Opinion

Developing a Progressive Control Pathway for African Animal Trypanosomosis☆

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Progressive control pathways (PCPs) are stepwise approaches for the reduction, elimination, and eradication of human and animal diseases. They provide systematic frameworks for planning and evaluating interventions. Here we outline a PCP for tsetse-transmitted animal trypanosomosis, the scourge of poor livestock keepers in tropical Africa. Initial PCP stages focus on the establishment of national coordination structures, engagement of stakeholders, development of technical capacities, data collection and management, and pilot field interventions. The intermediate stage aims at a sustainable and economically profitable reduction of disease burden, while higher stages target elimination. The mixed-record of success and failure in past efforts against African animal trypanosomosis (AAT) makes the development of this PCP a high priority.

Trends

Whilst great strides are being made in the elimination of tsetse-transmitted human African trypanosomosis (HAT or sleeping sickness), progress in the control of African animal trypanosomosis (AAT or nagana) is patchy at best.

Progressive pathways (or stepwise, staged approaches) are increasingly used for the control of a number of human and animal diseases, including foot-and-mouth disease, *peste des petits ruminants*, brucellosis, and rabies.

A range of tools are coming of age, which enable an evidence-based prioritization, planning, and monitoring of interventions against AAT, including geographic information systems (GIS), species distribution models, and population genetics.

Whilst the development of novel drugs against AAT lags behind, the array of techniques for vector control has broadened, and knowledge on their optimal field of application has improved.

Among growing concerns on the capacity of sub-Saharan Africa to feed itself in the coming decades, removing the constraints posed by AAT appears more urgent than ever.

Why a Progressive Control Pathway for AAT?

Progressive control pathways (**PCPs**) (see Glossary) and the related roadmaps are staged approaches increasingly used for the reduction, elimination, and eradication of a range of human and animal diseases, including foot-and-mouth disease (FMD) [1,2], *peste des petits ruminants* (PPR) [3], brucellosis [4], and rabies [5]. Within the PCP acronym, the word ‘control’ can be regarded as encompassing the full range of strategies against diseases, from reduction of the disease burden to **elimination** and **eradication**.

AAT, also known as ‘nagana’, is a family of parasitic diseases caused by different species of unicellular organisms, that is, *Trypanosoma vivax*, *T. congolense*, *T. brucei*, *T. simiae*, and *T. suis*. AAT is **cyclically transmitted** by blood-sucking tsetse flies (Diptera, genus *Glossina*). Some species of trypanosomes, in particular *T. vivax*, can also be transmitted mechanically by other biting flies (most notably *Tabanus* and *Stomoxys* spp.) [6,7]. AAT affects ruminants, swine, camels, equines, and carnivores, but the heaviest burden on subsistence livestock keepers in sub-Saharan Africa is caused by bovine trypanosomosis [8]. Tsetse-transmitted trypanosomosis is also listed by the World Organisation for Animal Health (OIE) as a notifiable disease (i.e., a disease that, as soon as suspected or detected, should be brought to the attention of OIE).

For over a century, efforts to study and control AAT have been substantial. Despite these efforts, the disease remains today the major constraint to the development of more sustainable and cost-effective crop–livestock agricultural systems in those areas of Africa having the greatest untapped potential [9]. The overall objective of the PCP for AAT is to promote

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interventions that alleviate poverty, increase income, and improve the livelihoods and resilience of smallholder farmers by creating and progressively expanding areas free of the AAT burden.

The PCP builds on many decades of research and on numerous technical and political achievements. Cost-effective tools against tsetse [10,11] and reliable diagnostics for AAT [12] are available. Success stories of sustainable tsetse and AAT control do exist [13–15]. Technical expertise is present within most endemic countries and from international development and research institutions. In a One-Health framework, synergies can be exploited for the elimination of human African trypanosomosis (HAT) [16] and for the control of other animal diseases (e.g., tick-borne diseases [17]). Commitment is strong at the national and international level, as demonstrated by the Pan African Tsetse and Trypanosomosis Eradication Campaign (PATTEC), an African Union (AU) initiative [18], and by the Programme against African Trypanosomosis (PAAT), which brings together the efforts of the relevant United Nations agencies (i.e., Food and Agriculture Organization of the United Nations (FAO), International Atomic Energy Agency (IAEA) and World Health Organization (WHO)) [19,20].

Many challenges also exist. There is no vaccine for AAT. Chemotherapy and chemoprophylaxis remain the mainstay of disease control, but available veterinary trypanocides are outmoded [21], substandard and counterfeit products are widespread [22,23], and drug resistance is increasing [21,24]. The presence of a wildlife reservoir makes AAT elimination very challenging, if at all possible, unless the vectors are removed in a sustainable way. In turn, the sustainable removal of tsetse populations has been achieved in less than 2% of the 10 million km^2 estimated to be infested [25], and AAT integrated management has very rarely been sustained [26]. The disease is often neglected by both endemic countries and donors, as it mostly affects poor smallholders in rural areas, it does not engage city-dwelling decision makers, it poses no immediate threat to wealthy nations, and it does not directly influence international livestock trade. Finally, while a country can self-declare, under its own responsibility, that the entire territory or a zone is free from AAT [27], there is no OIE official recognition of 'freedom from AAT' status so far.

The present opinion provides a first outline of the PCP for AAT, aiming to contribute to the rationalization of interventions against this persistent and pernicious disease. The development of the PCP appears particularly timely at a juncture when HAT elimination is progressing steadily whilst AAT control lags behind.

PCP for AAT

The PCP for AAT includes five stages and a pre-entry level named 'below Stage 1' (Figure 1). A regular step-wise progression is the rule (i.e., from Stage N to Stage N + 1) but **fast-tracking** is possible in specific circumstances. To move from one stage to the next, a set of minimum requirements must be met and a detailed plan to be implemented in the following stages must be prepared. Independent validation is required.

