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Operational research priorities to support the elimination of neglected tropical diseases in the South-East Asia Region

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Acronyms and abbreviations

CDS	Department of Communicable Diseases
DHF	dengue haemorrhagic fever
HSS	health system strengthening
IHIP	Integrated Health Information Platform
IRS	indoor residual spray
ITM	Institute of Tropical Medicine
IU	implementation unit
LF	lymphatic filariasis
MDA	mass drug administration
MMDP	morbidity management and disability prevention
NTD	neglected tropical disease
PCR	polymerase chain reaction
PKDL	post kala-azar dermal leishmaniasis
POC	point-of-care
RDT	rapid diagnostic test
SDG	Sustainable Development Goal
SE	South-East
TAS	transmission assessment survey
UHC	universal health coverage
VL	visceral leishmaniasis
WASH	water, sanitation and hygiene

Executive summary

Neglected tropical diseases (NTDs) continue to disproportionately debilitate the health and well-being of the poor and marginalized in the South-East (SE) Asia Region. Eliminating NTDs on the verge of elimination, namely leprosy, lymphatic filariasis (LF), schistosomiasis, trachoma, visceral leishmaniasis (VL) and yaws has been a flagship priority of WHO Regional Office for SE Asia since 2014. This has significantly contributed to progressing towards the Sustainable Development Goal (SDG) target of ending the epidemics of NTDs by 2030. However, there are remaining challenges and gaps that have stalled the control and elimination efforts.

"Ending the neglect to attain the Sustainable Development Goals: a road map for neglected tropical diseases 2021–2030" underscores an urgent need for innovation, research and knowledge sharing to achieve the 2030 elimination and control targets. Timely and coordinated operational research in dengue, leprosy, LF, schistosomiasis and VL has a strong potential to fill the knowledge gaps and accelerate the control and elimination efforts.

Consultation with the large group of disease experts convened between October 2021 and July 2022 highlighted various programmatic and knowledge gaps that are posing a challenge to the effective implementation of interventions and strategies. As many as 164 areas of operational research were identified (dengue – 38, leprosy – 20, LF – 30, schistosomiasis – 14, VL – 55 and overarching areas – 7) in the domains of diagnostics, treatment, vaccines, vector control, health systems and surveillance. The expert group consultation also yielded the top five areas of operational research that can guide the research agenda prioritization in WHO SE Asia Region. In this last mile of elimination, it is pertinent to fill the knowledge gaps and provide promising and rigorously researched solutions that will help to overcome the challenges that are stalling elimination and control efforts in the Region.

1. Introduction

Neglected tropical diseases (NTDs) impose devastating human, social and economic burdens on over a billion people worldwide. In the South-East (SE) Asia Region, at least one of 12 NTDs are endemic in all 11 Member States. The NTD burden is the highest in terms of the number of people requiring interventions for at least one NTD. NTDs disproportionately affect the poor, vulnerable and marginalized populations.

Eliminating NTDs on the verge of elimination, namely leprosy, lymphatic filariasis (LF), schistosomiasis, trachoma, visceral leishmaniasis (VL) and yaws has been a flagship priority of WHO SE Asia Region since 2014. This has significantly contributed to progressing towards the Sustainable Development Goal (SDG) target of ending the epidemics of NTDs by 2030.

Since 2016, six countries of the Region have eliminated at least one NTD, including lymphatic filariasis, trachoma and yaws, and a few more countries are in the pipeline for doing so in the coming years.

In the past seven years, new cases of kala-azar in the Region have reduced by 95%. By the end of 2021, 99% of implementation units (IUs) in the Indian subcontinent had achieved the elimination target.

Bhutan, Democratic People's Republic of Korea and Maldives continue to report fewer than 25 new leprosy cases per 1 million population annually. However, we still need to progress further to reach the elimination target in all endemic countries. At the same time, efforts to control dengue as a major public health problem will also be accelerated in this decade.

Burden in SE Asia Region: status of selected NTDs

Dengue: Over the previous decade, dengue cases have tripled from 0.19 million to 0.68 million. Dengue is endemic in all Member States, except for the Democratic People's Republic of Korea. All four serotypes are currently hyperendemic in these countries and the Region accounts for more than half of the global dengue burden.

Leprosy: In 2020, a total of 84 814 new leprosy cases were reported in the Region, with 90% of these cases reported from India and Indonesia alone. Bangladesh, India, Indonesia, Myanmar, Nepal and Sri Lanka are among the 23 global priority countries for leprosy elimination.

Lymphatic filariasis (LF): As many as 262 million people were treated with either two- or three-drug therapy in India, Indonesia and Nepal in 2021. Maldives, Sri Lanka and Thailand have been validated for the elimination of LF as a public health problem and are now in the post-validation surveillance phase. Bangladesh is finalizing the dossier for validation of elimination as a public health problem. Timor-Leste has passed the first transmission assessment survey (TAS) nationwide and is due for the final TAS in 2023.

Schistosomiasis: Indonesia is the only country in the Region with schistosomiasis endemicity; however, community prevalence has been <1% due to successful rounds of mass drug administration. Indonesia is targeting elimination by 2025. Myanmar will soon validate the suspected endemicity status.

Visceral leishmaniasis (VL): New cases of kala-azar in the Region have reduced by 96.2% between 2007 and 2021. By the end of 2021, the elimination target for kala-azar was achieved in all endemic *upazilas* of Bangladesh, 99% of all endemic blocks in India and 87% of endemic districts in Nepal. Bangladesh has sustained the target of less than one kala-azar case per 10 000 population in all

"Ending the neglect to attain the sustainable development goals: a road map for neglected tropical diseases 2021–2030" has identified critical gaps and actions that are impeding the achievement of elimination targets set for 2030. This includes a lack of effective, standardized and affordable diagnostics and interventions, poor targeting of interventions, low treatment coverage among marginalized groups, non-standardized disease surveillance with low sensitivity and specificity, lack of health system capacity and infrastructure, poor quality data, limited knowledge and understanding of disease epidemiology, emerging endemic areas and new foci and lack of funding and political support resulting from donor fatigue and political and programme complacency.

The NTD roadmap underscores an urgent need for innovation, research, knowledge sharing and increased domestic funding, including external resource mobilization to successfully achieve the 2030 targets. In this last mile of elimination, it is pertinent to fill the knowledge gaps and provide promising and rigorously researched solutions that will help to overcome the challenges that are stalling elimination and control efforts in the Region. To this end, WHO Regional Office for SE Asia convened an NTD operational research areas prioritization exercise from October 2021 to July 2022.

2. NTD operational research areas prioritization process

WHO Regional Office for SE Asia constituted an ad hoc group of NTD and research experts to identify areas of operational research for five NTDs (dengue, leprosy, LF, schistosomiasis and VL) that have a strong potential to accelerate control and elimination efforts in the Region. This ad hoc group represented government, non-government, donors/partners and research institutes of Bangladesh, Bhutan, India, Indonesia, Nepal, Sri Lanka, Thailand and Timor-Leste.

A preliminary review of the literature and interviews with key NTD experts by the Institute of Tropical Medicine (ITM), Antwerp, Belgium yielded 166 areas of critical research (dengue – 32, leprosy – 17, LF – 41, schistosomiasis – 21 and VL – 55) under the thematic areas of diagnostics, treatment, vaccines, vector control, public health/health systems, surveillance and integrated interventions. The review also highlighted various programmatic and knowledge gaps that have been stalling the progress towards NTD control and elimination in the Region.

After the preliminary listing of operational research areas, a review of five available approaches and methods for prioritization of research areas was undertaken. The scope, context, relevance, strengths, limitations and methodology of five available approaches were examined. Consequently, a hybrid consensus-based/metrics-based approach was followed to prioritize the areas of operational research in the Region. The hybrid approach was applied through a two-step process.

In the first step, 116 NTD and research experts reviewed the list of 166 areas of operational research during a virtual consultation meeting and ensured that all critical areas were listed. At the end of the virtual consultation, 164 areas of operational research were identified (dengue – 38, leprosy – 20, LF – 30, schistosomiasis – 14, VL – 55 and overarching areas – 7).

