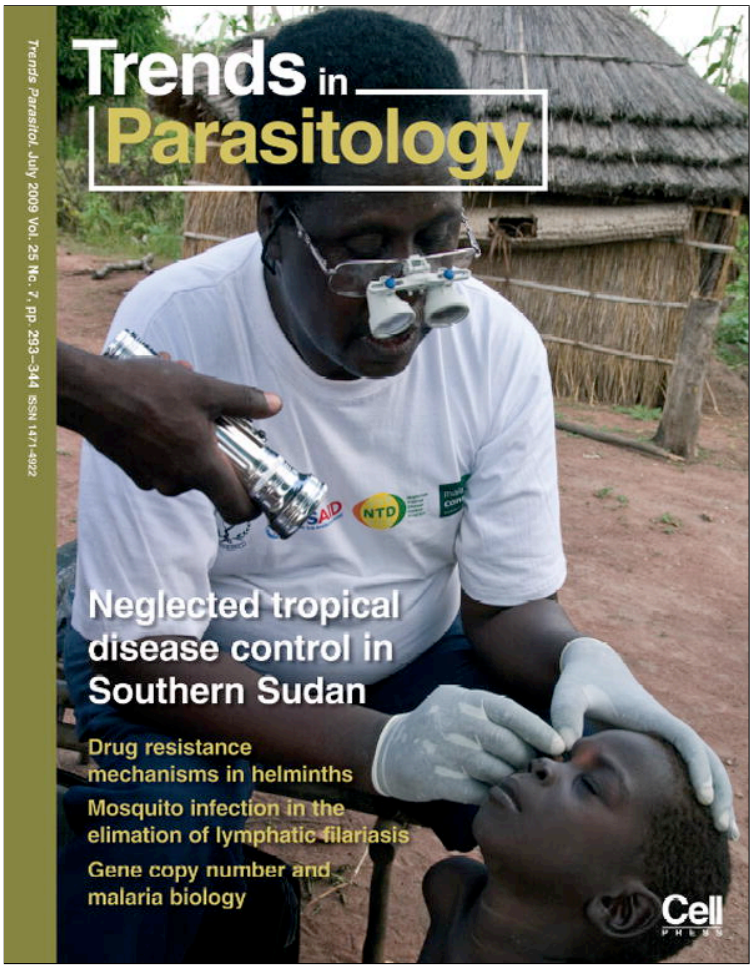

Opinion

Southern Sudan: an opportunity for NTD control and elimination?

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Southern Sudan has been ravaged by decades of conflict and is thought to have one of the highest burdens of neglected tropical diseases (NTDs) in the world. Health care delivery, including efforts to control or eliminate NTDs, is severely hampered by a lack of infrastructure and health systems. However, the post-conflict environment and Southern Sudan's emerging health sector provide the unprecedented opportunity to build new, innovative programmes to target NTDs. This article describes the current status of NTDs and their control in Southern Sudan and outlines the opportunities for the development of evidence-based, innovative implementation of NTD control.

An opportunity for coordinated control

Neglected tropical diseases (NTDs) are a range of diseases that occur in conditions of poverty and frequently overlap in endemic countries (http://www.who.int/neglected_diseases/en). Funding for their control and elimination has seen a dramatic expansion recently, with an emphasis on the co-administration of preventive chemotherapy (PCT) [1]. However, operational experience in delivering PCT packages, to date, has been from countries with well-established health systems (see, for example, Refs [2–5]). Little is known about implementation in post-emergency settings, in which delivery structures are less developed or absent. One such setting is Southern Sudan, which – until recently – was plagued by a series of conflicts since independence in 1956 [6]. The cessation of conflict, coupled with the commitment of the Ministry of Health (MoH) of the Government of Southern Sudan (GoSS), has yielded new opportunities and funding for NTD control, notably support from the US Agency for International Development to develop an integrated NTD control programme. There exists, therefore, a unique opportunity to develop an integrated programme from scratch and to generate crucial evidence on cost and cost-effectiveness in the process.

