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How can we better integrate the prevention, treatment, control and elimination of neglected tropical diseases with other health interventions? A systematic review

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ABSTRACT

Background Globally, about 1.7 billion people living in poverty are affected by one or more of a group of disabling, disfiguring and poverty-promoting conditions known as neglected tropical diseases (NTDs). Major global health actors, like the WHO, have endorsed a shift from vertical to integrated NTD management.

Objective This systematic review aimed to evaluate how integration is being conducted and how we can improve it.

Methods PubMed, Medline, Cochrane library, Web of Science, Trip, Embase, Global Health and Google Scholar were searched from 1 April to 22 July 2020.We included peer-reviewed articles published between 1 January 2000 and 22 July 2020 in English.

Results Database searches produced 24 565 studies, of which 35 articles met the inclusion criteria. Twenty of these articles were conducted in sub-Saharan Africa. Twenty articles were also published between 2015 and 2020. Literature revealed that NTDs have been integrated—among themselves; with water, sanitation and hygiene programmes; with vector control; with primary healthcare; with immunisation programmes; and with malaria management. Integrated mass drug administration for multiple NTDs was the most common method of integration. The three complex, yet common characteristics of successful integration were good governance, adequate financing and total community engagement.

Conclusion The dataset identified integrated management of NTDs to be cost effective and potentially to increase treatment coverage. However, the identified modes of integration are not exclusive and are limited by the available literature. Nonetheless, integration should urgently be implemented, while considering the programmatic and sociopolitical context.

PROSPERO registration number The study protocol was registered with PROSPERO number, CRD42020167358.

Key questions

What is already known?

- Global health actors have been advocating for integrated management of neglected tropical diseases. Integrated management of diseases is said to be cost effective and improves the quality of care being delivered.

What are the new findings?

- Neglected tropical diseases (NTDs) have been integrated with other NTDs; with water, sanitation and hygiene services; immunisation programs; with integrated vector control; with primary healthcare; and with malaria. Community engagement, intersectoral and multidisciplinary collaborations as well as adequate funding and political will have been some of the key facilitators to successful integration.
- Unfavourable policy environment, difference in target groups and inadequate resourcing were found to be barriers for successful integration.

What do the new findings imply?

- Knowing what facilitates a successful integration program will enlighten policymaker. The results from this review provides data that can be used to inform decision makers on how to better implement integrated NTD management.
- Deliberate and systematic planning and efforts are required to achieve an integrated NTD programme streamlined with the broader health system to achieve the NTD road map 2021–2030 goals.

INTRODUCTION

Neglected tropical diseases (NTDs) affect about 1.7 billion people globally.[1] The disease burden of NTDs disproportionately affects those in low and middle-income countries. A variable number of conditions have been classified as NTDs by different organisations including the US' Centres for Disease Control, the WHO and other organisations.[2 3] Twenty diseases were included in the WHO road map 2021–2030 to prevent, control, eliminate or eradicate NTDs, following gradual additions to the WHO NTD list between 2013 and 2019.[4] Many of these diseases can be controlled, and even eliminated through mass drug

administration (MDA), vector control and/or improved water, sanitation and hygiene (WASH).[5] Sustained reduction in NTD-related mortality and morbidity requires a multisectoral and interdisciplinary approach. This includes health promotion, disease prevention, mobilising and empowering human resources, and strengthening service delivery through primary healthcare.[3]

Traditionally, there has been a disease-specific approach to tackling NTDs, through community-based mass campaigns and clinical management.[6] For example, soil transmitted helminths (STH) and schistosomiasis are managed through MDA as preventive chemotherapy.[7] Due to geographical overlap, limited resources and changing environments, global health actors have been advocating for integrated disease management. To increase awareness, upgrade treatment coverage and improve patient outcomes, the WHO has suggested that stakeholders should improve intersectoral coordination (eg, with WASH and tropical diseases research and training); integration across diseases and continued improvements to the medicine and resources supply chain.[8 9]

The new 2021–2030 WHO roadmap emphasises integrated NTD management to sustain the efforts made over previous years under the theme 'Ending the neglect to attain the Sustainable Development Goals' (SDGs). The WHO, policy-makers and academics have also suggested that endemic countries should integrate NTD management strategies using existing resources and into existing health interventions, since many of these diseases are coendemic. The WHO recommended the integration of NTDs into well-established public health programmes such as HIV/AIDS, malaria, maternal and child health and WASH programmes, or within NTDs (for example those that manifest as skin conditions—skin NTDs).[10] Meanwhile, the UN has been advocating for Universal Health Coverage (UHC), in which communities are able to 'use the promotive, preventive, curative, rehabilitative, and palliative health services they need, of sufficient quality to be effective, while also ensuring that the use of these services does not expose the user to financial hardships'.[11] The SDGs are robust in recognising the relationship between poverty, politics and health. Thus, they acknowledge the importance of controlling NTDs while conceptualising the main mission of UHC, which is 'leaving no one behind'.[7] SDG 3 aims to achieve health equity through ensuring a healthy life and promoting well-being for all people.[12] Tackling these neglected diseases is vital in health and development because UHC cannot be achieved if marginalised communities are still suffering. It is also a major step to reducing global poverty. Bangert *et al* noted how the integrated management of NTDs can help achieve several of the SDGs and vice versa.[13] They indicated that integrated strategies to combat NTDs can boost global partnerships (SDG17), increase economic growth (SDG8) and generally reduce inequality (SDG10).