'Below Stage 1' and 'Stage 1' focus on creating the necessary political, institutional, and technical environment, and assessing disease risk and impact. Stage 2 looks at **sustainable reduction** of the AAT burden, while the following stages (i.e., from 3 to 5) target elimination. The PCP is consistent with the phased conditional approach recommended by FAO/IAEA for the implementation of area-wide integrated pest management programmes that might include the Sterile Insect Technique (SIT) [26].

'Below Stage 1' and 'Stage 1' are mainly national-level endeavours, whilst subsequent stages will normally target selected intervention areas. As a result, within a country, different AAT-affected areas can be at different PCP stages (Figure 2).

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At all stages of the PCP, various technical and managerial areas require attention (Figure 3), although emphasis and specific activities differ for different stages.

The main target group for the proposed PCP are the national authorities in charge of tsetse and AAT control, but the approach can be applied to multinational and regional initiatives as well. The PCP for AAT should also contribute to, and benefit from, a general reinforcement of the veterinary services in the affected countries, and all possible synergies in the control of other diseases should be exploited. Importantly, the PCP provides donors with a robust tool to monitor and evaluate progress and impacts, and gives them confidence in supporting AAT-endemic countries.

Laying the Groundwork: Below Stage 1, and Stage 1

Below Stage 1

A few minimum requirements have to be met to enter the PCP. Prior to that, a country is considered to be 'below Stage 1', meaning that it has not formally entered the PCP.

One key requirement to enter Stage 1 is political and financial commitment at the national level, which is translated into adequate core funding to establish and support a **Specialized National Structure** (**SNS**) dedicated to tsetse and AAT control. An SNS must be endowed with core technical and managerial competencies, although the strengthening of the SNS capacities is addressed to a larger extent in subsequent stages. Political commitment is also signalled through national level engagement in the AU-PATTEC initiative.

The second requirement relates to self-assessment and planning. Countries need to appraise their existing capacities, epidemiological knowledge, institutional arrangements, human and financial resources. Subsequently, a **work plan** must be developed, which will be implemented in the subsequent Stage 1.

Stage 1

The focus of Stage 1 is to develop technical capacities and to gain a sufficient understanding of AAT distribution, risk, and impact for an evidence-based planning of field activities. The latter will be implemented in Stage 2 and beyond.

Essential capacities include project management, veterinary and entomological competencies in **parasitological and serological surveillance**, trapping and identification of vector species, and AAT and vector control. Skills in data management and GIS to enable mapping, risk assessment, and monitoring are also needed [7,28].

Essential capacities must be built within the SNS, but more advanced ones (e.g., molecular diagnosis [29], geospatial modelling [30]), can be available from national or regional centres and laboratories, as well as from international institutions.

The establishment of a national-level information system is another pillar of Stage 1. All recent epidemiological and entomological data should be assembled, harmonized, geo-referenced, and centralized. National atlases can be developed [7], also using methodologies from the FAO continental Atlas of tsetse and AAT [31,32]. Targeted field investigations should be conducted where gaps exist or where available information is too old to inform decision making. More generally, all necessary data for an evidence-based, rational selection of intervention areas and strategies need to be collected in Stage 1. In particular, if a fast-tracking to the elimination pathway is envisaged (Stage 3 and beyond), genetics studies are likely to be needed to establish the degree of isolation of the target tsetse populations [33,34] and the related risk of reinvasion (Box 1).

Glossary

AAT elimination: reduction to zero of AAT incidence in a defined geographical area as a result of deliberate efforts. Continued measures to prevent re-establishment of transmission may be required. The concept finds application at Stages 3 to 5 of the PCP for AAT.

AAT eradication: permanent reduction to zero of the worldwide incidence of AAT as a result of deliberate efforts. Intervention measures are no longer needed.

AAT extinction: infectious agents causing AAT no longer exist in nature or in the laboratory.

AAT sustainable reduction: reduction of AAT incidence, prevalence, morbidity, mortality, burden, or impact to a locally acceptable, economically-profitable level as a result of deliberate efforts. Continued intervention measures are required to maintain the reduction. The concept finds application at Stage 2 of the PCP for AAT. 'AAT control' is used by certain authors in lieu of 'AAT sustainable reduction'.

African animal trypanosomosis (AAT) or 'nagana': a family of parasitic diseases caused by different species of tsetse-transmitted trypanosomes, that is, *Trypanosoma vivax*, *T. congolense*, *T. brucei*, *T. simiae*, and *T. suis*.

Baseline data: epidemiological, entomological, socioeconomic, and environmental data collected prior to the start of interventions against tsetse and AAT. Baseline data constitute the reference against which the impact of interventions is measured.

Cyclical transmission: AAT transmission by tsetse flies, whereby trypanosomes pathogenic for livestock undergo multiplication cycles within the mouthparts, midgut and/or salivary glands of the vector.

Fast tracking: possibility of skipping certain stages of the PCP, if conditions allow. In the PCP for AAT, fast tracking is possible from Stage 1 to Stage 3, and from Stage 1 to Stage 5.

Insecticide-treated cattle (ITC): epicutaneous application of insecticides on cattle, also known as the live-bait technique. Animals can be treated with pour-on formulations, spraying or dipping with aqueous formulations. The insecticide can be

Box 1. Novel Tools for Optimizing the Prioritization of Intervention Areas and the Execution of AAT Control

Atlases of Tsetse and AAT

Virtually all AAT-endemic countries lack a national-level, centralized system to manage field data on tsetse and AAT. Data collected over the years are generally scattered between different agents, locations or institutions, and they may even become lost altogether. This gap dashes hopes for an evidence-based decision making, as it makes it impossible to have a synoptic picture of the epidemiological situation at the country level. National atlases of tsetse and AAT, such as the one recently set up in Sudan [7], are now being developed in many countries. They provide a systematic, spatially explicit framework for data collation, storage, harmonization, and management. These initiatives benefit from the FAO-led continental atlas of tsetse and AAT [31,32], as the methodologies it developed can be adapted and applied at the country level. National-level information systems on tsetse and AAT, such as the atlases, ought to underpin data analysis and decision making throughout the PCP; they should be set up in Stage 1 and continuously updated in the following stages as new data are collected.

