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Operationalization of the test and not treat strategy to accelerate the elimination of onchocerciasis and lymphatic filariasis in Central Africa

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After 30 years of treatment with Mectizan (ivermectin), cutaneous and ocular complications of *Onchocerca volvulus* infection are now scarce in endemic communities. Indeed, transmission has been interrupted and the *O. volvulus*- associated disease has disappeared in some African foci. Despite this success, onchocerciasis elimination in *Loa loa* co-endemic areas is still constrained by severe adverse events (SAEs) occurring after ivermectin treatment in some individuals harbouring very high *L. loa* microfilaremia. One approach towards the prevention of these SAEs is to identify individuals with high *L. loa* microfilaremia and exclude them from ivermectin treatment. The development of the LoaScope has provided the tool that underlies this test and not treat (TaNT) strategy. The first successful TaNT campaign was conducted in a *L. loa* highly endemic focus in Cameroon in 2015 without any SAEs. To accomplish this within a research setting, 60 people were deployed for this campaign, making this 'research' strategy not sustainable from a cost perspective. We describe here a way of reducing the cost of the TaNT strategy with a smaller team (three people) selected within affected communities. We also suggest the organization of a TaNT campaign in affected countries.

Keywords: Test and not treat, Onchocerciasis, Lymphatic filariasis, Loiasis, Central Africa

Introduction

In 1987, the donation of the safe anthelminthic ivermectin (Mectizan) for control of the disease caused by *Onchocerca volvulus* dramatically changed the fight against onchocerciasis and set the stage for other control programmes. In 1996, the Community-Directed Treatment with Ivermectin (CDTI) strategy developed by the African Programme for Onchocerciasis Control (APOC) resulted in significant improvement in the treatment coverage for mass drug administration (MDA) in Africa. After 30 years of MDA with Mectizan, the skin and ocular diseases associated with onchocerciasis are now only infrequently seen in most endemic communities because of this sustained annual treatment.[1,2] Onchocerciasis transmission has been interrupted in some African foci thanks to either once- or twice-a-year mass administration of ivermectin.[3–5] The success of the CDTI strategy has provided convincing evidence of the possibility to move from control of disease to elimination of this infection from Africa,[6] leading the APOC to shift its goal from control to complete elimination.[7]

Despite the success of the onchocerciasis MDA-based programme and the paradigm shift from control to elimination, an important challenge appears in *Loa loa* co-endemic areas, with potential life-threatening (occasionally fatal) severe adverse events (SAEs) occurring after ivermectin in those few individuals harbouring very high *L. loa* microfilarial densities (>30 000 microfilariae [mf]/mL of blood).[8] As regards the high burden of onchocerciasis as well as the important socio-economic impact, and the fact that only those few individuals (<5%) harbouring very high *L. loa* microfilarial densities are likely to experience SAEs, it was considered that the benefits of treating highly endemic onchocerciasis outweigh the consequences related to SAEs. Mass treatments have therefore been conducted in loiasis-endemic areas under a surveillance system to closely follow up and manage individuals experiencing SAEs following ivermectin treatment in meso- and hyperendemic onchocerciasis foci. This heightened surveillance strategy has been somewhat effective in alleviating the communities' concerns. Despite these efforts, treatment coverage is commonly low in these co-endemic areas and individuals refusing treatment, so-called systematic non-compliers,

continue to host *O. volvulus*, the causative agent of onchocerciasis, and thus contribute to ongoing transmission.

In addition to the fear of ivermectin treatment and the constitution of systematic non-compliers, maintaining active transmission, ivermectin mass administration against hypo-endemic onchocerciasis was not recommended in loiasis co-endemic areas as a consequence of an unfavourable benefit–risk ratio. Two main approaches have been initiated to avoid the occurrence of these specific SAEs. The first approach was the utilization of a 'pretreatment drug' that could safely lower the *L. loa* parasitemia of heavily infected individuals to below the acceptable microfilarial density threshold prior to administration of ivermectin. To this end, low doses of ivermectin, albendazole, mebendazole and various antimalarial drugs have been unsuccessfully tried.[9–16]