For the purpose of this systematic review, integration has been defined as the process by which disease control activities are functionally merged or coordinated within multifunctional healthcare delivery.[6] Thus, healthcare systems are connected or combined with existing human services aimed at improving health outcomes. Integration is cost effective by reducing cost of delivery while minimising duplication of effort and resources in an already limited resource setting.[14] Integrated disease management approaches are also said to help combat felt and experienced stigma caused by visible disability or disfiguring diseases such as Leprosy.[15 16] Integration of disease management with existing health interventions can improve the quality of care being delivered.[4]

Integrated disease interventions have been implemented in three ways to manage both communicable and non-communicable diseases: integration of similar diseases in the same category for example, NCDs; integration of diseases with existing programmes that are not necessarily in the same category for example, malaria and HIV; and integrating at a systems level, such as primary healthcare and procurement and supply management.[17 18] After multiple failed attempts to control malaria through vertical approaches, success has been shown through multiple integrations including with maternal health and procurement and supply.[19 20] There has been an increase in research papers on integrated management of NTDs, nevertheless, it is still uncertain which components of these interventions have contributed to the effectiveness or sustainability of outcomes. This systematic review summarises the approaches taken to integration of NTD programmes, characteristics and outcomes of successful integration.

METHODS

We conducted a systematic review of literature following a protocol that was registered with PROSPERO, registration CRD42020167358 which can be accessed from https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020167358. We reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis. Between 1 April and 22 July 2020, we searched: Trip, Embase (Excerpta Medica dataBASE), Medline, PubMed, Cochrane library, Global Health and Web of Science for articles published between 1 January 2000 and 22 July 2020. We included peer reviewed articles that covered: preventing, improving the diagnosis of, treating, managing and monitoring NTDs; health promotion against NTDs; treatment compliance for NTDs and healthcare delivery and processes related to NTDs. Grey literature and articles that could not be Google translated into English were excluded.

We created a 22-disease list which was considered for this systematic review. Our search used a combination of population, intervention, comparison, outcome and advanced searches, which included exploded medical subject heading terms. Some search terms were truncated to capture various word endings (such as 'integration' and 'integrated'). When searching, methodological,

geographical and language filters were not applied. Key words were searched in combination with individual diseases using the Boolean operators AND and OR (online supplemental appendix 1). Titles and abstracts were reviewed, and only relevant papers had their full papers retrieved. For articles whose full text was not available online, the corresponding authors were emailed for further details. If the author did not respond, the article was excluded from the study.

Study selection

We included primary studies that were in or could be Google translated into English. We disregarded articles that did not report on the integrated management of an NTD. The authors GTB and KD checked relevant articles.

The quality of studies was assessed using the Newcastle-Ottawa Scale (NOS).The NOS is a tool used to score non-randomised studies for systematic reviews and meta-analysis which assesses participant selection, comparability and results/outcomes.[21] NOS follows a star rating. Poor quality studies scored 0 or 1 star across the assessed domains, while good quality studies scored a minimum of 2 stars across all domains. The critical appraisal skills programme[22] was used in place of the NOS for primary studies. The quality appraisal tools were copied into a table then scored and marked for each study.

After searching the databases, the references were exported to EndNoteX7 and Mendeley. We created a Microsoft excel data extraction form and recorded the following information: author, title, year of study and publication, country of study, study population, diseases of study, mode of integration, outcome and sponsors. Data were extracted by GTB and reviewed by all authors. We undertook a narrative synthesis of the extracted data.

ETHICAL CONSIDERATION

This study followed the registered protocol.

Patient and public involvement

Neither patients nor the public were involved in the study design and article selection.

RESULTS

Our keyword search yielded 24 565 studies (figure 1). After screening through titles, abstracts, and full texts, 35 articles met the inclusion criteria (table 1). Twenty-one studies were conducted in sub-Saharan Africa (AFR), and 20 papers were published between 2015 and 2020. Most articles reported integrated management of STH (n=20). None of the articles evaluated the integration of the management or control of snakebite envenoming, sleeping sickness, mycetoma, leishmaniasis, chikungunya, dengue fever, echinococcosis, fascioliasis or dracunculiasis. Overall, the included studies had fair-good methodological quality, with some studies providing insufficient

