INTRODUCTION

An extensive literature on treatment seeking for malaria and fever in sub-Saharan Africa demonstrates that medicine sellers are a widely used source of drugs for fever and malaria. The proportion of caregivers visiting shops during recent childhood illness ranged from 15% to 83%, with a median across studies of approximately 50%. For example, on the Kenyan coast, shop-bought medicines were used first, or solely, in 69% of childhood fevers treated. In Togo, only 20% of children less than five years of age with fever were seen at a health center, and 83% were treated at home with an antimalarial drug obtained from a street or market vendor. Medicine sellers are common in both rural and urban areas, among children and adults, and across socioeconomic groups.

Medicine sellers are generally closer to homes than formal facilities. For example, in coastal Kenya, 87% of rural households live within 1 km of a shop, but only 32% live within 2 km of a government dispensary or private clinic. Moreover, their service is faster, and their weekly opening hours may be twice as long as those in health facilities. Because drug stock-outs are common in public facilities, medicine sellers form an important alternative supply, and their staff are often perceived as more friendly and approachable. Finally, cost is an important motivation. In some settings, patients pay less at medicine sellers than at formal facilities, reflecting the lack of fees for consultation or diagnostic tests, illicit charges at some facilities, and the fact that sub-optimal drug doses can be purchased. Credit may also be more easily obtained at retail outlets. Even where inexpensive or free drugs are available at facilities, people may patronize medicine sellers to avoid the travel and time costs involved in accessing formal care.

However, concerns surround the appropriateness of drugs and information that medicine sellers provide. Often the type or dose of medicine is inappropriate for the complaint. In a baseline survey in Kenya, only 4% of children given store-bought chloroquine received an appropriate dose and only 2% received this dose over the recommended three-day period. Aspirin was widely used, although it is not recommended for children, with 22% receiving potentially toxic doses.

Polypharmacy may also be widespread, where providers prescribe additional unnecessary drugs such as antibiotics. Moreover, drugs may be of sub-standard quality because of poor manufacture and storage. Finally, in the new era of artemisinin-based combination therapy (ACT), there is concern that medicine sellers may continue to sell artemisinin derivatives alone (monotherapies), potentially jeopardizing ACT efficacy in the long-term.

The literature on malaria-related treatment seeking from medicine sellers has been well reviewed and summarized, but to date there has been no corresponding review of their characteristics and operations, despite increasing interest and experience in interventions to improve the care received. The World Health Organization now advocates strategies to improve home-based management of malaria, with retailer interventions seen as one possible channel, and international meetings addressing the topic have been held recently in Ghana and Uganda. Timely and appropriate treatment of children less than five years of age is particularly important in preventing mortality and curtailing morbidity. The Roll Back Malaria (RBM) Partnership has set a target of 80% receiving appropriate treatment within 24 hours by 2010, but in 2003 only 42% received any antimalarial drugs. It is increasingly recognized that medicine sellers can have a role in scaling-up coverage of appropriate malaria treatment, and their role could potentially extend to the provision of ACTs.
METHODS

Definition of medicine sellers. For the purposes of this review, medicine sellers were defined to include all commercial retailers selling fever/malaria drugs, except formal pharmacies that are required to be staffed by a qualified pharmacist. Medicine sellers are variously known as drug sellers, chemical sellers, and patent medicine vendors (PMVs), and operate in specialist drug shops as well as general shops, kiosks, and market stalls, and as itinerant hawkers. Such outlets are not permitted to stock prescription-only medicines, but in some cases are allowed to sell over-the-counter (OTC) products, such as cough syrups, painkillers, and some antimalarial drugs. No professional consultation is required for purchase, and staff are not required to be fully qualified pharmacists. We focused on these outlets because they are the most accessible and widely used, although many similarities can be recognized with the operation of some formal pharmacies, which are not always staffed by appropriate personnel, and with some basic private clinics.

Search strategy. We first identified papers on the practices of medicine sellers in sub-Saharan Africa, including studies focusing on antimalarial drugs and more general drug sales. Second, we identified all studies of interventions to improve the delivery of malaria-related treatment services involving medicine sellers in sub-Saharan Africa. The intervention review was based on a RBM commissioned report by Brieger, Unwin, Greer, and Meek. Malaria-related was defined to include fever and malaria because most malaria diagnoses in the region are based on febrile symptoms alone.

Internet searches using PubMed formed the first level of inquiry, using search terms related to the three inclusion criteria: medicine sellers, sub-Saharan Africa, and malaria. Because most work in this area has been done relatively recently, much is not yet formally published. Key terms were therefore used in general search engines, and gray literature libraries were searched. Personnel in various health and development agencies operating in Africa were contacted to identify additional studies. Finally, the team obtained contact information about each intervention project and made direct inquiries to fill gaps in project descriptions. Attempts were made to identify interventions continent-wide, but it is possible that there was some degree of anglophone bias in the search strategy.

RESULTS

Characteristics and operation of medicine sellers. A range of studies have looked specifically at the retail supply of antimalarial drugs in sub-Saharan Africa, and others have looked more broadly at the retail sector drug supply. The studies are roughly equally divided between rural and urban/peri-urban areas, with several covering both settings. Methods consisted mainly of structured questionnaires administered to sales staff, supplemented in some cases by in-depth interviews, undercover care-seekers, direct observation, outlet mapping, exit interviews, and household surveys.

There is considerable variation in retailer type across settings. In most areas, a limited range of drugs is sold by general grocery stores and kiosks, alongside a range of household goods such as soap powder, batteries, and cooking oil. In addition, in some areas of east and west Africa, a wider range of medicines is sold by small drug shops specializing in pharmaceuticals. In much of west Africa, itinerant vendors are important retail suppliers, although they are much less common in east and southern Africa. For example, in Ibarapa District in western Nigeria, medicine peddlers on motorcycles were found to provide the bulk of western health care to remote hamlets. In some settings, the drug seller market is extremely informal, including market traders with bowls of exposed tablets and capsules among which customers pick and choose, and hawkers wandering the streets, although most medicines are likely to be sold through more formal outlets.

The legal status of retailers varies, with each country having its own procedures and categories of licenses. Some operate entirely within the law, others are legal entities but perform some illegal activities, and others are completely illegal outlets. Because the legal boundaries for drug retailing vary across countries, a legal activity in one country may be considered illicit elsewhere. In some west African settings, retailers have formed trade associations, e.g., the Nigerian National Association of Patent and Propriety Medicine Dealers, founded in 1951, which requires prospective members to be inspected and interviewed. Such associations have not been documented in east or southern Africa, although medicine sellers may link with associations such as the Private Dispensers’ Association in Uganda, when they operate under the license of a qualified private dispenser.