The second approach was to develop a system to identify individuals at risk of post-ivermectin SAEs (i.e., those with *L. loa* mf levels of ≥30 000 mf/mL). To do this, an innovative, user-friendly diagnostic tool, the LoaScope, was developed for the rapid diagnosis of these 'at-risk' individuals[17] and a new so-called test and not treat (TaNT) strategy was developed and implemented for the first time in Cameroon in 2015 and 2017.[18]

The pilot phase of the TaNT strategy

The pilot phase of the TaNT approach was first implemented in the Okola Health District in Cameroon, where treatments had been halted in 1999 as a consequence of SAEs that had occurred after the first CDTI campaign. The campaign was organized in four phases: the census; community and individual sensitization; tests and treatments; and AE surveillance (Figure 1). During two TaNT campaigns, conducted in 2015 and 2017, nearly 37 500 individuals were tested and about 36 600 were treated with ivermectin. Importantly, no SAEs were recorded during these two TaNT campaigns.[18,19]

Despite this success, all the TaNT-related activities (census, sensitization, tests and treatments, AE surveillance) were conducted by central teams made up of researchers, graduate students and other technical and specialized staff (lab technicians, consultants, etc.). About 30 students were recruited for the census and supervised by a researcher. The sensitization team consisted of two individuals who spoke the local language, supported by a driver. Five teams were dedicated to the TaNT exercise itself. Each team was made up of one supervisor, two recorders (one collecting data on individual forms and the other recording data on an electronic tablet), a local community member to assist in translation and three laboratory personnel (one for blood sampling, one for making the calibrated thick blood smears and one to use the LoaScope). Finally, there was also a healthcare professional (nurse or medical doctor), who was assisted by a local community drug distributor (CDD) (Figure 1). After treatment, patients were closely monitored for AEs by the two AE surveillance teams, each made up of a driver and a physician.

Although the cost study of these two campaigns is ongoing, the pilot phase of the TaNT strategy was costly and hardly extendable to other settings similar to the Okola Health District (hypo-endemic for onchocerciasis and endemic for loiasis) in Cameroon and Central Africa. It therefore appears urgent to translate this successful interventional project into an operational activity that is sustainable.

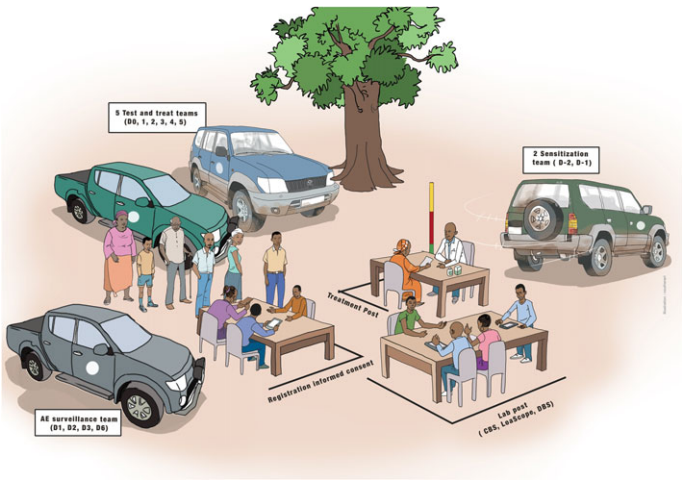

Figure 1. Organization of the TaNT team and the flow of participants during the research phase.

Translating the TaNT strategy into field operations

Translation of the TaNT strategy into field operations was inspired by the CDTI strategy, which had been quite successful. The CDTI strategy relies on the endemic communities themselves to conduct the MDA under the supervision of the local health system. Thus the treatment of a specific community is organized and conducted with the participation of the entire community. The CDDs for each village are selected by the local authorities and the population. These local staff conduct a census and communicate with the national health authorities to ensure that sufficient drugs are provided according to the number of eligible residents requiring MDA treatment.

In the operationalization plan, a CDD is necessary and will be chosen from among community members, as done in the classic CDTI strategy. This CDD will be trained to conduct the census, perform sensitization and administer ivermectin treatment. In addition to the CDD with the same prerogatives and job description as in the classic CDTI strategy, a testing team (blood drawer and LoaScope operator [LoaScopist]) will be needed to conduct the LoaScope tests and to define eligibility for ivermectin treatment. Regarding the profiles of these personnel, we thought that the blood drawer could be an assistant nurse or an assistant lab technician (who could be recruited from the area's healthcare community, private health facilities or the many training schools that exist in different health districts) and the LoaScopist could just be a literate individual from the community since the LoaScope is a user-friendly tool.