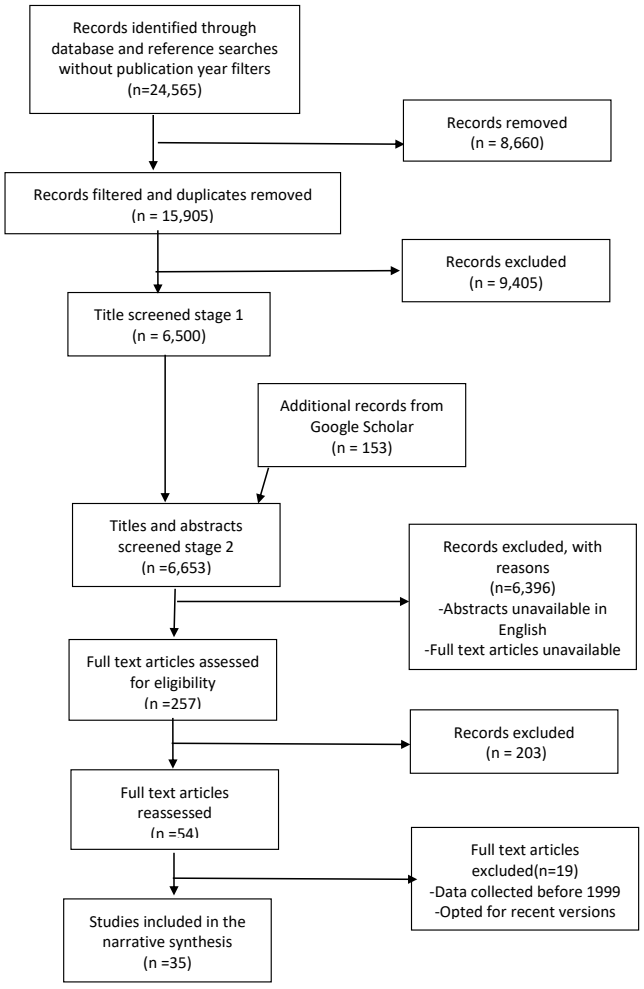

Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses study flow diagram.

information on outcome measures online supplemental appendix 2.

Identified integration modes

In these studies, six different modes of integration were identified; with other NTDs (n=21); with WASH services (n=7); with immunisation (n=3); with integrated vector control (n=4); with primary healthcare (n=4); and with malaria (n=6). It is important to note that some studies integrated multiple strategies. For example, Knopp *et al* conducted an open trial on the control of urogenital schistosomiasis with MDA, behaviour change facilitated by community education and vector control of the snails in Zanzibar.[23] They noted that neither communities that received MDA and behaviour change nor those that received MDA and snail control showed any significant difference in prevalence compared with the communities that only received MDA.[23] One of the studies integrated MDA for STH, lymphatic filariasis (LF) and onchocerciasis with primary healthcare in Mali.[24] They integrated the training of health workers for screening and referral where necessary. The significant gain of the integrated NTD programme was the scale-up of LF MDA which

Table 1 Summary of studies included

First author	Study location	Methodology	Year of study (publication year)	Diseases	Integrated health interventions	Type of outcome
Amparo *et al*[49]	Philippines	Cohort	2014 (2019)	Rabies	Health education curriculum	Social
Barogui *et al*[25]	Benin	Cross-sectional study	2016 (2018)	Leprosy, Buruli, Yaws	Screening, management, training, treatment	Epidemiological
Bronzan *et al*[27]	Togo	Cohort	2007–2015 (2018)	STH, schisto	MDA	Epidemiological
Clarke *et al*[52]	Timor-Leste	Non-randomised trial	2015–2016 (2018)	STH	WASH, MDA in schools and community	Epidemiological
Dembélé *et al*[24]	Mali	Cohort	2005–2010 (2012)	STH, Schisto, LF, Oncho	MDA, PHC	Social, epidemiological
Castro-Arroyave[63]	Guatemala	Mixed methods	2017 (2020)	Chagas	Social innovation, ecology	Epidemiological Economic
Emerson *et al*[53]	Ethiopia	Cross-sectional study	2006 (2008)	Trachoma	Malaria	Epidemiological
Evans *et al*[30]	Nigeria	Evaluation study	2008 (2011)	STH, Schisto, Oncho, LF	MDA	Epidemiological
Gunawardena *et al*[64]	Sri Lanka	Cross-sectional study	2012 (2014)	STH, LF	Surveillance, MDA	Epidemiological
Hashimoto *et al*[43]	Honduras	Retrospective analysis	2008–2011 (2015)	Chagas	PHC	Epidemiological
Hürlimann *et al*[32]	Cote d'Ivoire	Randomised trial	2011–2012 (2018)	STH, Schisto	Community led total sanitation (WASH)	Economic
Jacob *et al*[38]	Uganda	Cohort	2016–2017 (2018)	Oncho	MDA, Vector control	Epidemiological
Kaatano *et al*[33]	Tanzania	Cohort	2009–2013 (2015)	Schisto, STH	MDA, health education, WASH	Epidemiological
Kabatereine *et al*[45]	Uganda	Cross-sectional study	2009–2010 (2011)	Schisto, STH, Malaria	Survery, MDA, treatment	Epidemiological
Knipes *et al*[48]	Haiti	Non-randomised trial	2014–2015 (2017)	STH, LF, Malaria	Transmission assessment Surveys	Epidemiological
Knopp *et al*[23]	Zanzibar	Randomised controlled trial	2011–2017 (2019)	Schisto	MDA, vector control, behaviour change	Epidemiological
Koffi *et al*[26]	Cote d'Ivoire	Cross-sectional study	2016–2017 (2020)	Buruli, Leprosy, Yaws	Skin diseases	Social, coverage, Economic
Lankester *et al*[37]	Tanzania	Cohort study	2016 (2019)	STH, Rabies	MDA, MDRV	Epidemiological, social
Lee *et al*[34]	Sudan	Cohort	2009–2011 (2015)	Schisto	MDA, WASH, health education	Epidemiological
Lemoine *et al*[51]	Haiti	Evaluation study	2008–2014 (2016)	STH, LF	Social mobilisation, MDA, human resource	Epidemiological
Lemos *et al*[28]	Angola	Cohort	2012–2013 (2019)	Schisto, STH	Malaria, anaemia	Economic
Leslie *et al*[65]	Niger	Retrospective analysis	2005–2009 (2012)	STH, schisto, Trachoma, LF	MDA	Epidemiological Economic
Chen *et al*[41]	China	Cohort	2001–2014 (2017)	Schisto	Bovines, vector control, MDA	Epidemiological
Madon *et al*[66]	Tanzania	Case-control	2015–2016 (2018)	STH, Schisto, diarrhoea	WASH, social enterprise	Epidemiological
Mani *et al*[67]	India	Cohort	2001–2002 (2004)	LF, STH	MDA	Epidemiological
Midzi *et al*[47]	Zimbabwe	Cohort	2005=2007 (2011)	STH, Schisto	MDA, Malaria	Epidemiological