Of medicine seller clients, a high proportion are seeking care for fever or malaria, with other common complaints being colds/flu, headaches and stomach aches, diarrhea, and sexually transmitted infections (STIs). Of those with fever, malaria, a small proportion are reported to have severe disease, for which greater use is made of formal health facilities, or in some cases traditional healers. However in Tanzania, medicine seller clients reporting fever were as likely as health facility clients to have parasitemia, indicating that the provision of effective antimalarial drugs is important for both groups.

Similarities across drug retailers can be noted, particularly in stocking patterns. Nearly all stock modern manufactured medicines only, an exception being the Amayeza stores in South Africa’s Eastern Cape Province, which also stock a wide range of traditional remedies. Retailers tend to sell a wide variety of painkillers/antipyretics and the first-line antimalarial drug, which at the time of most studies was chloroquine or sulfadoxine-pyrimethamine (SP). These drugs were generally available under their generic (non-proprietary) name and under a variety of brand names, with 30 different SP brands identified in rural Kenya. Other products regularly stocked include anthelmintics, antihistamines, antiprotozoal drugs, and cough and stomach ache remedies. Most drug stores stock prescription-only medicines illegally,
such as antibiotics and tranquilizers, which are often kept under the counter.\textsuperscript{15,18,19,54,59,60,63,64,68,77}

Information on medicine seller sales volumes is available from only two sources, both of which indicate that they can be significant. In rural Tanzania, medicine sellers accounted for 39\% of total antimalarial drug volumes provided in the community, mainly through specialist drug stores.\textsuperscript{20} General stores stocking antimalarial drugs sold a mean of 74 equivalent adult doses per year (worth $38) and drug stores 2,310 per year ($1,731).\textsuperscript{20} In Lagos, Nigeria more than $4,076 worth of antimalarial drugs were sold in a week in 343 shops in three neighborhoods.\textsuperscript{23}

Medicine sellers often store and handle drugs in inappropriate ways, keeping them in conditions of excessive heat, light, and moisture that may endanger their potency, and storing them in re-used, wrongly labeled containers.\textsuperscript{15,18,20,29,57} Poor quality antimalarial drugs on the private market have been identified through laboratory testing in Cameroon, Nigeria, Tanzania, Kenya, and Uganda.\textsuperscript{76–85} For example, of samples collected from illegitimate outlets in urban and rural areas of Cameroon, 12\% of anti-folates (including SP), 38\% of chloroquine, and 74\% of quinine samples had either no active ingredient, an insufficient active ingredient, the wrong ingredient, or an unknown ingredient.\textsuperscript{30} This may reflect poor manufacture, inadequate storage, and in some cases deliberate counterfeiting. Packaging and labeling of products are also highly inadequate. Labeling is often unclear, instructions are rarely given in the local language, measuring devices are not provided for syrups, and dosing information is often inadequate or in conflict with national treatment guidelines.\textsuperscript{57} Even those medicine sellers officially allowed to sell drugs are usually permitted to sell pre-packaged products only, but this regulation is frequently flouted; of antimalarial tablets dispensed in rural Tanzania, packaged tablets made up only 22\% of tablet sales volumes from medicine sellers.\textsuperscript{20} Moreover, where packaged medicines are stocked, they are sometimes broken up to sell individual pills.\textsuperscript{18}

In most encounters with their customers, medicine sellers simply sell what the customer requests. Few sellers are presented with a prescription from a trained health professional, nor do they request one prior to making a sale.\textsuperscript{15,18,19,46,54,59,60,65} However, some sellers give a considerable amount of advice on drugs and doses.\textsuperscript{65,86} In Uganda, many customers asked for such advice, and drug shop staff often made instant diagnoses and drug recommendations, operating as storefront clinics.\textsuperscript{19} Common information sources for shopkeepers are the radio, their wholesalers, and the instructions provided by manufacturers.\textsuperscript{20,46,50} However, medicine sellers rarely ask customers questions about the illness\textsuperscript{65} and vary widely in the amount, accuracy, and quality of information given on how to take the medicines.\textsuperscript{28,29,63,77,87} Instructions are often unclear,\textsuperscript{29} and misinformation is often provided.\textsuperscript{87} Preventive information is rarely shared with the customer.\textsuperscript{29,63} However, poor quality treatment is not limited to the retail sector; the performance of formal health facility workers is often also poor, with frequent selection of inappropriate drugs and incorrect dosages.\textsuperscript{88}

Education levels vary across medicine sellers, but most have little or no formal training in medicine or pharmacy. Drug shop staff may be untrained, or trained as medical assistants or nurses, perhaps with some experience in the formal health sector.\textsuperscript{19,20,49,59} In some cases, government health personnel work in drug stores as well.\textsuperscript{19} Even where the official owner or licensee has health-related qualifications, outlets are often staffed by less qualified assistants.\textsuperscript{59,64,65,88} Staff in general shops rarely have any training or relevant experience, and in Uganda many were illiterate.\textsuperscript{19,20}

Relatively little is known about the distribution chain to medicine sellers beyond their immediate sources. Retailers usually obtain drugs from general wholesalers or large retail or wholesale pharmacies, although mobile distributors operate in some settings.\textsuperscript{72,52,53,64,76,90,91} In Nigeria, sales representatives from pharmacies and pharmaceutical companies were the main source of drugs for medicine sellers in a peri-urban area.\textsuperscript{88} Retailers may use formal as well as informal channels, and some studies have reported significant quantities of smuggled drugs in shops,\textsuperscript{18,67} including those labeled for exclusive government use (Unwin A, unpublished data).

In Abia, Nigeria, low staff turnover rates were found among medicine sellers, with more than half of shop owners and/or attendants working in the same shop for at least 4 years, and almost a quarter for at least 10 years.\textsuperscript{32} In contrast, in east Africa the retail market appeared to be highly dynamic, with a significant proportion of sellers entering and exiting the business in any given year.\textsuperscript{20,93} For example in rural Tanzania, during a one-year period 29\% of general stores stocking drugs had closed down, and an additional 7\% remained open but no longer stocked drugs; these reductions were more than compensated for by new stockists.\textsuperscript{90} The most commonly cited reason for closing down was erosion of capital. However, such high rates of closure appeared less common among drug stores and general wholesalers.