Distribution Models

Species distribution models enable us to map AAT risk [64] and optimize tsetse control operations [30]. They can be used to generalize point data on tsetse presence and density and AAT prevalence, such as those collected during Stages 1 and 2 of the PCP. The entomological inoculation rate (EIR) or tsetse challenge can be modelled in space and time using a range of environmental data [64]. This allows a fine-scale picture of the dynamics of AAT risk to be generated. Such models can be very useful to select the priority intervention areas and to inform interventions during Stage 2.

When an AAT elimination strategy is selected (Stage 3 and beyond), species distribution models can also be used to inform operations. In the Niayes area in Senegal, models of tsetse distribution were used throughout the campaign to optimize the targeting and cost-effectiveness of operations, including deployment of ITT, release of sterile males, and positioning of tsetse monitoring traps to assess progress [30].

Tsetse Population Genetics, Friction and Isolation

A new methodology combining GIS and population genetics was recently developed to identify natural barriers that isolate tsetse populations [35]. The methodology is based on the concept of landscape resistance to tsetse genetic flow (i.e., 'friction'). A statistical model of the genetic distance between tsetse populations is fitted using a set of predictors (i.e., remotely-sensed environmental data). By combining the modelled genetic distance with a species distribution model, the tool allows potentially isolated populations to be identified, and their genetic distance to the main tsetse population to be estimated. During Stage 1 of the PCP, this methodology could inform the choice on the most appropriate intervention strategies. For example, potentially isolated tsetse populations could be targeted for Stage 3 elimination activities, whilst for nonisolated populations a Stage 2 integrated management approach might be more appropriate. The most favourable areas to deploy artificial barriers to reinvasion could also be identified, thus optimizing sequential elimination programmes by dividing the target population into partially isolated subunits.

Spatially Explicit Benefit–Cost Analysis

The burden of AAT, and the potential benefits that can accrue from its removal, are not evenly distributed across endemic countries. Recent work on bovine trypanosomosis in Eastern Africa generated a suite of methodologies to estimate and map the costs [11], benefits [8], and benefit–cost ratios [10] of different intervention techniques. This spatially explicit information on the costs and benefits of different strategies can be a valuable aid to decision making, in particular in the prioritization of intervention areas and the selection of the most cost-effective tools.

Socioeconomic information on the burden of AAT is essential to justify investment and to prioritize areas for intervention. Spatially explicit benefit-cost analyses [8,10,11], tsetse and AAT distribution maps [7,31,32], and models of tsetse distribution and isolation [30,35] are tools that should support a rational selection of intervention areas and strategies (Box 1). The occurrence and risk of HAT [36–38] should be considered, as interventions promoting One-Health bring broader benefits and are more likely to attract resources [16,39,40]. Security constraints (i.e., civil strife, armed conflicts, etc.) should not be overlooked.

applied either to the full body or restrictedly on the legs and belly (by spraying or dipping).

Insecticide-treated targets (ITT): insecticide-impregnated devices used to kill pests. Tsetse targets can use both visual (i.e., shape, size, colours) and olfactory cues (i.e., natural or artificial odours) to attract flies.

Livestock protective fences (LPF): insecticide-incorporated netting that reduces the impact of nuisance and biting flies on livestock. The net is normally installed around pens, kraals, sheds, or sties, in which livestock spend a sizable part of the day. Attracted by the livestock hosts, biting flies are intercepted and killed by the insecticide-treated net.

Mechanical transmission: AAT transmission by biting flies such as Tabanidae and Stomoxynae, whereby trypanosomes pathogenic for livestock do not undergo cycles within the vector, or by veterinary agents using the same needle during vaccination campaigns targeting other diseases.

Parasitological surveillance: an activity involving the collection, analysis and interpretation of parasitological data, that is, data collected by means of parasitological diagnostic techniques. For AAT, the techniques include wet blood films, Giemsa-stained thick and thin blood films, centrifugation techniques such as the Haematocrit centrifuge technique, and the Buffy coat technique, and PCR detection of the parasites' DNA.

Progressive control pathway (PCP): stepwise, staged approach for the sustainable reduction, elimination and eradication of a disease (i.e., within the PCP acronym, the word 'control' can be regarded as encompassing the full range of strategies against the disease).

Roadmap: strategic plan and programmatic framework to advance in the progressive control and elimination of a disease. Roadmaps can be developed at the national, regional and global levels.

Rolling-carpet approach: a phased approach whereby the target pest population and the area it occupies are subdivided into a series of adjacent blocks. Blocks are treated sequentially, with a view to creating and progressively expanding pest-free areas. Generally, elimination

While substantive field interventions are the focus of subsequent stages, pilot field activities against tsetse and AAT should be carried out in Stage 1. Their aim is to develop national capacities, fine-tune and optimize intervention tools, and motivate donors. Furthermore, throughout the PCP, field interventions may be needed to tackle possible AAT epidemics [24], including in Stage 1.

Stage 1 should also look at coordination. A **steering committee** should be set up, for orientation and supervision of the SNS and its activities. Membership should include national stakeholders (i.e., all concerned ministries such as livestock, agriculture, health, environment, etc.), as well as regional and international actors (e.g., regional economic communities (RECs), international organizations, and research institutions).

Stage 1 culminates in the choice of priority intervention areas [41] and most appropriate strategies for the selected areas (AAT sustainable reduction or elimination). Importantly, the most likely strategy for subsequent stages can, to some extent, influence activities in Stage 1. For example, requirements in terms of data and capacities differ between the sustainable reduction and elimination scenarios, and this could affect activities and the duration of Stage 1.

Sustainable AAT Reduction: Stage 2

The focus of Stage 2 is a sustainable and economically-profitable reduction in AAT risk and burden by creating areas of low AAT incidence and impact, whereby only sporadic treatments with trypanocides are needed and the risk of emergence and/or spread of drug resistance is minimized [21,24].