Continued

Table 1 Continued

First author	Study location	Methodology	Year of study (publication year)	Diseases	Integrated health interventions	Type of outcome
Mwingira *et al*[36]	Tanzania	Report	2014 (2016)	Oncho, LF, STH	MDA	Epidemiological
Mwinzi *et al*[50]	Kenya	Cohort	2009 (2012)	Schisto, STH	MDA	Epidemiological
Ndayishimiye *et al*[35]	Burundi	Retrospective analysis	2008–2009 (2014)	STH, schisto. trachoma, oncho	MDA, immunisation	Epidemiological
Vaz Nery *et al*[31]	Timor-Leste	Randomised controlled trial	2012–2016 (2019)	STH	WASH	Epidemiological
Njenga *et al*[29]	Kenya	Cross-sectional study	2009–2010 (2014)	STH, schisto. LF	MDA	Economic
Okello *et al*[39]	Lao PDR	Cross-sectional study	2014–2016 (2019)	Taeniasis	STH, swine fever, pigs	Epidemiological
Page *et al*[42]	Australia	Cohort	2012–2016 (2020)	Strongyloidiasis	PHC	Epidemiological
Rao *et al*[44]	India	Cohort	1993–2001 (2002)	Leprosy	PHC	Epidemiological
Sun *et al*[40]	China	Cohort	2005–2015 (2017)	Schisto	Ecology, WASH, marsh clean, agriculture	Epidemiological

LF, lymphatic filariasis; MDA, mass drug administration; MDRV, mass dog rabies vaccine; Oncho, Onchocerciasis; PHC, Primary healthcare; Schisto, Schistosomiasis; STH, soil-transmitted helminthiasis; WASH, water, sanitation, and hygiene.

achieved full national geographic coverage in 2009. It is uncertain whether this intervention was cost effective or not, as the amount of money spent did not represent the full cost of logistics or staff salaries. For studies that integrated multiple strategies, only one method of integration has been chosen as a subheading for integration strategies.

With other NTDs

Skin-NTDs such as Buruli ulcer and yaws have been integrated with each other for diagnosis and treatment,[25 26] as well as other NTDs. Koffi *et al* trained nurses and community health workers together, in Côte d'Ivoire, in basic dermatology and disease management. Afterwards, health workers were more willing to implement integrated interventions to manage leprosy, Buruli ulcer and yaws than individual disease management, but they required capacity building and resources.[26] Barogui *et al* conducted a similar study in Benin but used both health workers and community volunteers following the World Health Assembly recommendations.[25] These allowed for continuous monitoring and sustainability of the programme. Both these studies trained nurses and peripheral health workers to be able to detect and treat skin conditions, with a focus on yaws, Buruli ulcer and leprosy. The combined training allowed the detection of other NTDs that were not targeted such as LF. Investigators discovered that health workers and volunteers were able to detect, manage and refer other skin conditions including scabies[26] and LF.[25]

Integrated MDA for two or more NTDs was also noted (table 2). A study in Mali looked at the integration of schistosomiasis, STH, LF and onchocerciasis MDA.[24] The team distributed drugs for either two diseases, or all four diseases, depending on the disease mapping results . They reported an increase in coverage of up to 100% for LF drugs but did not indicate a baseline coverage. Bronzan *et al*[27] reported no changes to treatment coverage but a significant reduction in the prevalence of schistosomiasis and STH after they integrated MDA among schoolchildren aged 6–10 years old in Togo. Out of these studies, two studies reported no changes in coverage of MDA or prevalence of STH[28 29]; however, one study reported a reduction in the prevalence of schistosomiasis only.[29] Evans *et al*,[30] and Dembélé *et al*[24] reported 'minor' adverse reaction to their drug combinations while Lemos *et al* did not indicate the intensity of the adverse reaction which were experienced by 52% of their participants.[28]

With WASH programmes

WASH programmes are often categorised into those addressing quality and quantity of water, storage of water, hygiene and sanitation. Clarke *et al* piloted a study which was later altered and conducted by Nery *et al*. The studies combined school-based interventions and surveys with community-targeted projects in Timor-Leste. Nery *et al* improved school sanitation by incorporating hygiene education into school programmes and construction