Determinants of medicine seller behavior. The determinants of medicine seller behavior have received relatively little attention compared with descriptive work on their characteristics and operation. One would expect their behavior to be influenced by a range of factors: their knowledge and clinical skills, client expectations, profit margins, pharmaceutical company promotions, and local regulation.\textsuperscript{41,94} Studies show that medicine seller knowledge of drugs and doses is often poor. For example, among retailers in rural Tanzania, knowledge of signs and symptoms of malaria was adequate, but 90\% did not know precise chloroquine doses for children.\textsuperscript{50} In Nigeria, only 1 of 49 patent medicine vendor owners knew the correct dose of chloroquine for a three-year-old child.\textsuperscript{59} Inadequate medicine seller knowledge is likely to be exacerbated by the recent introduction of ACT in Sub-Saharan Africa because these have new dosage regimens, and more than one product may be available with different dosages. For example, in Nigeria 95\% of medicine sellers incorrectly considered artesunate monotherapy to be an ACT.\textsuperscript{72}

Another important determinant of provider behavior is medicine sellers’ beliefs about patients’ attitudes and preferences. For example, even if they are aware that an oral therapy would be appropriate, they may sell injectable formulations if they know that patients believe injections to be more effective. However, careful interpretation of claims of such consumer pressure is required because providers may choose to blame consumers for their own profit-maximizing strategies.

One would also expect retailers behavior to be influenced by cost structure, profit margins, and competition from other providers, and to be more responsive to these financial incentives than would be their public sector counterparts. In the rural retail market in Tanzania, price competition for an-
timalarial drugs was limited because there were relatively few antimalarial drug retail stockers and the market was strongly segmented geographically, meaning that people did not generally travel far to seek care. This limited competition was associated with high retail markups, which were also documented in rural Kenya. However, in urban areas much greater price competition between retailers would be expected. It should also be noted that medicine seller incentives are unlikely to be purely financial; they may also include a desire to serve the community, to be seen as a respectable, trustworthy citizen, or to be viewed as professionally competent by their peers.

Last but not least, one would also expect regulation to affect medicine seller operations. The scope of such regulation generally concerns the availability, labeling, dispensing, and marketing of drugs, the qualifications of staff, the location and nature of the premises, and in some circumstances the prices charged. However, retail regulation is notoriously ineffective. For example, in Kano State, Nigeria, only 15% of drug sellers were registered with the Federal Government. In Uganda, 60% of chloroquine purchases reported in a household survey came from sources not authorized to provide antimalarial drugs. In Tanzania, 90% of drug stores illegally stocked prescription only antimalarial drugs, most stocked unregistered products, and all drug store serving staff were underqualified.

Strengthening regulatory control has posed great challenges because of the lack of enforcement capability. In a peri-urban area of Nigeria, only 33% of PMVs reported an inspection visit during the previous two years. In Dar es Salaam, more than half of pharmacy owners rated the government’s effectiveness in regulating the pharmaceutical sector as low or very low, for example, citing the failure to penalize shops flouting regulations and the lack of regular inspections. This was argued to reflect inadequate staffing and transport. In rural Tanzania, regulatory infringements were argued to reflect a combination of infrequent regulatory inspections, a failure of regulatory authorities to implement sanctions, and successful concealment of violations. In addition, there may be tacit permission of violations by local regulatory staff, who see enforcement as unfeasible and/or recognize that provision of prescription-only medicines in shops meets a genuine need in communities without formal pharmacies where government facilities frequently experience drug stockouts.

Interventions involving medicine sellers. A total of 16 interventions to improve malaria-related activities of medicine sellers in sub-Saharan Africa were identified and are summarized in Table 1. Five were based in Nigeria, four in Kenya, two each in Uganda and Ghana, and one each in Tanzania, Madagascar, and Zambia. It is notable that only one was found outside anglophone Africa; this may have reflected a greater likelihood of identifying English literature in the search, or greater reluctance to engage with medicine sellers on the part of francophone governments. The interventions varied considerably in scope and scale. All involved a combination of training, job aids, and demand generation/consumer information, with some including pre-packaged drugs. Franchise/accreditation networks were developed in three cases. In terms of health problems addressed, nine focused specifically on malaria treatment, two included acute respiratory infections (ARI) and/or diarrhea as well, and five had a more general primary health care orientation. All but one intervention involved working with existing medicine sellers, the exception being Child and Family Wellness (CFW) shops in Kenya where new outlets were established. In six interventions, medicine sellers were the primary focus, and in an additional six they had a major role, complemented with other strategies to improve medicine use. In the four remaining projects, medicine sellers had only a partial role as an adjunct to the main community health intervention. The number of medicine sellers involved ranged from 12 to more than 3,000. The earliest began in 1990, although all but three were initiated in 2000 or later, demonstrating that widespread interest in this area is a relatively recent phenomenon.

Four major intervention components were identified: 1) training/capacity building, 2) demand generation, 3) quality assurance, and 4) creating an enabling environment. Table 2 shows the number of interventions including each component and the activities covered.

All projects had an element of training and capacity building, including workshops, peer-in-shop education, and job aids. The three most common elements of training content were drug use, communication, and referral. Other topics included common health problems, safety, pharmacy law, management skills, and procedures unique to the intervention (e.g., franchising procedures). Management skills included finance, record keeping, business ethics, and stock maintenance. Six projects conducted in-shop or peer education visits. For 10 interventions, it was stated that take-home materials and job aids were provided to trainees. In one intervention, negotiation sessions were conducted, an approach in which the public health objectives and the factors influencing private practitioner behavior are taken into account in jointly devising what improvements to introduce.

Demand generation was addressed in 12 interventions using 2 approaches. Ten projects included mass media or public information components. For example, the KidCare intervention to socially market pre-packaged antimalarial drugs in Nigeria involved TV, radio, mobile video units, posters, billboards, leaflets, flyers, point of sale stickers, danglers, promotional material, and special events, with messages focusing on product information, malaria, and its treatment and prevention.

Five projects trained community volunteers to promote patronage of trained medicine sellers and appropriate medicines. Demand was also stimulated through subsidies on pre-packaged antimalarial drugs in Madagascar and at the initial introduction of pre-packaged drugs in Nigeria.

