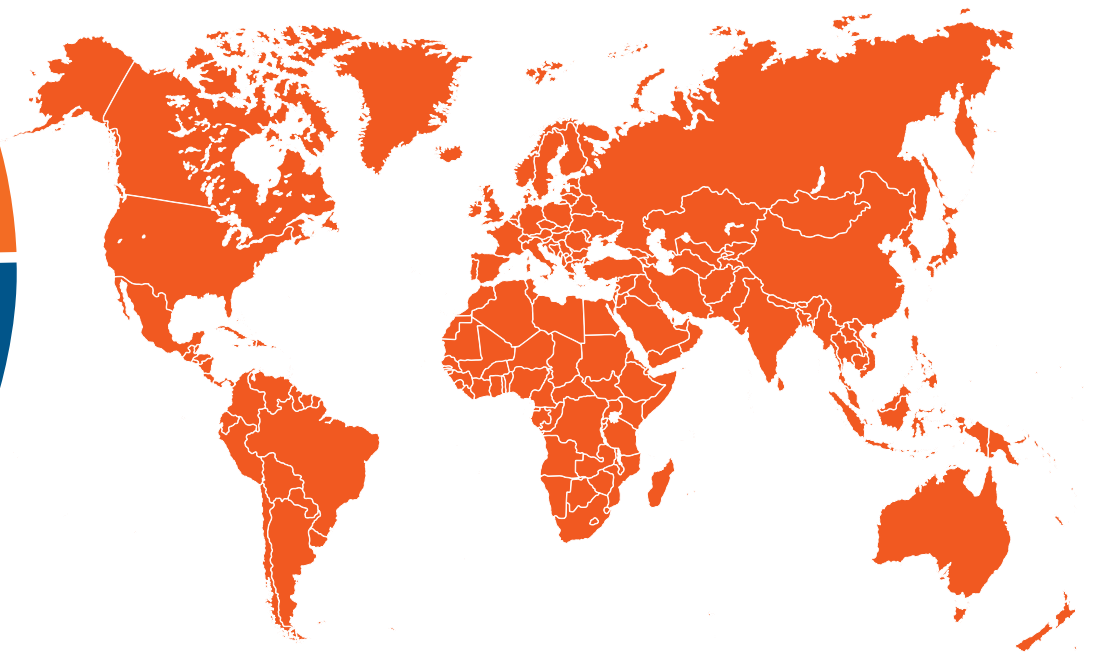




An assessment of German institutions' contribution to

RESEARCH ON NEGLECTED TROPICAL DISEASES



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IMPRINT

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IMAGE PROCESSING, LAYOUT

Gundula Scheele, Hamburg

PRINTING

RESET ST. PAULI Druckerei GmbH, Hamburg

EDITION

2nd Edition

LAST REVISION

June 2024

PREAMBLE

The World Health Organisation (WHO) estimates that over one billion people suffer from neglected tropical diseases (NTDs), a diverse group of diseases that occur particularly frequently, but not only, in low- and middle-income countries (LMICs). To date, 19 infectious diseases and snakebite envenoming have been categorised as NTDs by the WHO. Noma has recently been added as a further disease to the list. Combating NTDs is crucial to achieving the United Nations Sustainable Development Goals (SDGs).

By signing the Kigali Declaration, Germany has expressed its intention to contribute to the global fight against NTDs, not only in the area of research and development, but also by significantly strengthening capacities in endemic countries. An end to the burden of NTDs is possible, as the example of sleeping sickness shows, with fewer than 750 cases diagnosed in 2021. The expertise presented here is intended to show the state of the German NTDs research landscape in the period from 2018 to 2022 and compare it with the previous edition from 2018, which presented similar elements in the five-year period at that time. This study aims to connect researchers from different disciplines - from veterinarians to molecular biologists to implementation researchers - within the framework of One Health in order to generate and pool knowledge and resources in the field of NTDs.

This report brings together the expertise of 31 scientists which are experts of German NTDs research. The assessments in this report do not provide a judgement on the quality of research or a ranking of research institutions. The report succinctly identifies where gaps in current research and infrastructure exist, what actions may be needed to achieve the goals set by the WHO, and how German institutions and funders can help support equitable NTDs research and control. As scientists, we are committed to the fight against NTDs, which cause immeasurable suffering and have devastating health, social and economic consequences worldwide. Our common goal must be to alleviate the suffering of those affected and, together with our local partners in endemic countries, contribute to the development of health systems that leave no one behind.



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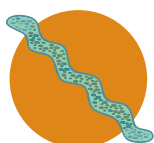
LEGEND



Toxins



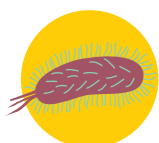
Ectoparasites



Flukes &
Helminths



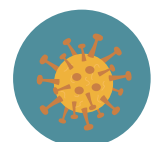
Fungi



Protozoa



Bacteria



Viruses

ABBREVIATIONS AND ACRONYMS

BMBF	Federal Ministry of Education and Research
BMZ	Federal Ministry for Economic Cooperation and Development
BNITM	Bernhard Nocht Institute for Tropical Medicine
CD	Chagas Disease
CMIA	Chemiluminescent Microparticle Immunoassay
DAHW	German Leprosy and Tuberculosis Relief Association
DALYs	Disability-Adjusted Life Years
DFG	German Research Foundation
DGP	German Society for Parasitology
DLR	DLR Project Management Agency
DNDi	Drugs for Neglected Diseases Initiative
DNTDs	German Network against Neglected Tropical Diseases
DTG	German Society for Tropical Medicine, Travel Medicine and Global Health
EDCTP	European and Developing Countries Clinical Trials Partnership
EKFS	Else Kröner-Fresenius-Foundation
ELISA	Enzyme-Linked Immunosorbent Assay
ESPEN	Expanded Special Project for Elimination of Neglected Tropical Diseases
FIND	Foundation for Innovative New Diagnostics
GIZ	German Association for International Cooperation
HAT	Human African Trypanosomiasis
ICT	Immunochromatographic Test
IIFT	Indirect Immunofluorescence Test
LMIC	Low- and Middle-Income Countries
MDA	Mass Drug Administration
PDP	Product Development Partnership
SDG	Sustainable Development Goal
WASH	Water, Sanitation and Hygiene
WHO	World Health Organization

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BACKGROUND

Neglected Tropical Diseases (NTDs) are a group of 21 diseases listed by the World Health Organisation (WHO) that occur frequently, but not exclusively, in low- and middle-income countries (LMICs). The people most affected by NTDs are often populations and minorities who are affected by poverty and lack access to adequate healthcare, education, water, sanitation and hygiene (WASH) and nutrition. Over one billion people worldwide are affected by NTDs. Despite the high burden of disease caused by NTDs, global attention is often focussed on other diseases such as HIV, malaria and tuberculosis.

In order to meet the call of the Sustainable Development Goal (SDG) 3.3 to end the global spread of NTDs by 2030, adapted research approaches and structural improvements to health systems are needed in a joint effort by affected and non-affected countries, research, governments and non-governmental organisations. This analysis aims to determine Germany's contribution to global NTDs research and to analyse progress, gaps and new challenges compared to the previous NTDs report published in 2018. ■

OBJECTIVES

This report presents the status of NTDs research in Germany in the period 2018-2022 and identifies changes, gaps and opportunities in NTDs research at German institutions. In addition, this report provides an overview of the political framework conditions such as the NTDs Roadmap 2030 and the associated Kigali Declaration. The results of the systematic research are presented and experts summarise the most important information for each of the 20 NTDs defined for the period 2018-2022. Finally, recommendations for action are given by comparing the results of the systematic literature, patent, clinical trial and funding searches with the experts' findings. ■

METHODOLOGY

This report was compiled by a project team of 31 authors from 16 German research institutions and organisations. Where possible, the work was carried out by a tandem of experts in the specific NTDs, providing evidence-based information and an assessment of the actions needed by German research institutions and networks to achieve the goals set out in the NTDs Roadmap 2030. In addition, a systematic literature search in the MEDLINE database and an analysis in the Dimensions environment (Digital Science & Research Solutions, Inc) was conducted. German patents related to NTDs were searched via the Questel Orbit FAMPAT database and a systematic search for clinical trials was conducted in the International Clinical Trials Registry Platform, the Pan African Clinical Trials Registry, ClinicalTrials.gov, ISRCTN and the European Clinical Trial Registry. Financial grants from funding organisations were retrieved via the G-FINDER data portal. The following were carried out:

- i. A systematic literature search for articles with at least one co-author from a German institution.
- ii. A systematic search for publication metrics, patents and clinical trials.
- iii. An expert-based information section and short tables with disease overviews. ■

RESULTS

The results of this report show that the German contribution of publications in NTDs research can be attributed to universities and some specialised non-university research institutions. The number of non-university research institutes among the ten most active institutions has decreased compared to 2013-2017. In contrast to the previous expertise, NTDs research in Germany increasingly contributed to translational research in the form of patents and clinical trials. In the last five years, the global publication volume on NTDs has increased by an average of 12%. The number of German publications has also increased, but was below this global average (8.5% increase in publications since 2018). The 1,550 papers

published at 270 German universities and non-university research institutions or companies accounted for 2.6% of the global publication volume, which represents a stable share compared to the last edition of the report. Among European countries, Germany ranks third after Spain and France.

The average 5-year impact factor of the top ten journals in which research articles on NTDs are published by German institutions was 3.5, which represents an increase of 21% compared to the period 2013-2017. Overall, the highest funding volumes invested were registered for lymphatic filariasis, schistosomiasis, onchocerciasis and sleeping sickness, in descending order. Most publications with German participation were published on leishmaniasis, followed by publications on schistosomiasis. The translational impact of German research can be seen in the 113 patents that were granted between 2018 and 2022, many of which are generic for several NTDs at the same time.

Worldwide, 513 clinical trials were recorded, of which 4.7% were initiated by a German trial sponsor. Based on our search methodology, clinical trials on Chagas and schistosomiasis were conducted most frequently. This is partly due to the strong involvement of the private sector in Chagas drug trials. Obtaining detailed information on the funding of German research in a holistic and systematic manner proved to be difficult in the context of this expertise. A database with comprehensive information on NTDs projects in the areas of basic research, clinical research and development as well as epidemiology, implementation research, operational research and capacity building projects and their funding is not available. The funding information in this report was mainly obtained through a search in G-FINDER, which, like the active surveys performed in the scope of this report, is also based on voluntary reports from research institutions and funders. The distribution of institutional funding for NTDs research is complex and diverse funding is not exclusively allocated to NTDs research.

Considering the aforementioned limitations and data gaps, the data indicate that funding for NTDs research in Germany showed a decline of around 10% in the first year of the COVID-19 pandemic, but then recovered and third-party funding for NTDs research in German institutions tended to increase. This contrasts with the year 2022, in which a 5-year low in the funding volume of German NTDs research can be observed. The German funding system is dominated by public funding organisations, which distribute 85% of the total approved funds. ■

CONCLUSION AND RECOMMENDATIONS FOR ACTION

In summary, this work emphasises Germany's commitment to research and research funding on NTDs, even if improvements are still needed to bring Germany into the global top group of NTDs research. We show that there have been changes over the years, and we can surmise that some of the positive results are due to the networking aspects that the projects have promoted over the years. Through our analysis and the assessment of the German NTDs experts, the main challenges in realising the global elimination target were described. Overall, we believe that initiatives such as this expertise should be continued in order to maintain attention to a global health problem that is constantly at risk of being underestimated and ignored by politicians, researchers, stakeholders and decision-makers. ■

I. BACKGROUND

In 2012, the WHO categorised a group of diseases - currently comprising 21 diseases - as NTDs, triggered by various causes such as viruses, bacteria, parasites, fungi and toxins. Intermediate hosts or vectors with an animal reservoir are often found in the life cycle of the pathogens. This classification is based on the categorisation of these diseases due to the low economic profit resulting from the marketing of treatments and preventive measures. However, in addition to these diseases recognised by the WHO, there are others that meet the criteria for NTDs. PLoS NTD, for example, proposes an expanded list of NTDs that includes diseases such as Loa Loa. In addition to the inclusion of noma in the official list of NTDs in December 2023, snakebite envenoming from the list of proposed potential NTDs was already successfully included in 2017. Since noma - a polymicrobial infection of soft tissue - was added to the list of NTDs in the final phase of the completion, it will not be referred to in this report. NTDs are closely linked to the cycle of poverty, lack of education, poor water and sanitation and social stigmatisation, yet various NTDs can also affect countries with a high availability of resources. These diseases are categorised by their geographical occurrence, even if their occurrence is not exclusively associated with tropical or subtropical countries.

Over one billion people worldwide are affected by NTDs. Despite the high morbidity burden, most of these diseases are not prioritised in the international agenda, which limits investment, especially in research. Global health guidelines such as the Sustainable Development Goals (SDGs), with target 3.3 published by the United Nations in 2016, identify tackling NTDs as a key component on the road to universal health coverage. This is emphasised by the successor to the NTDs Roadmap 2012-2020, the new NTDs Roadmap 2030, which was presented by the WHO in 2021 and endorsed by many stakeholders and governments by signing the Kigali Declaration in 2022 (see Fig. 1). However, these goals are not only being challenged by climate change, but also by conflicts and migration, as well as by health systems that are already under attack, e.g. due to the COVID-19 pandemic.

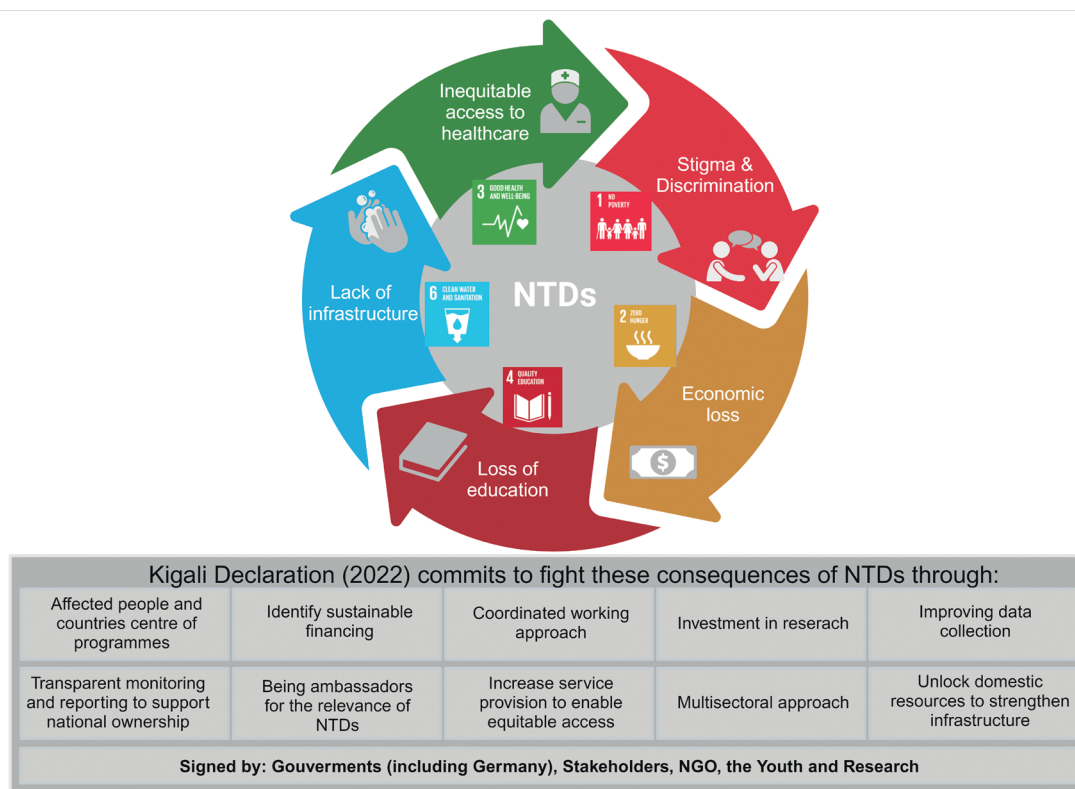


Figure 1: SDGs impacted by NTDs and the commitment of the Kigali Declaration

In addition, since the publication of the 2018 version of this report, there has been a paradigm shift in international guidance and commitment by national and international actors to advance efforts to combat NTDs through the new NTDs Roadmap and the Kigali Declaration, which supersede the previous 2012 Roadmap and London Declaration. The Kigali Declaration on NTDs is a political declaration that brings together governments, stakeholders, non-governmental organisations, youth organisations and the research community to promote the pursuit of international goals and their translation into national strategies to reduce or eliminate the multiple burdens caused by NTDs. Considering stakeholders around the world, the Declaration places affected countries and their citizens at the centre of the fight against NTDs. As shown in Fig. 2, the previous indicators in the categories of measuring success, approach to disease control and promoting country ownership have been adapted as part of the new roadmap.

Firstly, the criteria for evaluating the success of NTDs control measures have been adapted: From purely retrospective data analysis to a holistic assessment of success based on public health impact such as effective and sustainable interventions and actionable diagnostics. Secondly, in the area of cross-cutting approaches, the focus shifted from a more global, multi-country programme organisation to strengthening capacities in the affected countries with the support of the interdisciplinary global community. The third pillar of the roadmap shows the shift from dependence on external funders and partner funding to the involvement of local partners and regional actors in order to promote country ownership and improve sustainability. Local governments are therefore at the centre of implementation and coordination.

This issue of the NTDs Expertise is intended to inform stakeholders about the current status of NTDs research in Germany and the measures required to align the German agenda with the global agenda in the field of NTDs. Germany’s commitment is already evident in the signing of the Kigali Declaration, which supports a comprehensive national strategy to promote NTDs research in Germany and beyond through an interdisciplinary and multisectoral approach. Research into NTDs requires strong interdisciplinary work in the areas of human and animal health, water and sanitation, education, food safety and the environment. This emphasises once again the importance of a holistic view of health. This view, as described in the One Health concept, recognises the interrelationships between the health of humans, animals, plants and their shared environment.