In the second step, the metrics-based Delphi method was used to score and prioritize the identified operational research areas for each NTD. Various methods and processes for scoring and prioritization were reviewed, and 27 exclusive criteria that had been previously used for prioritization and ranking of research areas were identified. Of these 27, 11 exclusive criteria that suited the NTD context were selected for scoring and prioritization. A virtual "operational research areas prioritization survey" was sent to NTD and research experts. Results of the survey populated a list of top five operational research area for each NTD.

The detailed procedure of the operational research areas prioritization process is described in Annex 1.

3. Results – prioritised operational research areas for accelerating NTD control and elimination in WHO SE Asia Region

The process of identification and prioritization of operational research areas for dengue, leprosy, LF, schistosomiasis and VL finally yielded the top five areas of operational research that are considered critical for overcoming the programmatic challenges in the Region, as below. The full list of operational research areas identified for the five NTDs is given at Annex 4.

Dengue

(1) Determine affordable and effective referral systems to improve case management of dengue and dengue haemorrhagic fever (DHF)

(2) Evaluate the availability of better diagnostic tools for early detection of dengue outbreaks

(3) Determine effectiveness, cost-effectiveness and acceptability and evaluate the process of Wolbachia-mosquito rollout for control of dengue

(4) Evaluate use of biomarkers in dengue and DHF case management (severity/mortality as outcome)

(5) Determine effectiveness, cost-effectiveness, acceptability and evaluate the process of targeted IRS for dengue control.

Leprosy

(1) Develop more effective drugs or drug combinations or shorter regimens to treat leprosy

(2) Develop and validate laboratory or field-based point-of-care (POC) assays for leprosy diagnosis

(3) Develop and validate diagnostic tools for the detection and monitoring of nerve function impairment and reactions

(4) Optimize the use of available treatment for reactions and nerve function impairment and identification of new treatment options

(5) Develop and validate laboratory or field-based POC assays for leprosy infection.

Lymphatic filariasis

(1) Identify determinants of persistent hot spots, improve understanding of the same and develop a strategy to mitigate the problems

(2) Evaluate the impact of never treated and unreached on achieving elimination targets and evaluate practical, cost-efficient strategies to reduce it

(3) Evaluate current methodologies to estimate the burden of chronic disease manifestations and ability to identify Stage 1 to Stage 3 lymphoedema and hydrocele

(4) Explore opportunities and health system (6 HSS blocks) barriers for management of chronic LF patients in the essential package of care under universal health coverage (UHC), including assessment of how best to integrate morbidity management and disability prevention (MMDP) services into first-line routine health care in different settings

(5) Evaluate ongoing urban mass drug administration (MDA) campaign strategies including microplanning, training, social mobilization and supervision to improve coverage and compliance.

Schistosomiasis

(1) Identify effective, safe, cost-effective and sustainable snail control technology considering the environment and socioeconomic value

(2) Determine the effective approach to integrate multidisciplinary and multisectoral approaches through community empowerment, e.g. WASH, snail vector, education, animal for elimination of schistosomiasis

(3) Develop criteria/protocols as to whether or not elimination has been achieved and for stopping MDA

(4) Assess if and to what extent schistosomiasis elimination can be integrated into primary health care

(5) Develop more sensitive diagnostic tools adapted to *S. japonicum*/low-transmission settings (Indonesia).

Visceral leishmaniasis

(1) Investigate eye problems as a side effect of miltefosine use in post kala-azar dermal leishmaniasis (PKDL) patients

(2) Develop a syndrome-based approach for clinical management of fever in VL endemic areas

(3) Develop less invasive tests of cure for VL, PKDL and HIV-VL patients

(4) Do operational research to detect the proportion of unreported cases

(5) Develop new gold standard alternatives for laboratory confirmation of PKDL that can be widely used (instead of the current skin slit smear).

A large number (164) of critical areas of NTD operational research emerged during this process, which is a testimony to the knowledge and research deficiencies that exist in the NTD domain. The high volume of research areas also posed a challenge to ranking and prioritization, which was probably the reason for the low response rate (26%) to the virtual survey. The top five areas of operational research for each NTD need to be examined along with the complete list at Annex 4 where the bold text indicates the areas that were repeatedly mentioned and emphasized by experts during the various rounds of consultation. The full list of operational research areas with scores can be found in Annex 6.

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Annex 1

Detailed procedures and results

In accordance with the NTD roadmap 2030, the NTD team at the Department of Communicable Diseases (CDS), WHO Regional Office for SE Asia initiated the process of prioritization of areas of operational research for five NTDs (dengue, leprosy, LF, schistosomiasis and VL) for Member States of the Region in October 2021. The Department of Communicable Diseases consulted the NTD and research experts at the Regional Office, the Special Programme for Research & Training in Tropical Diseases (TDR), WHO headquarters and country offices (Annex 2) to facilitate the process of prioritization of areas of operational research for five NTDs in WHO SE Asia Region. The consultation with experts and review of documents helped with the drafting of the process. Institute of Tropical Medicine (ITM), Antwerp, Belgium undertook the preliminary review of the literature and interviews with NTD experts to draft a summary for each of the five selected NTDs. These summaries described the disease burden, epidemiology, control and elimination targets, challenges, existing gaps in research (clinical, interventional, operational and academic) and provided the first comprehensive and detailed list of areas for operational research. In the draft technical papers, the list of research areas for each NTD was categorized into the following thematic areas: diagnostics, treatment, vaccines, vector control, public health/health systems, surveillance and other (combined) interventions. This preliminary review yielded 166 areas of research: dengue (32), leprosy (17), LF (41), schistosomiasis (21) and VL (55). Among the thematic areas, research on surveillance yielded the most research areas (46).

To identify the most appropriate method for further prioritization of NTD operational research areas, eight peer-reviewed articles and reports were thoroughly reviewed. These peer-reviewed articles described any one of five approaches: essential national health research approach (ENHR), combined approach matrix (CAM), child health and nutrition research initiative (CHNRI) approach, James Lind alliance priority setting partnerships (PSPs) approach and Delphi approach. The scope, context, relevance, strengths, limitations and methodology of each were examined. At the same time, a complete list of NTD experts and stakeholders in WHO SE Asia Region was prepared. For each expert/stakeholder, an area of expertise (expertise in one or more disease, research expert) was identified based on educational qualification, contribution or role in the NTD programme domain to date. Experts were informed about their anticipated role and were requested to contribute to this process. A hybrid of consensus-based and metrics-based approaches was deemed the most suitable to meet the objectives of prioritization of operational research areas for NTDs in the Region. This hybrid approach was applied through a two-step process: in the first step, a virtual consultation meeting was organized to facilitate consensus-building among stakeholders about the complete listing of operational research areas for each NTD; and in the second step, the metrics-based Delphi method was used to score and prioritize the operational research areas for each NTD.

The first-step of the hybrid approach, i.e. 'virtual consultation meeting on identification of regional operational research priorities to support elimination of NTDs in WHO SE Asia

Region', was held from 16 to 18 November 2021. The programme of the meeting is given in Annex 3. All Member States of the Region were invited, as well as the government institutions, WHO country offices and WHO headquarters, relevant donors, development partners and research institutions. The consultation was attended by 116 NTD experts from eight of 11 countries of the Region (Bangladesh, Bhutan, India, Indonesia, Nepal, Sri Lanka, Thailand, Timor-Leste) (Annex 2). The experts who participated in the virtual consultation represented all NTD stakeholders of WHO SE Asia Region – research/academia (23), donors/partners (15), government (40) and WHO (38). There were 43 experts who were senior NTD professionals.

Prior to the consultation meeting, the following documents were shared with the participants: NTD roadmap 2030, 'A systematic approach for undertaking a research priority-setting exercise: guidance for WHO staff', Delphi method for research area prioritization and the draft technical papers developed by ITM that included the complete and detailed list of operational research areas for the five NTDs. Other than the above-mentioned documents, a brief description of the process to be followed during the breakout sessions and plenary sessions was shared with the speakers.

