007).

Quantitative component

This component consisted of measuring the effects of the user fees exemption intervention on the quality of drug prescription. The outcomes indicators were those recommended by WHO and INRUD (International Network for the Rational Use of Drugs) (WHO 1993): (i) the presence or absence of an antibiotic in the prescription; (ii) the presence or absence of an injectable product in the prescription; and (iii) the number of drugs per prescription (continuous variable). These indicators have been used in other similar studies related to drug practice (Van der Geest and Hardon 1988; Hazra et al. 2000; Maïga et al. 2003; Keohavong et al. 2006; Mouala et al. 2008).

The design was based on an interrupted time series. The window of observation covered 24 months, from September 2007 to August 2009. The variable of interest was the intervention (dichotomous variable emerging in the 13th month of the series). The observation month (1 to 24) was used to take into account the secular trend. Nine primary care health centres (CSPS) were selected that represented the Dori health district’s cultural and socio-economic diversity. The sources of data were the centres’ registries. In each centre, on a monthly basis, we drew a random sample of visit registrations for children in the target population (0–4 years). This was a systematic sampling. Information on the child’s condition and the drugs prescribed (nature and quantity of drugs, diagnosis, existence of a comorbidity, age) was extracted by a team of surveyors trained for this purpose. Rather than a selection, the entire population of prescriptions for children 5–10 years old who met the inclusion criteria were taken into account in the study, due to their small numbers.

To reduce the heterogeneity of the observations and facilitate data interpretation, we restricted the study to a limited number of diagnoses for which treatment protocols were available to the health workers. The cases included were children consulting for simple malaria or acute lower respiratory tract infection (ALRTI), the most common diagnoses in the region and the reasons for the great majority of visits. In 2008, malaria and ALRTI represented, respectively, 47% and 9% of diagnoses for
children under 5 years old (Ministère de la Santé 2008). We excluded upper respiratory tract infections (URTI) because they were poorly reported in the registries and their diagnoses were imprecise. Moreover, in this setting, parents rarely bring their children in for consultation for URTI. In Burkina Faso, URTI accounted for only 2.2% of the reasons for consultation in 2008.

Based on the diagnosis and the presence of a comorbidity, cases were grouped into four categories: (i) simple malaria without comorbidity; (ii) malaria associated with diarrhoea or ALRTI; (iii) ALRTI without comorbidity; or (iv) ALRTI associated with diarrhoea or malaria. When ALRTI was associated with malaria it was counted both in ‘malaria and comorbidity’ and in ‘ALRTI and comorbidity’. Table 1 presents the treatment protocols used by health workers to treat these cases.

To better understand the natural evolution of the prescription practices of health workers in the centres, we decided to include an analysis of how prescribing had evolved in another age group not targeted by the intervention, children aged 5–10 years. These children were received and treated during the same observation period, by the same prescribers and in the same health centres. In this way, we were able to compare prescription practices for children receiving free care, and for whom there could be incentives for over-prescribing, with children whose care was not free.

We determined the appropriateness of the prescription with respect to the three criteria by comparing the prescription with indications provided in the DTG (Table 1). Thus, for example, antibiotherapy is not indicated for malaria without comorbidity. Prescribing an antibiotic in such a case would constitute an inappropriate prescription. Antbiotherapy is always indicated for ALRTI.

We used hierarchical multiple regressions adapted to time series to estimate the effects of the intervention (Shadish et al. 2002). We used the XTREG and XTLOGIT functions in the Stata 9® software (StataCorp 2005). Variables included in the models were: the characteristics of the prescription, the diagnosis and the presence or absence of comorbidities (first level variables), the month (second level), and the health centre (third level). Models included an interaction term between intervention and comorbidity, in order to explore the existence of distinct effects of the intervention according to the severity of cases.