Quality assurance was addressed in 14 interventions in 5 main ways: 1) franchising or accreditation, 2) consumer accountability, 3) engaging a medicine seller association, 4) monitoring and supervision, and 5) pre-packaged drugs. Under franchising/accreditation, trained outlets obtaining accreditation or specific recognition received signs, posters, or stickers that identified them as an accredited outlet. The networks were publicized through identifiable names, brands, and logos. Franchising or accreditation was central to three projects, CFWshops in Kenya, accredited drug dispensing outlets (ADDOs) in Tanzania, and CAREshops in Ghana. An element of franchising was also found in the project promoting pre-packaged antimalarial drugs in Abia, Nigeria, in that medicine sellers were provided with...
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<tr>
<th>Study/project (year intervention began)</th>
<th>Providers</th>
<th>Disease focus</th>
<th>Nature of intervention</th>
<th>Evaluation type (outcome measures)</th>
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<td><strong>Nigeria</strong></td>
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<td>Nigeria: Primary care training for medicine vendors in Ibgo-Ora, western Nigeria (1990)</td>
<td>Patent medicine vendors (PMVs) and their apprentices n = 37</td>
<td>Primary health care</td>
<td>Training: 8 × 2 hour training sessions on primary care. Designed with a PMV training committee, selected by the local PMV association.</td>
<td>Pre-post with control (provider knowledge)</td>
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<td>Oshiname and Brieger (1992)⁵⁹</td>
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<td>Nigeria: Community partners for health (CPH): urban health coalitions, Kano Town, Nigeria (1994)</td>
<td>PMVs/community-based organizations (CBOs) n = 49 PMVs</td>
<td>Primary health care</td>
<td>Quality assurance plus training: Building on the successful partnerships formed between CBOs and private health facilities in Nigerian cities, attempts were made to encourage PMVs to join the partnership for training and community accountability in other areas.</td>
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<td>Brieger and Ogunlade (2001)¹⁰⁷</td>
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<td>Nigeria: Promoting prepackaged drugs for prompt and appropriate treatment of fever in rural Nigeria (2002)</td>
<td>PMVs, volunteer village health workers, and auxiliary health facility staff n = 12 PMVs</td>
<td>Febrile illness/malaria</td>
<td>Training plus demand generation plus pre-packaged drugs plus job aids: Three types of distributors trained to promote and sell age-specific prepackaged antimalarials and cotrimoxazole for preschool-age children. Community health education.</td>
<td>Pre-post (community drug use and provider choice)</td>
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<td>Brieger and others (2002–2003)¹⁰³</td>
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<td>Nigeria: Improving home based management of fever in Abia State, Nigeria (2003)</td>
<td>PMVs/catchment area planning and action (CAPA) committees n = 1,031 PMVs</td>
<td>Malaria</td>
<td>Training plus demand creation plus pre-packaged drugs plus job aids: Social marketing, mass media, community mobilization, and PMV training. Master trainers trained for one day cascade training of fellow PMVs. Supportive materials include shop danglers, stickers, job aids, customer handbills, and training handbooks.</td>
<td>Pre-post (provider behavior and knowledge)</td>
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<td>Greer and others (2004)⁹²</td>
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<td>Nigeria: Pre-packaged malaria treatment for children in Nigeria (KidCare) (2003)</td>
<td>Hospitals, clinics, pharmacies and PMVs n = 3,950 PMVs</td>
<td>Malaria</td>
<td>Social marketing of pre-packaged drugs: Pre-packaged chloroquine kits for two age groups for uncomplicated malaria, with clear labeling and instructions, mass media promotion, sold through major wholesalers and sub-distributors, job aids for PMVs. Detailers follow-up outlets to give information on correct usage and compliance. Training of pharmacists and PMVs. Phased replacement of chloroquine with antimalarial combination therapy in 2006, supported by mass media activities.</td>
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<td>PSI Nigeria/SPH⁹⁹</td>
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<td>Kenya: Changing home treatment by training shopkeepers in rural Kilifi, coastal Kenya (1999)</td>
<td>General retail shop keepers n = 285 shops</td>
<td>Malaria</td>
<td>Training plus demand generation: Skill-based participatory workshop training for groups of general retailers stocking drugs, provision of job aids, ongoing monitoring, and community information activities to promote appropriate sales of antimalarials</td>
<td>Pre-post with control (community drug use and provider choice and provider behavior)</td>
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<td>Marsh and others (2004)⁹⁹</td>
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<td>Training retailers in correct use of OTC antimalarials, Kisii Kenya (2001)</td>
<td>Untrained commercial drug sellers (i.e., retail drug shop owners located far from health facilities) n = 74</td>
<td>Malaria</td>
<td>Training plus job aids</td>
<td>Pre-post (provider knowledge)</td>
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<td>Demand generation activities in the community; two-day training sessions on malaria disease, referral, communications, record keeping, and stock management of over-the-counter antimalarial drugs; IEC job aids; supportive supervision.</td>
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<td>Vendor-to-vendor education in Bungoma, Kenya (2003)</td>
<td>Wholesale counter attendants, mobile suppliers, and retail drug outlets (shops, kiosks, pharmacies, private clinics) n = 73</td>
<td>Malaria</td>
<td>Training plus job aids</td>
<td>Controlled† (provider behavior and knowledge)</td>
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<td>District health management team one day training of wholesalers and mobile vendors as outreach educators. Participants equipped with job aids and posters for distribution to smaller drug outlets in the district. A neighbor-to-neighbor component, added later, aimed at increasing malaria knowledge and demand for antimalarials among caregivers.</td>
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<td>Child and family wellness shops (CFW shops™), Kenya (2003)</td>
<td>Community health workers (CHWs) operate shops and clinics under franchise n = 24 shops and 40 clinics</td>
<td>Primary health care (25% malaria diagnoses)</td>
<td>Quality assurance plus training</td>
<td>NA</td>
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<td>Establish new clinics and shops in underserved areas to provide quality, standardized products, run by trained and supervised CHWs. Manuals provided on diagnosis, treatment and drug management. Monthly inspections. Currently aiming to convert existing shops to clinics.</td>
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<td>Uganda</td>
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<td>Partnering with traditional healers and drugs sellers in Sembabule, Uganda (2001)</td>
<td>Traditional birth attendants (TBAs), traditional healers (THs), and drug vendors (DVs) n = 167 DVs</td>
<td>Malaria and diarrhea</td>
<td>Training plus job aids plus awareness-raising events</td>
<td>Pre-post (consumer knowledge and provider choice)</td>
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<td>Part of a district child survival project; TBAs, THs, and DVs trained for three days. Calendars and posters produced as communication aids for vendors</td>
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<td>Uganda</td>
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<td>Negotiation sessions plus policy formulation</td>
<td>Pre-post (provider behavior)</td>
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<td>The CORE Group and MIHV (2004)</td>
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<td>Negotiation sessions with private health practitioners targeting specific practices related to case management of childhood diarrhea, fever (malaria), and ARI. Moderators conducted negotiation sessions for 20–30 private practitioners, with follow-up monitoring and support visits.</td>
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<td>Using the potential of private health practitioners in child survival, Luwero, Uganda (2003)</td>
<td>Private health practitioners, including drug sellers n = 51 drug sellers</td>
<td>Malaria, ARI, and diarrhea</td>
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<td>Ghana</td>
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<td>Healthy happy homes, Volta and central regions, Ghana (2002)</td>
<td>Chemical shop owners and shop attendants Shop owners: n = 1,035 Shop attendants: n = 362</td>
<td>Malaria</td>
<td>Demand generation plus training</td>
<td>NA</td>
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<td>Radio drama from home-based care initiative communication campaign, to educate, motivate, and demonstrate issues related to malaria and other childhood illnesses. Pharmaceutical company conducted training. Chemical sellers distributed IEC materials.</td>
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<th>Study/project</th>
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<tr>
<td>Essential medicines franchise, Ghana (CAREshops) (2003)</td>
<td>Pre-existing licensed chemical sellers</td>
<td>n = 221</td>
<td>Primary health care</td>
<td>Franchising plus training plus marketing</td>
<td>Pre-post (provider knowledge)</td>
</tr>
<tr>
<td>Mensah (2005)</td>
<td>Primary focus</td>
<td>Conversion of existing chemical sellers shops into network of essential medicines franchises. Owners have access to pooled procurement of high-quality medicines at affordable prices.</td>
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<tr>
<td>Tanzania Accredited drug dispensing outlets (ADDOs), Ruvuma and Morogoro regions, Tanzania (2002)</td>
<td>Pre-existing small drug retailers (Duka la dawa)</td>
<td>n = 393</td>
<td>Primary health care</td>
<td>Accrediting plus training plus regulatory action plus brand marketing</td>
<td>Pre-post with control (provider behavior)</td>
</tr>
<tr>
<td>Ndomondo-Sigonda and others (2003)</td>
<td>Primary focus</td>
<td>Short-course formal training of drug retailers. Accreditation of participants and licensing to sell wider variety of essential drugs, including antibiotics and antimalarials. Creation of new cadre of pharmaceutical outlets (ADDO) combined with marketing and commercial incentives. Regulation decentralized to ward level.</td>
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<tr>
<td>Madagascar Pre-packaged malaria treatment for children in Madagascar (PaluStop) (2003)</td>
<td>Doctors, pharmacists, wholesalers, and general retailers in malaria-endemic zones; pharmacists only in epidemic zones</td>
<td>n = 2,800 general retailers</td>
<td>Malaria</td>
<td>Social marketing of pre-packaged drugs</td>
<td>NA</td>
</tr>
<tr>
<td>PSI Madagascar</td>
<td>Major role</td>
<td>Subsidized pre-packaged chloroquine kits for two age groups for uncomplicated malaria, with clear labeling and instructions, mass media promotion, marketed to doctors, pharmacists, wholesalers, and retailers. Training for medical detailers and commercial representatives. In-shop education of vendors and provision of information cards.</td>
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<tr>
<td>Zambia Improving household use of chloroquine in Nakonde, Zambia (2000)</td>
<td>Village health motivators (VHM) and drug vendors</td>
<td>n = 12 drug vendors</td>
<td>Malaria</td>
<td>Training plus community information</td>
<td>Pre-post with control (consumer knowledge)</td>
</tr>
<tr>
<td>Kaona and Tuba (2003)</td>
<td>Partial role in wider intervention</td>
<td>VHMs trained for seven days as communicators of malaria knowledge and correct dose information, and supplied with symptom manual. Drug vendors trained for one week and provided with dosage guides for distribution to clients.</td>
<td></td>
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</tr>
</tbody>
</table>