During the virtual consultation meeting, the participants were first briefed about the objectives of the meeting, the NTD roadmap 2030 and the elimination targets. Participants were divided into five NTD groups: dengue (23), leprosy (22), LF (29), schistosomiasis (11) and VL (31). The participants joined the five NTD breakout sessions. The breakout sessions were led by a group leader who was elected from the group by the participants and who facilitated a detailed discussion on each research area listed in the draft technical papers. The breakout sessions were scheduled for three hours over two days in order to provide adequate time for an in-depth discussion. During the breakout sessions, the participants discussed the potential of the listed research areas in facilitating the control and elimination efforts in the Region to meet the NTD 2030 targets. The discussion primarily focused on whether the proposed research areas: (a) were relevant in the context of control and elimination in WHO SE Asia Region; and (b) qualified as operational research (in contrast to academic research). Additional topics for discussion were: previously researched, intervention activity, clinical research, availability of time, technical capacity and resources, overlapping or cross-cutting areas within the NTD and across the five NTDs and rephrasing/rewording to add clarity to the research area. Two note takers in each breakout room simultaneously captured the qualitative discussion, documented the decisions of the group and prepared an updated list of agreed-upon research areas. The discussion of the breakout sessions was presented during the five disease-specific plenary sessions where the larger group of NTD experts could review and reflect upon the disease-specific list of research areas for the respective NTDs. The discussion during the plenary session was again captured by the note takers. The plenary session was followed by a deliberation about the overarching areas of NTD research. At the end of the virtual consultation, 164 areas of operational research that can accelerate control and elimination of NTDs in WHO SE Asia Region by 2030 were identified (Annex 3).

The virtual consultation meeting facilitated discussion and consensus-building among the stakeholders which is deemed vital to the process of identification of critical areas of research in public health. It also provided a complete and comprehensive list of research areas suggested by all stakeholders for the control and elimination of five NTDs in WHO SE Asia Region by 2030.

The virtual consultation was followed by the identification of criteria for scoring and prioritization that could be applied to the complete and comprehensive list of operational research areas generated thus far. A review of the eight peer-reviewed articles and documents helped identify the most appropriate method and process for scoring and prioritization. In the past, the Global Partnership for Zero Leprosy (GPZL) had used a metrics-based approach to score research topics for leprosy elimination. GPZL provided two sets of criteria to 26 experts via an online questionnaire to score and list the top 10 research topics to achieve leprosy elimination. In July 2019, the Scientific Advisory Committee of the Infectious Diseases Data Observatory (IDDO) group published priority areas of VL research; and in 2014, Lancet published a commentary where VL experts listed areas of critical VL research to achieve elimination in WHO SE Asia Region. The TDR Disease Reference Group on Helminth Infections, WHO followed a mix of consensus-based and metrics-based approaches to identify the top 10 research priorities for helminth infections including LF and schistosomiasis. Review of these documents revealed 27 exclusive criteria that have been previously used for prioritization and ranking of research areas. The Delphi method, a metrics-based approach, was now applied to proceed with the scoring and prioritization. The 27 criteria and scoring options were independently reviewed by three experts in context of relevance and potential to generate distinct scores. As a result, 11 criteria were selected and phrased as questions with multiple pre-coded response options to score and prioritize the previously identified research areas. A draft survey was tested with four NTD experts to verify the user-friendliness, validate the response options, data computation and analysis and interpretation of results. Results of the test run were used to make final edits to the survey and to the survey methodology. The 'operational research area prioritization survey' was hosted on the 'survey monkey' online platform for each NTD in April 2022 (Annex 5). Due to the high volume of operational research areas, the virtual survey was split into 12 identical sub-surveys. Research areas were split among the respondents and sub-surveys so that each respondent scored not more than 14 research areas and each research area had a minimum six experts to respond to. The survey respondents (n=91) were selected from the list of disease and NTD experts available with Regional Office for SE Asia. For leprosy, only one survey with all 20 research areas was administered on 114 leprosy experts in June 2022. Response options were pre-scored (0–4), wherein a high score earned by a research area resulted in high rank and prioritization. Scores for each research area were computed by multiplying the score with the number of respondents for question # 1–9. The scores of all nine questions were then added to generate the total score for the research area. The total scores of the research areas were arranged in descending order to identify the top five scores. Since questions S1 and S1a were screening questions, the research areas that were checked as 'not relevant' earned a score of 0. If Questions 1–9 were skipped, a score of 0 was assigned.

The surveys were emailed and were open to responses for four weeks. Of 91 respondents, 27 (30%) completed/partially completed the survey; similarly, for leprosy, 26 of 114 (23%) respondents completed the survey. The scores for each research area were computed and ranked (Annex 6).

Annex 2

NTD and research experts

Name	Designation	Institution	Country
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Dr Mitali Chaterjee		Department of Pharmacology, Institute of PG Medical Education & Research, Kolkata	India
Professor Nirmal Kumar Ganguly	Former Director General	ICMR, New Delhi	India
Dr Nilanthi De Silva	Senior Professor of Parasitology	Faculty of Medicine, University of Kelaniya	Sri Lanka
Professor Nadira Karunaweera	Senior Professor and Chair	Department of Parasitology (Leish) Faculty of Medicine, University of Colombo	Sri Lanka
Dr Indira Kahawita	Consultant Dermatologist	Chair – Leprosy Study Group College of Dermatologists	Sri Lanka
Ms Domingas da Consta Pereira	Executive Director	INS	

Name	Designation	Institution	Country
Dr Bhupendra Tripathi	Country Lead Elimination Programme – NTD	BMGF – India Country Office, New Delhi	India
Dr Be-Nazir Ahmad	Independent Expert (LF/VL)	Dhaka, Bangladesh	
Dr Murari Lal Das	Entomologist	Hetauda	Nepal
Dr Anand Joshi	Independent Expert		Nepal
Dr Dasaradha Ramaiah Kapa	Independent Consultant, LF expert		India
Dr Kaliannagounder Krishnamoorthy	Senior Consultant	Formerly Scientist G, Vector Control Research Centre, Indiranagar, Puducherry	India
WHO			
Dr Daniel Argaw	Coordinator UCN/NTD/PTC	WHO headquarters, Geneva	Switzerland
Dr Anthony Solomon	Chief Scientist (NTD) UCN/NTD/DOF	WHO headquarters, Geneva	Switzerland
Dr Jose Antonio Postigo	Medical Officer UCN/NTD/PTC	WHO headquarters, Geneva	Switzerland
Dr Saurabh Jain	Scientist UCN/NTD/PTC	WHO headquarters, Geneva	Switzerland
Dr Jonathan King	Scientist UCN/NTD/PTC	WHO headquarters, Geneva	Switzerland
Dr Amadou Garba Djirmay	Scientist UCN/NTD/PTC	WHO headquarters, Geneva	Switzerland
Dr Raman Velayudhan	Coordinator UCN/NTD/VVE	WHO headquarters, Geneva	Switzerland
Dr Rajpal Singh	Scientist UCN/NTD/VVE	WHO headquarters, Geneva	Switzerland

Name	Designation	Institution	Country
Dr Abraham Aseefa	Unit Head TDR/IMP	WHO headquarters, Geneva	Switzerland
Dr Megha Raj Banjara	Consultant TDR/IMP	WHO headquarters, Geneva	Switzerland
Dr Pemmaraju VR Rao	Team Lead Global Leprosy Programme	WHO Regional Office for SE Asia New Delhi	India
Dr Siswanto Siswanto	Senior Advisor – AMR	WHO Regional Office for SE Asia, New Delhi	India
Dr Suman Rijal	Director – CDS	WHO Regional Office for SE Asia, New Delhi	India
Dr Aya Yajima	Regional Advisor NTD	WHO Regional Office for SE Asia, New Delhi	India
Dr Hussain Rasheed	Regional Adviser Water, Sanitation and Climate Change HPN/SDH	WHO Regional Office for SE Asia, New Delhi	India
Dr Zaw Lin	Technical Officer NTD	WHO Regional Office for SE Asia, New Delhi	India
Dr Bhupendra Nagpal	Entomologist	WHO Regional Office for SE Asia, New Delhi	India
Dr Sabera Sultana	National Professional Officer	WHO Bangladesh, Dhaka	Bangladesh
Dr Anupama Hazarika	Medical Officer-CDS	WHO Bangladesh, Dhaka	Bangladesh
Dr M Mostafa Zaman	Advisor - Research & Publication unit	WHO Bangladesh, Dhaka	Bangladesh
Dr Shampa Saha	National Consultant – KA	WHO Bangladesh, Dhaka	Bangladesh
Dr Rashmi Shukla	National Professional Officer - Leprosy	WHO India, New Delhi	Bangladesh