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Post-conflict progress and challenges

On 9 January 2005, Southern Sudan and the Khartoum Government signed the Comprehensive Peace Agreement, ending decades of civil war. Health systems are now being rebuilt, providing opportunities and funding to integrate the control of multiple NTDs. However, the country's recent history, as well as its sheer size, poses several challenges [7]. Southern Sudan covers an area of 231 177 square miles (Figure 1) but has an estimated population of 11 million at most, which equates to 47 people per square mile. Migrant populations and the return of refugees and internally displaced persons result in constantly fluctuating population figures. In 2004, 98% of the population lived in rural areas (http://www.codecan.org/media/PLS-%20Facts%20about%20South%20Sudan%202008.pdf). Physical, health and education infrastructure is largely absent, and many areas are accessible only by plane, boat, four-wheel drive or foot, especially during the rainy season. The proportion of the population with access to a health facility has been estimated to be below 25% [7,8], and in 2002, just over 20% of school-aged children were enrolled in schools (http://www.unicef.org/media/media_21825.html).

Notwithstanding such challenges, the ongoing transition towards development and its associated lack of entrenched government structures and processes provide great opportunities to improve public health, including NTD control. For such improvements to take place, it is essential to build up a credible evidence base to understand the epidemiology of infection and disease and develop, as well as appropriately implement, intervention strategies.

Neglected tropical diseases in Southern Sudan

Twelve NTDs are endemic to Southern Sudan (http://malariaconsortium.org/~malaqkmt/userfiles/ntds_southern_sudan.pdf) (Table 1). However, as in all post-conflict settings, reliable disease surveillance data are sparse. Estimates of incidence or prevalence are based on either passive case detection [9,10] or localized surveys undertaken in areas where specific NTDs are known

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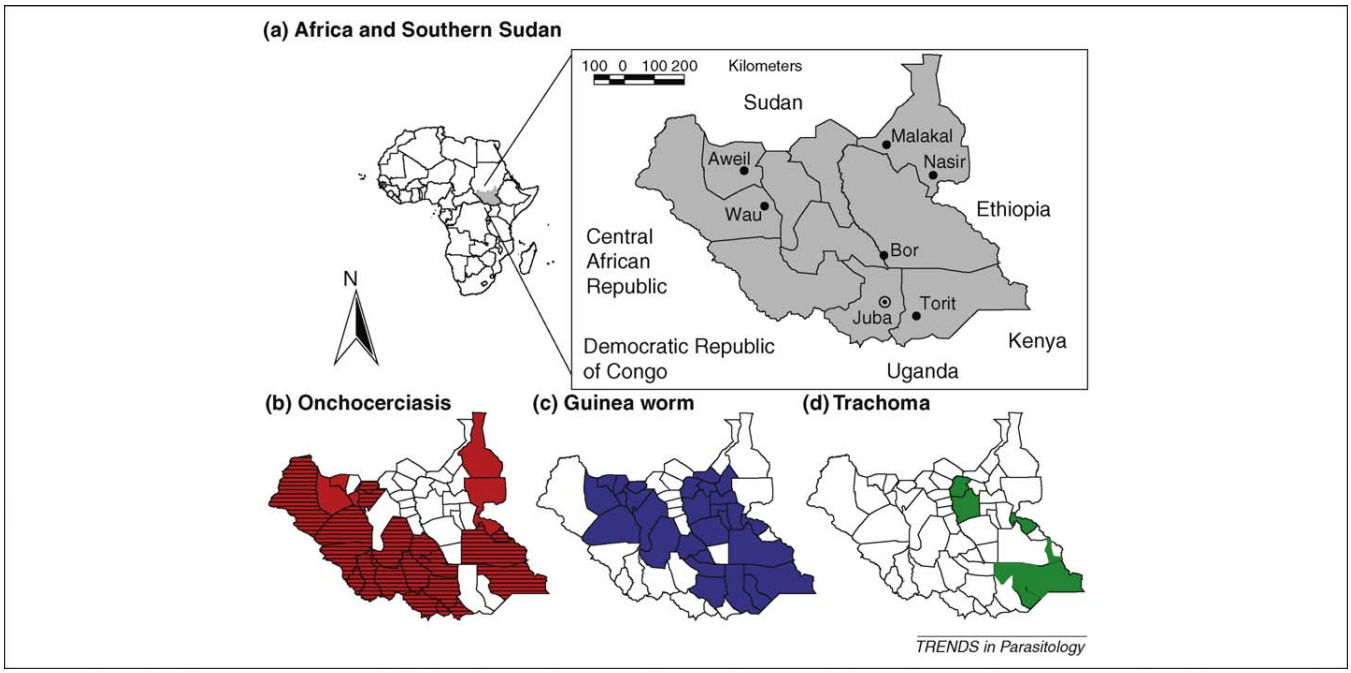