*NA = not applicable; OTC = over the counter; IEC = information, education, and communication; ARI = acute respiratory infection.
† Outlets were classified as intervention or control post-hoc based on whether they had obtained intervention materials from wholesalers; this may have led to selection bias.
shop stickers, posters, and danglers that designated them as trained providers of the RBM logo-branded pre-packaged drugs.

Three projects reported that some form of consumer accountability was built into the design, including the use of community-based organizations to identify, recruit, and monitor medicine sellers. Four projects mentioned the use of existing, or formation of new medicine seller associations, to assist in establishing norms and supporting/expanding training. Monitoring and supervision post-training was built into nine projects. Five projects addressed drug quality and packaging: four specifically focused on promoting pre-packaged antimalarial drugs, and the fifth focused on pooled procurement that was used for CAREshop franchised sellers to obtain bulk discounts and ensure drug quality.

Seven programs addressed the enabling environment; five addressed changes in drug policies and regulations. The ADDO program linked accreditation with enabling medicine sellers to sell both OTC drugs and limited prescription drugs, and decentralized regulation of accredited outlets from regional to ward level. In Nigeria, the national food and drug agency approved new pre-packaged drugs (Gilpin U, unpublished data), and later the Society for Family Health (KidCare project) played an influential role in the rescheduling of ACTs as OTC medicines, providing increased from 35% to 54% for uncomplicated malaria.

Medicine seller knowledge. Pre-training and post-training assessment of medicine seller knowledge was conducted through testing in five interventions, with several studies demonstrating improvements. For example, trained PMVs in Igbo-Ora, Nigeria, had significantly higher scores in a test on simple medicine use and appropriate practices for malaria management (increase from 46% to 70%), and in Kisii, Kenya, the percentage of sellers who knew the correct chloroquine dose for children less than five years of age increased from 0% to 59%. In Ghana, there was an increase in the proportion of franchised CAREshops scoring more than 60% on a test on managing simple ailments from 35% to 82%.

Medicine seller performance. Seller performance was assessed for five interventions. Because medicine sellers have incentives to put on their best behavior before an open observer, or present a wishful self-image under questioning, all studies evaluated provider behavior through mystery shoppers/simulated clients.

All interventions reported improvements in medicine seller performance. For example, in Bungoma, Kenya, the proportion of sellers stocking recommended antimalarial drugs was 62% in outlets that had received job aids compared with 23% in controls. In Tanzania, the proportion of drug stores stocking unregistered medicines was 2% in accredited stores compared with 10% in controls. The proportion giving appropriate drugs for uncomplicated malaria increased from 2% to 73% after negotiation sessions in Luwero, Uganda. The proportion of sellers recommending or giving a correct antimalarial drug dose also showed substantial improvements, increasing from 9% to 53% after training and introduction of pre-packed antimalarial drugs in Abia, Nigeria, and from 0% to 50% after negotiation sessions in Uganda.