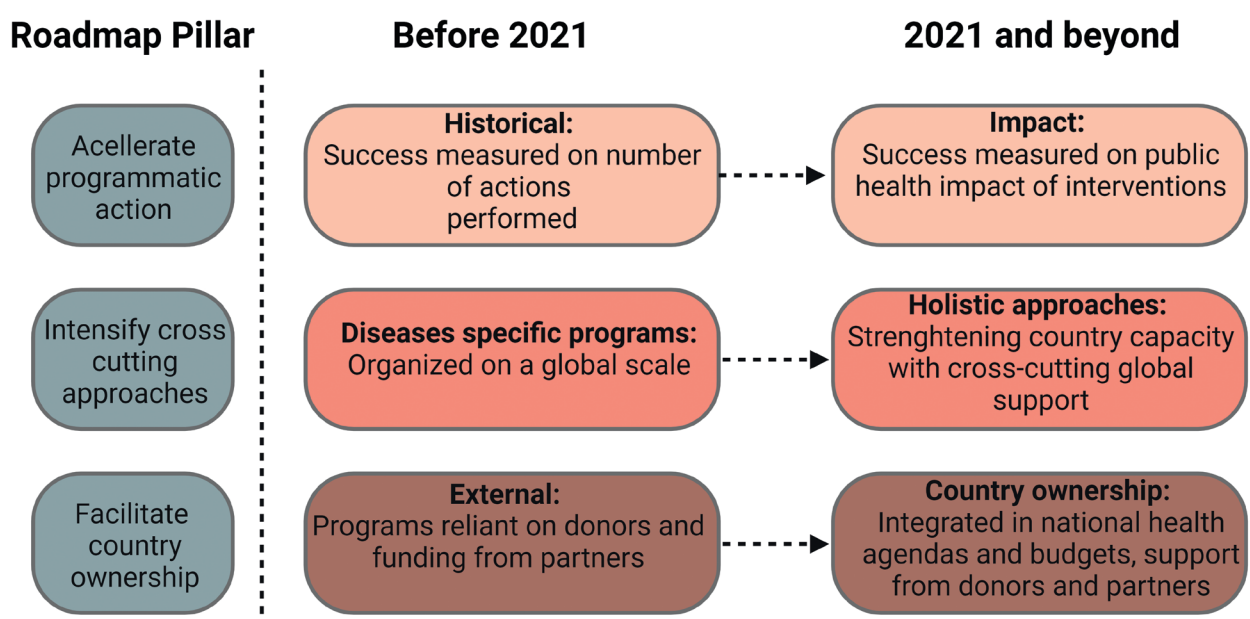


Figure 2: Paradigm shift in NTDs research through the NTDs Roadmap 2030



II. OBJECTIVES

Since 2018, the landscape of NTDs research and development in Germany has changed on an institutional, conceptual and political level. A paradigm shift can be observed due to the recognition of the Kigali Declaration by the Federal Government and numerous German stakeholders, as well as the new 2030 targets set by the WHO NTDs Roadmap. This report aims to provide an overview of the activities of German institutions in the field of NTDs research and development compared to the last edition in 2018. This publication pools the expert knowledge of NTDs researchers from German institutions to highlight and evaluate the potential of national scientific institutions in the field of NTDs. The previous edition of this report provided an initial overview of the most important players in NTDs research in Germany with a list of the research projects carried out and funded as well as a compact assessment of the research and development of drugs, active substances and diagnostics.

This second edition will highlight the changes since 2018 and build on the positive influences of the previous edition on the dialogue on NTDs in Germany. In addition to the contents of the previous edition, the current edition of the expertise will provide a detailed insight into project funding from public and private project sponsors and the progress of German NTDs research in the context of the Roadmap 2030. The study was initiated by the German Network against Neglected Tropical Diseases (DNTDs), the German Society for Tropical Medicine, Travel Medicine and Global Health (DTG), the German Society for Parasitology (DGP) and the Bernhard Nocht Institute for Tropical Medicine (BNITM) and conducted by the BNITM.

The contribution of German NTDs research to each of the 20 diseases is assessed on the basis of the following key questions:

1. How do German experts assess the status quo of the epidemiological situation and the possibilities for combating the disease?
2. What changes have been observed over the last five years in the various disease and funding landscapes?
3. What hurdles exist for NTDs research in Germany?



Permanent damage after snakebite envenoming (left) Healing process after buruli ulcer (right)



III. METHODOLOGY

From a project team of 31 scientists, one or two authors from different institutions have written a short description for each disease. These short descriptions contain a summary of the epidemiological data as well as an assessment of the current situation and the existing challenges. The individual results of the project organisers' research into the individual diseases can also be found in the brief descriptions. The research activities of German institutions were systematically researched in MEDLINE. In addition, various registers for clinical trials were searched using predefined key terms adapted to the respective database format, based on the MEDLINE search system. In this respect, the study is based on a methodology with three consecutive steps:

- I. A systematic literature search of articles with at least one co-author affiliated with a German research institution.
- II. A systematic search for publication metrics, patents and clinical trials.
- III. An expert-based information section and short tables with disease overviews.

First, all searches performed were narrowed down to the period from 1 January 2018 to 31 December 2022 and conducted in the MEDLINE database using a peer-reviewed search algorithm; the PubMed identifiers were then transferred to the Altmetric (Digital Science) Dimensions environment for data analysis. Each syntax was searched once for international articles and once for German institutions, affiliations of researchers and actors. Papers were included if at least one of the authors had an affiliation with a German institution. All search syntaxes validated by experts are listed in the appendix of this report. To ensure comparability for the period 2013-2017, the same search strategy was repeated for this period. Subsequently, existing patents relating to NTDs in Germany were searched via the Questel Orbit FAMPAT database, carried out by the Hamburg Chamber of Commerce. A systematic search for clinical trials was conducted in the International Clinical Trials Registry Platform, the Pan African Clinical Trials Registry, ClinicalTrials.gov, ISRCTN and the European Clinical Trial Registry. The financial contributions of third-party funders were taken from the G-FINDER data portal (Policy Cures Research). This was supplemented by a request for information on the funding of the ten leading institutions in NTDs research in Germany identified by the research of this expertise, which were asked to provide insights into their third-party funding for the years 2018-2022. Eight organisations responded, as well as the BMBF and the BMZ. The reported data was merged with the results of the G-FINDER database, which records annual investment in research and development for new products and technologies to address priority global health issues. In addition, information from organisations that have reported to G-FINDER but do not appear in the results of the data portal was included in the analysis.

Overall scientific productivity for NTDs

Compared to the years 2013-2017, there was an overall increase in global publications on NTDs between 2018 and 2022. Publications associated with researchers from German institutions remained stable in 9th place in an international comparison. The number of publications (1,550) associated with researchers from German institutions increased by 8.5%. Among the top ten countries, the average increase was 12% (standard deviation 9.1). Although the number of German publications also increased, only the USA, Switzerland and France showed a smaller increase in publications among the top ten countries. Among the European countries, the publication output of German NTDs research ranks third overall, after France and Spain.

Based on our search, a total of 513 clinical trials on NTDs were registered worldwide in the period under review. The diseases for which clinical trials were conducted most frequently were dengue with 24% of all trials and leishmaniasis with 14%. The lowest number of clinical trials was registered for mycetoma and dracunculiasis with 0.2% each. Most clinical trials on NTDs were funded by donors from the USA (12% of all trials), followed by India with 10% and France with its overseas departments (8.5%). Most patents were granted by organisations from the USA. The relationship between the number of publications and the number of patents in Germany is remarkable. With 25 patents found by searching the Dimensions database, Germany is the leading country in translating research into patents within the European Union. Leading countries in terms of political citations were the USA, the UK and Switzerland. It should be noted that many international organisations such as the Drugs for Neglected Diseases Initiative (DNDi) or the WHO are based in Switzerland, which increases the number of policy citations for this country.

Tab. 1: Country overview research statistics all NTDs (Change in percent from 2013-2017 to 2018-2022)

Country	Publications ¹	Authors ²	Trials ³	Policy ⁴	Patents ⁵
United States	7381 (+ 4.3)	29709	59	236	198
Brazil	6156 (+17.4)	21137	22	65	63
United Kingdom	3815 (+22.5)	16235	42	210	66
China	3167 (+30.2)	11166	26	24	44
India	3059 (+8.5)	10174	52	48	20
Australia	1673 (+10.1)	6852	14	84	15
France	1612 (-1.4)	8643	11	49	17
Spain	1608 (+11.8)	6845	42	26	16
Germany	1550 (+8.5)	8025	25	44	25
Switzerland	1376 (+10.4)	6519	38	158	22

Endemic treponematoses excluded due to limitations in literature search

¹ Publications retrieved through MEDLINE search and analyzed in the Dimensions environment

² authorships retrieved through MEDLINE search and analyzed in the Dimensions environment

³ Trials from International Clinical Trials Registry Platform, the Pan African Clinical Trials Registry, ClinicalTrials.gov, ISRCTN and the European Clinical Trial Registry,

⁴ Policies retrieved from Dimensions

⁵ Patents retrieved from Dimensions

German scientific productivity for NTDs

The total number of publications on NTDs with authors from 270 German research units rose to 1,550. The median increase in the number of publications among the top ten institutions between 2013-2017 and 2018-2022 is 20%. With the exception of the BNITM, the top ten institutions are all universities, while the Friedrich Loeffler Institute and the Robert Koch Institute were also among the leading non-university institutions in the period 2013-2017. The median number of senior researchers, defined as the first, last or corresponding author of a scientific publication, shows that half of the ten leading publishing institutions identified in our study have seen a decrease in the proportion of senior researchers publishing on NTDs, while the other five institutions have seen an increase. The institution with the highest number of authors was the BNITM (n=223), followed by the Charité (n=222). The highest number of senior authors came from Heidelberg University (n=89), followed by the BNITM (n=61).

Of all clinical trials, 4.7% can be attributed to a German sponsor. Of these 25 German clinical trials, 28% were sponsored by Bayer AG and two each by the Technical University of Munich, Heidelberg University Hospital, DAHW, Merck KGaA and Infecto-Pharm. Most of the German clinical trials are focused on Chagas disease and schistosomiasis. For the diseases dracunculiasis, mycetoma, human African trypanosomiasis, echinococcosis, food-borne trematodiasis, soil-transmitted helminths, endemic treponematoses, snakebite envenoming and trachoma, no clinical trials with a German trial sponsor were registered. A total of 113 patents relating to NTDs were granted to a patent holder based in Germany. The main owner of the newly granted patents is Merck KGaA with 4.5% (n=5), followed by the European Molecular Biology Laboratory (EMBL) and Prime Vector Technology and Boehringer Ingelheim Vetmedica with 3.6% each (n=4). Most of these patents were granted for multiple NTDs, between two and 14 diseases. Dengue was the most common disease (28%, n=32), followed by 21% (n=24) leishmaniasis patents. The only NTD for which no new patents with a German patent holder were granted in the period 2018-2022 is snakebite envenoming.

Tab. 2: Overview German institutions research statistics (Change in percent from 2013-2017 to 2018-2022)

Institution	Publication ¹	Senior German Authors ²	Authors ³	Trials ⁴	Patents ⁵
Heidelberg University	134 (+3.9)	89 (-7.3)	199	2	3
University of Tübingen	105 (+47.9)	50 (-2.0)	195	0	0
Bernhard Nocht Institut for Tropical Medicine	86 (+8.9)	61 (+10.9)	223	1	0
Charite University Medicine Berlin	84 (-5.6)	45 (-16.7)	222	0	1
Technical University of Munich	71 (+115.2)	41 (+105.0)	157	2	0
Ludwig-Maximilian University of Munich	67 (-19.3)	43 (-21.8)	173	0	2
University of Würzburg	64 (-26.4)	51 (-19.2)	173	0	1
University of Giessen	61 (+27.1)	45 (+32.4)	122	0	2
University Hospital Bonn	56 (+33.3)	30 (+15.4)	106	0	1
University Hospital Ulm	48 (+108.7)	41 (+141.2)	76	0	1

¹ Publications retrieved through MEDLINE search and analyzed in the Dimensions environment

² Authorships retrieved through MEDLINE search and analyzed in the Dimensions environment

³ Authorships retrieved through MEDLINE search and analyzed in the Dimensions environment

⁴ Trials from International Clinical Trials Registry Platform, the Pan African Clinical Trials Registry, ClinicalTrials.gov, ISRCTN and the European Clinical Trial Registry,

⁵ Patents retrieved from ORBIT FAMPAT through the Handelskammer Hamburg

Funding of German NTDs research

According to the G-FINDER report, research and development on NTDs is characterised by structural deficits worldwide, including Germany. Alarmingly, global funding for NTDs fell by 4% in 2020 compared to 2019 and has not recovered from this decline in 2021, as the G-FINDER report, published in 2022, shows. In addition, many of the targets set out in the NTDs Roadmap 2012-2020 have not yet been achieved by the global community. According to the report, it can be observed that global NTDs research is mainly funded by a few players such as the United States National Institute of Health (NIH), the Gates Foundation and the pharmaceutical industry. Germany plays only a minor role in the funding of projects in global comparison. The last edition of this report highlighted the urgent need to expand Germany's international presence in the field of NTDs research and emphasised the relatively low proportion of German gross national product invested in NTDs research compared to other countries such as the UK, the USA or France.

Determining the exact funding channels and amounts for German research in the context of this NTDs expertise proved to be difficult. Initially, an NTDs-specific search was conducted via the G-FINDER data portal as a tracker of annual investments in research, diagnostic products and technologies. However, many German research institutions do not report data to G-FINDER, and some NTDs, such as dracunculiasis, echinococcosis, food-borne trematodiasis or rabies, are not included in the G-FINDER report; yaws will be included in the 2022 analysis for the first time. In addition, operational research, capacity building or access- and health systems research do not fall within the scope of G-FINDER. Therefore, the top ten German NTDs research institutions and organisations were asked to provide information on their externally funded projects from 2018-2022. In addition, a request was sent to the most important donor organisations in Germany, such as the BMBF and the BMZ. A summarised list from this information, which includes projects from 2018-2022 and the G-FINDER results for 2018-2022, was used for this analysis. In addition, various projects that serve to strengthen health systems, such as those financed by the BMZ, were not listed as they are not explicitly NTDs research projects. Nonetheless, these projects clearly play a role in capacity building, support research and promote country ownership in the fight against NTDs.

Funds invested in Germany for NTDs (2018-2022)

The amount of funding for German NTDs research varies from year to year. German research funding is defined as funding awarded to a German institution, whereby these projects can be carried out either in Germany or in endemic countries.

Despite the global trend of declining overall funding, German NTDs research funding initially increased, with the exception of the first year of the COVID-19 pandemic in 2020, when a drastic decline in funding was observed. The total funding approved for German NTDs research is shown in Fig. 3. After a constant level of funding in 2018 (€12,198,193) to 2019 (€12,927,282), a decline of 10% to a funding amount of €11,670,983 was observed. Following this decline, the total amount of funding for German NTDs research recovered in 2021 (€21,428,046); a funding amount of over €8 million as part of a research project at two German research institutions deserves special mention here. In contrast to the global trend, German funding increased from 2020 to 2021. This development, contrary to the global trend, stagnated in 2022, which shows a 5-year low in the volume of funds in the form of an investment of €9,676,606 in NTDs research in Germany. In addition to the amounts shown, which are distributed via project funding, a total of almost €40,000,000 was awarded as basic funding by German public donors for research and development on NTDs and related diseases to organizations such as FIND, DZIF and EDCTP. However, this is only a rough estimate, as it is not possible to allocate the actual amount of institutional funds used only for NTDs research.

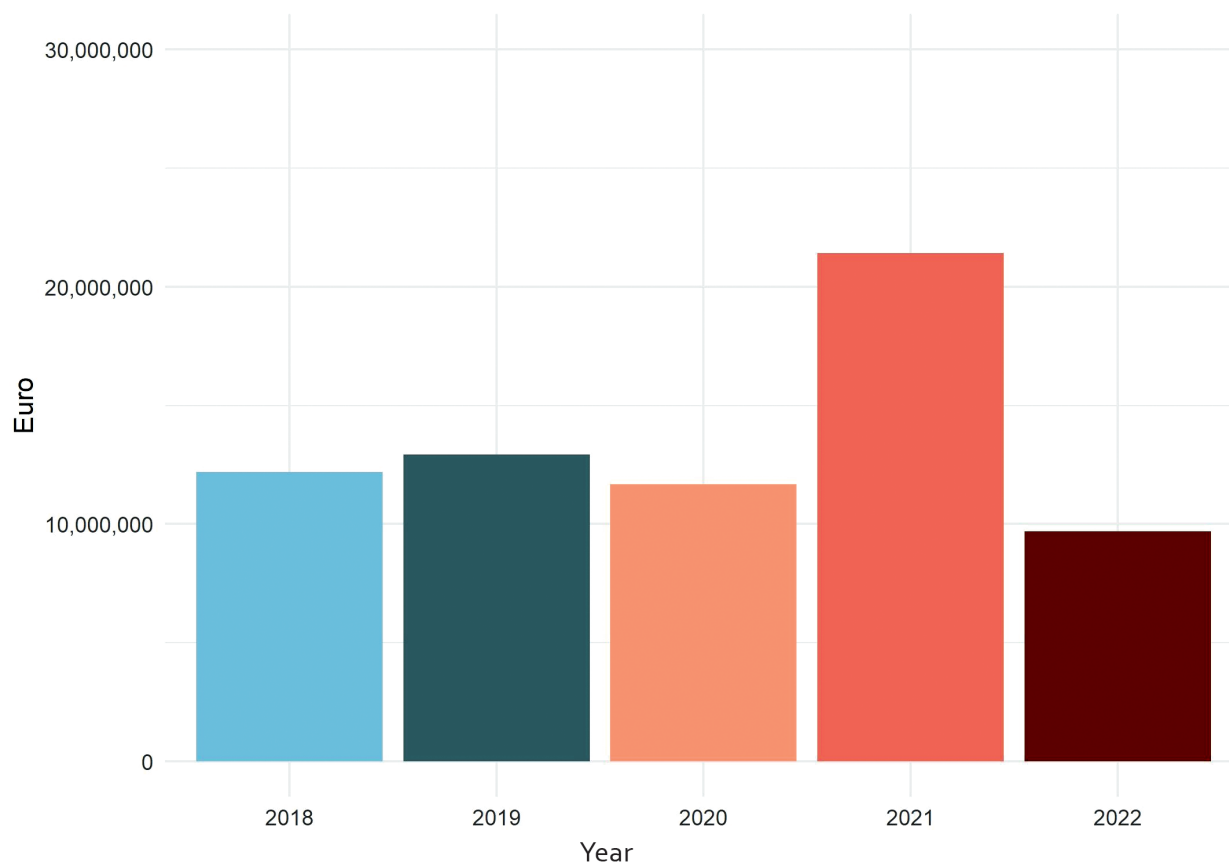


Figure 3: Financial contribution to NTDs research in Germany from 2018-2022

Funding structure of the German NTDs research landscape

The overall structure of the German NTDs funding landscape is dominated by public donors from the federal government and the European Union. Of the 256 grants awarded, 76% were financed by public donors with a funding volume of 85% of the total funds. Private sponsors accounted for 24% of projects and 15% of total funding. Overall, the highest funding volumes in descending order were for lymphatic filariasis, schistosomiasis, onchocerciasis and sleeping sickness.