The equation used in the modelling was:

\[
L(Y) = \exp\alpha + \beta_1\text{INTERV} + \beta_2\text{MO} + \beta_3\text{COM} + \beta_4\text{COM}^*\text{INTERV} + e_1 + e_2 + e_3
\]

\(L\) = Link function. Logistical function for the dependent variables \(Y\): use of antibiotics and use of injections. Linear function for the dependent variable \(Y\): number of drugs per prescription. 
\(\alpha\) = intercept
\(\exp\) = exponent
\(\beta\) = coefficient
\text{INTERV} = presence of intervention (0,1)
\text{MO} = month (from 1 to 24)
\text{COM} = presence of comorbidity (0,1)
\(e\) = error term

### Qualitative component

The study included a qualitative component to complement and facilitate the interpretation of the results of the quantitative component. The data collection was carried out in parallel with the quantitative data collection.

All the prescribing health care workers of the nine CSPSs who had been in service for more than a year were invited to participate. These were nurses and itinerant health workers, all prescribers. Fourteen participants were individually interviewed; each of the nine CSPSs was represented by at least one participant. Using a pre-tested semi-structured interview guide, the interviews dealt with the changes perceived in prescription practices since the start of the intervention. The interviews were all conducted in French and were carried out between 15 July and 30 August 2009.

The interviews were transcribed and condensed with closed coding, using a coding grid based on the interview guide (Lessard-Hébert et al. 1996). Qualitative Data Analysis (QDA)–Miner® software was used for the analysis. The results were interpreted by referring to the related quantitative results.

This study was approved by the research ethics committee of the University of Montreal and of Burkina Faso. Participants provided informed consent to the interviews with a signed consent form. Confidentiality and anonymity were assured.

### Table 1: Treatments corresponding to the diagnoses according to Burkina Faso’s Diagnostic and Therapeutic Guidelines (Ministère de la Santé 2003)

<table>
<thead>
<tr>
<th>Group of conditions</th>
<th>Pathology</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute lower respiratory tract</td>
<td>Bronchitis</td>
<td>Co-trimoxizole or Amoxicillin + Paracetamol</td>
</tr>
<tr>
<td>infections</td>
<td>Pneumonia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bronchopneumonia</td>
<td></td>
</tr>
<tr>
<td>Diarrhoeas</td>
<td>Amoebic dysentery: muculent bloody</td>
<td>Metronidazole + ORS</td>
</tr>
<tr>
<td></td>
<td>diarrhoea without fever</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bacillary dysentery: muculent bloody</td>
<td>Co-trimoxizole or Amoxicillin + ORS</td>
</tr>
<tr>
<td></td>
<td>diarrhoea with fever</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Febrile gastroenteritis: non-bloody</td>
<td>Etiological treatment (malaria, for example) + ORS</td>
</tr>
<tr>
<td></td>
<td>watery diarrhoea</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Toxic dietary infection (notion of</td>
<td>Carbon + ORS + Co-trimoxizole (if fever)</td>
</tr>
<tr>
<td></td>
<td>food infestation)</td>
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<tr>
<td></td>
<td>Digestive candidiasis</td>
<td>Nystatin</td>
</tr>
<tr>
<td>Malaria</td>
<td>Simple malaria</td>
<td>ACT + Paracetamol</td>
</tr>
</tbody>
</table>

Notes: ORS = Oral rehydration salts; ACT = Artemisinin-based combination therapy.
Results
In total, 14,956 prescriptions for children aged 0–4 years and 4,282 prescriptions for children aged 5–10 years (control group) were collected for analysis. For the qualitative component, 14 of the 33 agents approached agreed to be interviewed. Table 2 presents the distribution of cases according to morbidity in both groups.

Figures 1, 2 and 3 illustrate the evolution of drug prescription indicators over the 24 months of observation as well as the predictive values based on the analysis models. With regard to Figure 2(b), in the case of malaria with comorbidity, the start of the intervention was followed by a clear reduction in the use of injections. The increasing trend over time existed before the intervention and seemed to continue after the intervention. We can conclude that there was no change in the trend, but a beneficial effect of the intervention. However, this effect was not statistically significant. In the case of malaria without comorbidity, we saw an increasing trend in the use of injections, which continued after the intervention. The intervention did not appear to have an effect since the increase was not statistically significant. Overall, these figures show no obvious visual changes in prescription practices since the start of the intervention.

Figure 4 shows the evolution of indicators of drug prescribing for prescriptions for children aged 5–10 years in cases of malaria and ALRTI without comorbidity. No obvious visual change is observed during the study period.