There were also improvements in the provision of advice to consumers. The Ugandan negotiation sessions increased the proportion of sellers who explained how to give the medicine from 8% to 49%. In Abia, Nigeria, the proportion of sellers who asked whether the customer understood the information provided increased from 35% to 54% for uncomplicated malaria, but only from 29% to 33% for complicated malaria.
Not all indicators showed universally positive changes. For example, performance on referral practices was disappointing in Abia, Nigeria, where there were decreases in both the proportion explaining danger signs to caregivers and the proportion referring cases of convulsions. In Kilifi, Kenya, the proportion asking about danger signs was higher in intervention shops compared with controls (26% versus 0%) but still remained unacceptably low. In Tanzania, there was concern that referral rates for uncomplicated malaria may have increased too much, with 52% of accredited drug stores referring clients rather than providing antimalarial drugs themselves compared with 21% in controls, although it had been anticipated that most cases could be appropriately managed at medical seller level. Experience with preventive practices was also mixed, with three interventions showing little or no improvement in the proportion of sellers advising caregivers about prevention. This may have reflected a concern that such actions would decrease the medicine sellers’ sales.

Caregiver knowledge and choice of provider. Interventions that included community education also demonstrated an increase in caregiver knowledge. For example, after training and community mobilization in Zambia, caretakers were 32% and 51% more likely to identify simple and severe malaria, respectively. There is no evidence that working with community information activities had no significant impact on the proportion of fevers treated through shops. Interestingly, two interventions that included other groups in the training, such as VHWs and clinic staff, actually recorded a decrease in medicine seller use. In southern Nigeria, medicine sellers remained the most common source of treatment but there was a small increase in the use of VHWs. In Ssembabule, Uganda, there was a large decrease in medicine seller use from 47% to 4%, and the use of health units increased from 32% to 71%.

Rates of appropriate treatment. Only two studies assessed the impact on community drug use, with both using large-scale household surveys. In rural Nigeria, promotion of pre-packaged antimalarial drugs through community distributors including medicine sellers led to an increase in antimalarial drug use for reported fever from 38% to 50%, which could be attributed directly to the sale of project drugs. In Kilifi, Kenya, training general shopkeepers, accompanied by community mobilization and monitoring/supervision activities, was shown to lead to an increase in the proportion of shop-treated childhood fevers receiving an adequate amount of a recommended antimalarial drug from 2% to 15% after training on chloroquine and to 30% after subsequent training on SP.

Sustainability. The evidence of sustained improvement in medicine seller performance and lasting impact on caregiver behavior is limited, especially once outside involvement from researchers and/or donors has ceased. However, in Kilifi Kenya, persistent improvements in appropriate treatment were demonstrated over several years. Because the primary work of the medicine seller is to run a business, one aspect of potential sustainability that can be relatively easily assessed is whether sellers perceive commercial benefits from participation, such as increased prestige and/or higher profits. In general, sellers were highly enthusiastic, and in several cases expressed a desire for further training because they believed that the process either increased their turnover or gave them increased credibility within the community. However, high attrition rates among medicine sellers posed a challenge for sustainability in southern Nigeria, where 53% of sellers dropped out and in Ibgo-Ora, Nigeria, sustaining knowledge gains when apprentices graduated was problematic. In Kilifi, Kenya, 30% of trained shopkeepers had stopped selling drugs in the first year of the intervention, although this was reduced to 5% in subsequent years by selection of more stable retailers.

Cost. Another key factor influencing sustainability is the intervention cost. Cost data were available from six interventions, although comparison between studies is hampered by variation in the scope of costs included. The evaluation of general shopkeeper training in Kilifi, Kenya, provided the most comprehensive cost data, and was the only study to estimate the cost-effectiveness of the intervention in terms of treatment outcomes. During the early implementation phase, the full economic cost per year to the provider (including annualized development and set-up year costs) was $87.82 per trained shop, $0.46 per capita, and $4.00 per additional febrile episode appropriately treated (year 2000 US$). It was estimated that if the project were implemented at scale and run entirely by Ministry of Health staff, the costs would decrease to $18.41 per trained shop, $0.10 per capita, and $0.84 per additional febrile episode appropriately treated, with the latter figure varying between $0.37 and $1.36 in the sensitivity analysis. The investigators used a simple model to estimate the cost per death and disability-adjusted life year (DALY) averted, which predicted a cost per death averted of $505.42 for the early implementation phase and $105.92 for operation at scale, and a cost per DALY averted of $18.38 and $3.85, respectively, both of which would be considered highly cost-effective in relation to commonly used benchmarks.

Other training interventions provided a range for the cost per seller trained of $8–23. Training retailers and providing information, education, and communication materials in Kisii, Kenya, was estimated to cost $8 per trainee (2002 US$). Another Kenyan intervention in Bungoma found that providing training and materials to wholesalers cost $9–11 per retailer reached (2000 US$), excluding the time of district health personnel and outside technical advisors. In Abia, Nigeria, where training on the use of new pre-packaged antimalarial drugs was offered to medicine sellers as part of a social marketing campaign, $22.64 was spent directly on training and behavior change materials for each seller recruited (excluding staff time, travel, and program development costs) (2003 US$). Finally, negotiation sessions to improve key child care practices in Luwero, Uganda, cost $21 per provider, excluding the cost of community information (2003 US$).

The costs for establishing new outlets under the CFW franchise network in Kenya were understandably much higher, with an average start up cost per shop of US$5,000 over the first three years. No cost data were available for the fran-
chise/accreditation networks in Tanzania and Ghana, although the high costs of maintaining and scaling-up the networks have been noted as a major cause of concern by the projects.\textsuperscript{115}

**DISCUSSION**

This review has demonstrated that there are few reported interventions that have sought to work with medicine sellers to improve malaria treatment in Africa. This is in sharp contrast to the numerous published articles that not only document community use of medicine sellers, but also subsequently recommend that intervention should follow.