For several diseases, such as rabies, mycetoma or food-borne trematodiasis, no project sponsors were found as part of this search. This may indicate that there is a gap in the coverage of projects for these diseases and there is a possibility that projects on these diseases exist in Germany but were not covered by this search due to a lack of a common database.

Publication metrics of the published works

The 20 most covered journals that published research articles on NTDs involving German research institutions between 2018 and 2022 are shown in Fig. 4 (analysis of journal metrics of 651 published articles with a link to a German research institution 2018-2022). PLoS Neglected Tropical Diseases was the journal with the most published articles on NTDs included in this analysis, with a 5-year impact factor of 4.5. Compared to 2013-2017 (3.4), the average impact factor of the publications in the 20 journals with the most publications on NTDs in the period 2018-2022 increased to a 5-year impact factor of 3.9. Other journals with a high impact factor, such as Frontiers in Immunology and PLoS Pathogens, can now be found in the list of journals. For comparison, the chart from the period 2013-2017 can be found in the appendix of this report. In addition to these publications, the total number of publications decreased in 2022 after a steady increase since 2019. This decline is most noticeable in open access publications. However, in line with the general decline in publication volume, the total number of non-open access articles with the participation of a German institution has also fallen continuously, reaching its lowest level since 2013 in 2022.

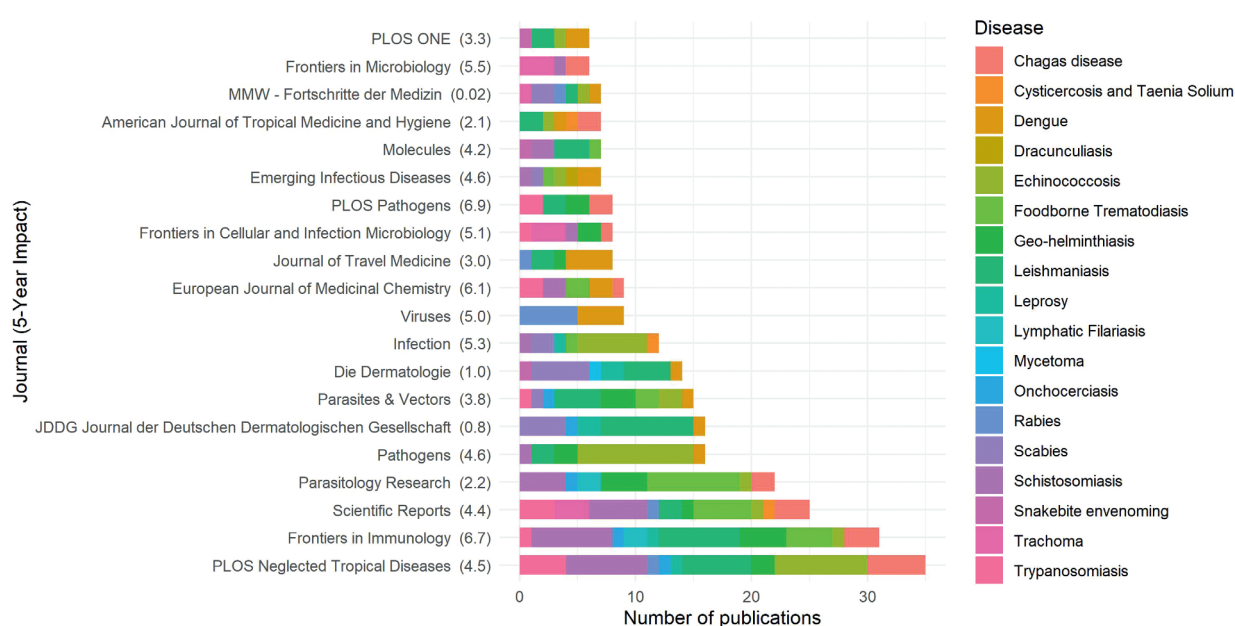


Figure 4: Name and 5-year impact factor on the number of publications per journal. Colour code indicating the different NTDs (5-year impact factor from 2023). Endemic treponematoses are not shown, as the limitation of the search algorithm made it impossible to differentiate between syphilis (not an NTD) and other treponematoses (which are NTDs)

Research priorities in Germany

The research priorities for the individual diseases were assessed by the authors of this report according to knowledge, experience and evidence (Fig. 5). The assessments by the experts are heterogeneous. Accordingly, the priorities in the area of development and implementation of diagnostics were often seen as the most urgent, followed by the development of targeted drugs as well as basic funding and other research and development measures. The strongly diverging priorities in drug research are particularly striking. While the authors ranked this topic among the lower priorities for eight diseases, drug research was classified as a higher priority for ten diseases. All priorities from diagnostics, vaccines, drugs, basic funding and other R & D to basic research were set as the highest, most urgent priority for some diseases and as the lowest priority for at least one disease. The development of vaccines was selected as the lowest priority overall, but this category was not considered applicable by the authors for three of the diseases (leishmaniasis, snakebite poisoning and food-borne trematodiasis) due to the nature of the disease or its transmission. In contrast, research into suitable vaccines is given the highest priority for leprosy and trachoma.

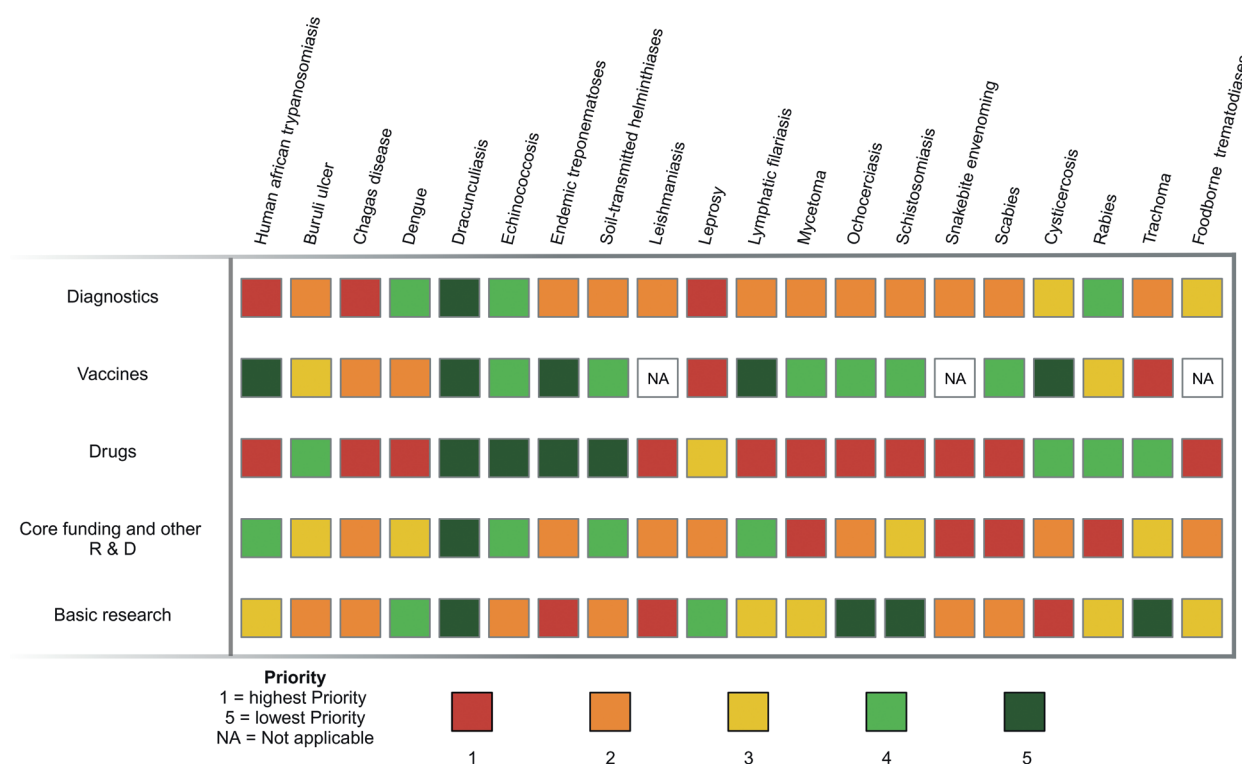


Figure 5: Research priority assessment for German NTDs research, priorities from 1 (highest priority in red) to 5 (lowest priority in green)



V. CONCLUSION AND SUMMARY

NTDs are a group of poverty-related diseases that are often underrepresented in research and development in relation to the number of people affected worldwide. Incentives to promote research and product development are rare, and without sufficient and continuous commitment there is a risk that the cycle of poverty and disease cannot be broken. Germany has taken a leading role by signing the Kigali Declaration and promoting initiatives to raise political, public and scientific awareness of NTDs. However, more effort is needed to achieve the SDGs and the control, elimination and eradication of NTDs. Furthermore, it is crucial that attention to these permanent health threats is maintained right now, as uncertain but more visible health threats attract more attention than possible pandemics due to NTDs.

In 2018, a first edition of this NTDs expertise was published to analyse the state of NTDs research, its funding and the commitment of German research institutions. The aim was to identify gaps and opportunities for NTDs research in Germany. This second edition attempts to outline the progress made since the last edition and new challenges that Germany needs to address in line with the global agenda. The main findings of this paper are that German research institutions have increased their publication volume in line with the global trend. Nevertheless, the increase in the number of publications with NTDs content is below the average increase of the ten most productive countries in the world. In contrast to the results of the previous report, a stronger contribution of German research institutions in the translational area of research and development was identified, which is reflected in clinical studies or patents. After the decline in funding volume in 2020 and the 5-year high in invested funds in 2021, the global trend of declining investment in NTDs research is also reflected in German NTDs research with the lowest funding volume of the period under review in the funding year 2022.

Overall, the highest volumes of funding invested were registered for lymphatic filariasis, schistosomiasis, onchocerciasis and sleeping sickness in descending order. This can be explained, among other things, by the high development costs for the corresponding drugs. Nevertheless, most publications with German participation were published on leishmaniasis, followed by publications on schistosomiasis. Overall, the scientific publications were published with a higher impact factor than in the period 2013-2017. One observed trend is the decreasing number of publications in 2022 after the all-time high in 2019, especially for open access publications. This could create barriers in knowledge access, especially in low- and middle-income countries (LMIC).

The challenge of the analysis presented was the reliable and comprehensive assessment of the financing of NTDs projects by German funders. The reasons for this are manifold: (i) the heterogeneous reporting of NTDs project funding; (ii) the difficulties in delineating the share of NTDs work in combined projects; (iii) the lack of complete databases on NTDs funding due to voluntary reporting; (iv) the absence of some NTDs in G-FINDER; (v) the incomplete responses from institutions on their project budgets for NTDs research; (vi) difficulties in allocating funding to specific funding periods (overlaps between the periods considered); (vii) the difficulty in allocating institutional funding from departments or institutions to NTDs research.

Among other things, we used one of the most comprehensive databases on investments in research and development on global health priorities with a focus on LMIC. The G-FINDER was introduced as an international instrument for monitoring the financing of poverty-related diseases. However, its completeness also depends on the individual reporting systems and the willingness of organisations to report. Furthermore, the G-FINDER project does not collect information on the funding of operational and implementation research. In addition, especially in the case of combined budgets at larger institutions or networks such as the DZIF (Translational Thematic Unit "TTU Malaria and NTDs"), the distribution of funds between the individual diseases is difficult to differentiate. Accordingly, it is only possible to measure the funding of NTDs precisely and compare it over time to a limited extent. We recommend setting

up a more structured database in Germany for all aspects of NTDs funding.

Despite these unavoidable methodological weaknesses, it can be stated that Germany's financial contribution remains moderate compared to other countries. Although Germany's contribution is rather low in relation to its gross national product, NTDs research benefits greatly from funding from public donors such as the BMBF and other ministries as well as the DFG or, at international level, the European Commission. Although this shows the commitment and recognition of the German government for NTDs research, it also harbours risks and dependencies for the research institutions. It is to be feared that under the increasing pressure of economic challenges, research in the field of global health will be given even less priority and the impact of global health problems on our society will be underestimated.

A change in the commitment of German institutions in the field of translational research on NTDs addresses the need for relevant implementations of research findings in endemic contexts. This is evident in the number of patent applications and clinical trials. Investment in innovation is particularly important in the fight against NTDs and requires joint efforts with basic research on pathogens, epidemiology, research and development and implementation research, which must be coordinated. Germany's efforts show that a substantial part of NTDs research is focussed on the development of new diagnostics, drugs and vaccines for endemic countries.

Experts in NTDs have identified diagnostics and drugs as priorities in NTDs research, as they recognise the complexity of vaccine development for most NTDs. On the positive side, experts from German institutions are increasingly active in WHO advisory bodies and collaborate with organisations such as FIND and DNDi and other Product Development Partnerships (PDPs) that focus on the development of drugs, vaccines or diagnostics for NTDs. The networking opportunities on NTDs topics should be utilised to a greater extent in Germany. The example of noma and the inclusion of this disease in the list of NTDs in 2023 shows the influence that active networking can have. The DNTDs, for example, is committed to promoting the topic and organising information events. Nevertheless, the neglect of these diseases requires a more proactive commitment, including from scientists, in order to make themselves visible for NTDs research as a tool for better disease control and to achieve the desirable goals of the NTDs Roadmap.



VI. RECOMMENDATIONS FOR ACTION

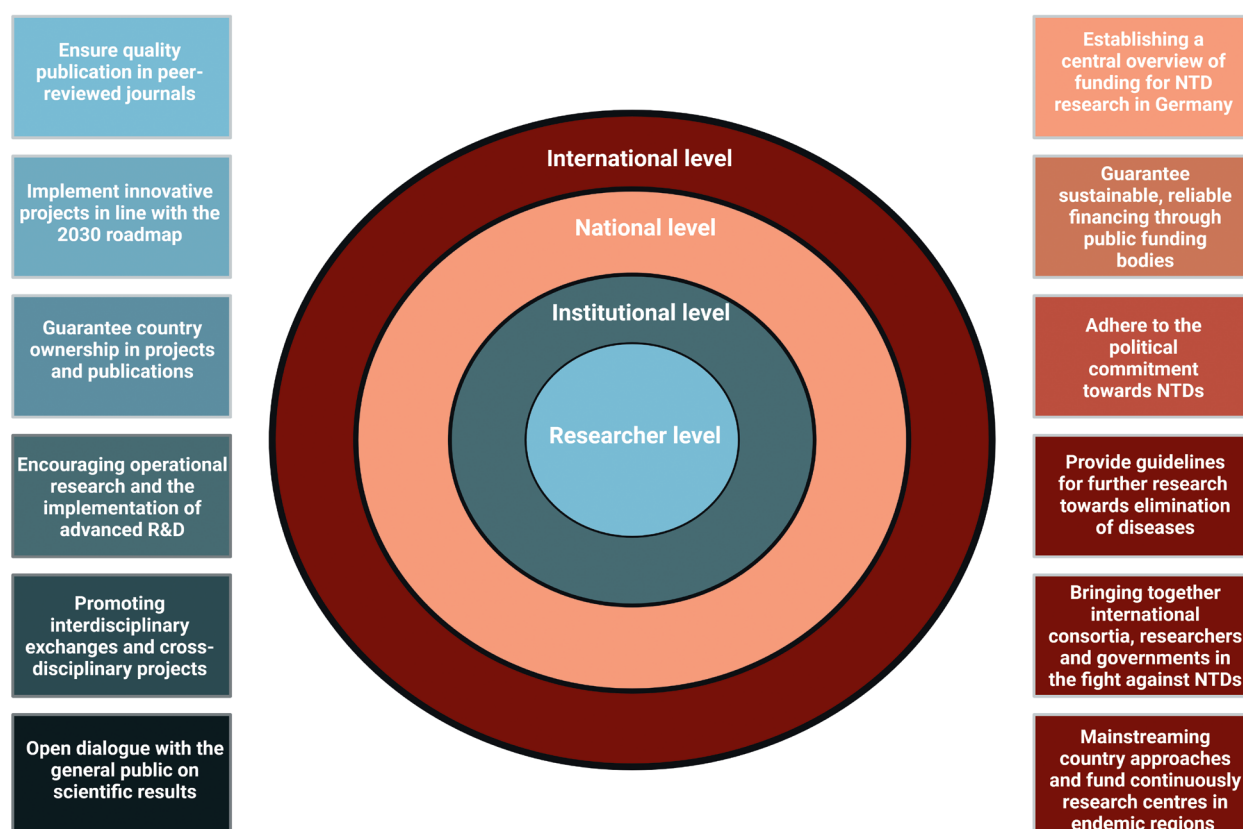


Figure 6: Recommendations for action for German NTDs research at individual, institutional, national and international level

In conclusion, the following recommendations for action can help to further support research and development on NTDs and their thematization in politics and the public in Germany and beyond. An interdisciplinary, international approach is required in the fight against NTDs. Most NTDs are clearly related to One Health: A holistic approach involving human medicine, veterinary medicine and environmental research is essential to achieve the desired goals. Researchers should publish in peer-reviewed and freely accessible journals (open access). Research and development projects should primarily be carried out in line with the WHO's 2030 Roadmap. In addition, it must be ensured that partners in endemic countries have ownership and equal rights in both the projects and the publications. German institutions should promote the translation of scientific results and convert research- and diagnostic methods into operational and implementation-oriented output. Cooperations with established international product development partnerships such as DNDi or newly established PDPs harbour potential for the translation of research into a market-ready product. These implementation projects can support the interdisciplinary exchange between researchers, experts and political decision-makers.