Figure 1. Maps. These show **(a)** the location of Southern Sudan in Africa, its ten states and major towns, highlighting its large size and low population density; **(b)** areas of Southern Sudan with structures for onchocerciasis control, in the form of either community drug distributors (red, hatched) or supervision centres for community-directed treatment with ivermectin (red, not hatched); **(c)** areas covered by the community-based network for Guinea worm eradication; and **(d)** trachoma-endemic areas already targeted with the SAFE strategy through the Guinea worm network. Both community-based structures shown in (b) and (c) are suitable for additional mass drug administration of preventive chemotherapy.

Table 1. NTDs in Southern Sudan

Parasite	Disease	Etiologic agent	Distribution[a]	Burden	Refs
Protozoan	Visceral leishmaniasis	*Leishmania donovani*	Unity, Jonglei, UN and EE	Cyclic: 500–9000 cases per year	[10]
	Human African trypanosomiasis	*Trypanosoma brucei gambiense*	WE, CE, isolated foci in EE	1–2 million people at risk	[21],[b,c]
		T.b. rhodesiense	Historical reports in Jonglei and EE	No recent reports	
Bacterial	Trachoma	*Chlamydia trachomatis*	Surveyed areas include counties in EE, CE, Jonglei and UN and one county in NBEG	At least 3.9 million	[11–13]
	Buruli ulcer	*Mycobacterium ulcerans*	WE	1000+ cases	[c]
	Leprosy	*Mycobacterium leprae*	Population in all ten states at risk	In 2006, 1060 new cases were reported	[c]
Helminths	Soil-transmitted helminths	*Ascaris lumbricoides, Trichuris trichiura,* hookworm (species unconfirmed)	Probably all ten states, especially EE, CE and WE	Unknown	[c]
	Lymphatic filariasis	*Wuchereria bancrofti*	Integrated mapping ongoing; four states known to be endemic but probably distributed much more widely	Unknown	[c]
	Loiasis	*Loa loa*	Equatoria region; predominantly WE	Unknown	[d]
	Onchocerciasis	*Onchocerca volvulus*	Hyperendemic in WBEG, NBEG, Warrab, Lakes, WE, CE and parts of EE; parts of Unity bordering Warrab; in Jonglei border with Ethiopia; UN on border with BN	4.1 million at risk, of which 3.6 million are eligible for treatment	[40],[c]
	Dracunculiasis	*Dracunculus medinensis*	All states except WE and Unity	3618 cases in 2008, down from 5815 cases in 2007	[41],[e]
	Schistosomiasis	*Schistosoma haematobium*	Probably Warrab, Lakes, Unity and UN	Unknown	[c,f]
		S. mansoni	EE, CE and WE; probably Jonglei, Warrab and Lakes	Unknown	

[a]Abbreviation of States: BN, Blue Nile; CE, Central Equatoria; EE, Eastern Equatoria; NBEG, North Bahr el Ghazal; UN, Upper Nile; WBEG, Western Bahr el Ghazal; WE, Western Equatoria.
[b]Human African trypanosomiasis (sleeping sickness): epidemiological update (http://www.who.int/wer/2006/wer8108.pdf).
[c]Neglected tropical disease in Southern Sudan: situation analysis, gap analysis and intervention options appraisal (http://malariaconsortium.org/~malaqkmt/userfiles/ntds_southern_sudan.pdf).
[d]APOC (2005) Rapid assessment of loiasis and onchocerciasis in Equatoria region of Southern Sudan. Mission Report, African Programme for Onchocerciasis Control, 4–24 April 2005.
[e]Southern Sudan Guinea Worm Eradication Program, Ministry of Health, Government of Southern Sudan, Final Report, 2008
[f]Atlas of the Global Distribution of Schistosomiasis (http://www.who.int/wormcontrol/documents/maps/en/).