Table 2 Summary of studies that integrated mass drug administration

Study author	Diseases	Who distributed the drugs	Who managed the programme	Outcome
Lemos *et al*[28]	Schistosomiasis STH Malaria Anaemia	Centro de Investigação em Saúde de Angola lab workers	Government and researchers	All anaemia cases were associated with schistosomiasis –13.5% reduction in schistosomiasis infections with no significant changes in anaemia
Lemoine *et al*[51]	LF STH	Community drug distributors,	ENVISION project	100% coverage from as low as 30%
Njenga *et al*[29]	Hookworm (STH) Urogenital Schistosomiasis	Trained schoolteachers	Authors	Did not change both the overall prevalence and intensity of hookworm infection.
Ndayishimiye *et al*[35]	STH Schistosomiasis Onchocerciasis Trachoma	Community drug distributors and community health workers	Ministry of Health	Increase in total population covered from 3 209 521 in 2007 to 4 179 495 in 2010
Leslie *et al*[65]	STH Schistosomiasis LF Trachoma	–	Government	Integrated programme cost 21% less than vertical programmes
Evans *et al*[30]	STH Schistosomiasis Onchocerciasis LF	Community drug distributors	Ministry of Health	98%–100% coverage, reduction in cost by 41.1%
Mwinzi *et al*[50]	STH Schistosomiasis	Community drug distributors	Ministry of Health	52.3% to 91.9% coverage with a 69% prevalence reduction for hookworm
Mani *et al*[67]	STH LF	Community health workers	–	77% prevalence reduction compared 15% reduction for single drug (3× increase in control)
Bronzan *et al*[27]	STH Schistosomiasis	–	Ministry of Health	Decrease in STH prevalence from 31.1% in 2009 to 11% in 2015 -Schisto 23.5% to 5%

'-' means not clear.
LF, lymphatic filariasis; STH, soil transmitted helminths.

of concrete-lined pit latrines for both students and teachers.[31] In the communities, they constructed taps, and encouraged a total sanitation approach. This saw an increase in latrine usage from 65.9% to 84.9%, an increase in reported hand-washing practices and an STH prevalence reduction of 88.2% (95% CI 70.2 to 100.0).[31] The intervention group also saw a reduction of the odds of STH by 57% compared with the control group (which only received school-based intervention). They also noted that half of the study population were adults, 40% of whom had never received formal education.

Hürlimann *et al*[32] conducted a controlled trial in Cote d'Ivoire on the general population. They integrated the control of schistosomiasis and STH with community-led total sanitation (an expansion of the WASH programme that discourages open community defecation). They noted that the intervention reduced the prevalence of schistosomiasis but did not show any effect on the prevalence of STH. Interestingly, Nery *et al* also noticed that their WASH and MDA programme for STH did not result in a significant change in the prevalence of the disease compared with MDA alone.[31] Kaatano *et al* improved the quality of water that families used and tried to reduce their contact with lake water by constructing pump wells on Kome island in Tanzania.[33] This was combined with health education and MDA. The intervention resulted in a reduction in the prevalence of schistosomiasis by 90.5% in children and 83% in adults. They also noted a STH reduction of 93.3% in children and 56.9% in adults. Similarly in Sudan, investigators constructed a filtered drinking water supply to supplement MDA.[34] A clean water supply within the intervention village contributed significantly to the reduction in the prevalence of urogenital schistosomiasis (from 28.5% to 13.5%), in comparison to the control village.

With immunisation programs

The Burundian Ministry of Health ran a campaign to incorporate MDA for STH, schistosomiasis, onchocerciasis and trachoma.[35] Treatment for STH was incorporated countrywide, while MDA for the other diseases was only distributed in endemic districts. They integrated these with immunisation programmes for children aged up to 59 months, antenatal clinics for pregnant women,

primary schools and in communities. The drugs were distributed by community drug distributers and local health facility staff. For trachoma, community health workers were the only ones that assessed, diagnosed, confirmed and provided medication. For all diseases, reported coverage in children was 95%–100%.[35] Mwingira *et al* integrated NTD programmes (MDA) with the measles and rubella immunisation programme (MR) in Tanzania.[36] The MR vaccines were delivered to children aged 9 months to 15 years (to accommodate catch-up doses) together with mebendazole for those aged 1–5 years. The MDA was for LF, onchocerciasis and STH for those aged over 5 in the same geographical area. They integrated the two programmes by planning, sensitising the community, drug distribution (and vaccination) and postadministration evaluation. The vaccination coverage remained at 97% while the MDA coverage increased from 86% to 93%. Lankester *et al* also integrated the vaccination of dogs with the MDA of STH drugs in Tanzania.[37] They followed three cohorts of community dwellers. Cohort A received combined deworming and mass dog rabies vaccine, cohort B received deworming drugs, and cohort C received the rabies vaccine only. The group that received the combined delivery of MDA and MRDV saved 32 min walking time. This group also experienced a 33% lower cost per deworming dose and a 16% lower cost per rabies vaccination. It was unclear how the savings came about, but could be from cutting logistical costs.[37]

With vector control programmes

In Uganda, Jacob *et al*[38] supplemented the MDA programme for onchocerciasis with community-directed slashing and clearing of vegetation which served as potential breeding areas. This clearing led to 89%–99% decline in vector biting rates. However, this study did not record the effect of this, combined with the MDA on disease prevalence. Okello *et al* also reported a 63% reduction in disability-adjusted life years (DALYs) after integrating human-alone Taeniasis management with that of STH and Taeniasis in humans and pigs in northern Lao.[39] They compared the cost (in monetary value and DALYs) of control of Taeniasis alone or with three possible combinations. Thus, Taeniasis/cysticercosis in the human population (the base case), *Taenia solium*/cysticercosis and STH in the human population; *T. solium*/cysticercosis alone in the human and pig population (which also acts a vector of transmission to humans); *T. solium*/cysticercosis in the pig population and STH in humans; and finally *T. solium*/cysticercosis, STH and classical swine fever in humans and pigs. They estimated US$214 and US$93 per DALY averted in both pigs and humans, respectively.[39]

China has moved the control of schistosomiasis from disease-based to environmental through improvement of marshland areas[40 41] which has taken 10–15 years to achieve. The integrated environmental improvement project included clearing marshland, building of boat factories and burying of soil with contaminated snails. They also introduced fish in some of the marshland areas to serve as biological control agents. They reported a reduction in infection rates in both humans and cows to 0 in 2015, from 0.4 in humans and 1.3 in livestock in 2003. They also reported a reduction in human cases from 61 in 2004 to 0 from 2005 to 2015.[40] The multisectoral involvement showed the feasibility of eliminating schistosomiasis.