We recommend that researchers and their institutions should also maintain an open dialogue with the public and policymakers on scientific findings to highlight the importance of NTDs and related research and to communicate progress. The national and state level play a key role in the promotion of NTDs research with German participation. As most research projects are funded by public project organisations, the government bears a high level of responsibility for contributing to the success of the fight against NTDs. Fortunately, by signing the Kigali Declaration, the German government has also committed itself to providing appropriate support in the fight against NTDs. As the data collection for this report showed, there are no reliable and complete sources on the funding of research and development to combat NTDs

in Germany. This makes the assessment of Germany's actual contribution difficult and prone to underestimation. A database to record funding amounts, at least from the various ministries, could facilitate reliable reporting on Germany's contribution. This would enable continuous transparency regarding the actual volume of funding invested in basic research, implementation research and capacity building.

The international community defines the objectives of NTDs research by providing the NTDs list, creating the roadmap, providing guidance and bringing together international consortia, researchers and government representatives to promote evidence-based dialogues and decision-making processes. Greater involvement of actors from German institutions would be desirable in this area. The international community must incorporate country-specific approaches and support research centres in endemic regions in particular. German funding institutions can contribute to this, especially as there are already a large number of long-term and stable collaborations, especially with African institutions. The long-term funding of already well-established and newly established research centres in endemic countries should be a next step in connection with the expansion of capacities in endemic countries, as is also practised by other European countries.



A midwife in primary health care performs a colposcopy as part of a screening for female genital schistosomiasis



INDIVIDUAL ASSESSMENTS OF NEGLECTED TROPICAL DISEASES

Appendix

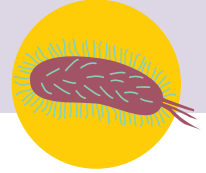
The appendix contains the complete search syntax, supplementary results and a discussion of the methodology. The attachment is available via the following link:

<https://www.bnitm.de/forschung/forschungsgruppen/population/abt-infektionsepidemiologie/laborgruppe-fusco/dissemination-and-awareness-activities/ntd-expertise>



VII. INDIVIDUAL ASSESSMENT OF THE NEGLECTED TROPICAL DISEASES

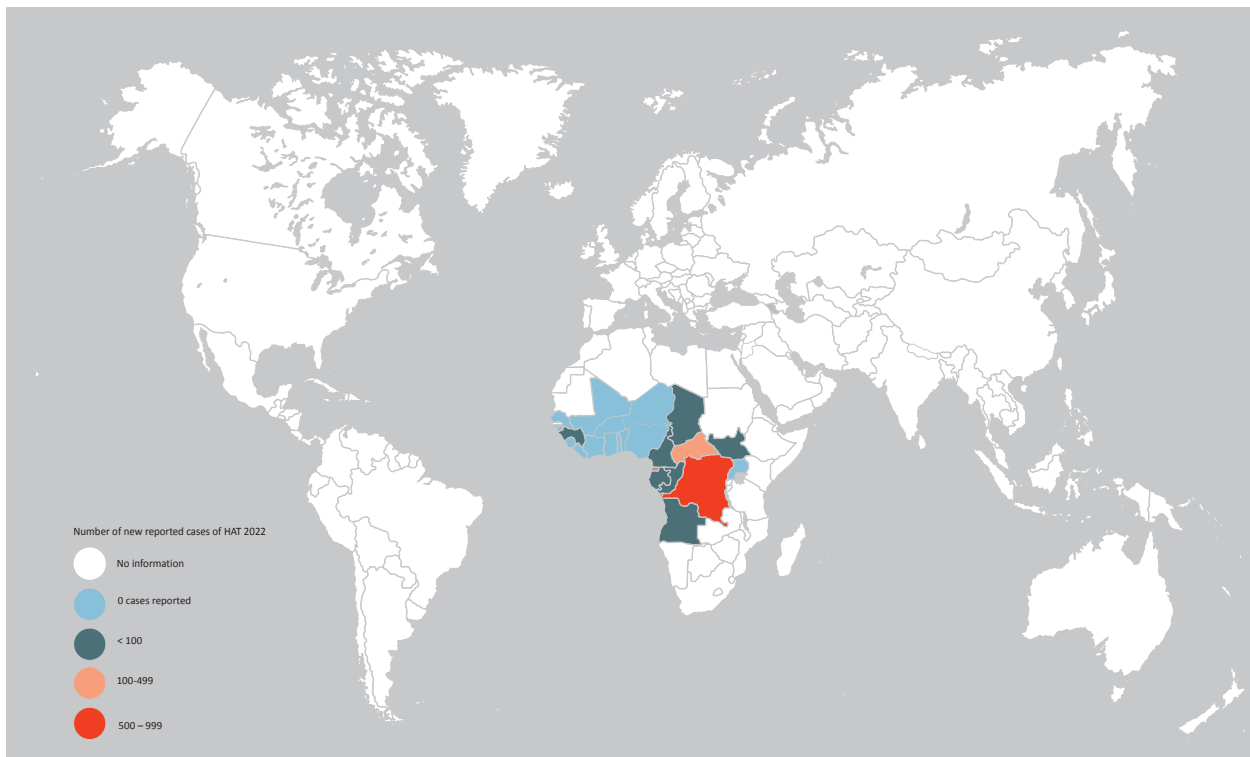
- 1 Human African Trypanosomiasis (sleeping-Sickness)**
Markus Engstler, August Stich
- 2 Buruli Ulcer**
Thorsten Thye
- 3 Chagas Disease (Trypanosoma cruzi Infection)**
Günter Fröschl, Michael Pritsch
- 4 Dengue**
Pietro Scaturro, Jonas Schmidt-Chanasit
- 5 Dracunculiasis (Medina worm, guinea worm)**
Inge Kroidl, Jürgen May
- 6 Echinococcosis**
Joachim Richter, Valentina Marchese
- 7 Endemic treponematoses (yaws, bejel, pinta)**
Sascha Knauf
- 8 Soil transmitted-helminths (STH)**
Valentina Marchese, Georg von Samson-Himmelstjerna
- 9 Leishmaniasis**
Joachim Clos
- 10 Leprosy**
Christa Kasang
- 11 Lymphatic filariasis**
Achim Hörauf, Inge Kroidl
- 12 Mycetoma**
Andrea Vanegas Ramirez, Marcellus Fische
- 13 Onchocerciasis**
Achim Hörauf, Marc P. Hübner
- 14 Schistosomiasis**
Daniela Fusco, Andrea Kreidenweiss
- 15 Snakebite Envenoming**
Jörg Blessmann, Benno Kreuels
- 16 Scabies (Sarcoptes-Scabiei-Infection)**
Ghyslain Mombo-Ngoma
- 17 Taeniasis / cysticercosis (Pork tapeworm)**
Andrea Sylvia Winkler, Clarissa Prazeres da Costa
- 18 Rabies**
Thomas Müller, Conrad Freuling
- 19 Trachoma**
KH Martin Kollmann
- 20 Foodborne Trematodiasis**
Norbert Mencke, Christian Griebenow



SHORT SUMMARY

Sleeping sickness (HAT), although limited to Africa, is one of the most dangerous tropical diseases. It is caused by unicellular parasites of the genus *Trypanosoma* and transmitted by the bite of infected tsetse flies. There are two forms: West African sleeping sickness by *T. brucei gambiense* and East African sleeping sickness by *T. b. rhodesiense*. If left untreated, HAT leads to death. Diagnostics and therapy are complex and require a high degree of expertise. Even though the number of newly infected people has now fallen to well below 1,000 per year, sleeping sickness remains an important threat in many regions of sub-Saharan Africa.

DISTRIBUTION



EPIDEMIOLOGY AND OPTIONS FOR CONTROL

Population affected	Approximately 60 million at risk of contact with potentially infected tsetse flies (<i>Glossina spp.</i>). <i>T. b. gambiense</i> in 24 countries of West and Central Africa, 92% of reported cases and causes a chronic illness. <i>T. b. rhodesiense</i> in 13 countries of Eastern and Southern Africa, 8% of reported cases and leads to an acute severe disease.
New cases/ death rate (per 100,000/year)	Worldwide since 2015 under 3000 new cases per year, since 2020 less than 1000 new cases per year.
WHO control strategy	Support for national control programmes; Public-private partnerships (PPPs) to ensure the free supply of medicines; continuation of active case search measures in severely affected regions. Goal: Elimination as a public health problem. WHO Roadmap: Interruption of transmission until 2030.
Status of therapy (side effects)	Fexinidazole has been recommended as first-line therapy for <i>T. b. gambiense</i> infection since 2019. This is the first time that oral therapy is available for all stages of West African HAT, which is considered a breakthrough. Studies on its use in <i>T. b. rhodesiense</i> are ongoing. The other approved drugs suramin, pentamidine, melarsoprole, eflornithine and nifurtimox (all with significant, sometimes life-threatening side effects) are also still in use.
Available vaccinations	No vaccinations available.
Diagnostics available	Default is still the microscopic detection of pathogens in blood, lymphatic fluid and cerebrospinal fluid; Rapid tests for <i>T. b. gambiense</i> are in use. Serology for <i>T. b. gambiense</i> possible, simplified antibody diagnosis (CATT) for screening. For staging a CSF puncture is mandatory.

STATUS QUO, PROBLEMS AND SETBACKS

HAT is still a significant health risk in sub-Saharan Africa. War, displacement and migration are causing a resurgence. The complex diagnostics and therapy require an experienced medical team. Sanofi collaborated with DNDi on the development of the orally available medication fexinidazole, which was submitted to the EMA in 2017 and is based on a molecule from Höchst AG. Oral administration represents a breakthrough in treatment for patients. The pathophysiological basis of HAT is still poorly understood. There is a need for research in basic scientific questions, improved diagnostics, simplified therapies and modern strategies for disease control. African trypanosomes are also causative agents of widespread livestock diseases that cause billions of dollars in damage every year. Trypanosomiasis is a prototypical One Health problem.

RESEARCH IN GERMANY 2018-2022

Funding & Sponsors German projects	Public funding	Private funding
Funding in euro	5.752.235 €	168.316 €
Sponsors	European Commission, DFG	Volkswagen Foundation, German-Israelitan Foundation

Publication & Authorship	Overall publications (% Change 2013-2017)	German publications ¹ (% Change 2013-2017)	German affiliations (Leading position) ²
Publications	1.178 (-12.1%)	138 (+2.2%)	616 (138)

¹ An overview of the included German publications can be found in the appendix,

² Total number of all German researchers named in publications, multiple naming of individual researchers by inclusion in different publications, as well as multiple affiliation possible; leading authors are first- last- or corresponding authors Positions

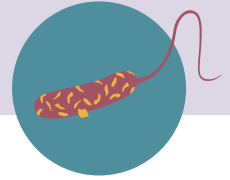
Scientific transfer of German research	Number of German trials (international)/ patents
Clinical trials	0 studies with German, 7 studies without German participation (Phase 2-3)
Patents	10 Patents, 3 HAT specific

ASSESSMENT OF THE GERMAN RESEARCH CONTRIBUTION

- ▶ Due to the current decline in HAT cases, attention to the disease is decreasing and so is the funding of research. Globally, research on trypanosomes and sleeping sickness has declined by about 95% in the last three years. There are only three laboratories active in Germany. At the moment the national expertise is extremely reduced and limited.
- ▶ HAT is a classic example of the close connection between the weaknesses of local health systems and the resurgence of an epidemic that was thought to have been overcome. Combating them is thus a model for an interdisciplinary solution strategy. Germany is predestined for research into the One Health aspect due to the existing networks between research institutes and NGOs as well as its increasing international importance in the global health context.

NEEDS ASSESSMENT AND CONCLUSION

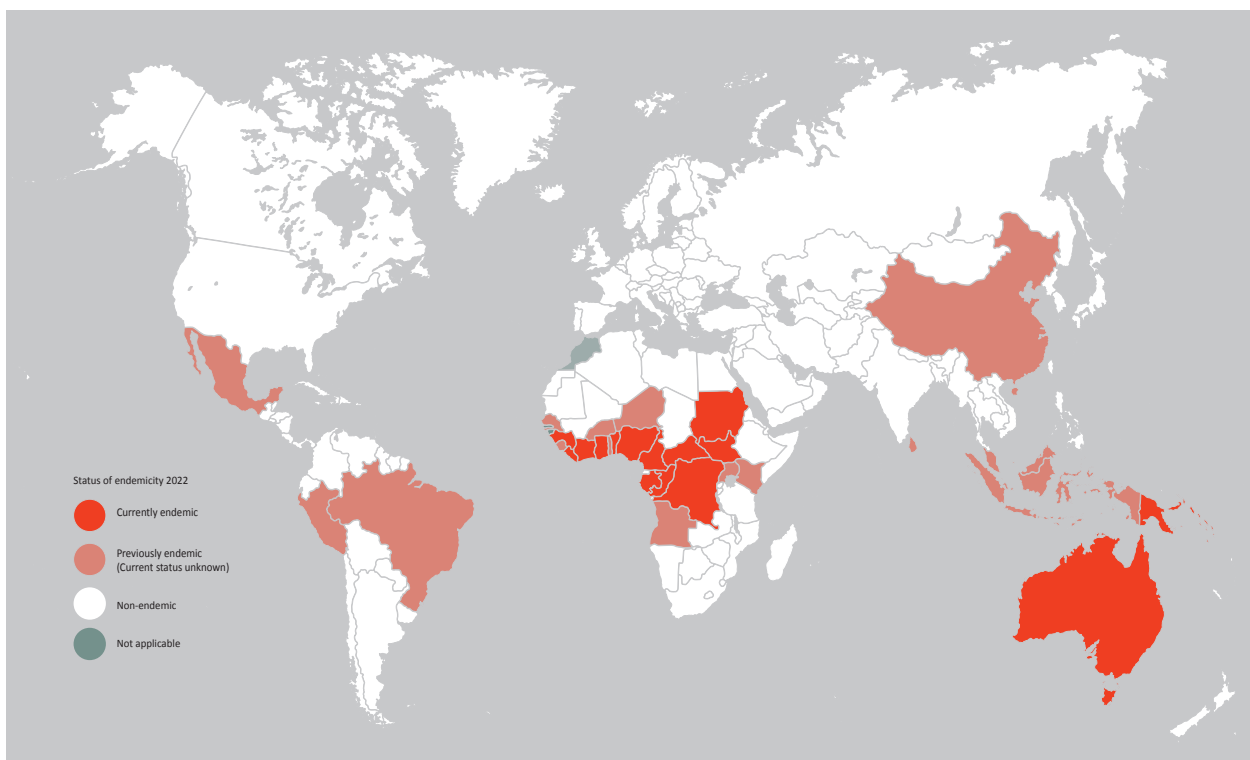
The WHO aims to interrupt transmission by 2030 (NTD Roadmap). In view of the current decline in the number of cases, this goal seems achievable with appropriate effort and resources. This requires the development of adapted diagnostics and simplified therapeutic procedures. Even if the transmission is interrupted, there is a risk of resumption. The countries in which HAT still occurs are among the poorest and structurally weakest in the world: The continuation of control measures, even with low case numbers, as well as the preservation of expertise in the diagnosis and treatment of sleeping sickness are necessary. It requires the integration of activities to combat HAT into the general health care of countries, despite their complexity. All these measures require professional scientific support that combines expertise in basic sciences, tropical medicine and public health.



SHORT SUMMARY

Buruli ulcer is a chronic, necrotizing disease of the skin and subcutaneous tissue caused by the environmental bacterium *Mycobacterium ulcerans*. It predominantly affects children in rural areas of tropical countries with a focus on West Africa. The route of transmission is still unclear, but it seems to be connected to contacts with stagnant or slow-flowing water. The disease begins with nodules or patchy skin lesions. If left untreated, large areas of the skin are destroyed. In advanced stages, disfigurement and permanent disability result. Diagnosis and therapy are difficult under the living conditions of most patients.

DISTRIBUTION



EPIDEMIOLOGY AND OPTIONS FOR CONTROL

Population affected	Over 33 countries, mainly in Africa and the Western Pacific.
New cases/ death rate (per 100,000/year)	Little reliable data, ca. 1600 cases worldwide in 2020 and 2021 (WHO).
WHO control strategy	Information campaigns; finding patients in the early stages of the disease (community screening); free treatment; reduction of patient numbers in affected areas.
Status of therapy (side effects)	WHO-recommended oral combination therapy with rifampicin and clarithromycin daily for eight weeks. Rifampicin has considerable side effects (i.e. liver toxicity).
Available vaccinations	No vaccinations available.
Diagnostics available	In principle, yes (Ziehl-Neelsen stain, PCR, culture, histopathology), but difficult to perform in the most affected areas.