The intervention strategy hinges on the integrated management of AAT [24,25], a community/farmer-based approach that relies on the collaboration of local veterinary services and farmers associations, taking into account eco-epidemiological settings, livestock production systems [42], and cattle breeds. Effective strategies will require the combined use of tsetse control methods, diagnostic tests, and trypanocidal drugs. Improved nutrition and the control of other parasitic diseases would also be beneficial [43,44].

Baseline and monitoring data, including parasitological, entomological, and socio-economic data, need to be collected in the intervention areas to guide field activities, fine-tune intervention strategies, and measure progress and impact. The possible presence of drug resistance should be considered, and if necessary investigated.

Regarding capacity development, all actors involved in the integrated AAT management should be targeted, including livestock keepers and farming communities at large, public and private veterinary services, as well as the SNS. Emphasis should go on the correct use of trypanocides to limit the emergence and spread of drug resistance [21] and on efficient and cost-effective vector control techniques, particularly **insecticide-treated cattle** (**ITC**) [45,46], **livestock protective fences** (**LPF**) in the case of zero-grazing rearing systems [47], and **insecticide-treated targets** (**ITT**), especially where tsetse pressure from protected areas has to be prevented [48].

The main challenge in Stage 2 is sustainability, which will have to rely on the sensitization and training of veterinary services, farmer associations, and individual farmers. Funding mechanisms must be put in place to ensure that interventions are sustained with minimal support from extension services [49]. The latter should focus on maintaining awareness and securing the availability and appropriate use of affordable, efficient and cost-effective control tools [22]. Importantly, farmer communities must be fully involved in the devolvement of the integrated disease management strategies to ensure that they are adapted to the target

within one block and suppression in the adjacent one are carried out simultaneously to avoid the risk of reinvasion of the cleared blocks. In the process, temporary barriers may also be required between blocks to prevent reinvasion.

Sequential aerosol technique (SAT): the application in sequence of several ultra-low-volume sprays of nonresidual insecticides, usually by aircraft.

Serological surveillance: an activity involving the collection, analysis and interpretation of serological data, that is, data collected by means of antibody detection techniques. For AAT, the enzyme-linked immunosorbent assay (ELISA) is the most commonly applied serological test.

Specialized National Structure (SNS): dedicated entity with national level mandate for AAT control and elimination. Examples of SNS include specialized units within the mandated ministries, dedicated institutes, coordination structures, and statal or parastatal bodies.

Steering committee: a body set up to orient and supervise the Specialized National Structure and its activities. Membership should include national stakeholders (i.e., all concerned ministries such as livestock, agriculture, health, environment, etc.), as well as regional and international actors (e.g., regional economic communities (RECs), international organizations and research institutions).

Sterile insect technique (SIT): a method of pest control using area-wide inundative releases of sterile insects. Sterile males reduce reproduction in a field population of the same species by inducing sterility in wild females.

Tsetse elimination: complete removal of a tsetse species from a defined geographical area. The concept finds application at Stages 3 to 5 of the PCP for AAT. 'Local eradication', or even 'eradication' tout-court, are used by certain authors in lieu of 'elimination'.

Tsetse eradication: removal of all wild populations of a given tsetse species from the whole planet.

Tsetse suppression: deliberate reduction of fly numbers as a precursor to elimination. The concept finds application at Stage 3 of the PCP for AAT.

livestock–agricultural production systems and more generally to local constraints. Adoption of new technologies, such as tiny targets, LPF, restricted application of insecticide on animals and repellent–insecticide associations, normally requires external support, a good knowledge of local sociotechnical networks, a strong participatory approach and colearning processes to adjust the techniques to the users [25]. The degree of adoption of the proposed strategy by stakeholders will depend on their appreciation of the benefits and risks derived from the intervention activities and the associated changes required within their farming system [50].

Stage 2 could be sustained indefinitely, with AAT management becoming a fixed production cost [10]. However, the strategy should be reassessed at regular intervals (3–5 years). Should the epidemiological and socioeconomic conditions become favourable, a shift towards an elimination strategy (Stage 3) can be envisaged.

Tsetse sustainable reduction: deliberate reduction of fly numbers to locally acceptable levels; the reduction is maintained by continued intervention. The concept finds application at Stage 2 of the PCP for AAT. ‘Tsetse control’ is used by certain authors in lieu of ‘tsetse sustainable reduction’.
Work plan: detailed plan of action for specific intervention areas and for a well defined time period (in general, of a few years), aimed at advancing in the progressive control of AAT.

Eliminating AAT: Stages 3 to 5, and beyond

The focus of the PCP’s final stages (3 to 5) is to create sustainable AAT-free areas. Models for AAT transmission, as well as for other vector-borne diseases, indicate that in certain agro-ecological settings (i.e., endemic AAT cycle where wild fauna are absent [48]) the disease might be eliminated through a substantial and **sustained reduction** in tsetse densities [51]. However, real-life examples of this approach are lacking, and AAT elimination normally requires the local **elimination** of the tsetse vector. This is the approach described in this PCP.

In the selection of target areas for tsetse elimination, the level of isolation should be assessed [33,34], and isolated populations should be given priority. In principle, larger, nonisolated populations could be tackled sequentially through the **rolling-carpet approach** [52], which has been used very successfully for other insect pests [53,54]. However, real-life, sustainable examples of the approach for tsetse flies are rarer. A recent example is the sequential elimination of a sizable belt of *Glossina morsitans centralis*, which cuts across Botswana, Angola, and Zambia; the programme was largely based on aerial spraying, namely the **sequential aerosol technique (SAT)** [15,55].