Table 2. Current NTD control strategies in Southern Sudan[a]

Disease	Primary interventions currently used	Progress to date	Limitation of current intervention	Suitable for MDA?
Onchocerciasis	Annual CDTI implemented since 1995.	1.3 million individuals (36% of eligible population) treated in 2007.	Incomplete coverage; high attrition rate of CDDs.	Yes
Dracunculiasis	Active case surveillance, detection and containment, and prevention activities including water filtration, provision of safe water, treatment of water sources and health education.	In 2008, 89% of endemic villages were providing regular reports, 49% of cases were contained, and cases were reduced by 38% when compared to 2007.	Incomplete coverage of surveillance and interventions.	No
Soil-transmitted helminths	Single-dose albendazole, distributed alongside NIDs.	2.5 million doses distributed in all ten states in 2006, reaching 87% of the targeted 1–5-year-olds. Similar coverage achieved in 2007.	Lack of prevalence data and intervention strategy.	Yes
Schistosomiasis	No large-scale campaigns for schistosomiasis control have been undertaken to date. Praziquantel is rarely available at health facilities.	Small, *ad hoc* treatment campaigns.	Insufficient prevalence data and lack of large-scale intervention strategy.	Yes
Lymphatic filariasis	No targeted interventions to date.	Regular distribution of ivermectin in CDTI areas will have reduced infection levels in areas where LF and onchocerciasis are co-endemic.	Lack of prevalence data, limited funds for surveys and to conduct MDA, no palliative care, and co-endemicity of *Loa loa* in Equatoria region.	Yes
Loiasis	No targeted interventions to date. Pathology not considered worth treatment at the present time. Important because co-infection with onchocerciasis can provoke SAEs.	Regular distribution of ivermectin in CDTI areas will have reduced infection levels in areas where *L. loa* and onchocerciasis are co-endemic but might have caused SAEs.	Boundaries of loiasis endemic area not clearly delineated. No treatment suitable for MDA.	No
Trachoma	SAFE strategy consisting of trichiasis surgery, antibiotics for active trachoma, facial cleanliness and environmental improvements.	SAFE is being delivered as an integrated component of the Guinea worm eradication program in parts of Eastern Equatoria and Jonglei States.	Limited coverage and varying uptake of interventions by communities.	Yes
Visceral leishmaniasis	Passive case detection at a few health facilities equipped to treat the disease; treatment with pentavalent antimonials.	Case-management and supply chain of drug and diagnostic supplies improved.	Limited number of facilities with equipment and skills for diagnosis and treatment, cost of drugs, emerging drug resistance, and lack of awareness and prevention (LLINs) in affected communities.	No
Human African trypanosomiasis	Passive case detection at a few health facilities; treatment with pentamidine, eflornithine and melarsoprol.	Number of cases reported have decreased as a result of interventions carried out since 2003 [21].	Inadequate surveillance and limited number of treatment facilities and trained health workers.	No
Buruli ulcer	Antibiotic treatment using, for example, rifampicin and aminoglycoside.	Some interventions (treatment, awareness campaigns, health education) have been carried out over recent years.	Disease distribution not clearly established; limited access to treatment and surgery.	No
Leprosy	MDT blisterpacks provided free of charge by WHO.	Some interventions (treatment, awareness campaigns, health education) have been carried out over recent years.	Limited MDT coverage.	No

[a]Abbreviations: CDD, community drug distributor; CDTI, community-directed treatment with ivermectin; LF, lymphatic filariasis; LLIN, long-lasting insecticidal net; MDA, mass drug administration; MDT, multi-drug therapy; NID, national immunization day; SAE, severe adverse event; SAFE, strategy for trachoma control consisting of eyelid surgery (S), antibiotics to treat the community pool of infection (A), facial cleanliness (F) and environmental changes (E).

(or suspected) to occur [11–14]. Although comprehensive empirical data are few, those that do exist indicate that lymphatic filariasis (LF), schistosomiasis, soil-transmitted helminth (STH) and trachoma are endemic over large areas, whereas visceral leishmaniasis (VL), human African trypanosomiasis (HAT), Buruli ulcer and leprosy occur more focally. To date, comprehensive epidemiological mapping has been undertaken for only onchocerciasis, loiasis and Guinea worm. Determining the prevalence and distribution of the other NTDs remains an important operational necessity because NTD transmission is heterogeneous and scarce resources for control need to be geographically targeted [15].