STATUS QUO, PROBLEMS AND SETBACKS

The route of transmission is still unclear, so that no prevention strategies can be established. Most Buruli ulcer patients live in poor, rural regions of tropical countries. Reporting data underestimate the actual number of people with the disease. Diagnosis in the early stages of the disease is difficult because existing tests are not sensitive or accessible to most patients. The newly implemented oral therapy consisting of rifampicin plus clarithromycin has shown to be effective. However, the combination of specific therapy, general wound care, and rehabilitation is not available for a large proportion of patients.

RESEARCH IN GERMANY 2018-2022

Funding & Sponsors German projects	Public funding	Private funding
Funding in euro	635.525 €	Not reported
Sponsors	BMBF	Not reported

Publication & Authorship	Overall publications (% Change 2013-2017)	German publications ¹ (% Change 2013-2017)	German affiliations (Leading position) ²
Publications	234 (-17.7%)	13 (-23.6%)	25 (8)

¹ An overview of the included German publications can be found in the appendix,

² Total number of all German researchers named in publications, multiple naming of individual researchers by inclusion in different publications, as well as multiple affiliation possible; leading authors are first- last- or corresponding authors Positions

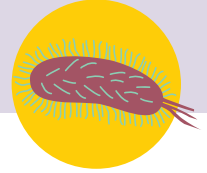
Scientific transfer of German research	Number of German trials (international)/ patents
Clinical trials	3 studies with German, 6 studies without German participation (Phase 2-3)
Patents	5 Patents, 0 Buruli Ulcer specific

ASSESSMENT OF THE GERMAN RESEARCH CONTRIBUTION

The German research contribution is internationally visible, but should be broader, in particular for research into better on-site diagnostics and new vaccines.

NEEDS ASSESSMENT AND CONCLUSION

Research on the route of transmission of *Mycobacterium ulcerans* is necessary to develop non-pharmaceutical prevention strategies. Development of point-of-care tests for diagnosis confirmation and therapy monitoring in regions with poor infrastructure. Exploring of therapeutic options that can be used locally in the early stages of the disease. Clinical trials are difficult to perform due to the low case numbers. Rare, but in the chronic stage extremely disfiguring and functionally limiting diseases such as Buruli ulcer need to be differentially addressed and treated in the context of local skin diseases. Synergies should be generated in the face of scarce resources.



SHORT SUMMARY

Chagas disease (CD) is a zoonosis caused by the protozoan *Trypanosoma cruzi*. Predatory bugs of the *Triatominae* family serve as vectors; non-vectorial routes of transmission also exist (e.g. via blood transfusions, organ and tissue donations, contaminated food, or from mother to child). Acute symptoms after infection are usually nonspecific and may consist of swelling at the site of entry and/or febrile illness. After several weeks to months, an asymptomatic phase of illness occurs that lasts for years to decades, after which approximately 20-30% of chronically infected individuals experience organ manifestations (e.g. cardiomyopathy, megaesophagus, and/or megacolon), some of which may be severe or fatal.

DISTRIBUTION



EPIDEMIOLOGY AND OPTIONS FOR CONTROL

Population affected	Poorer populations in endemic areas of Latin America and migrant populations. The disease is currently endemic in 21 Latin American countries, but through migration and non-vector transmission routes it occurs worldwide. The WHO currently estimates that there are approximately 6-7 million infected people, 68,000 to 122,000 of whom are estimated to live in Europe. In addition to humans, many mammals in endemic areas act as reservoirs of the pathogens, including domesticated animals.
New cases/ death rate (per 100,000/year)	No reliable figures available.
WHO control strategy	Vector control; improvement of living conditions; education; food hygiene; screening of blood, organ, or tissue donations; screening of childbearing women.
Status of therapy (side effects)	Trypanocidal therapy with benznidazole and nifurtimox; not available in Germany, must be obtained from WHO. In 10% therapy discontinuation necessary due to side effects.
Available vaccinations	No vaccinations available.
Diagnostics available	Direct detection: blood smear microscopy, PCR. Indirect detection: antibodies by ELISA, HAI, ICT, IIFT, CMIA, Western blot.

STATUS QUO, PROBLEMS AND SETBACKS

CD is underdiagnosed in endemic areas as well as in Germany. There is a lack of education to make patients and physicians aware. The data base is insufficient to make evidence-based decisions, and CD is associated with stigma. Diagnostic methods have improved, but follow-up after therapy is problematic because of antibody persistence. PCR assays have a high specificity but cannot reliably rule out infection and are available in only a few centers.

Adverse drug reactions of therapeutics not available in Germany lead to discontinuation of therapy in one out of ten adults.

RESEARCH IN GERMANY 2018-2022

Funding & Sponsors German projects	Public funding	Private funding
Funding in euro	3.511.700 €	210.701 €
Sponsors	European commission, BMBF	DNDi, Industry, DAHW, Fresenius Foundation

Publication & Authorship	Overall publications (% Change 2013-2017)	German publications ¹ (% Change 2013-2017)	German affiliations (Leading position) ²
Publications	3317 (+12.4%)	101 (+32.9%)	569 (110)

¹ An overview of the included German publications can be found in the appendix,

² Total number of all German researchers named in publications, multiple naming of individual researchers by inclusion in different publications, as well as multiple affiliation possible; leading authors are first- last- or corresponding authors Positions

Scientific transfer of German research	Number of German trials (international)/ patents
Clinical trials	7 studies with German, 26 studies without German participation (Phase 1-4)
Patents	12 Patents, 3 Chagas specific

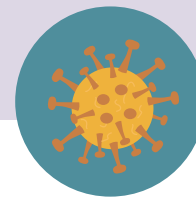
ASSESSMENT OF THE GERMAN RESEARCH CONTRIBUTION

- ▶ A guideline working group led by the German Society for Tropical Medicine, Travel Medicine and Global Health (DTG) e.V. published the first recommendations on CD in Germany on the AWMF platform in October 2022.
- ▶ Research groups based in Germany collaborate with partners in endemic regions as well as other European countries (e.g. Italy and Spain).
- ▶ Contribution of industry:
Merck Germany: Participation in the “NTD Drug Discovery Booster” project of the Drugs for Neglected Diseases Initiative (DNDi)

NEEDS ASSESSMENT AND CONCLUSION

CD remains underdiagnosed and undertreated in Germany, with individual and societal consequences. The first AWMF recommendations for Germany were published in 2022. A statement on the assumption of costs of screening examinations by health insurance companies is pending.

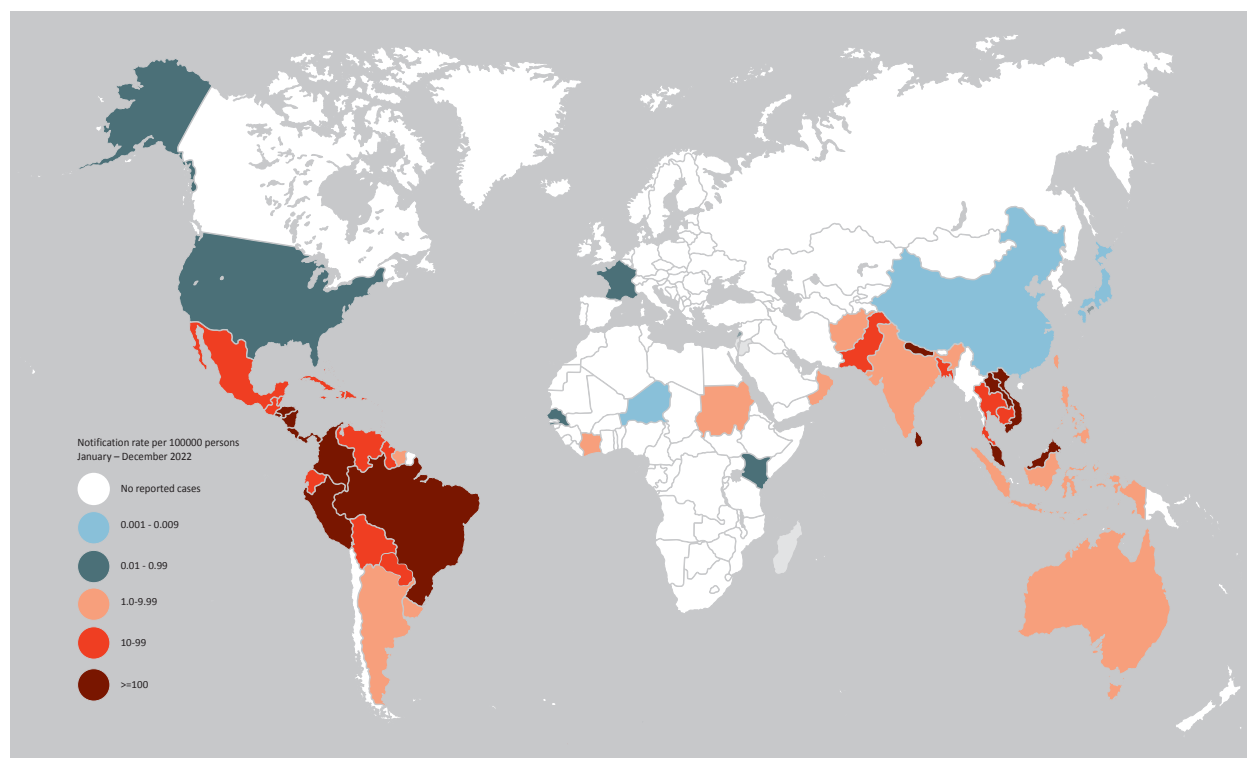
Important for Germany is the interruption of all non-vectorial transmission routes (blood and tissue donations, congenital) as well as enabling adequate diagnostics and therapy. This requires a reliable database as well as education. Important research goals are progression markers and more tolerable therapeutics.



SHORT SUMMARY

Dengue virus (DENV) comprises four serotypes and is the causative agent of dengue fever. *Aedes aegypti* is the primary DENV vector in urban settings, while *Ae. albopictus* is a secondary vector in suburban/rural areas. DENV causes more deaths and illness than any other arboviral infection in human populations from across tropics and subtropics. It was estimated that 390 million dengue infections occur every year, of which about 96 million manifest clinically, and 500,000 develop severe symptoms with a case fatality rate of about 2.5%, of which a high proportion are children. After an incubation period of 5-7 days, the first clinical features of dengue include fever with rash, severe headache, pain behind the eyes, myalgias and arthralgia. Recovery from DENV infection provides lifelong immunity against the same DENV serotype, but confers only partial and transient protection against subsequent infection by the other three serotypes. Sequential infections with different serotypes increase the risk of developing dengue hemorrhagic fever.

DISTRIBUTION



EPIDEMIOLOGY AND OPTIONS FOR CONTROL

Population affected	390 million infections estimated worldwide per year, and almost half of the World population lives in risk regions.
New cases/ death rate (per 100,000/year)	Highly heterogeneous, see map according to region.
WHO control strategy	Diagnostics and clinical management; integrated surveillance and outbreak preparedness; vector controls; vaccination; operational accompanying research for implementation Aim: reduction in mortality to 0% for 2030.
Status of therapy (side effects)	To date no antiviral therapy available.
Available vaccinations	Two vaccines (Dengvaxia and Qdenga) approved, several vaccine candidates are being clinically tested. Dengvaxia only recommended in people with previous DENV infection, because others have a risk for severe illness in cases of subsequent infection after vaccination.
Diagnostics available	Real-Time RT-PCR from blood and urine; PoC for NS1 antigen and IgM and IgG possible; serology due to cross-reactivity with related (flavi)viruses may cause unspecific results.

STATUS QUO, PROBLEMS AND SETBACKS

The goals of the global strategy for dengue prevention and control set for 2020 have not been achieved, and dengue continues to spread worldwide. However, dengue mortality has been reduced in certain countries through the implementation of early case detection and appropriate management of severe cases. Decreasing dengue morbidity could be accomplished by adopting improved outbreak prediction and detection methods, achieved through coordinated epidemiological and entomological surveillance. Effective communication will play a crucial role in achieving behavioral changes that enhance prevention programs. It will be imperative to manage dengue outbreaks using non-insecticidal approaches, including the suppression of mosquito populations and their potential elimination through attractant traps, repellents, genetically modified mosquitoes, and *Wolbachia*-based strategies.

RESEARCH IN GERMANY 2018-2022

Funding & Sponsors German projects	Public funding	Private funding
Funding in euro	1.439.628 €	349.152 €
Sponsors	European commission, DFG, BMBF, BMWK	Colciencias, Industry

Publication & Authorship	Overall publications (% Change 2013-2017)	German publications ¹ (% Change 2013-2017)	German affiliations (Leading position) ²
Publications	1.565 (+ 13.8%)	72 (-1.4%)	274 (67)

¹ An overview of the included German publications can be found in the appendix,

² Total number of all German researchers named in publications, multiple naming of individual researchers by inclusion in different publications, as well as multiple affiliation possible; leading authors are first- last- or corresponding authors Positions

Scientific transfer of German research	Number of German trials (international)/ patents
Clinical trials	1 study with German, 111 studies without German participation (Phase 1-4 & Postmarket)
Patents	32 German patents, 23 Dengue specific

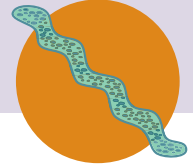
ASSESSMENT OF THE GERMAN RESEARCH CONTRIBUTION

- ▶ The EU has invested a significant amount in dengue research in the past years. However, at the moment a continuation is not to be expected.
- ▶ In international comparison and considering the worldwide significance of dengue, the German contribution is relatively low compared to the international landscape.

NEEDS ASSESSMENT AND CONCLUSION

Research is required to explore alternative methods of fluid management, addressing dengue in pregnancy and in cases with co-morbidities, and providing more precise guidance regarding the utilization of blood products. The development of user-friendly tests that can accurately detect levels of protective immunity would be helpful. Investigations into transmission dynamics are necessary to assess the influence of virus population structure, urbanization, land-use changes, human behavioral interactions, and climate parameters on dengue epidemiology. Establishing universally accepted clinical endpoints is crucial for the comparative evaluation of interventions. These endpoints should effectively mirror the severity of clinical conditions and require prospective validation.

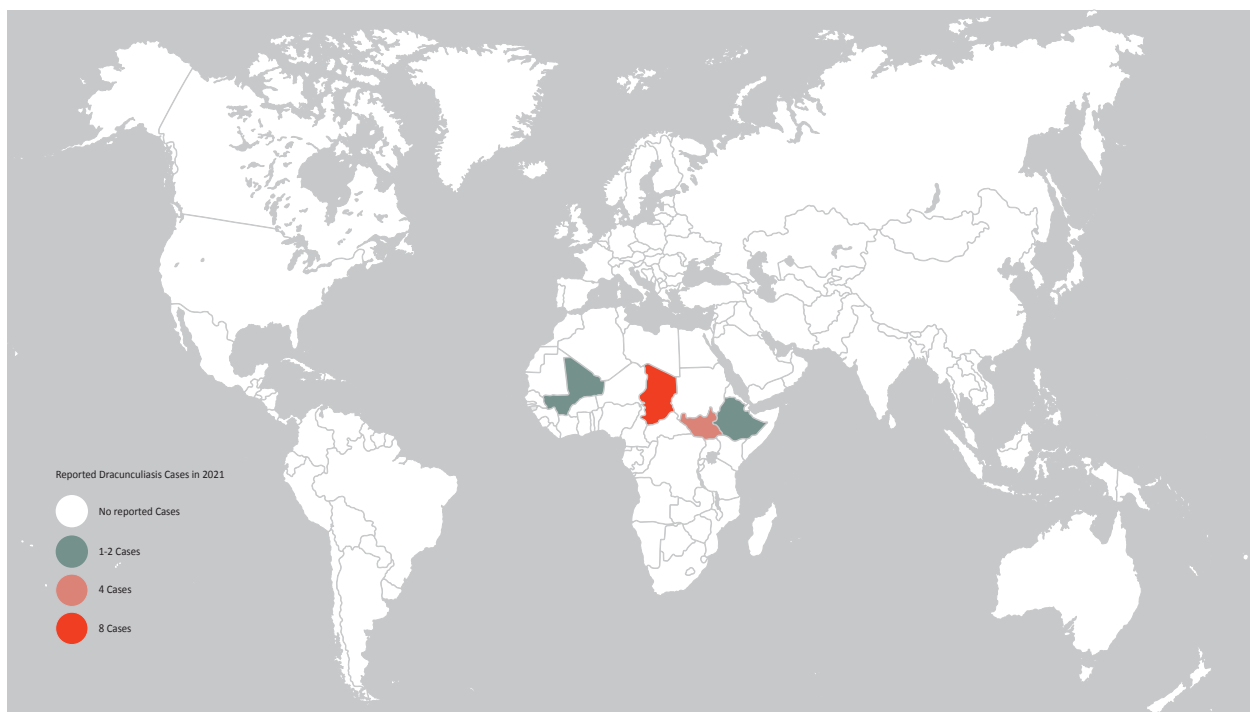
For vector control interventions, there is a need for a technically validated proposal that outlines standardization and offers best practice recommendations for combined approaches. Collaborative research institutions in the Global South should be more deeply engaged to evaluate the disease burden. Furthermore, research efforts in regions where dengue is endemic, notably in Asia, Latin America, and the Caribbean, should be intensified. The role of immunological enhancement as a trigger for severe cases requires clearer elucidation, particularly in comparison to other risk factors.