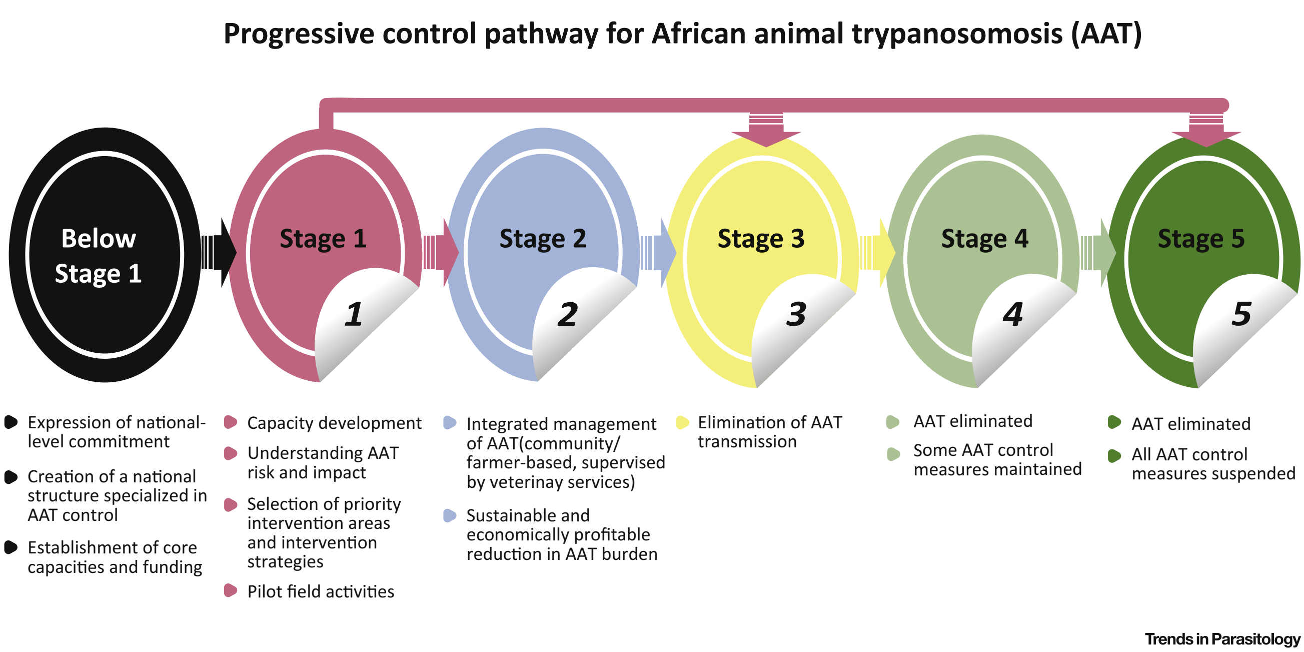

Figure 1. Progressive Control Pathway for African Animal Trypanosomosis (AAT).

Trends in Parasitology

Figure 2. Examples of Geographically-Explicit Roadmap (Panel A) and Work Plan (Panel B) for the Progressive Control of African Animal Trypanosomosis (AAT) in One Hypothetical Country (Country X). In panel A, Country X's initial situation is shown to be 'Below Stage 1'; it then moves to 'Stage 1' at the national level, and subsequently control activities are carried out in selected zones, thus enabling these selected zones to advance to higher progressive control pathways (PCP) stages. In panel B, one specific work plan by zone is illustrated (in this example, it is a 5-year work plan). Zone A is an AAT-free area, in which the absence of AAT was confirmed through surveys carried out in previous steps of the roadmap. Zone B is an area where AAT occurs and which has been prioritized for AAT elimination; elimination activities are planned to start in year N + 3. Zone C is an area where AAT is in the process of being eliminated, and where AAT transmission is planned to be interrupted by the year N + 4; some control measures are planned to be maintained after year N + 4. Zone D is an area where AAT transmission has been interrupted, but some control measures are still in place; all control measures are planned to be suspended as of year N + 3. Zone E is an area where AAT has been reduced, and which has been prioritized for AAT elimination as of year N + 3. Zone F is an area where AAT has been reduced, and where the reduction is planned to be sustained during the 5-year period. Zone G is an area where AAT occurs, and which has been prioritized for AAT reduction/integrated management as of year N + 2. Zone H is an area where AAT occurs, but which has not been prioritized for either reduction/integrated management or elimination activities during the present 5-year work plan.

Stage 3

The focus of Stage 3 is the interruption of AAT transmission. Many activities already described for Stage 2 have to be carried out (or continued) in Stage 3, but emphasis differs. The collection of baseline and monitoring data is more intensive than in Stage 2, so as to address the higher information requirements of an elimination campaign [56,57]. Focus is on tsetse data, including longitudinal monitoring of tsetse densities [30], age structure, and natural abortion rates (the latter only needed to measure SIT-induced abortion rates, if an SIT component is planned) [26]. At very low tsetse densities, advanced statistical analysis of tsetse catches is needed to measure the probability of having achieved tsetse elimination [30]. Despite the emphasis on tsetse data, essential AAT [29,58,59] and socioeconomic data [60] are still needed.

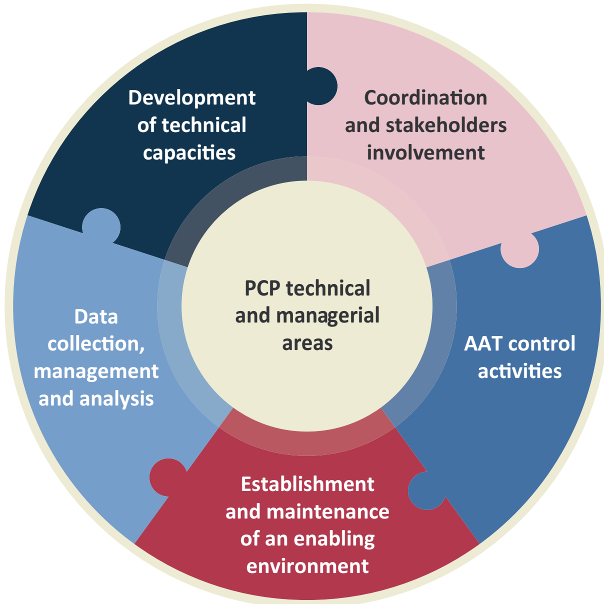

Figure 3. Progressive Control Pathway (PCP) Technical and Managerial Areas. Whilst each PCP stage is characterized by specific goals and activities, five components cut across all stages, albeit with different emphasis. Coordination and stakeholders involvement points to the notion that African animal trypanosomosis (AAT) control must be a collective endeavour, which should mobilize and harness the commitment of donors, decision-makers, farmers, and extension services alike. Capacity development plays a major role in the early stages of the PCP, but it must be sustained throughout, so as to address the specific technical requirements of the various stages. Epidemiological and socio-economic data are crucial for an evidence-based decision making, starting from the feasibility assessment and prioritization, and culminating in the demonstration of the impact of interventions. The creation of an enabling environment must ensure that the normative, legal, and technical frameworks are conducive to a successful and sustainable roll-out of AAT control interventions. Finally, AAT control in the field begins with pilot activities in Stage 1, continues in different ways through the following stages, until it is interrupted in Stage 5.