Current NTD control strategies

Despite decades of civil unrest, progress has been made with the control of some NTDs (Table 2). These efforts can be broadly categorized as: (i) large-scale programmes, targeting at least 10% of the population (onchocerciasis and Guinea worm; Figure 1); (ii) smaller, *ad hoc* public health campaigns (STH and trachoma); or (iii) treatment provided, to varying degrees, by health facilities on an in-patient basis (VL and HAT) and through outreach (Buruli ulcer and leprosy). Because the populations at risk are not precisely known, it is generally not possible to reliably estimate coverage rates or their change over recent years.

Implementation of both onchocerciasis and Guinea worm control is through community-based structures, utilizing volunteers for community-directed treatment with ivermectin (CDTI) and for distribution of water filters and surveillance, respectively. Trachoma control is currently integrated with the Guinea worm eradication program in Eastern Equatoria and Jonglei States and consists of the SAFE strategy with its four components of eyelid surgery (S), antibiotics to treat the community pool of infection (A), facial cleanliness (F) and environmental changes (E). To date, de-worming against STH has been carried out during national immunization days, and schistosomiasis treatment is being provided by some health facilities.

Treatments for VL, HAT, leprosy and Buruli ulcer are considered too toxic, lengthy or difficult to be delivered through community-based mechanisms and are available only at health facilities or through outreach, if at all. Historically, treatment services for VL and HAT were provided by non-governmental organizations during epidemics (see, for example, Ref. [16]), enabling temporary expansion of service coverage [17,18]. Activities were scaled back shortly after the disease was considered to be under control, creating an opportunity for disease resurgence [19–21]. Current access to and quality of treatment for VL and HAT, as well as leprosy and Buruli ulcer, remains inadequate [10].

Building on existing MDA structures

Ongoing post-conflict reconstruction provides several key opportunities to improve on current NTD control, which are outlined below and in Box 1. An immediate opportunity for expanding NTD control is through integration of PCT delivery into the CDTI onchocerciasis network. Delivery of albendazole can readily be added to annual ivermectin distribution in areas where onchocerciasis and LF are co-endemic, with the collateral benefit of controlling STH, scabies and lice [22]. Southern Sudan plans to start co-administration of ivermectin and albendazole through CDTI structures in 2009.

In some Guinea worm endemic areas, health education and distribution of antibiotics for trachoma control have been integrated into the community-based Guinea worm activities. Anecdotal reports suggest that this has been popular with the communities. Once the transmission of Guinea worm has been interrupted and the network needs to be maintained for surveillance, Southern Sudan will have the opportunity to expand the existing integration, both geographically and in scope.

Together, the CDTI and Guinea worm network provide approximately 80% geographic coverage (Figure 1). This means that other mechanisms are required to deliver PCT to parts of the country where neither onchocerciasis nor Guinea worm are endemic, as well as within administrative units where distribution of these two diseases is focal, and where the existing networks do not reach all individuals eligible for other treatments. This is particularly relevant for elimination of LF, a disease that tends to be endemic over large areas [23]. Co-administration through the expanded programme on immunization provides one alternative delivery structure; it was successfully used in 2006 and 2007 for mass de-worming with albendazole. Another option might be de-worming for schistosomiasis and STH through schools, an approach that is already well established elsewhere in the region [24–26]. However, distribution through schools (as well as modification of the curriculum to improve knowledge, attitudes and practices related to NTD control) will only become viable once rebuilding of infrastructure has progressed and school attendance has increased substantially. Meanwhile, ongoing campaigns for the distribution of long-lasting

Box 1. Key opportunities and outstanding key questions for Southern Sudan

Opportunities

To build on existing solid structures for mass drug administration (MDA) developed during the war and expand their scope and geographical coverage at a unique time of health sector rebuilding. In the medium term, a common delivery platform for preventive chemotherapy (PCT) and other interventions (e.g. LLINs and vitamin A supplementation) could be developed as part of a health-facility–community linkage.