Name	Designation	Institution	Country
Dr Kamalakar Lashkare	National Professional Officer -LF	WHO India, New Delhi	India
Dr Sonam Wangdi	National Professional Officer	WHO Bhutan, Thimphu	Bhutan
Dr Kamar Rizwan	Technical Officer	WHO Democratic People's Republic of Korea, Pyongyang	Democratic People's Republic of Korea
Dr Serene Joseph	Technical Officer – NTD	WHO Indonesia, Jakarta	Indonesia
Dr Achmad Naufal Azhari	National Profession Officer	WHO Indonesia, Jakarta	Indonesia
Dr Badri Thapa	Scientist – Malaria	WHO Myanmar, Yangon	Myanmar
Dr San San Win	National Technical Officer	WHO Myanmar, Yangon	Myanmar
Dr Khin Oo Mon	Project Coordinator (VBDC)	WHO Myanmar, Naypyitaw	Myanmar
Dr Deyer Gopinath	Medical Officer – Malaria & Border Health	WHO Thailand, Bangkok	Thailand
Dr Khin Pa Pa Naing	Technical officer	WHO Nepal, Kathmandu	Nepal
Dr Usha Kiran	National Professional Officer	WHO Nepal, Kathmandu	Nepal
Dr Mirzaya Cader	National Professional Officer	WHO Sri Lanka, Colombo	Sri Lanka
Dr Preshila Samaraweera	National Consultant (CDS)	WHO Sri Lanka, Colombo	Sri Lanka
Dr Aisath Thimna Latheef	National Professional Officer	WHO Maldives, Malé	Maldives
Dr Debashish Kundu	Technical Officer (CDS)	WHO Timor-Leste, Dili	Timor-Leste
Dr Younghee Jung	Technical Officer (NTD)	WHO Timor-Leste, Dili	Timor-Leste

Annex 3

Agenda of the virtual consultation meeting

Day 1: Tuesday 16 November 2021 (all times are in Indian Standard Time – GMT + 5.30 hrs)		
14:00–14:10	Opening remarks	Dr Suman Rijal, Director CDS
14:10–14:20	Meeting objectives	Dr Zaw Lin
14:20–14:40	NTD road map 2030 and operational research for NTDs: global efforts	Dr Anthony Solomon
14:40–14:50	Break	
14:50–15:20	NTD operational research areas identification: method and process	Dr Zaw Lin
15:20–15:30	* Five breakout and plenary sessions: process	Dr Ekta Saroha
15:30–17:00	* Five breakout sessions (dengue, leprosy, LF, schistosomiasis): deliberations on identified list of operational research areas	
Day 2: Wednesday 17 November 2021 (all times are in Indian Standard Time – GMT +5.30 hrs)		
14:00–15:45	* Five breakout sessions (dengue, leprosy, LF, schistosomiasis, VL): deliberations on identified list of operational research areas	
15:45–15:55	Preparation of presentation for plenary session	Disease note takers & group leaders
15:55–16:00	Break	
16:00–16:30	Plenary: dengue	Disease group leader Dr Veerle Vanlerberghe (moderator) Dr Usha Kiran (note taker)
16:30–17:00	Plenary: LF	Disease group leader Dr Ekta Saroha (moderator) Dr Kamalakar Arjun Lashkare (note taker)

Day 3: Thursday 18 November 2021 (All times are in Indian Standard Time – GMT +5.30 hrs)		
14:00–14:30	Plenary: schistosomiasis	Disease group leader Dr Katja Polman (moderator) Dr Achmad N Azhari (note taker)
14:30–15:00	Plenary: VL	Disease group leader Dr Kristien Cloots (moderator) Dr Amresh Kumar (note taker)
15:00–15:30	Plenary: leprosy	Disease group leader Dr Epco Hasker (moderator) Dr Rashmi Shukla (note taker)
15:30–15:40	Break	
15:40–16:15	Overarching areas of operational research in five NTDs	Dr Epco Hasker
16:15–16:30	Way forward	Dr Zaw Lin
16:30–16:55	TDR support for operational research for NTD elimination	Dr Abraham Aseffa/ Dr Megha Raj Banjara
16:55–17:00	Closing remarks	Dr Suman Rijal, Director CDS

***Breakout sessions: deliberations on identified list of operational research areas (Days 1 and 2)**

Group	Presenter	Moderator	Note taker
Dengue	Dr Veerle Vanlerberghe	Dr Raman Velayudhan/ Dr Rajpal Singh Yadav/ Dr BN Nagpal	Dr Usha Kiran
Leprosy	Dr Epco Hasker	Dr Pemmaraju Venkata R Rao	Dr Rashmi Shukla
LF	Dr Ekta Saroha	Dr Jonathan King	Dr Kamalakar Arjun Lashkare
Schistosomiasis	Dr Katja Polman	Dr Amadou Garba Djirmay/ Dr Aya Yajima	Dr Achmad N Azhari
VL	Dr Kristien Cloots	Dr Daniel Argaw Dagne/ Dr Jose Antonio Postigo/ Dr Saurabh Jain/Dr Zaw Lin	Dr Amresh Kumar

Annex 4

Full list of operational research areas for five NTDs

(Bold text indicates the areas that were repeatedly mentioned and emphasised during the various rounds of consultation)

Data source: Plenary presentation during the virtual consultation meeting

Dengue

Category: diagnostics

1. Evaluation of the added value of polymerase chain reaction (PCR) diagnosis of dengue in comparison to rapid diagnostic tests (RDTs)
2. Evaluation of decentralisation of RDTs to primary health-care settings (also in rural areas) on morbidity and case fatality rate of dengue cases (in comparison to clinical/general blood-cell diagnosis being currently followed)
3. Evaluate the availability of better diagnostic tools for the early detection of outbreaks
4. Evaluation of adherence of health professionals to the use of RDT and how this enters within the clinical management algorithm
5. Evaluation of performance of locally available RDTs
6. Evaluate the use of biomarkers in case management (severity/mortality as outcome).

Category: treatment

1. Evaluate efficacy of use of anti-dengue drugs (once available) in routine settings
2. Implementation research on affordable and effective referral systems to improve case management
3. Implementation research on acute fever case management when dengue is suspected.

Category: vaccine

None

Category: vector control

1. Implementation research (effectiveness, cost-effectiveness, acceptability and process evaluation) on Wolbachia roll-out
2. Implementation research (effectiveness, cost-effectiveness, acceptability and process evaluation) on targeted indoor residual spray (IRS)
3. Evaluate impact of water, sanitation and hygiene (WASH) measures on dengue transmission
4. Evaluate the impact of improved water provision on dengue transmission
5. Evaluate the impact of improved housing structures (roof gutters/architecture) on dengue transmission
6. Evaluate the impact of wall paints/linings on dengue transmission
7. Define indicators to use in the evaluation of impact of control interventions

8. Applied research to optimize and scale-up programmatic delivery of vector control in an environmentally safe and sustainable manner
9. Design strategies on how to coordinate environmental management activities with WASH stakeholders to manage outbreaks
10. Develop insecticide resistance monitoring strategies (frequency/level) and insertion within decision-making on control methods
11. Define control strategy based on knowledge on resting, biting and breeding behaviour of *Aedes aegypti* and *Aedes albopictus*
12. Evaluate the importance of hidden breeding sites (construction sites) for entomological infestation
13. Undertake mapping distribution of *Aedes* species and define control strategy adapted to distribution of *Aedes* species
14. Develop vector surveillance strategies (in relation to early warning and hotspots of transmission) and sampling tools for better decision-making (early warning system, targeting of control measures).