In order to eliminate tsetse flies in the target area, a **suppression** phase focuses on the reduction of tsetse densities, while a second mop-up phase completes the elimination. A range of tools can be used in the process, either alone but preferably in combination following an integrated pest-management approach. These include the methods already mentioned in Stage 2, such as ITC and ITT. However, more expensive methods can be used in an elimination context [10], such as SAT [15] and SIT [14,61]. Some of the tsetse control methods are more appropriate for suppression, while others are more effective for elimination. For example, SIT is the only technique with inverse density dependent efficiency (i.e., it works best when wild tsetse densities are very low), so it is particularly efficient for elimination [62].

Once tsetse flies are eliminated, the need to clear the parasite reservoir in livestock should be evaluated. A blanket treatment may be particularly important to eliminate *T. vivax*, whose **mechanical transmission** can occur in the absence of tsetse. Control and surveillance of livestock movement may also be necessary to reduce the risk of disease reintroduction.

Compared with Stage 2, AAT elimination requires more centralized, top-down management and coordination. Despite this, farmers' sensitization and involvement remains crucial. Public information campaigns (e.g., radio, TV, etc.) ensure the engagement and support of the beneficiaries, who can also contribute directly to the campaign (e.g., if ITC is used).

Transition from Stage 3 to Stage 4 is linked to the interruption of AAT transmission (i.e., not directly to the elimination of the tsetse vector).

Stages 4 and 5

The focus of Stage 4 is the elimination of AAT transmission and the establishment of AAT-free areas. In Stage 4 the maintenance of some of the control measures deployed in Stage 3 is still required. In Stage 5 all control measures are lifted, and the free-status should be maintained in their absence.

A monitoring system, including sentinel herds to assess AAT incidence, is required to ensure the absence of circulation of parasites and the absence of tsetse (when tsetse elimination was targeted in Stage 3). Serological tests for the detection of antibodies against trypanosomes [12] or tsetse saliva antigens [63] could be useful to demonstrate the absence of parasite circulation or the absence of tsetse.

Beyond Stage 5

Exit from the PCP (i.e., 'Beyond Stage 5') should be linked to the demonstration of AAT-free status. The OIE has developed a procedure for the official recognition of disease-free status. To date, six diseases are included in this procedure (i.e., bovine spongiform encephalopathy, FMD, contagious bovine pleuropneumonia, African horse sickness, *PPR*, and classical swine fever); AAT is not one of these six, meaning that the OIE does not officially recognize 'freedom from AAT'. However, by providing the relevant epidemiological evidence, a country can prove to a potential importing country that its entire territory or a zone is free from AAT. This would be considered as a self-declaration. The OIE member countries can request OIE to publish their self-declaration of AAT freedom, recognising that this self-declaration remains under the full responsibility of the country in question.

Concluding Remarks and Future Perspectives

The PCP for AAT provides affected countries and stakeholders with a rational tool to plan and implement stepwise AAT control campaigns. In this opinion paper, focus is on Stages 1 to 3, because most countries and affected areas will have to tackle these early stages. Also, taking sound initial decisions is crucial in a stepwise approach, especially regarding the choice between sustainable reduction or elimination of AAT. Research has recently provided improved tools and methodologies to prioritize intervention areas and to select the most appropriate intervention strategy for each of them, taking into account the environmental, epidemiological, and socioeconomical settings (Box 1). In this context, the development of updated maps of tsetse and AAT at a range of scales appears particularly relevant [7,30–32].

Based on the present outline, a detailed PCP will be developed, also by drawing on the expertise from AAT-affected countries and a broader range of experts. In particular, the requirements for transition between stages will be discussed and more accurately defined.

The overall PCP approach was presented and debated in two workshops for AAT-affected countries in Eastern Africa, organized by FAO in collaboration with AU-PATTEC. Interactions with country representatives and other stakeholders enabled the approach to be improved and tentative **roadmaps** to be developed. The tool was appreciated for its capacity to support the formulation of rational national policies and to promote regional integration.

The main goal of this PCP is to help lift the burden of AAT. In this light, the existing normative gaps (e.g., OIE AAT-specific Terrestrial Animal Health Code Chapter and official AAT status recognition) are not considered as major hurdles, and an effective roll-out of the PCP appears both attainable and eminently desirable. To achieve this goal, the support of all stakeholders,

Outstanding Questions

How can a rational use of existing trypanocides be more effectively promoted in the field?

How can investment in the development of novel veterinary drugs against such neglected diseases as AAT be stimulated?

How can we improve the quality assurance of AAT control tools available in the field?

How can novel decision support tools be scaled up and more broadly adopted (i.e., national and continental atlases of AAT and tsetse, distribution models, maps of landscape resistance to tsetse dispersal, spatially explicit benefit-cost analyses; see Box 1)?

How can we involve the social sciences to foster innovation in the context of farmer-based integrated AAT management (i.e., Stage 2 of the PCP)?

What mechanisms need to be put in place to ensure the sustainability of farmer-based integrated AAT management (i.e., Stage 2 of the PCP)?

including resource partners, will be crucial. In particular, funding AAT-endemic countries through the early stages of the PCP will be critical before the benefits of more advanced PCP stages can be fully reaped.

Disclaimer

The views expressed in this publication are those of the authors and do not necessarily reflect the views or policies of the Food and Agriculture Organization of the United Nations.