To address the control of NTDs not suitable for MDA through appropriate integration into multi-functional health care delivery at facility level and through strengthening of the link between communities and health facilities.

To ensure that new policies and strategies incorporate MDA of PCT and other NTD treatment and prevention as part of Primary Health Care.

To generate essential evidence that might enable better coordination and/or integration of mapping and MDA activities, thus reducing time and costs associated with operating in very difficult terrain, as well as contributing to the international understanding of the cost and cost-effectiveness of NTD control or elimination.

Questions

Which NTDs are endemic where? Both MDA and health-facility-based NTD interventions need to be targeted based on disease prevalence. For the majority of NTDs, this information is not available in sufficient detail.

How best to integrate the various criteria for NTD mapping? Trachoma, in particular, requires costly and detailed epidemiological surveys before azithromycin donation can be requested. There is an urgent need to develop simplified mapping procedures for trachoma and to establish how best to integrate survey procedures for LF, schistosomiasis and STH, as well as trachoma.

What is the actual cost of conducting MDA of PCT? Few cost data for delivery of integrated MDA are currently available. A cost analysis, following guidelines for economic evaluation of health care programmes, will be required to allow appropriate budgeting and to be used in the cost-effectiveness evaluation of integrated MDA.

What is or are the vector(s) of lymphatic filariasis and what is the vectorial capacity? It is assumed that *Anopheles gambiae* and *Anopheles funestus* mosquitoes are responsible for LF transmission in Southern Sudan, based on data from neighbouring Uganda [38]. Whether this is the case and what the competence of the vector(s) is should be determined because it is an important determinant of the number of MDAs required and, hence, of the overall cost of LF elimination [39].

How should the integrated NTD programme be evaluated and monitored? There is a need for standardized tools for monitoring and evaluation that address issues such as: (i) how best to collect data, particularly once prevalence decreases; (ii) which data collection methods can be integrated; and (iii) how frequently data need to be collected, particularly in areas where communications are poorly developed and where population access is intermittent and expensive.

insecticidal nets (LLINs) present an interim opportunity for PCT distribution until LLIN coverage has been scaled up [3].

In the medium term, Southern Sudan will have the opportunity to develop an innovative platform for community-directed delivery of PCT and other interventions (e.g. LLINs and vitamin A supplementation). Building on a recent TDR study (http://www.who.int/tdr/svc/publications/tdr-research-publications/community-directed-interventions-health-problems), a standardized delivery platform could be developed. A common set of interventions could be identified that address Southern Sudan's needs and are suitable for integration; donors would then be asked to invest into the platform, instead of supporting specific diseases. The delivery platform could be part of a health-facility–community linkage, and pre-service training of the country's new nurses and doctors could emphasize supervision and management of the platform as a central part of their job. To inform the development of such platform, more in-country experience with integration will be needed.

For VL, HAT, leprosy and Buruli ulcer, whereby confirmative diagnosis is required before infected individuals receive treatment [27–30], the existence of community-based MDA structures cannot be harnessed to provide mass treatment but presents an opportunity to improve treatment outcomes and reduce transmission through prevention. CDDs can be trained to provide health education, case identification, early referral and community follow-up.

Integration into multi-functional health care delivery

For those NTDs not suitable for MDA, both diagnosis and treatment are available only at a few facilities, often many hours (if not days) away from endemic communities. As a result, infected individuals generally present late or not at all, resulting in high morbidity and mortality (see, for example, Ref. [31]). With Southern Sudan having the highest caseload of VL in Africa [32] and being among the top three endemic countries for HAT [21], there is an obvious and urgent need for improvement. As mentioned above, such improvement should involve the affected communities where feasible but also requires better and more accessible case management. Ongoing upgrading of facility-based health care undertaken by the MoH–GoSS and partners provides an important opportunity to ensure that the skills and supplies to provide routine NTD diagnosis and treatment are put in place and that a link between the facilities and the communities is being established. Initial steps to do so have been taken by the MoH–GoSS, with considerable support from the World Health Organization and other agencies. The required drugs and other supplies have been included in the essential drug kit list, and training of national staff, including those operating at the periphery, on diagnostic and treatment procedures is ongoing.