Category: surveillance

1. Estimate the disease burden (epidemiologic impact, social costs and cost of illness)
2. Develop and evaluate the predictive value of an early warning system in different settings and determine the most sensitive indicators as early warning signals of increased risk for dengue outbreaks (prediction thresholds)
3. Evaluate added value of virus identification in mosquitoes as an early warning sign
4. Evaluate interventions applied based on an early warning system in comparison to preventive measures
5. Develop a methodology to do risk mapping, capturing spatial areas at high risk for transmission and target control measures
6. Implementation research on differentiated interventions according to the risk profile of geographical zones/popular spots (evaluation effectiveness, process and feasibility of a flexible approach)
7. Evaluate the impact of virus population structure, urbanization and other land-use changes, human behavioural interactions and climate parameters on dengue transmission dynamics
8. Evaluate the importance of human mobility and places where people stay/gather during the daytime (school/work/market) on transmission dynamics of dengue
9. Evaluate the added value of monitoring serotypes (genotypes and linkages) for estimating the magnitude of outbreak prediction
10. Implementation research on evaluation impact of interventions in large urban settings, where community participation is difficult
11. Evaluate impact of multimedia tools on human behaviour related to dengue control
12. Design advocacy strategies and funding strategies to bring *Aedes*-borne diseases higher on the political agenda
13. Developing community engagement strategies for implementing integrated vector control
14. Evaluate the impact of behavioural change intervention on the incidence of dengue

15. Evaluate the impact of activities of schoolchildren within schools and at their houses to decrease breeding sites.

Leprosy

Category: diagnostics

1. Further development and validation of lab or field-based POC assays for leprosy diagnosis
2. Further development and validation of lab or field-based POC assays for leprosy infection
3. Development and validation of diagnostic tools for the detection and monitoring of nerve function impairment and reactions.

Category: treatment

1. Optimize the use of available treatment for reactions and nerve function impairment and identification of new treatment options
2. More effective drugs or drug combinations, or shorter regimens, to treat leprosy
3. Feasibility and impact of PEP.

Category: prevention and vaccines

1. Vaccines:
    a. *Mycobacterium indicus pranii* (MIP)
    b. T and cell vaccines (LepVax)
2. Post exposure prophylaxis
3. Causes of disability and ways to prevent it.

Category: health system

1. Determining cost-efficient active case-finding strategies under different epidemiological settings and local contexts
2. Development of methods for eLearning and hands-on training for health workers and community health volunteers
3. Interventions to reduce stigma: peer counselling, peer-to-peer networks, socioeconomic development
4. Involvement of persons affected by leprosy.

Category: surveillance

1. Determine the geospatial distribution of leprosy in countries and estimate the number of hidden cases
2. Determine numbers and distribution of people disabled due to leprosy
3. Development of mapping tools for leprosy surveillance and response monitoring
4. Defining data needs and data collection tools for programme monitoring and epidemiological monitoring.

Category: others

1. Risk factors for transmission of leprosy
2. Epidemiological modelling and investment case
3. Impact of COVID-19 pandemic.

LF

Category: diagnostics

1. Develop and improve diagnostics (fecundity of adult worms after IDA, biomarker for microfilaria density, recent exposure to infection) to help stop-DA and stop-IDA decisions and to be used in post-mass drug administration (MDA) surveillance for Wb, Bm, Bt
2. Evaluate performance, quality control and cost-effectiveness of current and new diagnostic tests and methodologies in a range of settings
3. Perform landscape analysis of potential new manufacturers of NTD diagnostics.

Category: treatment

1. Evaluate new drugs in the pipeline and treatment regimens that potentially kill or sterilize adult worms for efficacy and safety, to be used in MDA
2. Developing methods for remapping of urban areas (according to socioeconomic status) with identification of priority target areas (hotspots) for MDA implementation
3. Identify practical approaches to ensure better drug compliance among the adult male population
4. Operational research on management of chronic manifestations (psychosocial issues, different medical/surgical approaches, economic issues, programmatic issues)
5. Evaluate the cost and benefits of MMDP essential package of care implemented under UHC
6. Access and availability to Ivermectin to meet demand for IDA

Category: vaccine

None.

Category: vector control

1. Assess the opportunities, long-term impact and cost-effectiveness of country- and site-specific integrated vector management approaches (control and surveillance) to achieve and sustain elimination.

Category: health system

1. Evaluate current methodologies to estimate the burden of chronic disease manifestations and ability to identify Stages 1–3 lymphoedema and hydrocele
2. Ensure routine quality control in qualitative diagnosis in terms of skills of personnel (microscopy, FTS, etc.)
3. In low-transmission settings, evaluate cost-effectiveness of different survey and treatment strategies versus large-scale MDA
4. Evaluate impact of never treated and unreached on achieving elimination targets and evaluate practical, cost-efficient strategies to reduce it
5. Evaluate ongoing urban MDA campaign strategies including microplanning, training, social mobilization and supervision to improve coverage and compliance
6. Create evidence on feasibility and best strategies to integrate surveillance within other routine health-care processes in different settings (surveillance or disease-elimination systems i.e., Integrated Health Information Platform (IHIP), malaria, VL, Integrated Disease Surveillance Prohect (IDSP), noncommunicable diseases (NCDs), etc.)
7. Investigate innovative digital applications as tools to improve programme performance

8. Explore opportunities and health system (6 HSS blocks) barriers for management of chronic LF patients in the essential package of care under UHC, including assessment of how best to integrate MMDP services into the first-line routine health care in different settings.

Category: surveillance

1. Identification of high transmission areas, persistent hotspots and missed populations; increase understanding of determinants, improve identification and develop a strategy to mitigate the problem
2. Develop and pilot new surveillance strategies and interventions to be sustained post-validation
3. Investigate determinants of risk for resurgence after validation of elimination
4. Define criteria to demonstrate interruption of transmission
5. Develop a system for cross-border surveillance, patient notification and case management
6. Develop surveillance/evaluation strategies for zoonotic *Brugia malayi* and explore the role and impact of zoonotic transmission from cats/dogs for *B. malayi* infections
7. Develop/identify biomarkers to differentiate resurgence versus reinfection after interruption of transmission
8. Validation of geostatistical transmission assessment surveys (TASs).

Category: other

1. Perform return-on-investment analysis on previous 20 years to support investments in the coming years
2. Methods to enhance communication and advocacy
3. Integration with soil-transmitted helminthiases (STH) programme
4. Impact of COVID-19.

Schistosomiasis

Category: diagnostics

1. Develop more sensitive diagnostic tools adapted to *S. japonicum*/low-transmission settings (Indonesia)
2. Develop tests and standardized protocols for diagnosis of schistosomiasis in animal reservoirs, snails and environment
3. Evaluate available novel (antigen-based and molecular) diagnostic tests for *S. japonicum*

Category: treatment

1. Develop protocols for treatment and drug efficacy monitoring in animals
2. Study the effectiveness of selective treatment/test and treat for elimination of schistosomiasis in low-transmission settings.

Category: vaccine

None.

Category: vector control

1. Study to identify effective, safe, cost-effective and sustainable snail control technology considering the environment and socioeconomic value.

Category: health system

1. To assess if and to what extent schistosomiasis elimination can be integrated into primary health care
2. Health financing research to estimate the cost-effectiveness of elimination of schistosomiasis, with focus on the pre-elimination phase.

Category: other

1. Understand zoonotic transmission and interventions to address zoonotic reservoirs, with focus on wild animals (including rats)
2. Study how to improve integration of multidisciplinary and multisectoral approaches through community empowerment (e.g., WASH, snail vector, education, animal) for elimination
3. Pilot projects in cross-sectoral cooperation at village level.

Category: surveillance

1. Further clarify the status of schistosomiasis in SE Asia through proper surveys with accurate diagnostic tests (Myanmar, India, Thailand, Nepal)
2. Develop criteria/protocols as to whether or not elimination has been achieved and for deciding on stopping MDA
3. (Re)mapping and surveillance of intermediate snail hosts.