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References

1. Sumption, K. *et al.* (2012) Progressive control of FMD on a global scale. *Vet Rec.* 170, 637–639
2. FAO/OIE (2012) *The Global Foot and Mouth Disease Control Strategy: Strengthening Animal Health Systems through Improved Control of Major Diseases,* World Organisation for animal Health (OIE)/Food and Agriculture Organization of the United Nations (FAO)
3. FAO/OIE (2015) *Global Strategy for the Control and Eradication of PPR,* FAO/OIE
4. El Idrissi, A. (2012) A stepwise approach for progressive control of brucellosis in animals and humans. *EMPRES Transbound. Anim. Dis. Bull.* 41, 4–8
5. FAO (2012) *Developing a Stepwise Approach for Rabies Prevention and Control,* FAO
6. Desquesnes, M. *et al.* (2009) Development of a mathematical model for mechanical transmission of trypanosomes and other pathogens of cattle transmitted by tabanids. *Int. J. Parasitol.* 39, 333–346
7. Ahmed, S.K. *et al.* (2016) An atlas of tsetse and bovine trypanosomosis in Sudan. *Parasit. Vectors* 9, 194
8. Shaw, A. *et al.* (2014) Mapping the economic benefits to livestock keepers of intervening against bovine trypanosomosis in Eastern Africa. *Prev. Vet. Med.* 113, 197–210
9. Alsan, M. (2014) The effect of the tsetse fly on African development. *Am. Econ. Rev.* 105, 382–410
10. Shaw, A. *et al.* (2015) Mapping the benefit–cost ratios of interventions against bovine trypanosomosis in Eastern Africa. *Prev. Vet. Med.* 122, 406–416
11. Shaw, A.P. *et al.* (2013) Estimating the costs of tsetse control options: an example for Uganda. *Prev. Vet. Med.* 110, 290–303
12. OIE (2013) Trypanosomosis (Tsetse-transmitted). In *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals, World Organisation for Animal Health*. OIE (Chapter 2.4 .17)
13. Kappmeier, K. *et al.* (1998) Review of tsetse flies and trypanosomosis in South Africa. *Onderstepoort J. Vet. Res.* 65, 195
14. Vreysen, M.J. *et al.* (2014) Sterile insects to enhance agricultural development: the case of sustainable tsetse eradication on Unguja Island, Zanzibar, using an area-wide integrated pest management approach. *PLoS Negl. Trop. Dis.* 8, e2857
15. Kgori, P.M. *et al.* (2006) The use of aerial spraying to eliminate tsetse from the Okavango Delta of Botswana. *Acta Trop.* 99, 184–199
16. WHO (2013) *Control and Surveillance of Human African Trypanosomiasis,* Technical Report Series, WHO
17. Eisler, M.C. *et al.* (2003) Integrated control of vector-borne diseases of livestock – pyrethroids: panacea or poison? *Trends Parasitol.* 19, 341–345
18. Kabayo, J.P. (2002) Aiming to eliminate tsetse from Africa. *Trends Parasitol.* 18, 473–475
19. Hursey, B.S. (2001) The programme against African trypanosomiasis: aims, objectives and achievements. *Trends Parasitol.* 17, 2
20. Mattioli, R. *et al.* (2016) The programme against African trypanosomosis. *EMPRES Anim. Health* 360 (46), 9–13
21. Giordani, F. *et al.* (2016) The animal trypanosomiases and their chemotherapy: a review. *Parasitology* 1–28
22. Sutcliffe, O.B. *et al.* (2014) Animal trypanosomosis: making quality control of trypanocidal drugs possible. *Rev. Sci. Tech. OIE* 33, 813–830
23. Tchamdja, E. *et al.* (2016) Drug quality analysis through high performance liquid chromatography of isometamidium chloride hydrochloride and diminazene diaceturate purchased from official and unofficial sources in Northern Togo. *Prev. Vet. Med.* 126, 151–158
24. Van den Bossche, P. and Delespaux, V. (2011) Options for the control of tsetse-transmitted livestock trypanosomosis. An epidemiological perspective. *Vet. Parasitol.* 181, 37–42
25. Bouyer, J. *et al.* (2013) Community- and farmer-based management of animal African trypanosomosis in cattle. *Trends Parasitol.* 29, 519–522
26. Vreysen, M.J. *et al.* (2013) Tsetse flies: their biology and control using area-wide integrated pest management approaches. *J. Invertebr. Pathol.* 112, S15–S25
27. OIE (2016) *Terrestrial Animal Health Code,* OIE
28. Cecchi, G. and Mattioli, R. (2009) *Geospatial Datasets and Analyses for an Environmental Approach to African Trypanosomiasis,* FAO (Food and Agriculture Organization of the United Nations)
29. Seck, M. *et al.* (2010) The prevalence of African animal trypanosomoses and tsetse presence in Western Senegal. *Parasite* 17, 257–265
30. Dicko, A.H. *et al.* (2014) Using species distribution models to optimize vector control in the framework of the tsetse eradication campaign in Senegal. *Proc. Natl. Acad. Sci. U.S.A.* 111, 10149–10154
31. Cecchi, G. *et al.* (2015) Developing a continental atlas of the distribution and trypanosomal infection of tsetse flies (*Glossina* species). *Parasit. Vectors* 8, 284
32. Cecchi, G. *et al.* (2014) Assembling a geospatial database of tsetse-transmitted animal trypanosomosis for Africa. *Parasit. Vectors* 7, 39
33. Solano, P. *et al.* (2010) Population genetics as a tool to select tsetse control strategies: suppression or eradication of Glossina palpalis gambiensis in the Niayes of Senegal. *PLoS Negl. Trop. Dis.* 4, e692
34. Adam, Y. *et al.* (2014) Genetic comparison of *Glossina tachinoides* populations in three river basins of the Upper West Region of Ghana and implications for tsetse control. *Infect. Genet. Evol.* 28, 588–595

35. Bouyer, J. *et al.* (2015) Mapping landscape friction to locate isolated tsetse populations that are candidates for elimination. *Proc. Natl. Acad. Sci. U.S.A.* 112, 14575–14580