Moreover, evaluation data from these interventions are relatively weak; only 11 interventions had been formally evaluated, and peer-reviewed publications were available for only 5. In most cases, evaluation measures were limited to intermediate outcomes (such as provider knowledge and behavior), rather than those more closely linked to health outcomes (such as community drug use). Few studies provided comprehensive cost or cost-effectiveness data. Limitations in study design were also noted. No evaluations involved randomization of outlets/areas to intervention and control groups, which probably reflects the complexity of undertaking a randomized controlled trial while maintaining realistic program implementation and working with pilot projects. Most evaluations had no control group, relying instead on pre and post data, which may be subject to numerous confounding factors. Moreover, because the post-intervention assessments were often undertaken only three or four months after implementation, long-term impact is difficult to predict.\textsuperscript{42,92,101}

Despite these limitations, some tentative conclusions are possible. Two key findings are that medicine sellers are interested and willing to participate, and that interventions involving them can increase the frequency of appropriate treatment of malaria and other childhood illnesses. All interventions reported improvements in medicine seller knowledge and/or performance. The proportion of retailers who stocked approved drugs, dispensed age-appropriate dosages, and advised caregivers about appropriate management were all shown to improve. The one study that used community surveys to assess the impact on rates of appropriate treatment showed strongly positive results. However, even where major improvements were documented, a significant proportion of febrile cases were still inappropriately treated. Post intervention, for example, 60% of shop treated fevers still did not receive an adequate dose of a recommended antimalarial drug in Kilifi, Kenya,\textsuperscript{90} and 50% of private practitioners failed to give the correct antimalarial dose in Luwero, Uganda.\textsuperscript{42}

Because medicine sellers were already active in many communities, interventions did not in general require investment of external funds to establish outlets (an exception was the CFW network). The resources required to implement the programs were still significant, with costs ranging from $10 to $30 per outlet trained when operating at a reasonable scale. However, if significant changes in treatment outcomes are achieved, this may still represent a highly cost-effective use of resources.

These conclusions are supported by evidence from interventions focusing on other health issues, such as diarrheal diseases, ARI, STIs, and contraceptives, and those working with pharmacies rather than medicine sellers, both within and outside Africa.\textsuperscript{118–137} Reproductive health and STI interventions have changed the knowledge and sales behavior of medicine sellers, reducing inappropriate use of antibiotics and encouraging use of syndromic management guidelines.\textsuperscript{124–126,128,135–137} For example, in Kampala, Uganda, social marketing of pre-packed STI treatment (Clear Seven) led to significant improvements in cure rates, compliance, and condom use.\textsuperscript{129} Face-to-face educational outreach on diarrhea treatment in Kenyan pharmacies led to a significant increase in the knowledge of counter attendants, an increase in sales of oral rehydration salts, and a decrease in antidiarrheal sales.\textsuperscript{118} However, a similar intervention to improve ARI treatment in pharmacies and drug shops in Kampala, Uganda did not improve dispensing practices, with persistent provision of antibiotics and little advice provided.\textsuperscript{119} This was attributed to client demand for particular drugs, competition among drug outlets, and the inability of most clients to afford the recommended treatments.

There is insufficient evidence to conclude that any one approach to working with medicine sellers is superior in improving malaria treatment. Similarly, it is not possible to isolate the additional benefits of each component in these generally multi-faceted interventions. However, a number of key features of successful interventions can be suggested, based primarily on the views of their implementers and evaluators.

First, the planning process should begin with a comprehensive situation analysis, including the legal and market environment. For example, the regulatory framework in which medicine sellers operate, the channels through which they obtain drugs, and nature of competition between providers should all be understood. It is also important to document rates of closures and new start-ups because interventions that focus resources on relatively permanent sellers are likely to be more sustainable and cost-effective. Guidance on undertaking a situation analysis for home care of malaria including medicine sellers has been developed.\textsuperscript{138}

Second, interventions with the widest buy-in were generally more successful. The involvement of medicine sellers, public health officials, and community representatives in curriculum development, training, and supervision was believed to contribute to acceptability and effectiveness, and political support from central and local officials was essential. The two interventions that appeared to have worked most closely with national drug regulatory authorities and other Ministry of Health partners achieved the most significant policy changes. As a result of the Ugandan negotiation session intervention in Luwero, a national strategy for involving private health practitioners in child survival was developed.\textsuperscript{111} In Tanzania, new legislation was drafted creating a separate class of accredited medicine sellers.\textsuperscript{104}

Third, effective interventions require a combination of approaches, which should go beyond short-term shopkeeper training. Because client knowledge is a strong determinant of the outcome when drugs are bought from a retailer, concurrent community information programs are important. Pre-packaged medicines also facilitate the provision of correct medicines and dosages.

Finally, it should not be assumed that knowledge assessed at the end of a period of training will be fully transferred into practice once the trainee returns to his or her place of work.
This may be addressed to some degree through ongoing refresher training, continued monitoring of performance, and supervision of trained sellers. However, where sellers lack financial incentives to behave as they have been trained, such problems are likely to prove persistent.

In deciding on the appropriate scope for an intervention, it is useful to categorize interventions as targeted at either behavior change or role change. Behavior change interventions focus on improved sales practices, such as selling an effective antimalarial drug, not selling antibiotics, distributing pre-packaged drugs, and asking appropriate questions. Role change interventions train medicine sellers to be active health care providers, as shown in the various franchising studies, and may require enabling legislation to legitimize their expanded role. Key components for behavior and role change interventions are proposed in Table 3. Those focused on behavior change can provide short-term and relatively rapid responses through brief, highly focused training. In contrast, role change interventions involve more extensive engagement with the health system, and more fundamental changes to the sellers’ organization and management of their businesses. These may lead to broader benefits in the long-term, but are likely to have greater cost and capacity requirements.

In certain areas evidence is limited. No studies attempted to evaluate the distribution of benefits across socioeconomic groups. It is therefore not clear to what degree these interventions reach the poorest groups within their target areas, although there is evidence that they are effective in generally poor communities.99,105,110

The evidence is limited of sustained impact and capacity to operate at a nationwide scale. Several approaches are in the process of scaling up: 33 Kenyan districts have successfully applied for Global Fund finance to adopt the Kilifi model of shopkeeper training (Marsh V, unpublished data), CARE-shops operate in 20 districts in Ghana, and the Tanzanian accredited drug store model has expanded to cover approximately 400 shops (Briggs J, unpublished data). Social marketing of pre-packaged antimalarial drugs already operates nationwide in Madagascar, and is supported in 19 states in Nigeria (Chavasse D, unpublished data). However, major logistical and financial challenges in maintaining large networks of outlets with trained personnel have been noted, such as the capacity to provide refresher training, supervision and regulation, and the high cost of training courses.105,112