VL

Category: diagnostics

1. **Develop a single marker to detect asymptomatically infected individuals**
2. **Develop a biomarker to identify the risk of progression to disease**
3. **Develop a diagnostic test (more specific than rK39 RDT) for low-incidence settings (antigen-based?), allowing for diagnosis of relapse cases and allowing diagnosis within first 14 days of fever**
4. **Develop a syndrome-based approach for clinical management of fever in VL endemic areas**
5. **Develop a biomarker to distinguish reinfection from relapse**
6. **Need for validation of the PCR test for Post-kala-azar dermal leishmaniasis (PKDL), especially for macular cases**
7. **Develop a new gold standard alternative for lab confirmation of PKDL that can be widely used (instead of the current skin slit smear)**
8. **Develop a test of cure for PKDL**
9. **Develop better diagnostic tools for HIV-VL**
10. **Develop a diagnostic test differentiating between different species level (for areas where several species co-exist)**
11. **Develop a test detecting drug resistance**
12. **Develop less invasive, highly specific tests to measure the parasite level**
13. **Develop less invasive test of cure for VL, PKDL and HIV-VL patients.**

Category: treatment

1. **Develop highly effective, safe, new, short-duration oral/topical treatments for VL and PKDL that can be used at community level**

2. **Investigate eye problems as a side effect of miltefosine use in PKDL patients**
3. **Evaluate the risk of relapse and PKDL for different drug regimens (single-dose vs 3-day LAMB), with long-term follow up of patients to assess rate of PKDL**
4. **Evaluate determinants for relapse and develop biomarkers to predict risk of relapse**
5. **Evaluate determinants for VL mortality and develop biomarkers to predict risk of mortality in patients**
6. **Develop treatment guidelines/regimens for relapse cases**
7. **Develop new HIV-VL treatment guidelines.**

Category: vaccine

1. Research on new, pipeline preventive and therapeutic candidate vaccines to prevent *Leishmania* infection and disease and vaccines to block transmission of *Leishmania*.

Category: vector control

1. **Research on vector population characteristics and behaviour, including insecticide resistance to guide vector control activities**
2. **Investigate role of alternative vector species in new/doubtful endemic areas**
3. **Investigate the contribution of exophagic/exophilic vectors to transmission**
4. **Research on/development of new vector control technologies adapted to the biological characteristics of each parasite species and its eco-epidemiology**
5. **Develop strategies for appropriate vector control, (e.g. when to stop IRS, use of alternative approaches, implementation of vector surveillance at sentinel sites to detect changes in vector infection and a rapid response of targeted vector control)**
6. **Assess the potential contribution (and acceptability) of long-lasting insecticidal nets (LLINs) to reduce transmission in persistent hotspots, areas with routine LLIN use for malaria (mesh-size)**
7. **Develop proxy markers for sandfly infectivity**
8. **Develop markers of successful vector control**
9. **Evaluate potential integrated vector control/surveillance**
10. **Develop and evaluate new insecticides against field populations of sandflies, including two new WHO prequalified insecticides (pirimiphos-methyl and clothianidin).**

Category: health systems

1. **Investigate the full impact of COVID-19, including the use of overlapping drugs (LAMB)**
2. **Include care for all skin NTDs in an integrated approach regardless of the specific causative agent**
3. **Develop a syndrome-based approach for clinical management of fever (or other clinical features) in VL endemic areas**
4. **Evaluate and ensure availability of all diagnostics and drugs in terms of local production versus monopolies**
5. **Develop a standardized approach for mapping and surveillance of VL**
6. **Evaluate the most suitable approach for active case detection of VL and PKDL in a low-incidence setting**
7. **Develop confirmation strategy for each VL case treated (PCR-based?)**

8. Develop integrated skin NTD approach regardless of the specific causative agent.

Category: surveillance

1. **Carry out operational research on integration of VL disease control and surveillance**
2. **Develop the most adequate response strategy to an outbreak**
3. **Develop the most adequate response strategy to a suspected case of local transmission in a non-endemic setting**
4. **Carry out transmission assessment in endemic doubtful districts/areas to investigate the current extent of endemicity**
5. **Investigate the causative leishmania species in new/doubtful endemic areas in case of atypical presentation in selected settings (CL, increased treatment failure, increased relapse)**
6. **Operational research to detect the proportion of unreported cases**
7. **Define strategy to validate zero reporting**
8. **Develop strategies to monitor leishmania transmission (rather than cases)**
9. **Assess the role of asymptomatically infected individuals in transmission**
10. **Investigate the potential role of animals in leishmania transmission**
11. **Monitoring of drug resistance**
12. **Monitoring of insecticide resistance**
13. **Monitoring of quality of programme implementation**
14. **Research on post-validation prevention of resurgence**
15. **How best to ensure continued advocacy and resource allocation post-validation? Lessons learned from other diseases, e.g. leprosy**
16. **Investigate the importance of CL as a potential threat to the elimination of VL (parasite species, vector, progress to VL – biomarkers, infectiousness)**

Overarching areas

Category: surveillance/health systems

1. Integrated surveillance
2. Poverty alleviation and integrated NTD management
3. Data sharing platforms
4. MDA donations management, resource forecasting at country level and supply chain management
5. Integrated management of skin NTDs (CL, scabies, PKDL, leprosy)

Category: other

1. COVID-19 effect on NTDs; new disease management/data/information systems post-COVID-19
2. Schistosomiasis: environmental DNA research and xenomonitoring; combine it with other NTDs.

Annex 5

Sample 'Operational research area prioritization survey'

Operational research area prioritization survey
Dengue
WHO Regional Office for SE Asia
April 2022

Welcome to the 'Operational research area prioritization (ORA)' virtual survey!
This ORA survey is for dengue.

At the end of the consultative meeting, the dengue expert group had listed 38 operational research areas (RAs). You are requested to screen and rank only 13 (RA# 1–13) of the 38 areas through this survey. (The remaining areas are being screened and ranked by other experts).

The RAs are numbered and stated in green text. Please read the research areas carefully before answering the questions. All responses are pre-coded. For some questions, we are requesting detailed information/comments. We will use your qualitative responses to substantiate the screening and ranking.

Please note that the first (screening) question (Q. S1) of each research area asks, 'if research is relevant or not'. If you select 'yes, relevant', you will continue to the scoring questions (Q. 1–9); if you select 'not relevant' you will be asked to justify (Q. S1a) and you will auto-skip to the next research area (RA #xx). Therefore, please carefully review the research area before answering the first question.

Your responses are very critical for scoring and prioritization of ORA in WHO SE Asia Region. Thank you again, for your continued support and expertise!

RA#1: Evaluation of the added value of PCR diagnosis of dengue in comparison to RDTs

Q#	Question	Response options	Score	Comment
S1	For RA#1 (Evaluation of the added value of PCR diagnosis of dengue in comparison to RDTs), please let us know if the research is **relevant or not**	• Yes, relevant • Not relevant	1 0	Skip to Q1 Skip to S1a Response required
S1a	Research on this topic is **not relevant** because	• research is already available • ongoing interventions/policies can be modified without undertaking this research • proposed research topic cannot be translated into a clear research question • of ethical concerns		Multiple responses allowed; no scoring; skip to next RA

Q#	Question	Response options	Score	Comment
		Please elaborate on available research, ongoing interventions, existing policies, anticipated ethical concerns, or any other critical information about this research area		
Q1	This research will accelerate the **progress** towards dengue control	A great deal A lot A moderate amount A little None at all None of the above Other (please specify)	4 3 2 1 0 0	
Q2	This research will make an **impact** in dengue control	A great deal (large population groups in WHO SE Asia Region) A lot (small population groups) A little (selected population groups) None at all None of the above Please specify the anticipated impact	3 2 1 0 0	
Q3	This research will **reduce dengue burden**	A great deal A lot Moderately Little Not at all None of the above Other (please specify)	4 3 2 1 0 0	
Q4	There are research **institutes in WHO SE Asia Region** that can complete this research	Yes, more than one Yes, one No Not sure Please share the name(s) of institute(s)	2 1 0 0	
Q5	This research will offer solutions/interventions at least a year prior to the control/elimination target date	Yes No Other (please specify)	1 0	