With primary healthcare

Page *et al* integrated screening for strongyloidiasis within primary healthcare among aboriginal Australians.[42] Primary health providers incorporated screening for strongyloidiasis with routine medical check-ups and noticed an increase in the proportion screened from 40.3% to 81.9%.[42] In Honduras, Hashimoto *et al*[43] integrated Chagas disease vector control into routine disease prevention at health centres. Health centre staff promoted bug searching and vector reporting and supplied educational materials for community dwellers. They noticed a reduction in DALYs by 92%, saved US$65 876 and improved disease surveillance from about 46% to 84%. A similar approach was applied in Mali where community health workers are responsible for distribution of drugs and recruiting/ training community volunteers to work as drug distributors.[24] They also reported an increase in coverage for all diseases that were included in the MDA (LF, onchocerciasis, schistosomiasis, STH and trachoma) with a coverage between 76% and 100% from as low as 39.6%.[24] After noticing that vertical approaches to the management of leprosy were no longer cost effective, the Indian government decided to integrate leprosy management into primary healthcare.[44] They assigned one leprosy worker at a primary health centre who was a case detector and followed up patients through the same primary health centre. They noted an increase in older patients who presented themselves to the health facility.[44]

With malaria programs

Malaria was the only priority disease that was integrated with NTD interventions in the studies included.[45 46] In Uganda, investigators integrated the management of schistosomiasis, STH and malaria to evaluate the prevalence of each disease, as well as the prevalence of coinfection.[45] They recruited and trained community medicine distributors, who also acted as community mobilisers. All the participants received PZQ (Praziquantel) and ALB (Albendazole) and only those who tested positive for malaria through microscopy were given Artemisinin-based combined therapy.[45] Overall prevalence of coinfection with malaria and STH was 13.8%.[45] Prompt malaria tests and treatment with school-based MDA for STH and schistosomiasis were conducted every 6 months for a year and a half in Zimbabwe. STH and malaria coinfections reduced by 68%, schistosomiasis and malaria by 84%, and schistosomiasis and STH by 90.7%.[47] The final study was a pilot study conducted to assess the feasibility of an integrated LF–STH and malaria survey in Haiti.[48] Surveys

for LF–malaria were administered in 12 communities, for LF only in one and for LF–malaria and STH in one. Each survey was administered by a different team but at the same time, with the LF–STH–malaria team spending five more days collecting samples than the LF–STH and LF–malaria teams. The cost of the LF–STH–malaria evaluation was 49% higher than the cost for the LF-only evaluation, but did not disclose how much the malaria-only cost.[48]

Health education programs

An integral part of the intervention studies included in this systematic review was health education. Health education was conducted alongside MDA,[23 33 34] immunisation and WASH programmes.[32 34] Health education included education on health promotion, disease progression and signs and symptoms. Amparo *et al* integrated the rabies elimination programme into all elementary school curricula in The Philippines.[49] Information on rabies, animal bite prevention, bite management and responsible pet ownership were strategically designed to be incorporated into all lessons including Maths, English, Filipino and the arts. Rabies knowledge among students significantly improved and bite incidents almost halved. From the included studies, three overarching themes which influenced the success or challenged the integrated interventions are collated within the label of barriers and facilitators.

Facilitators of successful integration

This review has shown that barriers and facilitators to integration cannot be viewed independently but as interlinked. For most studies, intersectoral and multidisciplinary collaborations, political will and community engagement facilitated the interventions (table 3). Community engagement was one of the most common themes that emerged from this review, especially for community-directed interventions.[42 50] Evans *et al*[30] stated that community mobilisation and the usage of community-directed distributors was an important factor in the integration of MDA for STH, schistosomiasis, onchocerciasis and LF. Likewise, Lemoine *et al*[51] reported that community engagement was a key strategy to the success of their programme. This included selecting community members to train for the drug administration and education campaigns and ensuring community awareness of the programme. Effective communication was reported to increase community engagement and participation[24] and brought a sense of programme ownership.[30]

Barriers to integration

Clarke *et al* failed to randomise their study groups because they were unable to find partners who would sponsor the study.[52] This suggests that adequate funding is fundamental to high-quality studies and successful integrated programmes. Lack of community mobilisation was a threat to interventions as shown in Kenya where it led to a low treatment coverage of 46% for LF and schistosomiasis.[29] Both studies that integrated the management of skin NTDs reported the lack of a dermatologist in their