For the prescription group of children aged 0–4 years, in eight of the 11 reported odds ratios (OR) and coefficients, no association was found between the intervention and drug prescription practices (Table 3). In three cases, there was a significant association. There were some significant interactions between the intervention and the presence of comorbidity. In fact, changes attributable to the intervention were observed only in the absence of comorbidity. In the presence of comorbidity, no significant changes were observed. The intervention was observed to be associated with a reduction in inappropriate use of antibiotics in malaria without comorbidity (OR = 0.48; P < 0.0005). It was also associated with a reduction in the use of injectable products (OR = 0.28; P < 0.005) and in the number of drugs per prescription (coefficient = −0.14; P < 0.005) in the case of ALRTI without comorbidity.

For the prescription group of children aged 5–10 years, the post-intervention period was associated with an increase in the use of injectable products and a slight increase in the number of drugs per prescription (Table 3).

Prescribers’ perceptions regarding changes in their practices
We did not observe any consensus among prescribers regarding the evolution of their drug prescription practices.

Health worker (HW)-1: “Now it is easier for us to prescribe. If the treatment is for a week, I don’t hesitate; I prescribe the molecules for a week. In the past, I had to prescribe for 5 days if the patient didn’t have the means to cover a whole week’s dose.”

HW-3: “Our prescribing hasn’t changed, in the sense that we are required to follow the flow chart in the DTG, whether it’s free or not.”

However, the positive effects of the training and supervision were very much highlighted by the people we interviewed.

HW-5: “For example, a child who comes with malaria... me, for example, I used to include an antibiotic. But in the supervision they said there was no point in putting in an antibiotic systematically.”

HW-12: “The training we received improved how we prescribe.”

Finally, some prescribers perceived an increase in their workload related to this intervention. According to them, this state of affairs could negatively affect the quality of their prescriptions.

HW-3: “Well, the fact that drugs are free has made our work very, very intensive because not many people came here before. Now lots of people come.”

Discussion
Analyses of prescriptions for children aged 0–4 years showed that the intervention induced prescribers to maintain or improve their practices. These positive effects were seen in cases of malaria and of ALRTI without comorbidity. No effect was observed when there was comorbidity present.

These results are comparable to those of some evaluations of interventions aimed at improving the quality of drug prescriptions. These were interventions based on training and
supervision, which are two of the three components of the intervention implemented in Burkina Faso. Also, the diagnoses considered in these studies were not exactly the same as those used in our study. Studies in Indonesia (Santoso et al. 1996), Zambia (Bexell et al. 1996), Brazil, Uganda and Tanzania (Gouws et al. 2004) showed a reduction in the use of antibiotics. In Yemen (Walker et al. 1990) and Indonesia (Hadiyono et al. 1996), there was a reduction the use of injectables. In India (Chaudhury et al. 2005) the number of drug prescriptions decreased. Evaluations of interventions in Zimbabwe (Trap et al. 2001), elsewhere in Zambia (Bexell et al. 1996) and in Kenya (Tumwikirize et al. 2004) revealed better adherence of treatment to national therapeutic guidelines.

We noted a lack of consensus in the prescribers’ statements about changes in their practices since the start of the intervention. The prescription practices they adopted varied depending on whether or not they were dealing with children targeted by the intervention. From their statements, it was clear that supervision and training enabled some of them to adopt better practices. Even though the intervention had the effect of increasing demand for services (Ridde et al. 2012), the issue of the negative effect of workload on practices did not appear to be justified. Indeed, there was no sign of any negative effect.

The results were somewhat different in the group of children aged 5–10 years, where the intervention appeared to be associated with maintenance or deterioration of drug prescription practices. These results reinforced the notion that the intervention had a positive effect. Still, it is not clear why the prescribers seemed to deviate from prescription norms after the start of the intervention when dealing with children not targeted by the intervention.

Figure 1 Evolution of prescriptions for antibiotics and injectables in the case of ALRTI for children ages 0–4 years.