SHORT SUMMARY

Dracunculiasis is caused by the nematode *Dracunculus medinensis* (medina worm, guinea worm). The nematode is transmitted by small crabs (cyclops) living in water. Humans become infected when they ingest the crabs, which contain infectious larvae, by drinking water. The larvae penetrate the intestinal wall and develop in the retroperitoneum to become adult worms. After impregnation the female (approximately 75 cm long) moves into the connective tissue of the lower extremities. This can lead to inflammation. One year after infection a cyst forms at the genital opening on the front end of the worm, which ruptures on contact with water, emitting thousands of larvae. The larvae are consumed by the crabs and develop within two weeks to become infectious larvae.

DISTRIBUTION



EPIDEMIOLOGY AND OPTIONS FOR CONTROL

Population affected	In 1986, 3.5 million people were infected in 20 countries before large control measures commenced. Remaining dozens of cases are found in Sub-Saharan Africa, mainly in Chad, Ethiopia, Mali, and South Sudan. Sudan is in the prequalification stage and two countries have been certified but considered under reintroduction of transmission: Cameroon, and Central African Republic.
New cases/ death rate (per 100,000/year)	In 2019, 54 cases were reported globally. These numbers dropped to 27, 15 and 13 cases in 2020, 2021 and 2022, respectively. In addition to the above confirmed cases of dracunculiasis, also suspected cases had to be taken care of, mainly in Chad, Ethiopia, and South Sudan (>10.000 suspected cases each), but also in Angola, Mali, Sudan and Cameroon (<500 suspected cases each).
WHO control strategy	Education of the population, avoidance of water contact by infected persons, safe water supply, filtration of water using cotton cloths, boiling of drinking water; eradication of cyclops using insecticide „Temephos“. Treatment of infected animal populations with flubendazol.
Status of therapy (side effects)	Carefully rolling the worm piece-by-piece onto a wooden stick. This is painful and can take weeks. No drug treatment is available.
Available vaccinations	No vaccinations available.
Diagnostics available	Visual identification of the specific ulceration or penetration of the skin by the worm.

STATUS QUO, PROBLEMS AND SETBACKS

Remaining endemic villages are located in isolated, difficult to access parts of countries, some of which are politically unsafe. Tracking down the most recent isolated cases is therefore a difficult and cost-intensive challenge. Since several years' infections in dogs, cats, and baboons have been verified in Chad, Ethiopia and Mali, with more than 1,500 animal infections in 2020. This makes eradication considerably more difficult. Treatment of infected animals with Flubendazol was added. In the last years it was shown that frogs and fish species can act as paratenic hosts, which can add to the distribution of dracunculiasis.

RESEARCH IN GERMANY 2018-2022

Funding & Sponsors German projects	Public funding	Private funding
Funding in euro	Not reported	Not reported
Sponsors	Not reported	Not reported

Publication & Authorship	Overall publications (% Change 2013-2017)	German publications ¹ (% Change 2013-2017)	German affiliations (Leading position) ²
Publications	63 (+ 53.6%)	4 (+400%)	9 (0)

¹ An overview of the included German publications can be found in the appendix,

² Total number of all German researchers named in publications, multiple naming of individual researchers by inclusion in different publications, as well as multiple affiliation possible; leading authors are first- last- or corresponding authors Positions

Scientific transfer of German research	Number of German trials (international)/ patents
Clinical trials	Not reported
Patents	1 German patent, 0 Dracunculiasis specific

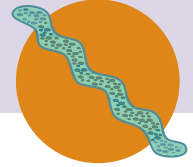
ASSESSMENT OF THE GERMAN RESEARCH CONTRIBUTION

At the moment there is no significant contribution to research from the German community.

NEEDS ASSESSMENT AND CONCLUSION

Although the disease is on the verge of eradication, the training of (future) local health workers (early detection and reporting) is essential to ensure the disease is eradicated. Implementation research, including medical anthropology and health communication might be useful to evaluate empirically most efficient approaches. The goal of eradicating dracunculiasis in the near future may be regarded as realistic since (i) Diagnosis is simple and unambiguous; (ii) Intermediate hosts are almost exclusively found in stagnant water which makes control easier; (iii) Control interventions are low-cost and relatively easy to implement.

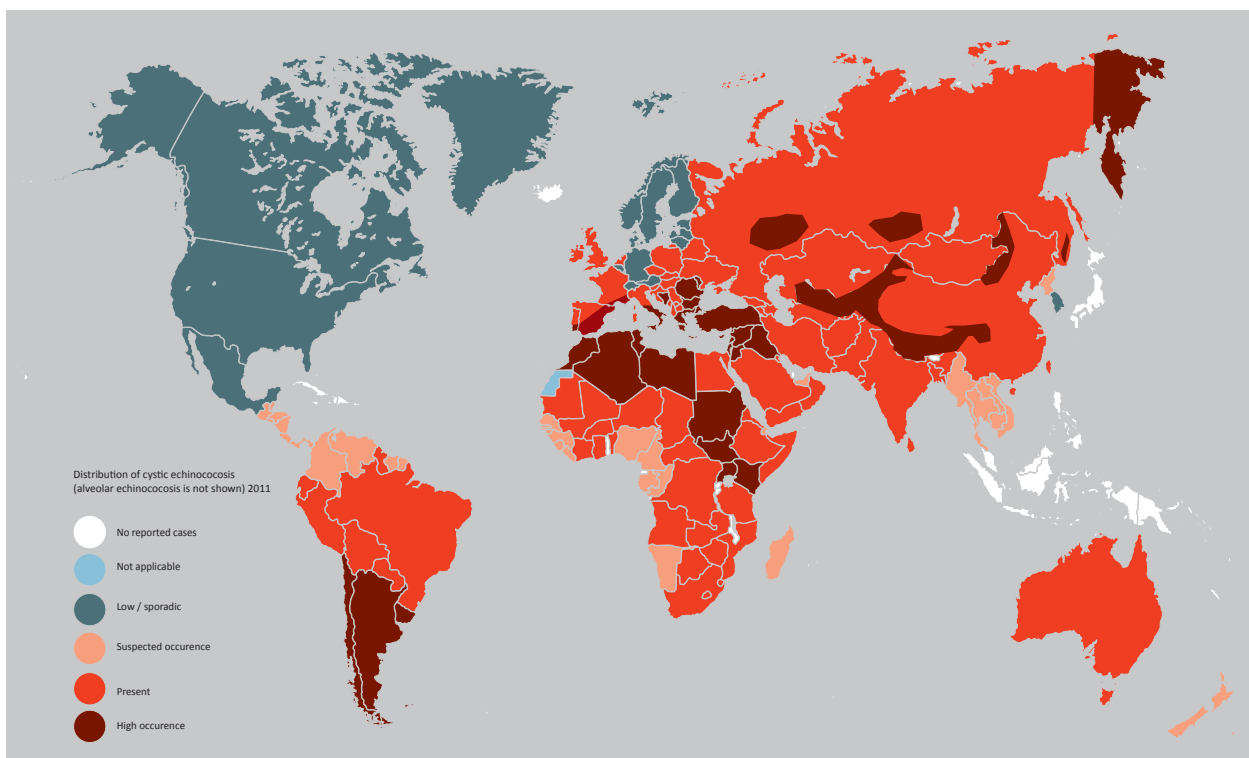
Nevertheless, tight surveillance and vector control as well as health education and prevention are essential in order to prevent new endemic areas arising. Infection of dogs presents an increasing difficulty when it comes to eradicating the disease as well.



SHORT SUMMARY

Cystic echinococcosis (CE) is caused by *Echinococcus (E.) granulosus*, alveolar echinococcosis (AE) by *E. multilocularis*. Worm ova are ingested by the human host after hand-to-mouth contact with contaminated matrices, such as dog fur. Canides are definitive hosts and are infected through ingestion of infected farm animals or wild rodents. Echinococcosis does not cause indicative symptoms. Rupture of a cyst or compression of organs by the growing cyst can be life-threatening. Lethality is unknown for CE. If untreated AE, leads to death. Stage-specific treatment options include surgery, radiological procedures and anthelmintic drugs.

DISTRIBUTION



EPIDEMIOLOGY AND OPTIONS FOR CONTROL

Population affected	Estimated one million people infected at any time, CE is highly endemic in Southern Eastern Europe, Mediterranean countries, the Middle East, eastern Africa, Central Asia, Northwestern China and South America; AE in China and East Asia, Northern Europe and America.
New cases/ death rate (per 100,000/year)	Up to 50 per 100.000/year. Mortality of CE unknown, of untreated AE 100%.
WHO control strategy	Health education and regulatory slaughter measures. Periodic anthelmintic treatments of dogs.
Status of therapy (side effects)	Stage specific therapy: combinations of anthelmintic, interventional or surgery. Problems: drug toxicity; interventions: anaphylaxis, dissemination.
Available vaccinations	Vaccination only for sheep available.
Diagnostics available	Imaging is crucial. Serology specificity and sensitivity relatively low and may miss a number of cases. Microscopy, PCR of samples.

STATUS QUO, PROBLEMS AND SETBACKS

Echinococcosis is the only helminthic disease which may not be curable. Control of CE is hampered by limited resources in endemic rural areas. Notification of human cases must be established. Due to poverty and political unrest patients migrate to urban areas and non-endemic countries where physicians are not familiar with CE. There is insufficient knowledge among doctors, about less invasive therapy options, and among radiologists about staging CE. Treatment of osseous CE is unsatisfactory. The use of praziquantel as a protoscolicidal agent is encouraging. AE among rodents is expanding in Europe and an increase of human cases is to be expected. Control measures in wild animals is mostly not realized. Therapy of AE is unsatisfactory. If benzimidazoles are not tolerated, no salvage therapy is at hand. There is limited research on alternative drugs.

RESEARCH IN GERMANY 2018-2022

Funding & Sponsors German projects	Public funding	Private funding
Funding in euro	Not reported	Not reported
Sponsors	Not reported	Not reported

Publication & Authorship	Overall publications (% Change 2013-2017)	German publications ¹ (% Change 2013-2017)	German affiliations (Leading position) ²
Publications	2.208 (+21.3%)	149 (+52%)	613 (164)

¹ An overview of the included German publications can be found in the appendix,

² Total number of all German researchers named in publications, multiple naming of individual researchers by inclusion in different publications, as well as multiple affiliation possible; leading authors are first- last- or corresponding authors Positions

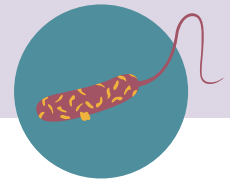
Scientific transfer of German research	Number of German trials (international)/ patents
Clinical trials	No German studies, 15 studies without German participation
Patents	3 German patents, 0 Echinococcosis specific

ASSESSMENT OF THE GERMAN RESEARCH CONTRIBUTION

- ▶ The German contribution is low in terms of number of publications, but German researchers contributed significantly to the standardization of diagnosis and therapy (participation in the informal WHO working group on echinococcosis).
- ▶ The national register is contributing both to the improvement of diagnosis and treatment, and to the assessment of disease epidemiology, the later one being explored by German researchers also in other countries.
- ▶ German researchers are also contributing in a multicenter international project for the harmonization of existing parasitological and molecular methods, the development of innovative molecular tools to detect *Echinococcus* species in the food chain, and the production of epidemiological data in vegetables on canine feces in selected endemic countries.

NEEDS ASSESSMENT AND CONCLUSION

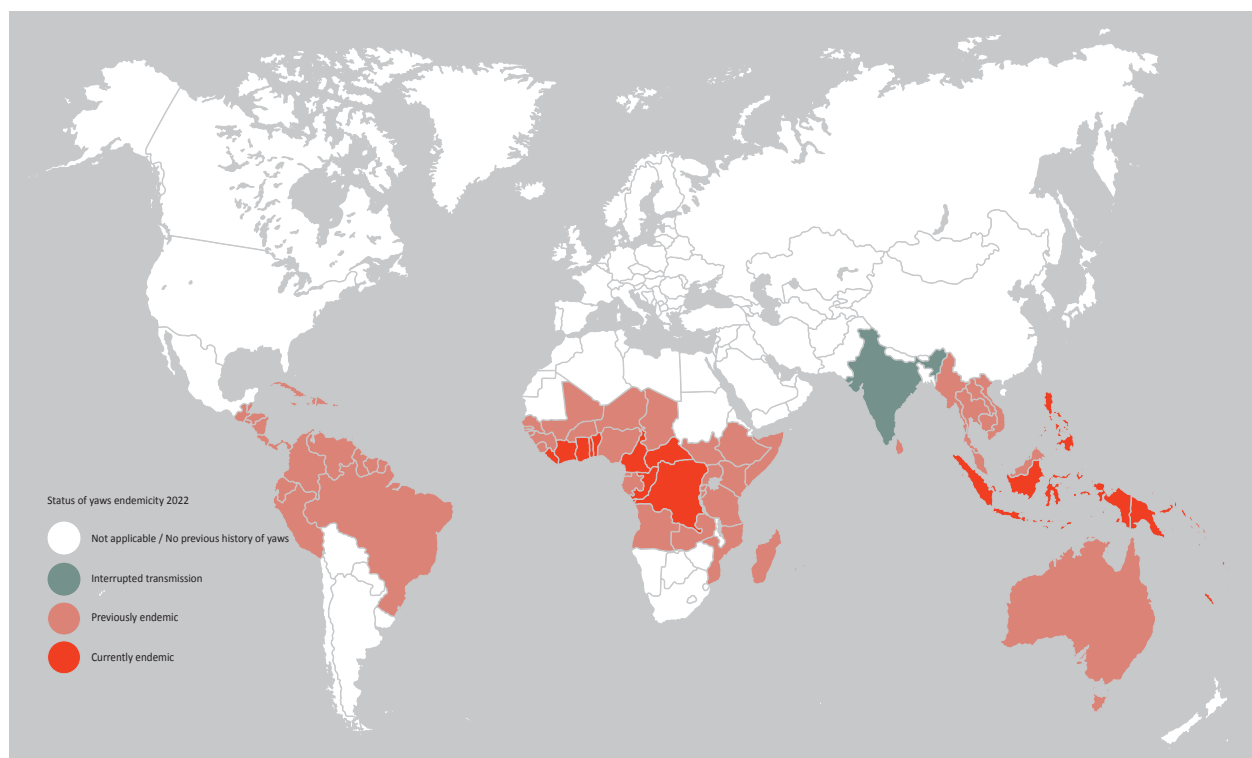
Actions required to achieve the 2030 WHO sub target of disease control in 17 endemic countries: Improvement of epidemiological knowledge and national surveillance in endemic countries; development of guidelines for prevention and control interventions; ensurance of access to ultrasound evaluation and cooperation with surgical and radiological community. Knowledge gaps to be filled: Improvement of treatment strategies: clinical trials on optimal duration of albendazole treatment, use of praziquantel instead of topical scolicides. Development of optimal diagnostic tools for human disease (without the need of imaging).



SHORT SUMMARY

Endemic treponematoses is the term used to describe diseases caused by *Treponema pallidum* subsp. *per-tenu* (yaws), *T. pallidum* subsp. *endemicum* (bejel) and *T. carateum* (pinta). The geographical distribution is mainly in the tropics. The main route of transmission is direct contact with infected persons. Infections are generally chronic and, if left untreated, lead to disfigurement and disability. Affected persons have severe limitations in their quality of life. In the meantime, it has been proven that nonhuman primates in sub-Saharan Africa are naturally infected with the yaws pathogen. For some years now, there have been bejel infections that show the clinical picture of syphilis. The current distribution of pinta disease is unknown.

DISTRIBUTION



EPIDEMIOLOGY AND OPTIONS FOR CONTROL

Population affected	Approximately 630 million people live in yaw-endemic countries. An estimated 89 million people are exposed to yaws.
New cases/ death rate (per 100,000/year)	123,866 yaws cases were reported to the WHO in 2021, of which 1,102 cases were confirmed from a total of nine countries. In many countries where yaws occurred historically, the status is unknown today.
WHO control strategy	Initial mass treatment with azithromycin and a population coverage of 90%, followed by case-oriented treatment of the remaining individual cases and their contacts.
Status of therapy (side effects)	Azithromycin orally at a single dose of 30 mg/kg (max. 2 g). Any person who fails treatment must be tested for macrolide resistance and treated with benzathine penicillin (single intramuscular dose) at a dosage of 0.6 million units for patients under and 1.2 million units for patients over ten years of age.
Available vaccinations	No vaccinations available.
Diagnostics available	Various antibody tests and nucleic acid test procedures for direct detection of the pathogen are available. New point-of-care tests for rapid detection are being established (e.g. LAMP-based methods).

STATUS QUO, PROBLEMS AND SETBACKS

The WHO's goal is to eradicate the disease by 2030. The current control strategy is suitable for eliminating yaws in humans. Even though the epidemiological link between infections in humans and nonhuman primates is unclear, a One Health approach and permanent surveillance are needed to detect a possible new infection by a potential animal reservoir in sub-Saharan Africa. In addition, the occurrence of macrolide resistances and (co-)infection with *Haemophilus ducreyi* as a differential diagnosis is a cause for concern. With regard to diagnostics, the detection of latent infections is a problem in the case-oriented control strategy.

RESEARCH IN GERMANY 2018-2022

Funding & Sponsors German projects	Public funding	Private funding
Funding in euro	Not reported	Not reported
Sponsors	Not reported	Not reported

Publication & Authorship	Overall publications (% Change 2013-2017)	German publications ¹ (% Change 2013-2017)	German affiliations (Leading position) ²
Publications	856 (+0.3%)	45 (+15.3%)	N/A

¹ An overview of the included German publications can be found in the appendix,

² Total number of all German researchers named in publications, multiple naming of individual researchers by inclusion in different publications, as well as multiple affiliation possible; leading authors are first- last- or corresponding authors Positions

Scientific transfer of German research	Number of German trials (international)/ patents
Clinical trials	No German studies, 5 studies without German participation (Phase2-4)
Patents	15 German patents, 9 endemic treponematoses specific

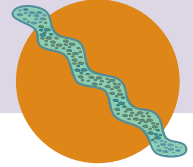
ASSESSMENT OF THE GERMAN RESEARCH CONTRIBUTION

- ▶ There is little research activity on endemic treponematoses in Germany.
- ▶ In an international comparison, however, the German contribution to the elucidation of a possible animal reservoir is clearly visible.
- ▶ German researchers are supporting the WHO's eradication campaign by establishing and testing rapid test methods suitable for the tropics (e.g. LAMP4Yaws).