Table 3 Factors that facilitated the integration of neglected tropical disease

Modes of integration	Logistics	Good governance	Motivated actors	Policy	Community engagement
With other NTDs	Availability of public health infrastructure[64] Adequate funding[53]	Multilevel stakeholders[43 50 63]	Health workers willingness to provide integrated services[25 26]		Use of trusted community health workers[51] Community sensitisation[24 26 64] Health promotion campaigns,[23 33 34]
Water, sanitation and hygiene programmes	Good coordination between community workers and supervisors.[31]				Community education and sensitisation.[32 34]
Immunisation programmes		Government ownership[35]		Policy supporting integrating methods[46]	Timely communication.[3736]
Vector control					Community sensitisation[38]
Primary healthcare		National strategic plan ownership[24 44]	Willingness of health workers[43 44]		
Malaria programmes			Use of trusted community drug distributors[45]		Community mobilisation and sensitisation[45]

study as a limitation.[25 26] They also acknowledged the lack of medication or affordable drugs for the patients as being counterproductive to their efforts.[26] Unfavourable national policies had a negative impact, as in the case of Zimbabwe,[47] where only certified medical personnel are allowed to administer any form of medication, which limited MDA coverage. Similarly, Emerson *et al* successfully managed to conduct a survey on malaria and trachoma but noted that integrated management of these two diseases may not work.[53] The policy for malaria net distribution is to give two nets per household and only requires one household member, while the trachoma management would need the entire household to be present.

DISCUSSION

This systematic review presented the available literature regarding the integration of NTD management with existing health interventions. The new 2021–2030 WHO roadmap emphasises that integrated NTD management to sustain reductions in NTD related mortality and morbidity, requires a multisectoral and interdisciplinary approach.[10] We conducted a systematic review of 35 articles, predominantly from sub-Saharan Africa, to synthesise evidence of applying integrated management methods to NTDs. The literature has shown six dominant ways in which the integration of NTDs is applied in different policy settings and different sociocultural environments. These are with: other NTDs; WASH programmes; immunisation; integrated vector control; primary healthcare; and malaria.

We acknowledge these modes of integration are not exhaustive and are limited by the available literature. With the disfiguring and disabling nature of NTDs, we expected to find literature on integrated morbidity management as this is also a vital part of disease management.[54] Alleviating the suffering caused by disease morbidity should also be a priority. The fact that most studies integrated the management of multiple NTDs supports that there is high level of coendemicity and geographical overlap, as reported by Hotez *et al*.[55] The study has also shown that interventions against similar diseases, such as skin NTDs, are relatively easy to integrate, as suggested by Foster.[56] The skin-NTDs studies support Narain *et al*'s observation that integrated disease management boosts the skills of the health workers.[17] Molyneux and Nantulya advocated for linking malaria control programme to onchocerciasis, LF, schistosomiasis, measles and trachoma.[57] This systematic review shows how this has been done for LF, STH and schistosomiasis. None of the literature covered integration of malaria with onchocerciasis nor trachoma. This may reflect a missed opportunity.

An important part of the integration, especially for school and community-based interventions, was health education. Health education integrated into school curricula has been shown to have a positive impact on children. Ejike *et al* modified the 'snakes and ladders' game to 'schisto and ladders' to educate students about schistosomiasis in Nigeria.[58] The game included information on schistosomiasis transmission and safety of praziquantel. They noted a significant improvement in the knowledge of risk behaviours, prevention and control of schistosomiasis among the group that played schisto and ladders compared with the group that played the traditional snakes and ladders. This supports Amparo *et al*'s approach of creatively integrating educational information into school-appropriate lessons and activities.[49] It is imperative that the use of edutainment be incorporated in health promotion for school-going children.

Studies have shown that barriers to integrating disease management go beyond the availability of resources. The findings showed that community participation and adequate funding, as well as good governance (political will) are key to the success of integrated programmes. The three facilitators included interlinked subthemes. For example, good leadership and literacy can be associated with community engagement and communication. Good leadership and government ownership, combined with availability of resources and infrastructure *tha*t is, for referrals, are important when implementing integrated services. Governments should ensure that NTDs are integrated into national health plans and budgets for accountability and ensuring adequate funding. The findings showed that MDA programs that included health education and selected community members as drug distributors were successful. Parker and Allen[59] noted that the success of MDA programs was also determined by the relationship between drug distributors and the study participants. Baker *et al* proposed that integrated programmes should continually be evaluated for impact as opposed to just 'pushing integration for the sake of integration'.[60] This will limit duplication from other settings and ensure that challenges are being addressed. Health systems are not uniform, so the facilitators identified in this study should be analysed and adapted to specific country needs to ensure that strategies are impact oriented.

As discourse on how we can improve the integration of NTDs occurs, we should also look at how vertical approaches are impacting NTDs and how NTD control can impact other diseases. Indeed, health interventions targeting other diseases have positively impacted the control of NTDs, especially those with similar approaches. For example, the use of insecticidal nets to combat malaria in The Gambia led to the interruption of LF transmission since they have a common vector.[61] Deliberate efforts to tackle NTDs can benefit from strengthened health systems while themselves contributing to improved health systems. National programme managers should consider ways in which NTDs can help with other disease burdens, especially those that may benefit from community health workers, water and sanitation and similar skilled workers. For example, community workers trained in active case-finding can be used to survey and monitor emerging diseases.