In some settings the sheer number of medicine sellers and the high turnover of outlets and staff may render face-to-face training of each one infeasible on a national scale. One may question whether the significant financial resources and long-term supervision required to maintain a comprehensive training program or accreditation network are available in countries that currently struggle to provide regular supervision and commodities to their own primary care facilities.75 However, several projects have demonstrated the potential to outsource these activities to non-governmental organizations and commercial companies.105,110,139

Despite the success stories reported above, enthusiasm for medicine seller interventions is not universally shared. In many countries, calls for a more active role for retailers have met with resistance from at least some government health personnel, who favor stricter enforcement of pharmaceutical laws or outright banning of medicine sellers.61,140 Several sources of objection can be identified: that public-private collaboration with providers who routinely infringe current regulations is inappropriate; that such interventions confer legitimacy on sellers with minimal training who may then be perceived locally as health professionals; and that such interventions reduce health facility use. However, there is no evidence of large increases in medicine seller use after interventions; in some cases use actually decreased. Moreover, standards of treatment are also often poor in formal health facilities.88 and in some settings the quality of facility care obtained is no better than that provided by medicine sellers.20,26 Although poor facility performance clearly needs to be addressed, discouraging medicine seller use may not improve the quality of care received overall.

There is also concern that interventions that facilitate the sale of previously prescription-only drugs by medicine sellers may lead to indiscriminate use, increasing the risk of adverse events and the development of drug resistance. These issues have been raised in the context of the on-going introduction of ACT in Africa. There are already plans to introduce ACT through medicine seller interventions in Nigeria through the KidCare social marketing program and in Tanzania through ADDOs.72,141 Some argue that although it was appropriate to deliver the old monotherapy regimens such as chloroquine and SP through medicine sellers and other community-based delivery systems, this would be inappropriate for ACTs because of the greater complexity of the dosing schedule, the need for large subsidies to ensure affordability, the necessity of prioritizing scarce ACT supplies, and the potential development of resistance to these valuable and effective medicines.142 Moreover, provision of highly effective ACTs at health facilities may lead to a decrease in shop use for febrile illness, as observed in Rufiji District in Tanzania (IMPACT-TZ collaboration, unpublished data), reducing the need for medicine seller programs. However, many of the perceived advantages of retailers highlighted in the introduction will persist, particularly their accessibility and importance as an alternative drug source when public facilities stock out. It is therefore likely that significant medicine seller use will continue in most settings, and it is questionable whether the RBM target of 80% coverage of appropriate malaria treatment in children less than five years of age can be achieved.

### Table 3

<table>
<thead>
<tr>
<th>Behavior change: relatively rapid but limited change in case management practices</th>
<th>Role change: longer-term change in medicine seller roles to enhance health systems</th>
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<tbody>
<tr>
<td>Medicine seller inventory</td>
<td>Standards of practice</td>
</tr>
<tr>
<td>Medicine seller involvement, e.g., through association</td>
<td>Recruitment criteria</td>
</tr>
<tr>
<td>Training of trainers: health workers, medicine sellers, or others</td>
<td>Franchising procedures</td>
</tr>
<tr>
<td>Short training: workshops, seminars</td>
<td>Training of trainers: health workers, medicine sellers, or others</td>
</tr>
<tr>
<td>National treatment guidelines</td>
<td>Detailed training courses</td>
</tr>
<tr>
<td>Pre-packaged drugs in age-specific packets</td>
<td>Standard treatment protocols</td>
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<tr>
<td>Supportive behavior change materials in the form of job aids, hand-outs for customers</td>
<td>Record keeping and accountability systems</td>
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<tr>
<td>Follow-up supervision</td>
<td>Branding, logos, and identification</td>
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<td></td>
<td>Credit facilities</td>
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<td></td>
<td>Central drug stocks of quality products at reasonable prices</td>
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<td>Follow-up supervision</td>
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</table>
CONCLUSIONS

Medicine sellers offer a service to patients that is widely used for the treatment of fever and malaria in most of Africa. Their popularity alone does not justify their use, but indicates the importance of ensuring that they have the capacity to provide safe and appropriate medicines in correct amounts in the communities they serve.

Despite the limited number of evaluations conducted, there is credible evidence that well-planned and implemented interventions can improve quality of service. Experience from the 16 malaria-related medicine seller interventions identified in sub-Saharan Africa indicated that where medicine sellers were taught about approved drugs, had the opportunity to stock such drugs, and saw the benefits of providing guidance on dosing, the proportion of clients that received the correct dose of an effective drug could be substantially increased. This provides a strong rationale for further exploring the largely untapped potential of medicine seller interventions to contribute to the achievement of the RBM targets.

In view of the limited evaluation base and on-going introduction of ACTs, there is an urgent need for further operational or intervention research to adapt these interventions to the ACT era, and provide more comprehensive evaluations of their impact, value for money, sustainability, and potential to scale up to a national level.

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Authors’ addresses: Catherine Goodman, Health Economics and Policy, Health Policy Unit, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK. E-mail: catherine.go...; and Kenya Medical Research Institute/Wellcome Trust Collaborative Programme PO Box 43640, Nairobi, Kenya. Telephone: 254-20-272-0163, Fax: 254-20-271-1673; William Brieger, Health Systems Program, Department of International Health, Bloomberg School of Public Health, The Johns Hopkins University, 615 North Wolfe Street, Room ES141, Baltimore, MD 21205. Telephone: 443-787-4042, Fax: 443-787-0217, E-mail: bbrieger@yahoo.com or bbrieger@jhsp...; Alasdair Unwin, Plan International, International Headquarters, Chobham House, Christchurch Way, Woking, Surrey, GU21 0JG, UK. Telephone: 44-1483-73-3338, Fax: 44-1483-73-6505, E-mail: alasdair.unwin@planinternational.org; Anne Mills, Nyanzuru MB, WHO, Health Policy, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK. Telephone: 44-207-927-2534, Fax: 44-207-436-3611, E-mail: Anne.mills@lshtm.ac.uk; Sylvia Meek, Malaria Consortium, Development House, 56-64 Leonard Street, London EC2A 4LT, UK. Telephone: 44-20-7549-0214, Fax: 44-20-7549-0211, E-mail: s.meek@malariaconsortium.org; George Greer, Child Survival and Infectious Diseases Bureau for Africa, Health Team, U.S. Agency for International Development, 1300 Pennsylvania Ave, NW, Washington, DC 20523-4600. Telephone: 202-712-0504, Fax: 202-216-3373, E-mail: ggreer@usaid.gov

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