NEEDS ASSESSMENT AND CONCLUSION

There is still a lack of current and basic epidemiological (prevalence, reservoir, transmission routes, antibiotic resistance, etc.) and biological parameters (e.g. proteome) for all endemic treponematoses. Closing these knowledge gaps is important and requires the promotion of long-term projects in the One Health sector, including capacity building in the endemic areas.

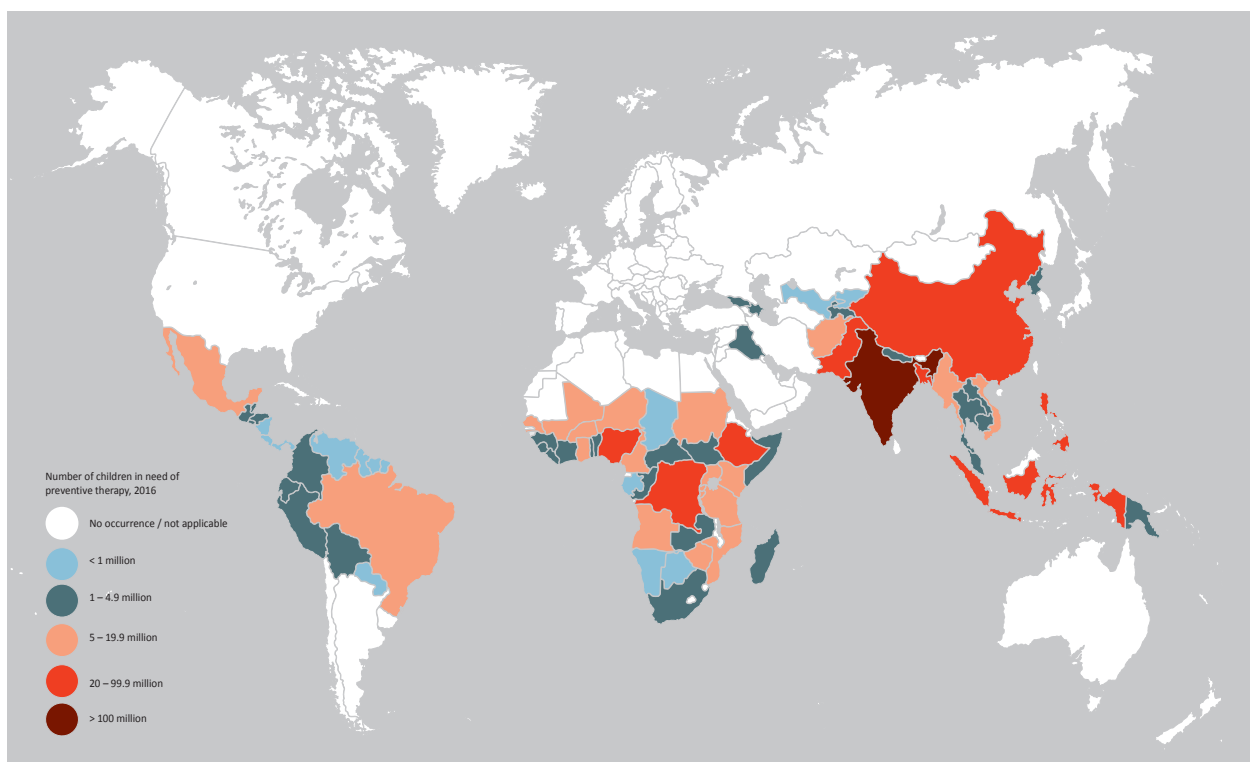
Research on efficient primary interventions (vaccination) is crucial, not least because of animal infections and because of the rapid development of macrolide resistance. There is a need for significantly better financial support for research projects, One Health surveillance and capacity building in endemic areas.



SHORT SUMMARY

Soil-transmitted helminthiasis (STH) are infections (often zoonoses) caused by intestinal nematodes: Hookworms (*Necator americanus* and *Ancylostoma duodenale*), whipworms (*Trichuris trichiura*), roundworms (*Ascaris lumbricoides*) and *Strongyloides stercoralis*. Transmission to humans occurs through contact with eggs (ingestion) or larvae (penetration of the skin). An estimated 1.5 billion people are infected, mainly in tropical and subtropical areas. Symptoms correlate with the intensity of infection and include: Anaemia, malnutrition, developmental disorders, diarrhoea, intestinal obstruction. *S. stercoralis* can be fatal in immunocompromised individuals. Mebendazole or albendazole are effective against STH, ivermectin is the treatment of choice for *S. stercoralis*.

DISTRIBUTION



EPIDEMIOLOGY AND OPTIONS FOR CONTROL

Population affected	1.5 billion people (24% of the world population); estimated over 600 million for <i>S. stercoralis</i> (exact epidemiology unknown).
New cases/ death rate (per 100,000/year)	6,300 reported deaths in 2016, unknown for <i>S. stercoralis</i> .
WHO control strategy	MDA (albendazole or mebendazole); ivermectin as supplement for areas with high prevalence of <i>T. trichiura</i> (since 2017) and against <i>S. stercoralis</i> at prevalence >10 %; WASH; health education.
Status of therapy (side effects)	Albendazole and mebendazole against hookworms, whipworms and roundworms; ivermectin against <i>S. stercoralis</i> and in combination against <i>T. trichiura</i> ; alternatively pyrantelpamoate; risk of ivermectin-related serious adverse events in people with high-grade <i>Loa loa</i> infection.
Available vaccinations	No vaccinations available.
Diagnostics available	Microscopy; rapid tests desirable; various diagnostic methods for <i>S. stercoralis</i> .

STATUS QUO, PROBLEMS AND SETBACKS

The current level of albendazole/mebendazole MDA coverage for preschool and school-aged children is 59%, far from the target of 75% set for 2020. WHO has added the containment of morbidity caused by *S. stercoralis* as a target for 2030, but the exact epidemiology and disease burden still need to be assessed. Rapid, easy-to-use point-of-care diagnostics are needed for mapping and surveillance, including for *S. stercoralis*. More effective drugs and drug combinations are needed. Moxidectin, tribendimine and Oxantel pamoate are promising options for combination. Monitoring of treatment success is currently notoriously inadequate in MDA programmes, which poses both an ethical weakness and the risk of unnoticed development of anthelmintic resistance – a serious problem for the long-term impact of current worm control interventions

RESEARCH IN GERMANY 2018-2022

Funding & Sponsors German projects	Public funding	Private funding
Funding in euro	1.188.006 €	Not reported
Sponsors	DFG, European Commission, DZIF, BMBF	Not reported

Publication & Authorship	Overall publications (% Change 2013-2017)	German publications ¹ (% Change 2013-2017)	German affiliations (Leading position) ²
Publications	1.977 (+18.9%)	84 (+42.3%)	600 (118)

¹ An overview of the included German publications can be found in the appendix,

² Total number of all German researchers named in publications, multiple naming of individual researchers by inclusion in different publications, as well as multiple affiliation possible; leading authors are first- last- or corresponding authors Positions

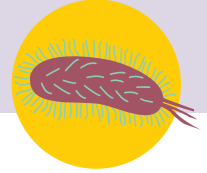
Scientific transfer of German research	Number of German trials (international)/ patents
Clinical trials	No German studies, 24 studies without German participation (Phase2-4)
Patents	9 German patents, 2 STH specific

ASSESSMENT OF THE GERMAN RESEARCH CONTRIBUTION

- ▶ The national contribution is small given the global importance of STH.
- ▶ One German institution participated in an EU-funded project to develop a vaccine against hookworms.

NEEDS ASSESSMENT AND CONCLUSION

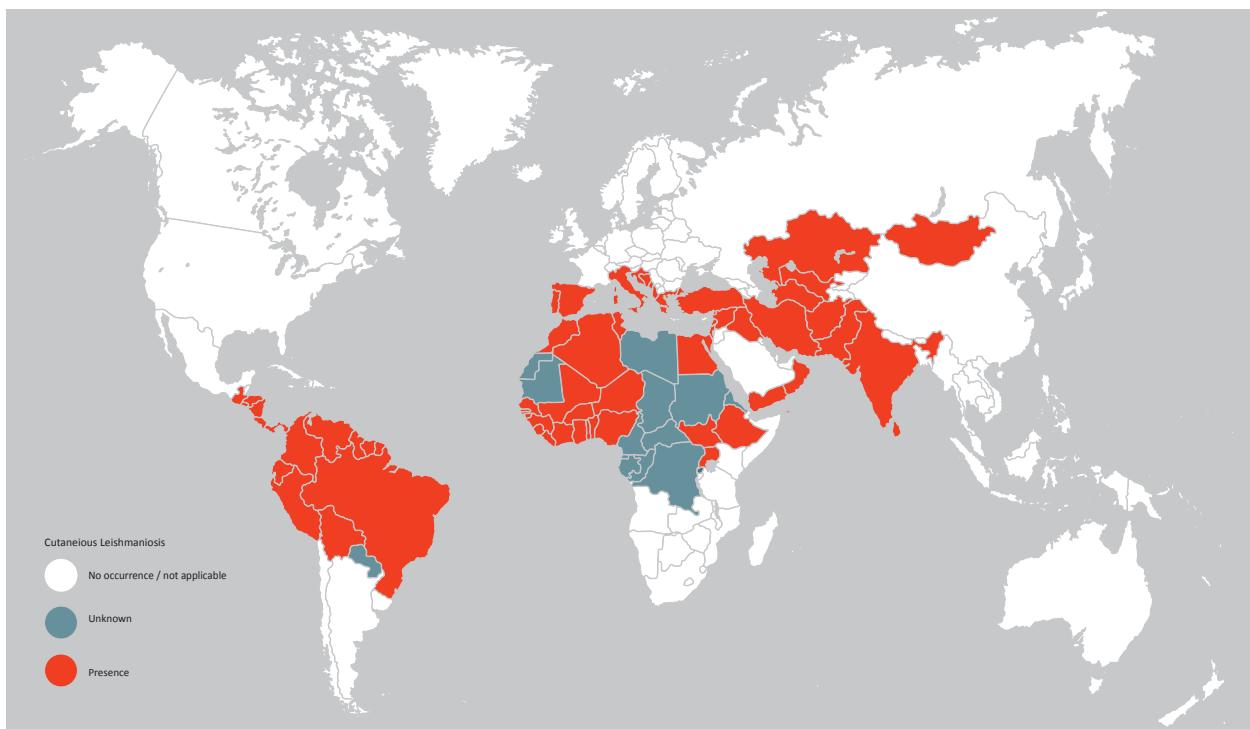
Adequate MDA coverage and routine monitoring of treatment success are urgently needed. Additionally, there is need of: Epidemiological surveys of *S. stercoralis* for the planning of the ivermectin MDA. There is a need for rapid tests, including for *S. stercoralis*. Knowledge on causes, mechanisms and prevention of AR needs to be increased. New groups of anthelmintics for MDA and vaccine development should be pursued. WASH measures need to be implemented and evaluated comprehensively. Collaboration between human and veterinary medicine and environmental sciences must take place in line with the One Health concept.



SHORT SUMMARY

Leishmaniasis is one of the few NTDs with an increasing burden of disease and is the parasitic tropical disease with the second highest mortality rate worldwide after malaria. Transmission occurs through female sandflies, which transmit the flagellated form of the parasites. In the host organism, the flagella-free parasite stage develops, which nests and multiplies in phagocytic immune cells. Depending on the species of leishmania and the immune status, cutaneous leishmaniasis (CL), mucocutaneous leishmaniasis (MCL) or visceral leishmaniasis (VL), in which internal organs such as the spleen, liver and bone marrow are affected, occur. CL and MCL heal with often disfiguring scarring. If left untreated, VL is fatal. HIV-Leishmania co-infection is associated with rapid disease progression, high relapse and mortality rates.

DISTRIBUTION



EPIDEMIOLOGY AND OPTIONS FOR CONTROL

Population affected	About 350 million live in risk areas, about 14 million are ill.
New cases/ death rate (per 100,000/year)	CL: 0.6 - 1.0 million new cases/year; VL: 200,000-390,000 new cases/year, mortality rate >95% in untreated cases.
WHO control strategy	Vector and reservoir control; early diagnosis and therapy; surveillance; educating the population.
Status of therapy (side effects)	Frequent severe side effects: cardiotoxicity of antimony agents, teratogenicity of miltefosine. Treatment choice depends on several factors (i.e., type of disease, co-morbidities, parasite species and geographic location). For <i>L. infantum</i> infection: pentavalent antimonials (PA) and liposomal amphotericin B (LAMB) (natural resistance to miltefosine); For <i>L. donovani</i> infection: PA, LAMB, paromomycin and miltefosine. Drug costs is a problem for major endemic countries, progress through single-dose LAMB treatment of patients (India/Nepal/Bangladesh).
Available vaccinations	No vaccinations available.
Diagnostics available	Microscopic smear of bone marrow punctures, PCR detection, serology only for late VL cases.

STATUS QUO, PROBLEMS AND SETBACKS

Leishmaniasis is a major public health problem in endemic countries, especially in war zones. In the NTD Roadmap, leishmaniasis is targeted for elimination as a public health problem. The main problem with CL therapeutics is the lack of clinical studies that scientifically validate their use and the elevated costs. Oral and topical treatments not requiring cold chain that can be used at community level are needed. The goal of an effective and well-tolerated vaccine is a major challenge and hardly achievable in the short/medium term. Other preventive measures, such as vector and reservoir control, as well as early treatment of patients, are more realistic. There are newly discovered groups of pathogens in previously unknown endemic areas with unclear transmission, reservoir and vectors. VL in Southern Europe: increasingly unclear reservoir situation, focus on dog reservoirs may be insufficient. Propagation: A vector capacity in Germany of isolated transphlebotomines is speculated, but urgently needs a systematic clarification.

RESEARCH IN GERMANY 2018-2022

Funding & Sponsors German projects	Public funding	Private funding
Funding in euro	2.184.411 €	95.123 €
Sponsors	DFG, European Commission, BMBF	WHO-TDR

Publication & Authorship	Overall publications (% Change 2013-2017)	German publications ¹ (% Change 2013-2017)	German affiliations (Leading position) ²
Publications	6.148 (+12.5%)	214 (-11.6%)	1.129 (243)

¹ An overview of the included German publications can be found in the appendix,

² Total number of all German researchers named in publications, multiple naming of individual researchers by inclusion in different publications, as well as multiple affiliation possible; leading authors are first- last- or corresponding authors Positions

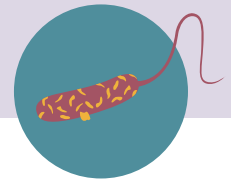
Scientific transfer of German research	Number of German trials (international)/ patents
Clinical trials	1 German study, 71 studies without German participation (Phase2-4)
Patents	24 German patents, 10 Leishmaniasis specific

ASSESSMENT OF THE GERMAN RESEARCH CONTRIBUTION

- ▶ Germany's contribution lies particularly in the field of basic immunological and parasitological research. Clinical research (e.g. diagnostic/therapeutic studies in endemic countries) is underrepresented.
- ▶ With a share of 3.4% of all publications on leishmaniasis, the participation of scientists from German institutions is relatively high despite moderate funding.

NEEDS ASSESSMENT AND CONCLUSION

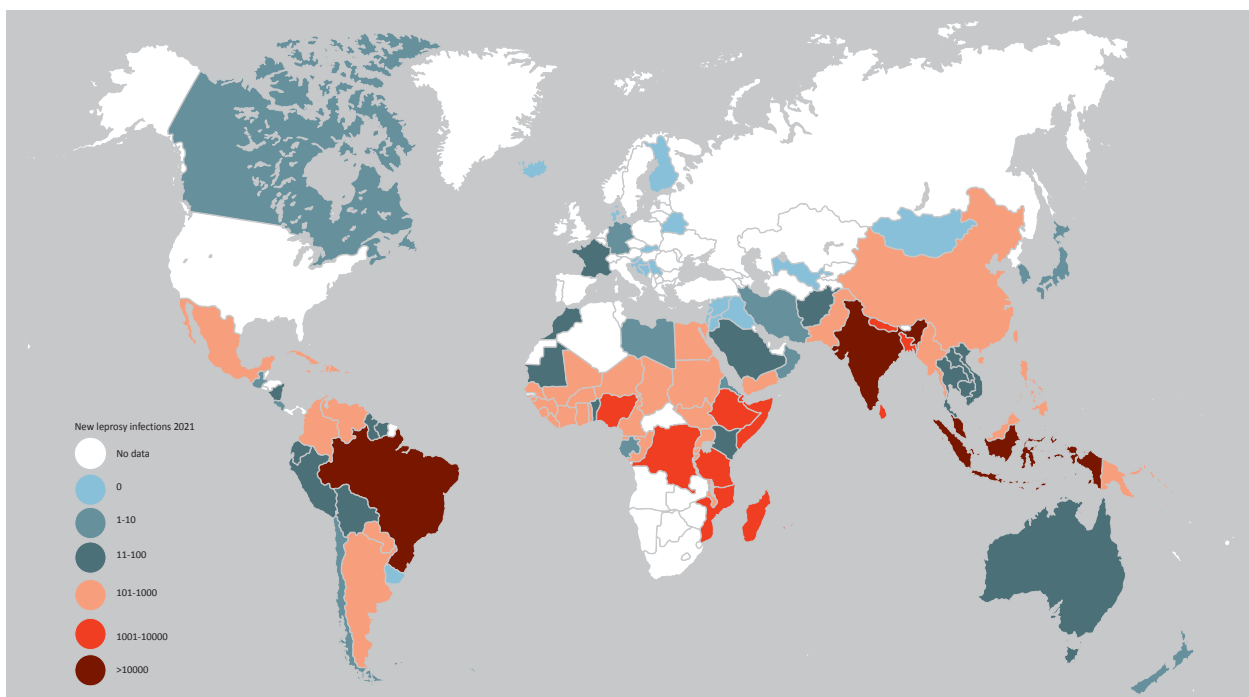
Conducting epidemiological studies in endemic countries (vector, parasite and disease prevalence), especially for newly discovered Leishmania species. Preclinical development and testing as well as for the clinical evaluation of new therapeutic concepts and vaccines, in particular for drugs not requiring cold chain. Development of tools to support intervention, e.g. smartphone apps for electronic clinical documentation (e.g. of skin lesions during the course of therapy). Research on the implementation of preventive measures. Development and use of sandfly effective repellents and small-mesh mosquito nets for exposure prophylaxis.