New policies and strategies

Until 2005, communicable diseases in Southern Sudan were managed either using strategies developed by the Khartoum Government or according to the protocols of individual aid agencies. Since then, the MoH–GoSS has put in place a number of new or revised strategies with the aims of standardizing diagnosis, treatment and prevention among implementing partners operating in the South, and providing a framework for the MoH–GoSS and development partners to allocate funding. The most recent addition specifically addresses integrated NTD control (http://www.malariaconsortium.org/~malaqkmt/userfiles/ntd_ss_strategic_plan_june_2008_final.pdf).

Revision or development of new strategies continues to provide opportunities to include new evidence and to identify specific areas requiring further in-country research (see below). Because of the absence of large government bureaucracies, such strategic planning processes can be undertaken quickly and with extensive consultation. This dynamic environment also allows for specific implementation needs, such as a strong government commitment to community-based delivery, to be readily incorporated into emerging health policies.

More generally, improvements in environmental hygiene are the ultimate answer to the control and elimination of many NTDs, but for Southern Sudan (as for many low-income countries), these are expensive and represent long-term objectives. Multiple agencies are working with the GoSS to strengthen water, hygiene and sanitation infrastructure, and efforts should be made to ensure integration between NTD control and government departments coordinating the provision of water and sanitation. Here, there is opportunity for cross-sectoral collaboration and influencing strategies and policies (for example, to formulate standardized, rather than disease-specific, education on water and sanitation) and to target the construction of new boreholes and latrines to areas with high population densities and a high risk of specific NTDs.

Strengthening the evidence base

Integrated NTD control has now been initiated in at least ten African countries, although, to date, there are few empirical data on the health benefits and cost savings of an integrated approach over and above single-disease control programmes [4,33,34]. Thus, there remains an urgent need to strengthen the evidence base for integrated control. Southern Sudan provides particular opportunities to do so because all of the targeted NTDs are endemic and most of them have not been mapped. This means that extensive epidemiological surveys are needed. With the aim of saving time and money, the feasibility of an integrated survey tool covering a range of NTDs is being investigated. Integrated surveys will need to overcome a number of important differences in epidemiologies and survey methodologies of NTDs [15,35] and, thus, generate useful information to guide similar undertakings elsewhere.

It is also apparent that the commonly quoted annual MDA costs of US$0.4–0.5 per person [36,37] are not applicable in Southern Sudan. Actual cost data are being collected and will be used to generate evidence of the cost and cost-effectiveness of this approach. The methodology and costing templates used will be available for similar data collection elsewhere, providing an opportunity to generate figures that can be readily compared between countries.

Finally, the planned expansion of co-administration of PCT through community-based structures and campaigns will require exploration of new and innovative delivery approaches to ensure that full coverage (both geographically and of the eligible population) is achieved and can be retained. This will provide opportunities to contribute to the evidence base on recruitment, training, supervision and retention of community drug distributors (CDDs) and on factors associated with coverage. At present, the Southern Sudan Onchocerciasis Task Force already faces the challenge of approximately 30% of CDDs discontinuing their involvement in CDTI every year, resulting in considerable costs for the recruitment and training of new volunteers. Useful insight on improving CDD retention has been gained from other countries with well-established onchocerciasis control programmes (see, for example, Ref. [42]), as has insight on factors associated with coverage (see, for example, Ref. [43]). However, there is as yet limited evidence on how best to address these issues once a package of drugs or other interventions is delivered through community-based mechanisms, though TDR and others have recently started to fill this knowledge gap [44] (http://www.who.int/tdr/svc/publications/tdr-research-publications/community-directed-interventions-health-problems).

Concluding remarks

Information on the distribution and burden of NTDs in Southern Sudan is limited, but existing data consistently indicate that this is a country with a high burden and great need. In itself, this is not unlike many other developing countries. What sets Southern Sudan apart is that most NTDs are endemic, that most of them have benefited from little control and that infrastructure and systems are practically absent. Although this presents great challenges, it also offers great potential to increase treatment coverage for co-endemic NTDs, integrate more complex case management into facility-based health care delivery and strengthen the link between communities and health facilities. This unprecedented opportunity to build evidence-based systems for NTD control or elimination needs to be maximized now while rebuilding of the health sector is ongoing.

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