(a) Antibiotics

ATB with com: values observed in the use of antibiotics in the case of ALRTI without comorbidity
Pred_ATB with com: values predicted according to the analysis model in the case of ALRTI without comorbidity
ATB without com: values observed in the use of antibiotics in the case of ALRTI with comorbidity
Pred_ATB without com: values predicted according to the analysis model in the case of ALRTI with comorbidity

(b) Injections

INJ without com: values observed in the use of injections in the case of ALRTI without comorbidity
Pred_INJ without com: values predicted according to the analysis model in the case of ALRTI without comorbidity
INJ with com: values observed in the use of injections in the case of ALRTI with comorbidity
Pred_INJ with com: values predicted according to the analysis model in the case of ALRTI with comorbidity.
Some actors have warned of the potential for decline in drug prescription quality in interventions that abolish user fees for drugs. However, our study shows that if these interventions include training and supervision components, the quality of drug prescription can be maintained.

There is a need for new studies in the field of evaluation to examine the effects of interventions to abolish user fees that are either associated or not with supervision and training. First, there is a need for a qualitative study to better understand the perceptions of changes in prescription practices observed after the intervention. Second, a study on quality of care in its broader sense that would take into account the entire consultation process would make it possible to examine some aspects that our study could not uncover, such as accuracy of diagnosis.

**Limitations**

With regard to the external validity of our study, the intervention evaluated here was implemented as part of a pilot project under supportive conditions that may not necessarily exist in a large-scale intervention. Caution is therefore advisable in attempting to generalize from the results of such a study. In terms of statistical validity, having more observation points could have provided more robust estimates and greater statistical power for assessing changes that might be attributable to the intervention. Drug availability could be a potential confounding factor, but we did not measure it because the health centres did not have up-to-date documentation about the management of drug stocks. However, prescribers noted that drug availability had been good since the beginning of the intervention. This may be explained by the rapidity of reimbursement (about 33 days). Patient attendance could also be a confounding factor, but we excluded it from the model at the outset because of a high correlation with the intervention. The duration of prescriptions such as for antibiotics could have been modified by the intervention. We did not measure duration because this information was not available in the registries.

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**Figure 2** Evolution of prescriptions for antibiotics and injectables in the case of malaria for children ages 0–4 years.

(a) Antibiotics

ATB$_{with\ Com}$: values observed in the use of antibiotics in the case of malaria without comorbidity

Pred$_{ATB\ with\ Com}$: values predicted according to the analysis model in the case of malaria without comorbidity

(b) Injections

INJ$_{without\ Com}$: values observed in the use of injections in the case of malaria without comorbidity

Pred$_{INJ\ without\ Com}$: values predicted according to the analysis model in the case of malaria without comorbidity

INJ$_{with\ Com}$: values observed in the use of injections in the case of malaria with comorbidity

Pred$_{INJ\ with\ Com}$: values predicted according to the analysis model in the case of malaria with comorbidity.
In addition, only one dimension of quality of care was considered here; this study did not assess the quality of the clinical exam nor the appropriateness of the diagnosis reached. In fact, the diagnoses are reported as recorded in the registries by the prescribers. Also, the 5–10 years age group is not really a completely comparable control group for the 0–4 years age group. Results should therefore be interpreted with caution.

Upper respiratory tract infections were excluded from the study because of the poor quality of the data for them. They would have provided a better picture of abusive use of antibiotics, since they require fewer antibiotics compared to lower respiratory tract infections.

Finally, because the three components of the intervention were intertwined and simultaneously implemented, it was not possible to disentangle the respective effects of the free access to medication, the training activities and the supervision.

**Conclusion**

This tripartite intervention, which combined free access to medications, training and supervision, did not produce any deterioration in drug prescription practices. The combination of these three components seems to have maintained and even improved prescription practices. Likewise, the exemption from user fees had a major effect on demand in this intervention, as elsewhere. These results should encourage health authorities in African countries to implement such interventions in their countries.
Figure 4  Evolution of drug prescribing indicators for children ages 5–10 years in cases of malaria and ALTRI without comorbidity.
(a) Antibiotics
ATB_ALTRI: values observed in the use of antibiotics in the case of ALTRI without comorbidity
ATB_malaria: values observed in the use of antibiotics in the case of malaria without comorbidity