Q#	Question	Response options	Score	Comment
Q6	This research will offer or support **affordable solutions/interventions** to WHO SE Asia Region Member States	A great deal A lot A moderate amount A little None at all None of the above	4 3 2 1 0 0	
Q7	**Benefits** of this research will outweigh the potential **risks**	A great deal A lot A moderate amount A little None at all Not applicable Other (please specify)	4 3 2 1 0 0	
Q8	This research will improve **equity** (research findings will benefit socially, economically, demographically, geographically, or sexually disadvantaged groups)	A great deal A lot A moderate amount A little None at all Not applicable Please specify the population groups	4 3 2 1 0 0	
Q9	This research will be **cost-effective** (cost of doing the research outweighs the anticipated gain in health or not)	A great deal A lot A moderate amount A little None at all None of the above Other (please specify)	4 3 2 1 0 0	

Annex 6

Scores and ranks of operational research areas

Operational research area	Score	Rank
Dengue		
Evaluation of the added value of PCR diagnosis of dengue in comparison to RDTs	35	
Evaluation of decentralization of RDTs to primary health-care settings (also in rural areas) on morbidity and case fatality rate of dengue cases (in comparison to clinical/general blood cell diagnosis being done currently)	28	
Evaluate the availability of better diagnostic tools on the early detection of outbreaks	68	2
Evaluation of adherence of health professionals to the use of RDT and how this enters within the clinical management algorithm	0	
Evaluation of performance of locally available RDTs	0	
Evaluate use of biomarkers in case management (severity/mortality as outcome)	60	4
Evaluate efficacy of use of anti-dengue drugs (once available) in routine settings	49	
Implementation research on affordable and effective referral systems to improve case management	79	1
Implementation research on acute fever case management when dengue is suspected	57	
Implementation research (effectiveness, cost-effectiveness, acceptability, process evaluation) on Wolbachia roll-out	63	3
Implementation research (effectiveness, cost-effectiveness, acceptability, process evaluation) on targeted IRS	58	5
Evaluate impact of WASH measures on dengue transmission	37	
Evaluate the impact of improved water provision on dengue transmission	51	
Evaluate improved housing structures (roof gutters/architecture) on dengue transmission	17	
Evaluate the impact of wall paints/linings on dengue transmission	0	
Define indicators to use in the evaluation of impact of control interventions	0	
Applied research to optimize and scale-up programmatic delivery of vector control in an environmentally safe and sustainable manner	0	
Design strategies on how to coordinate environmental management activities with WASH stakeholders to manage outbreaks	0	
Develop insecticide resistance monitoring strategies (frequency/level) and insertion within decision-making on control methods	0	
Define control strategy based on knowledge on resting, biting and breeding behaviour of *Aedes aegypti* and *Aedes albopictus*	0	

Operational research area	Score	Rank
Evaluate the importance of hidden breeding sites (construction) for entomological infestation	0	
Mapping distribution of *Aedes* species and define control strategy adapted to distribution of *Aedes* species	0	
Develop vector surveillance strategies (in relation to early warning and hotspots of transmission) and sampling tools for a better decision-making (early warning system, targeting of control measures)	0	
Estimate the disease burden (epidemiologic impact, social costs and cost of illness)	0	
Develop and evaluate the predictive value of an early warning system in different settings and determine the most sensitive indicators as early warning signals of increased risk for dengue outbreaks (prediction thresholds)	0	
Evaluate added value of virus identification in mosquitoes as an early warning sign	0	
Evaluate interventions applied based on an early warning system in comparison to preventive measures	0	
Develop methodology to do risk mapping, capturing spatial areas at high risk for transmission and to target control measures	48	
Implementation research on differentiated interventions according to the risk-profile of geographical zones/popular spots (evaluation effectiveness, process and feasibility of flexible approach)	42	
Evaluate the impact of virus population structure, urbanization and other land-use changes, human behavioural interactions and climate parameters on dengue transmission dynamics	47	
Evaluate the importance of human mobility and places where people are staying/gathering during day-time (school/work/market) on transmission dynamics of dengue	0	
Evaluate the added value of monitoring serotypes, (genotypes and linkages) for estimating magnitude of outbreak prediction	49	
Implementation research on evaluation impact of interventions in large urban settings, where community participation is difficult	48	
Evaluate the impact of multi-media tools on human behaviour related to dengue control	40	
Design advocacy strategies and funding strategies to bring *Aedes*-borne diseases higher on the political agenda	49	
Developing community engagement strategies for implementing integrated vector control	47	
Evaluate impact of behavioural change intervention on incidence of dengue	44	
Evaluate impact of activities of school children within schools and at their houses to decrease breeding sites	0	

Operational research area	Score	Rank
Leprosy		
Further development and validation of lab or field-based POC assays for leprosy diagnosis	504	2
Further development and validation of lab or field-based POC assays for leprosy infection	421	5
Development and validation of diagnostic tools for the detection and monitoring of nerve function impairment and reactions	469	3
Optimize the use of available treatment for reactions and nerve function impairment and identification of new treatment options	462	4
More effective drugs or drug combinations, or shorter regimens, to treat leprosy	506	1
Feasibility and impact of PEP	398	8
Mycobacterium indicus pranii (MIP)	348	11
T and cell vaccines (LepVax)	321	14
Post-exposure prophylaxis	402	7
Causes of disability and ways to prevent it	377	9
Determining cost-efficient active case finding strategies under different epidemiological settings and local contexts	416	6
Development of methods for e-learning and hands-on training for health workers and community health volunteers	340	12
Interventions to reduce stigma: peer counselling, peer-to-peer networks, socioeconomic development	349	10
Involvement of persons affected by leprosy	317	15
Determine the geospatial distribution of leprosy in countries and estimate the number of hidden cases	302	18
Determine numbers and distribution of people disabled due to leprosy	276	20
Development of mapping tools for leprosy surveillance and response monitoring	329	13
Defining data needs and data collection tools for programme monitoring and epidemiological monitoring	303	17
Risk factors for transmission of leprosy	314	16
Epidemiological modelling and investment case	301	19
Impact of COVID-19 pandemic	228	21
LF		
Develop and improve diagnostics (fecundity of adult worms after IDA, biomarker for microfilaria density, recent exposure to infection) to help stop-DA and stop-IDA decisions and to be used in post-MDA surveillance for Wb, Bm, Bt	37	
Evaluate performance, quality control and cost-effectiveness of current and new diagnostic tests and methodologies in a range of settings	39	
Perform landscape analysis of potential new manufacturers of NTD diagnostics	26	
Evaluate new drugs in the pipeline and treatment regimens that potentially kill or sterilize adult worms, for efficacy and safety to be used in MDA	18	

Operational research area	Score	Rank
Developing methods for remapping of urban areas (according to socioeconomic status) with identification of priority target areas (hotspots) for MDA implementation	0	
Identify practical approaches to ensure better drug compliance among the adult male population	28	
Operational research on management of chronic manifestations (psychosocial issues, different medical/surgical approaches, economic issues, programmatic issues)	47	
Evaluate the cost and benefits of MMDP essential package of care implemented under UHC	0	
Access and availability to ivermectin to meet the demand for IDA	0	
Assess the opportunities, long-term impact and cost-effectiveness of country- and site-specific integrated vector management approaches (control and surveillance) to achieve and sustain elimination	37	
Evaluate current methodologies to estimate the burden of chronic disease manifestations and ability to identify Stage 1–3 lymphoedema and hydrocele	106	3
Ensure routine quality control in qualitative diagnosis in terms of skills of personnel (microscopy, FTS, etc.)	94	
In low-transmission settings, evaluate cost-effectiveness of different survey and treatment strategies versus large-scale MDA	75	
Evaluate the impact of never treated and unreached on achieving elimination targets and evaluate practical, cost-efficient strategies to reduce it	107	2
Evaluate ongoing urban MDA campaign strategies including microplanning, training, social mobilization and supervision to improve coverage and compliance	95	5
Create evidence on feasibility and best strategies to integrate surveillance within other routine health-care processes in different settings (surveillance or disease-elimination systems, i.e. IHIP, malaria, VL, IDSP, NCDs, etc.)	73	
Investigate innovative digital applications as tools to improve programme performance	85	
Exploring opportunities and health system (6 HSS blocks) barriers for management of chronic LF patients in essential package of care under UHC, including assessment of how best to integrate MMDP services into first-line routine health care in different settings	99	4
Identification of high transmission areas, persistent hotspots and missed populations; increase understanding of determinants, improve identification and develop a strategy to mitigate the problem	114	1
Develop and pilot new surveillance strategies and interventions to be sustained post-validation	78	
Investigate determinants of risk for resurgence after validation of elimination	53	
Define criteria to demonstrate interruption of transmission	0	