The deployment of such a community-based TaNT strategy in the field will be aligned and based on the experience of the classic CDTI strategy. First, meetings for advocacy will be organized regarding the voluntary aspect of involvement in this activity.

The training will be done in a staggered manner, aligning with the health pyramid. In general, the health pyramid is made

up of three levels: a central level encompassing the Ministry of Health, which oversees disease-specific programmes, and general and reference hospitals; an intermediate level involving the regional/provincial Delegations of Health and the regional/provincial hospital; and a peripheral level with Health District (HD) (or health zone) services and HD hospitals. Within the HD (or health zone), there are health areas comprised of communities. The health centre lies at the centre of the health area. The national manager of the onchocerciasis (or onchocerciasis and lymphatic filariasis [LF] or neglected tropical disease [NTD], according to the country) programme and their technical staff, as well as the regional delegates and the technical staff in charge of NTDs, should be briefed on the TaNT strategy, the shift from control to elimination of onchocerciasis, use of the LoaScope, the surveillance and management of AEs, and the diagnosis and management of SAEs. This training should be done by the TaNT expert team. The teams at all levels will also be trained in basic maintenance of the LoaScope.

After training at the national/regional level, training should be continued, using the same agenda, at the HD level. In the first year it is probably optimal that the regional (intermediate) level and the TaNT expert teams train the HD and health area staff. In subsequent years, the training could be done by intermediate-level staff, supervised by the onchocerciasis (or onchocerciasis-LF or NTD) programme manager and his technical team.

A sensitization campaign should be carried out in all HDs eligible to implement the TaNT strategy to inform the residents about the programme. The campaign should focus on details concerning the diseases (onchocerciasis, LF and loiasis), their consequences and their treatment. Emphasis should also be placed on the possible AEs that can occur after ivermectin treatment and contrast this with the important fact that with the new TaNT strategy there should be no resulting SAEs. The TaNT strategy should be organized at the district level. In each community, one member (the CDD) will be selected to take care of an average of 100 inhabitants (20 households). This selection will be organized by local authorities and the CDD should be designated by the area population. The CDD will be trained as stated above to conduct the census and administer treatment (dosage of ivermectin according to patient height). He/she will also be trained in the indications and contraindications of ivermectin and albendazole administration, patient registration and completion of the treatment report. The head of the health centre will select an assistant nurse or assistant lab technician, or any other health personnel who will be trained to collect blood samples for the LoaScope and a literate community member will receive training on use of the LoaScope. An operational TaNT team will be deployed in three to five communities, depending on the size of the communities, to reduce the distances covered by each team (Figure 2). Following training, the CDDs will organize the census, then the nurse and the TaNT teams will plan and organize treatments. For the first year, the TaNT teams will start in contiguous areas to facilitate supervision by the head of the health centre. The health area could be split into two zones, with the first half of the health area starting in the first week, followed by the other half in the second week. The treatments in the overall health area should be supervised by the HD team.

Considering that this strategy cannot be deployed following a door-to-door strategy, the TaNT team will organize the procedures

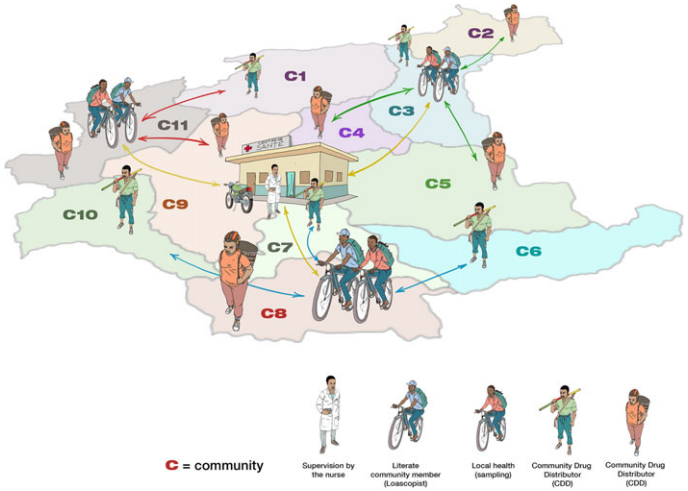

Figure 2. Core TaNT operational teams and deployment of the campaign in 11 communities in a single health area.