36. Simarro, P.P. *et al.* (2010) The Atlas of human African trypanosomiasis: a contribution to global mapping of neglected tropical diseases. *Int. J. Health Geogr.* 9, 57

37. Simarro, P.P. *et al.* (2012) Estimating and mapping the population at risk of sleeping sickness. *PLoS Negl. Trop. Dis.* 6, e1859

38. Simarro, P.P. *et al.* (2015) Monitoring the progress towards the elimination of gambiense human African trypanosomiasis. *PLoS Negl. Trop. Dis.* 9, e0003785

39. Scoones, I. (2014) The politics of trypanosomiasis control in Africa. Working Paper Series, STEPS Centre, ISBN 978-1-78118-144-7

40. Grant, C. *et al.* (2015) Stakeholder narratives on trypanosomiasis, their effect on policy and the scope for One Health. *PLoS Negl. Trop. Dis.* 9, e0004241

41. Mattioli, R. *et al.* (2004) Tsetse and trypanosomiasis intervention policies supporting sustainable animal-agricultural development. *J. Food Agr. Environ.* 2, 310–314

42. Cecchi, G. *et al.* (2010) Geographic distribution and environmental characterization of livestock production systems in Eastern Africa. *Agric. Ecosyst. Env.* 135, 98–110

43. Mungube, E.O. *et al.* (2012) Best-bet integrated strategies for containing drug-resistant trypanosomes in cattle. *Parasit. Vectors* 5, 164

44. Katunguka-Rwakishaya, E. *et al.* (1997) The influence of supplementation with cotton seed cake on the resistance of Ugandan goats to primary and secondary challenges with *Trypanosoma congolense* and on their response to treatment. *Vet. Parasitol.* 70, 67–76

45. Bouyer, J. *et al.* (2009) Control of bovine trypanosomosis by restricted application of insecticides to cattle using footbaths. *Vet. Parasitol.* 161, 187–193

46. Torr, S.J. *et al.* (2007) Less is more: restricted application of insecticide to cattle to improve the cost and efficacy of tsetse control. *Med. Vet. Entomol.* 21, 53–64

47. Bauer, B. *et al.* (2011) Managing tsetse transmitted trypanosomosis by insecticide treated nets—an affordable and sustainable method for resource poor pig farmers in Ghana. *PLoS Negl. Trop. Dis.* 5, e1343

48. Van den Bossche, P. (2010) A changing environment and the epidemiology of tsetse-transmitted livestock trypanosomiasis. *Trends Parasitol.* 26, 236–243

49. Catley, A. and Leyland, T. (2001) Community participation and the delivery of veterinary services in Africa. *Prev. Vet. Med.* 49, 95–113

50. Bouyer, F. *et al.* (2011) Restricted application of insecticides: a promising tsetse control technique, but what do the farmers think of it? *PLoS Negl. Trop. Dis.* 5, e1276

51. Hargrove, J.W. *et al.* (2012) Modeling the control of trypanosomiasis using trypanocides or insecticide-treated livestock. *PLoS Negl. Trop. Dis.* 6, e1615

52. Hendrichs, J. *et al.* (2005) Strategic options in using sterile insects for area-wide integrated pest management. In *Sterile Insect Technique* (Dyck, V., ed.), pp. 563–600, Springer

53. Enkerlin, W. *et al.* (2015) Area freedom in Mexico from Mediterranean fruit fly (Diptera: Tephritidae): a review of over 30 years of a successful containment program using an integrated area-wide SIT approach. *Fla. Entomol.* 98, 665–681

54. Wyss, J.H. (2000) Screwworm eradication in the Americas. *Ann. N. Y. Acad. Sci.* 916, 186–193

55. Kgori, P.M. and Modo, S. (2009) *Transboundary Programme to Eliminate Tsetse from the River Frontiers of Botswana and Namibia Using the Sequential Aerial Spraying Technique.* 30th Meeting of the International Scientific Council for Trypanosomiasis Research and Control (ISCTRC), African Union Interafrican Bureau for Animal ResourcesKampala, Ugandapp. 461–470

56. Bouyer, J. *et al.* (2010) Stratified entomological sampling in preparation for an area-wide integrated pest management program: the example of *Glossina palpalis gambiensis* (Diptera: Glossinidae) in the Niayes of Senegal. *J. Med. Entomol.* 47, 543–552

57. Percoma, L. *et al.* (2016) Enquêtes entomologiques préparatoires à une lutte à grande échelle contre les glossines, assistées par un système d'information géographique: cas de la Pattec au Burkina Faso. *Rev. Elev. Med. Vet. Pays Trop.* 68, 157–165

58. Adam, Y. *et al.* (2012) Bovine trypanosomosis in the Upper West Region of Ghana: entomological, parasitological, and serological cross-sectional surveys. *Res. Vet. Sci.* 92, 462–468

59. Sow, A. *et al.* (2013) Baseline survey of animal trypanosomosis in the region of the Boucle du Mouhoun, Burkina Faso. *Res. Vet. Sci.* 94, 573–578

60. Bouyer, F. *et al.* (2014) Ex-ante benefit-cost analysis of the elimination of a Glossina palpalis gambiensis population in the Niayes of Senegal. *PLoS Negl. Trop. Dis.* 8, e3112

61. Vreysen, M.J. *et al.* (2000) *Glossina austeni* (Diptera: Glossinidae) eradicated on the island of Unguja, Zanzibar, using the sterile insect technique. *J. Econ. Entomol.* 93, 123–135

62. Bouyer, J. *et al.* (2010) Trypanosomosis: control methods. In *Infectious and Parasitic Diseases of Livestock* (Lefèvre, P.-C., ed.), pp. 1936–1943, Éditions Lavoisier (Tec & Doc)

63. Somda, M.B. *et al.* (2016) Identification of a Tsal152-75 salivary synthetic peptide to monitor cattle exposure to tsetse flies. *Parasit. Vectors* 9, 149

64. Dicko, A.H. *et al.* (2015) A spatio-temporal model of African animal trypanosomosis risk. *PLoS Negl. Trop. Dis.* 9, e0003921