Operational research area	Score	Rank
Develop a system for cross-border surveillance, patient notification and case management	0	
Develop surveillance/evaluation strategies for zoonotic *Brugia malayi* and explore the role and impact of zoonotic transmission from cats/dogs for *B. malayi* infections	54	
Develop/identify biomarkers to differentiate resurgence versus reinfection after interruption of transmission	45	
Validation of geostatistical TAS	54	
Perform return-on-investment analysis on previous 20 years to support investments in the coming years	0	
Methods to enhance communication and advocacy	53	
Integration with STH programme	49	
Impact of COVID	54	
Schistosomiasis		
Develop more sensitive diagnostic tools adapted to *S. japonicum*/low-transmission settings (Indonesia)	22	5
Develop tests and standardized protocols for diagnosis of schistosomiasis in animal reservoirs, snails and environment	21	
Evaluate available novel (antigen-based and molecular) diagnostic tests for *S. japonicum*	15	
Develop protocols for treatment and drug efficacy monitoring in animals	0	
Study the effectiveness of selective treatment/test and treat for elimination of schistosomiasis in low transmission settings	0	
Study to identify effective, safe, cost-effective and sustainable snail control technology considering the environment and socioeconomic value	30	1
To assess if and to what extent schistosomiasis elimination can be integrated into primary health care	23	4
Health financing research to estimate the cost-effectiveness of elimination of schistosomiasis, with focus on the pre-elimination phase	22	
Understand zoonotic transmission and interventions to address zoonotic reservoirs, with focus on wild animals (including rats)	0	
Study how to improve integration of multidisciplinary and multisectoral approaches through community empowerment (e.g., WASH, snail vector, education, animal) for elimination	28	2
Pilot projects in cross-sectoral cooperation at village level	0	
Further clarify the status of schistosomiasis in SE Asia through proper surveys with accurate diagnostic tests (Myanmar, India, Thailand, Nepal)	17	
Develop criteria/protocols as to whether or not elimination has been achieved and for stopping MDA	26	3
(Re)mapping and surveillance of intermediate snail hosts	0	

Operational research area	Score	Rank
VL		
Develop a single marker to detect asymptomatically infected individuals	35	
Develop a biomarker to identify risk of progression to disease	11	
Develop a diagnostic test (more specific than rK39 RDT) for low-incidence setting (antigen-based?), allowing for diagnosis of relapse cases and allowing diagnosis within first 14 days of fever	0	
Develop a syndrome-based approach for clinical management of fever in VL endemic areas	50	2
Develop a biomarker to distinguish reinfection from relapse	19	
Need for validation of the PCR test for PKDL, especially for macular cases	34	
Develop new gold standard alternative for lab confirmation of PKDL that can be widely used (instead of current skin slit smear)	36	5
Develop a test of cure for PKDL	30	
Develop better diagnostic tools for HIV-VL	34	
Develop diagnostic test differentiating between different species level (for areas where several species co-exist)	27	
Develop test detecting drug resistance	28	
Develop less invasive, highly specific tests to measure parasite level	0	
Develop less invasive test of cure for VL, PKDL and HIV-VL patients	45	3
Develop highly effective, safe, new, short-duration oral/topical treatments for VL and PKDL that can be used at community level	0	
Investigate eye problems as a side effect of miltefosine use in PKDL patients	59	1
Evaluate the risk of relapse and PKDL for different drug regimens (single-dose vs 3-day LAMB), with long-term follow up of patients to assess rate of PKDL	26	
Evaluate determinants for relapse and develop biomarkers to predict risk of relapse	16	
Evaluate determinants for VL mortality and develop biomarkers to predict risk of mortality in patients	0	
Develop treatment guidelines/regimens for relapse cases	24	
Develop new HIV-VL treatment guidelines	23	
Research on new, pipeline preventative and therapeutic candidate vaccines to prevent *Leishmania* infection and disease and vaccines to block transmission of *Leishmania*	30	
Research on vector population characteristics and behaviour, including insecticide resistance to guide vector control activities	30	
Investigate role of alternative vector species in new/doubtful endemic areas	0	
Investigate the contribution of exophagic/exophilic vectors to transmission	0	
Research on/development of new vector control technologies adapted to the biological characteristics of each parasite species and its eco-epidemiology	30	
Develop strategies for appropriate vector control, (e.g. when to stop IRS, use of alternative approaches, implementation of vector surveillance at sentinel sites to	30	

Operational research area	Score	Rank
detect changes in vector infection and a rapid response of targeted vector control)		
Assess the potential contribution (and acceptability) of LLIN to reduce transmission in persistent hotspots, areas with routine LLIN use for malaria (mesh-size)	0	
Develop proxy markers for sandfly infectivity	0	
Develop markers of successful vector control	24	
Evaluate potential integrated vector control/surveillance	24	
Develop and evaluate new insecticides against field populations of sandflies, including two new WHO prequalified insecticides (pirimiphos-methyl and clothianidin)	19	
Investigate the full impact of COVID-19, including the use of overlapping drugs (LAMB)	14	
Include care for all skin NTDs in an integrated approach regardless of the specific causative agent	17	
Develop a syndrome-based approach for clinical management of fever (or other clinical features) in VL endemic areas	25	
Evaluate and ensure availability of all diagnostics and drugs in terms of local production versus monopolies	23	
Develop a standardized approach for mapping and surveillance of VL	24	
Evaluate the most suitable approach for active case detection of VL and PKDL in a low-incidence setting	26	
Develop a confirmation strategy for each VL case treated (PCR-based?)	28	
Develop integrated skin NTD approach regardless of the specific causative agent	25	
Carry out operational research on integration of VL disease control and surveillance	23	
Develop the most adequate response strategy to an outbreak	24	
Develop the most adequate response strategy to a suspected case of local transmission in a non-endemic setting	0	
Carry out transmission assessment in endemic doubtful districts/areas to investigate the current extent of endemicity	31	
Investigate the causative leishmania species in new/doubtful endemic areas in case of atypical presentation in selected settings (CL, increased treatment failure, increased relapse)	0	
Operational research to detect proportion of unreported cases	43	4
Define strategy to validate zero reporting	13	
Develop strategies to monitor Leishmania transmission (rather than cases)	0	
Assess the role of asymptomatically infected individuals in transmission	0	
Investigate the potential role of animals in Leishmania transmission	14	
Monitoring of drug resistance	17	
Monitoring of insecticide resistance	25	
Monitoring of quality of programme implementation	26	
Research on post-validation prevention of resurgence	18	

Operational research area	Score	Rank
How best to ensure continued advocacy and resource allocation post-validation? Lessons learned from other diseases, e.g. leprosy	12	
Investigate the importance of CL as a potential threat to the elimination of VL (parasite species, vector, progress to VL – biomarkers, infectiousness)	5	
Overarching areas		
Integrated surveillance	0	
Poverty alleviation and integrated NTD management	0	
Data-sharing platforms	0	
MDA donation management, resource forecasting at country level and supply chain management	0	
Integrated management of skin NTDs (CL, scabies, PKDL, leprosy)	0	
COVID-19 effect on NTDs; new disease management/data/information systems post-COVID-19	15	1
Schistosomiasis: environmental DNA research and xenomonitoring – combine it with other NTDs	0	