The integration of NTDs within the general health system requires careful and deliberate planning. Countries should address this systematically. Leadership and governance of the health system at all levels should include NTDs. Countries should include NTD prevention and treatment services in their essential healthcare packages and universal healthcare benefit packages. The national health information system should also include NTD indicators and data collection systems to sustainably track progress and inform decision making at all levels. Integration of the NTD drug supply system within the national medical supplies and logistic system is required. Integration of NTDs with the training curriculum of health workforce is also required to ensure preservices training of health providers. To ensure a multisectoral response to NTD control, elimination and eradiation, it is critical to establish or strengthen multisectoral coordination body, engage other sectors such as education; WASH; gender and social inclusion; agriculture sector in the planning and financing of NTD interventions.

The impact of COVID-19 on health systems and the global economy also means that integrated delivery of health programmes is critical to optimally use the available budget. Integration will play an important role in leveraging resources in different health programmes and campaigns and provide services that attain the highest standards of public health measures against COVID-19, protecting both the public and those who deliver the services. Molyneux *et al* suggest that safe MDA distribution can mitigate the impact of COVID-19.[62] In addition, integration will also improve adherence to COVID-19 prevention methods such as social distancing by reducing the number of contacts with community health workers and with the healthcare system.

CONCLUSION

The review identified six modes of integration. These are with: other NTDs; WASH programmes; immunisation, vector control; primary healthcare and malaria. The application of integrated management of diseases is context-dependent and may not be applied universally. Thus, the wider sociocultural and sociopolitical contexts must be analysed during the needs assessment stage. Despite this, these studies can serve as guidance for future integration studies. In these studies, three main themes that acted as barriers or facilitators to integration emerged. These included good governance, political will, funding and community engagement. This has shown that the effectiveness and success of such programmes go beyond the availability of resources.

Ultimately, integrated management of NTDs appears promising, with endemic countries producing research papers on how they are implementing strategies. With continual support and monitoring of progress by larger organisations such as the WHO, the accountability endemic countries have towards achieving their goals is likely to increase. The results from this review provide data that can be utilised to inform decision makers on how to better implement NTD management.

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Appendix 1: Full EMBASE search strategy

1. (Chagas disease and (Management or treatment or prevention or control or restrict*) and (integrat* or Combin*)).af

Chikungunya
1. ((Chikungunya management or treatment or prevention or control) and integrat*).m_titl

Cysticercosis
((Cysticercosis management or treatment or prevention or control) and integrat*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

Dengue
1. ("Dengue fever" and (Management or treatment or prevention or control or Restrict*) and (integrat* or Combin*)).af.

Dracunculiasis
1. ("Dracunculuasis" or "Guinea worm disease" or "guinea worm").m_titl.
2. ("Guinea worm disease" or "guinea worm" or "Dracunculiasis").mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
3. ("Management" or "treatment" or "prevention" or "control").m_titl.
4. (integrat* or combin*).m_titl.
5. 1 and 2 and 3 and 4

Echinococcosis
1. ("Management" or "treatment" or "prevention" or "control").m_titl.
2. (integrat* or combin*).m_titl.
3. Echinococcosis.m_titl.
4. 1 and 2 and 3

fascioliasis
1. (Fascioliasis and (Management or treatment or prevention or control or Restrict*) and (integrat* or Combin*)).af.

Leishmaniasis
1. (Leishmaniasis and (Management or treatment or prevention or control or Restrict*) and (integrat* or Combin*)).af.

leprosy
1. (("Leprosy" or "Hansen's disease") and (Management or treatment or prevention or control or Restrict*) and (integrat* or Combin*)).af.

mycetoma

1. (("Mycetoma" or "Chromoblastomycosis" or "Madura Foot" or "eumycetoma*" or "mycetomapedis" or "actinomycetoma*") and (Management or treatment or prevention or control or Restrict*) and (integrat* or Combin*)).af.

onchocerciasis

1. (("Onchocerciasis" or "River blindness") and (Management or treatment or prevention or control or Restrict*) and (integrat* or Combin*)).af

podoconiosis

1. (("Podoconiosis" or "nonfilarial elephantiasis") and (Management or treatment or prevention or control or Restrict*) and (integrat* or Combin*)).af.

scabies

1. (scabies and (Management or treatment or prevention or control or Restrict*) and (integrat* or Combin*)).af.

Schistosomiasis

1. (("Schistosomiasis" or "Bilharzia") and (Management or treatment or prevention or control or Restrict*) and (integrat* or Combin*)).af.

sleeping sickness

1. (("Sleeping sickness" or "Human African trypanosomiasis" or "Tsetse fly disease") and (Management or treatment or prevention or control or Restrict*) and (integrat* or Combin*)).af.

Snakebite

1. (("Snakebite envenoming" or "antivenins" or "snakebite*" or "venoms" or "envenoming" or "snake poison") and (Management or treatment or prevention or control or Restrict*) and (integrat* or Combin*)).af.

Soil-transmitted helminthiasis

1. (("Soil-transmitted Helminths" or "Hookworm" or "Whipworm" or "Soil-transmitted helminth*" or "soil transmitted helminth*" or "intestinal worm* OR helminth" or "Helminthiasis") and (Management or treatment or prevention or control or Restrict*) and (integrat* or Combin*)).af.

Strongyloidiasis

1. (("Strongyloidiasis" or "strongyloidesstercoralis" or "Stronyloidiasis") and (Management or treatment or prevention or control or Restrict*) and (integrat* or Combin*)).af.

Yaws

1. (YAWS and (Management or treatment or prevention or control or Restrict*) and (integrat* or Combin*)).af.