(b) Injections
INJ_ALRTI: values observed in the use of injections in the case of ALRTI without comorbidity
INJ_malaria: values observed in the use of injections in the case of malaria without comorbidity

(c) Average number of drugs per prescriptions
Nbr_ALRTI: average number of drugs observed in the case of ALRTI without comorbidity
Nbr_malaria: average number of drugs observed in the case of malaria without comorbidity.
Table 3 Changes in prescriptions in the post-intervention period for children ages 0–4 years and for children ages 5–10 years

<table>
<thead>
<tr>
<th>Outcome indicator</th>
<th>Diagnosis</th>
<th>Assessment parameter (c)</th>
<th>Effect measure Condition (comorbidity) for children ages 0–4 years</th>
<th>Effect measure Condition (comorbidity) for children ages 5–10 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Without comorbidity</td>
<td>With comorbidity</td>
</tr>
<tr>
<td>Presence of antibiotics</td>
<td>Malaria (a)</td>
<td>Odds ratio</td>
<td>0.48** [0.33; 0.70]</td>
<td>n.a. [0.78; 1.99]</td>
</tr>
<tr>
<td></td>
<td>ALRTI (b)</td>
<td>Odds ratio</td>
<td>1.93 [0.66; 5.62]</td>
<td>1.32 [0.22; 7.69]</td>
</tr>
<tr>
<td>Presence of injectables</td>
<td>Malaria (b)</td>
<td>Odds ratio</td>
<td>1.22 [0.85; 1.71]</td>
<td>0.62 [0.32; 1.16]</td>
</tr>
<tr>
<td></td>
<td>ALRTI (b)</td>
<td>Odds ratio</td>
<td>0.28** [0.17; 0.46]</td>
<td>0.81 [0.36; 1.81]</td>
</tr>
<tr>
<td>Number of drugs prescribed</td>
<td>Malaria (b)</td>
<td>Coefficient (Linear regression)</td>
<td>0.03 [-0.009; 0.08]</td>
<td>0.002 [-0.05; 0.05]</td>
</tr>
<tr>
<td></td>
<td>ALRTI (b)</td>
<td>Coefficient (Linear regression)</td>
<td>-0.14** [-0.20; -0.08]</td>
<td>0.019 [-0.04; 0.084]</td>
</tr>
</tbody>
</table>

Notes:
(a) Variables in the model: intervention, month.
(b) Variables in the model: intervention, month, comorbidity, comorbidity*intervention.
(c) Variables in the model: intervention, month, comorbidity
n.a. = Non-applicable. In the case where only the inappropriate use of antibiotics is of interest, only cases of malaria without comorbidity are taken into account.
** Statistically significant results.

Table 4 Sample sizes of prescriptions per month

<table>
<thead>
<tr>
<th>Months</th>
<th>Children aged 0–4 years</th>
<th>Children aged 5–10 years</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Episodes of malaria</td>
<td>Episodes of ALRTI</td>
</tr>
<tr>
<td>1</td>
<td>387</td>
<td>119</td>
</tr>
<tr>
<td>2</td>
<td>636</td>
<td>291</td>
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<td>3</td>
<td>345</td>
<td>291</td>
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<td>5</td>
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<td>6</td>
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<td>440</td>
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</tbody>
</table>

Acknowledgements
We wish to thank the NGO Hilfe zur Selbsthilfe e.V. (HELP), the Sahel Regional Department of Health, the health workers in the Dori Health District and Mr Rolf Heinmuller for their collaboration. Valéry Ridde is a New Investigator of the Canadian Institutes of Health Research. Our thanks also to Donna Riley for translation and editing support for this article.

Funding
Funding was received from the Humanitarian Aid service of the European Commission (ECHO) and the the University of Montréal Grant for Master Student.

Conflicts of interest
The NGO HELP is responsible for the intervention we evaluated and also participated in funding the evaluation.

References
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Note: (a) Variables in the model: intervention, month.
(b) Variables in the model: intervention, month, comorbidity, comorbidity*intervention.
(c) Variables in the model: intervention, month, comorbidity
n.a. = Non-applicable. In the case where only the inappropriate use of antibiotics is of interest, only cases of malaria without comorbidity are taken into account.
** Statistically significant results.