in the community so as to shorten the distance between the households and treatment points; for example, arrangements could be made for villagers to join neighbouring treatment sites if this is more practical for them. The treatment activities should start at 10:00 h (to take into account the diurnal periodicity of *L. loa* mf) and, depending on the number of inhabitants to be treated at a particular site, the team will stay at each site for 1 or 2 h before moving on to the next treatment site. In subsequent years, the CDD will register and treat directly (without LoaScope examination) all the populations that were tested and treated the first year, as *L. loa* microfilaremia is reduced by 90% the year following the first treatment with ivermectin.[20] The LoaScope tests will be done in those who have never been tested previously. The follow-up for AEs will be done in the same manner as indicated in the Mectizan Expert Committee/Technical Consultative Committee guidelines.[21]

It will be important to have technical support always available at the national level that can address the concerns of the TaNT teams in the field. The technical support team will be fully accessible to help solve any technical problems with the LoaScope and ensure maintenance and software updates according to the manufacturer's and developer's recommendations. Such a national-level team should be under the direction of the national NTD programme, thus ensuring that there is a good flow of information between the different bodies involved in NTD programme, the Ministry of Health and supporting partners.

Pending questions and/or challenges to the success of the operationalization plan

The first challenge is the management of heavily infected individuals excluded from ivermectin mass administration. Those excluded individuals will be invited to attend the health centre, where they will undergo a test with the SD Bioline Biplex (Wb123- and Ov16-based POC) tests for onchocerciasis and LF[22] and treated accordingly (doxycycline 100 mg/day for 5 weeks for *O. volvulus* or albendazole every 6 months for *Wuchereria bancrofti*). Those

who are not infected by either LF or onchocerciasis will have the opportunity to receive 200 mg albendazole twice daily for 21 days[14] to lower their *L. loa* mf load. If, during the following year's treatment campaign, their mf level is below the risk threshold, they will receive ivermectin.

The second challenge is the ability of these community personnel to conduct this strategy. Because of the low complexity of the strategy (as compared with other community interventions), the strategy is likely to be successful. We really hope this system will work, as the Community Directed Intervention Group showed that community members could implement a significantly more complex intervention. Indeed, a large-scale study showed that the CDI process provides an effective platform for the delivery of health interventions in the model of core principles of primary healthcare. Many public health interventions are now based on community partnership. Active community participation in the organization and delivery of interventions and a structured and systematic partnership of communities and health systems are key factors in the success of the interventions.[23] Also, blood drawers will be selected from among technical personnel (retired or just trained but not yet employed by the government), and the LoaScope is a user-friendly tool. However, we would advise that there be a technical support team to manage technical issues that may occur during a community-based TaNT campaign.

Conclusion

The TaNT interventional project was conducted with success in 2015 and 2017 in a loiasis-endemic area, the Okola HD. Indeed, mass ivermectin administration was conducted without a single SAE being recorded. Despite this success, the TaNT strategy was costly and hardly applicable in similar settings, and there was an urgent need to develop an operational plan to deploy such a strategy. We have proposed a community-based approach for the TaNT strategy, modelled on the CDTI approach, taking into consideration the success of the CDTI approach in improving ivermectin treatment coverage and the capacity of community members in implementing public health interventions. We now hope that this community approach of the TaNT strategy will be successfully implemented by community members and accelerate the elimination of onchocerciasis in *L. loa*–endemic countries of Central Africa.

Authors' contributions: JK, HCND, CDM, TBN and MB prepared the first draft. All authors critically reviewed and approved the final manuscript.

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Competing interests: None declared.

Ethical approval: This study received ethical clearance (no. 2013/11/370/L/CNERSH/SP) from the National Ethics Committee of Cameroon. The administrative authorization (no. D30-571/L/MINSANTE/SG/DROS/CRSPE/BBM) was delivered by the Division de la Recherche Operationnelle en Santé (DROS). All volunteers provided written signed consent (or parental consent in the case of minors) before undergoing blood sampling and again before receiving treatment.

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