SHORT SUMMARY

Leprosy is a bacterial infection caused by *Mycobacterium leprae*, which affects the skin and nerves and sometimes leads to severe disabilities. The nerve damage causes paralysis and mutilation, especially of the hands and feet, as well as blindness. Early diagnosis can prevent this. Infection occurs via droplets. Prolonged, close contact over months with someone with untreated leprosy is needed to contract the disease. Leprosy can be completely cured with 6-12 months of antibiotic therapy. It is present in more than 120 countries around the world, with approximately 200,000 new cases reported each year. A high number of undetected cases are to be feared worldwide, exacerbated by the suspension of case searches during the Corona pandemic. Leprosy is a stigmatizing disease with strong social consequences for those affected.

DISTRIBUTION



EPIDEMIOLOGY AND OPTIONS FOR CONTROL

Population affected	At least 4 million people worldwide affected by disability and discrimination.
New cases/ death rate (per 100,000/year)	133,008 new cases in 2021. The number of unreported cases is considerably higher.
WHO control strategy	„Zero Leprosy Strategy 2021-2030“ will be implemented through active case search; prevention through a single dose of rifampicin for contacts and promotion of inclusion, treatment and rehabilitation measures. The objectives are: „Zero Transmission“: no new leprosy cases in 120 countries, 70% reduction in global case numbers and 90% reduction in child infection „Zero Disability“: 90% fewer cases with grade 2 disability and „Zero Stigma and Discrimination“; by promoting inclusion and no state discrimination against leprosy patients.
Status of therapy (side effects)	Donations of medicines enable therapy worldwide. Treatment options for leprosy complications are inadequate; the resistance monitoring system needs to be improved.
Available vaccinations	No vaccinations available.
Diagnostics available	Leprosy in endemic areas is often only clinically diagnosed; microscopic detection of bacteria from tissue fluid (Slit Skin Smear); histological examination of skin biopsies; PCR and rapid test in development. Existing antibody tests have little informative value.

STATUS QUO, PROBLEMS AND SETBACKS

Leprosy remains a public health problem in countries with highly endemic regions. The goal of disrupting transmission in 120 countries can only be achieved through active case search and contact tracing. Geographical studies of the occurrence of leprosy are required. The introduction of a single dose of rifampicin as prevention for leprosy contacts successfully reduces transmission. Antibiotic treatment (6-12 months) is effective, but treatment of immunological leprosy reactions is difficult. Vaccines are under development; however, the cost of studies is high. So far, there is no field-compatible rapid test for the diagnosis of leprosy. Clinical and operational studies led to the WHO recommendation of leprosy prevention with a single dose of rifampicin for contacts in 2018. German non-university institutions played a key role in this.

RESEARCH IN GERMANY 2018-2022

Funding & Sponsors German projects	Public funding	Private funding
Funding in euro	291.617 €	1.694.726 €
Sponsors	DFG, GIZ	EDCTP, LRI, NLR, ALM, DAHW

Publication & Authorship	Overall publications (% Change 2013-2017)	German publications ¹ (% Change 2013-2017)	German affiliations (Leading position) ²
Publications	1.549 (+ 32.4%)	36 (+63.6,0%)	351 (46)

¹ An overview of the included German publications can be found in the appendix,

² Total number of all German researchers named in publications, multiple naming of individual researchers by inclusion in different publications, as well as multiple affiliation possible; leading authors are first- last- or corresponding authors Positions

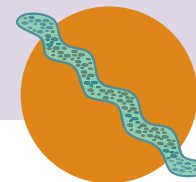
Scientific transfer of German research	Number of German trials (international)/ patents
Clinical trials	1 German study, 23 studies without German participation (Phase1-4)
Patents	13 German patents, 2 Lepra specific

ASSESSMENT OF THE GERMAN RESEARCH CONTRIBUTION

- ▶ Germany's contribution is particularly in the field of operational and implementation research and is mainly carried out by non-university institutions.
- ▶ Particularly in view of the still high importance of leprosy worldwide, contribution of Germany's universities is extremely low in international comparison.

NEEDS ASSESSMENT AND CONCLUSION

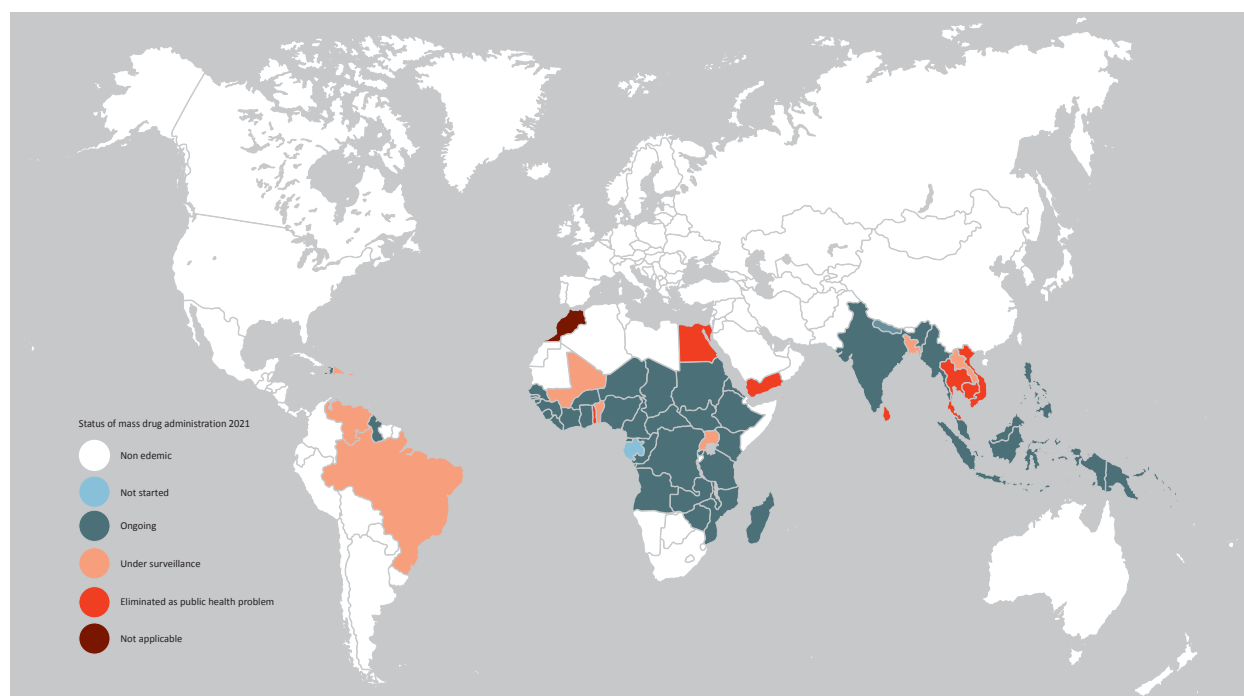
- Diagnostics: A field-ready (rapid) test that also detects subclinical infections must be developed.
- Prevention: Further implementation studies, e.g. the combination of vaccination and medication, are urgently needed.
- Drug resistance: A surveillance system of drug resistance in leprosy needs to be expanded.
- Operational: Studies on the geographical distribution of leprosy cases and implementation studies on existing and developing control measures must be carried out.



SHORT SUMMARY

Lymphatic filariasis (LF) is caused by the filariae *Wuchereria bancrofti*, *Brugia malayi* and *B. timori*. Mosquitoes (Anopheles and others) transmit worm larvae, from which adult worms develop. These are located in lymphatic vessels that are destroyed by chronic inflammation. The consequences are lymphedema and hydrocele, those affected are stigmatized and often unable to work (estimated >2 million DALYs in Africa, just as many in Asia). Mass chemotherapy (MDA) control programs have reduced the number of infected people by 74%, 17/72 countries have eliminated LF as a public health problem. For worldwide elimination, drugs are needed that kill the adult worms; these are being developed with the visible participation of German institutions and subsidies.

DISTRIBUTION



EPIDEMIOLOGY AND OPTIONS FOR CONTROL

Population affected	51 million infected/885 million „at risk“, at least 40 million with the disease sequelae (25 million hydroceles, 15 million lymphedema), which do not disappear even by eliminating the infection.
New cases/ death rate (per 100,000/year)	Approx. 0.5 -1% new cases/year (i.e. 1,000 per 100,000/year) No robust data on the death rate; limitations due to morbidity are significant: 2-4 million DALYs.
WHO control strategy	Mass chemotherapy (MDA) with the anthelmintic drugs ivermectin, albendazole and/or diethylcarbamazine in all endemic regions with a prevalence of > 1% of people with microfilariae in the blood. The intervention aims to interrupt transmission by reducing the number of microfilariae (MF), which are transmitted by mosquitoes, not primarily at individual cure, because the adult worms remain in the body for years and produce MF. Without new drugs, the goals of the WHO Roadmap are difficult to achieve. The second, no less important pillar of the „Global Program for the Elimination of LF“ (GPELF) is the „Morbidity Management and Disease Prevention“ program, in which the WHO „Essential Package of Care“ (hygiene) is implemented. Implementation is the responsibility of endemic countries as part of the commitment to SDG 3.8, Universal Health Coverage.
Status of therapy (side effects)	Anthelmintic drugs ivermectin, albendazole and/or diethylcarbamazine. Of the 72 countries affected, 17 (3 in Africa: Togo, Egypt, Malawi; many small island states in the Pacific) have met the criteria for elimination, but remain under surveillance. 45 countries are endemic and require MDA, of which nine have not yet started or have not implemented the MDA in all endemic regions.
Available vaccinations	No vaccinations available.
Diagnostics available	Test for circulating antigen in the blood; microscopy of MF in the blood; Antibody diagnosis is specific only when monovalent, recombinant antigen WB123 is used.

STATUS QUO, PROBLEMS AND SETBACKS

The extension from dual to triple therapy with ivermectin (IVM), albendazol (ALB) and diethylcarbamazine (DEC) (IDA, = IVM, ALB and DEC) in regions without onchocerciasis has accelerated the reduction of prevalence, i.e. in Asia. However, Covid has shown that the MDA, which has to be repeated over many years (only against worm larvae), is vulnerable: Interruptions for one year mean setbacks of several years. Therefore, drugs must be developed that kill the adult, long-lived worms and thus eliminate the LF more quickly. There is already an adulticidal therapy principle that kills adult worms by eliminating their endobacteria (*Wolbachia*) (e.g. doxycycline). New drugs with shorter therapy durations are currently being developed on the basis of this principle (by DNDi). The already existing pathological changes such as lymphedema and hydroceles are no longer improved by MDA. Here, morbidity management must be improved, including medication; the first step is to more accurately record the cases, 90% of which are not recorded.

RESEARCH IN GERMANY 2018-2022

Funding & Sponsors German projects	Public funding	Private funding
Funding in euro	15.288.620 €	67.026 €
Sponsors	BMBF, DFG	Industry

Publication & Authorship	Overall publications (% Change 2013-2017)	German publications ¹ (% Change 2013-2017)	German affiliations (Leading position) ²
Publications	624 (+3.0%)	30 (+36.4%)	80 (16)

¹ An overview of the included German publications can be found in the appendix,

² Total number of all German researchers named in publications, multiple naming of individual researchers by inclusion in different publications, as well as multiple affiliation possible; leading authors are first- last- or corresponding authors Positions

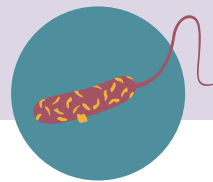
Scientific transfer of German research	Number of German trials (international)/ patents
Clinical trials	1 German study, 21 studies without German participation (Phase 1-4)
Patents	4 German patents, 1 LF specific

ASSESSMENT OF THE GERMAN RESEARCH CONTRIBUTION

- ▶ In an international comparison and with regard to the global significance of the LF, the German contribution to drug development is clearly visible (collaborations of DNDi with German institutions via PDP funding, as well as DZIF and EDCTP) and internationally very well networked (DNDi, Gates Foundation, etc.). The very successful drug development so far has led to three candidates in clinical development, and one in late preclinical stage. Development will soon be completed [7].
- ▶ The promotion of this program must be maintained until at least one of these new drugs against the adult worms has been registered. Otherwise, the hitherto very visible share of German funding in this development would fizzle out.
- ▶ One German researcher is a member of the WHO DTAG commission (Diagnostic Technical Advisory Group) aimed at identifying diagnostic solutions for lymphatic filariasis.

NEEDS ASSESSMENT AND CONCLUSION

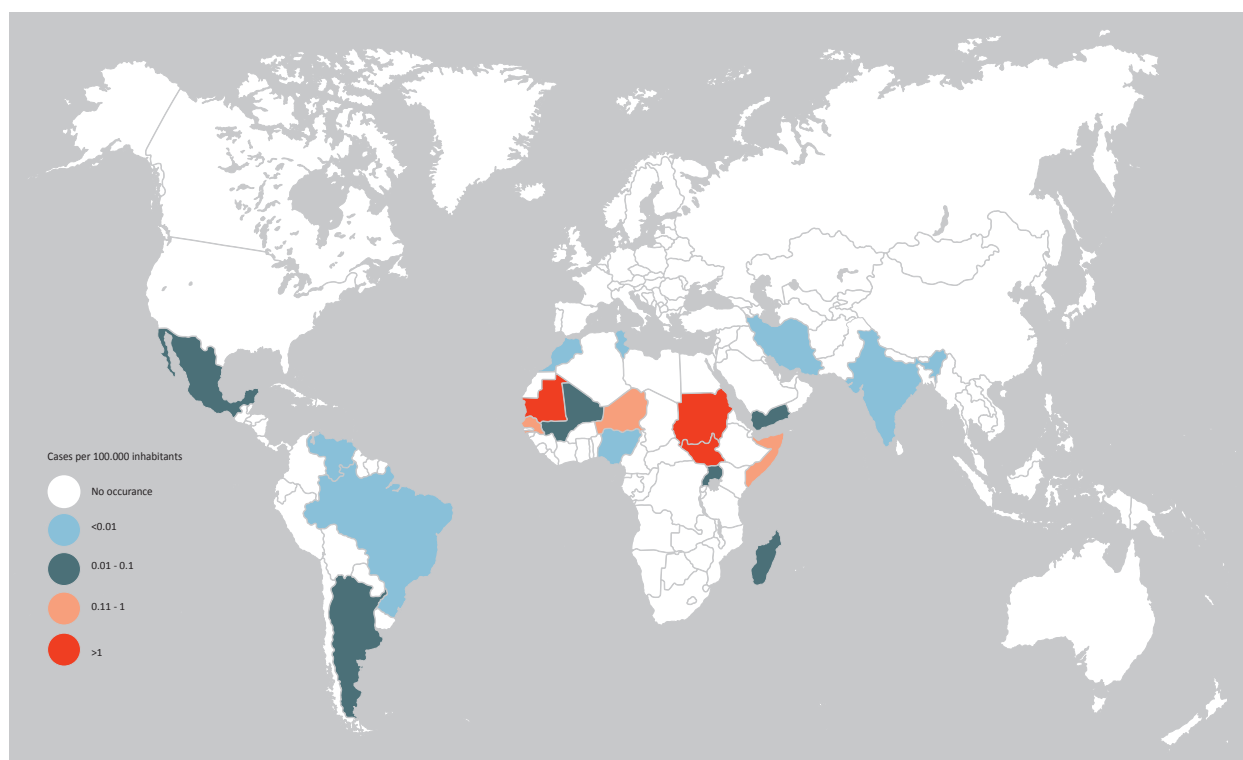
New therapeutics have already been developed, e.g. in collaboration with DNDi; they have completed the litmus test of preclinical development and are currently in clinical trials. These programs must continue until success in phase 3 trials and drug registration. Dosages and formulations, especially for children, must be tested in additional clinical trials. Research on diagnostics and operational research is hardly taking place at the moment, but is urgently needed.



SHORT SUMMARY

Mycetoma is a chronic infection of the skin, soft tissues and bones caused by fungi (eumycetoma) or bacteria (actinomycetoma) that occurs in tropical and subtropical climates. Men and farmers living in remote regions are largely affected. Mycetomas are caused by bacterial and fungal species implanted in the subcutaneous tissue through mild microtrauma. If left untreated, the infection can lead to enormous tissue damage. Long-term antibiotic or antifungal therapy should always accompany a possible surgical rehabilitation. There is a need for research in the areas of epidemiology, prevention, transmission, diagnostics and therapy.

DISTRIBUTION



EPIDEMIOLOGY AND OPTIONS FOR CONTROL

Population affected	9,000 cases are estimated to occur annually worldwide. Men get sick more often than women (4:1); Farmers have increased exposure. The majority of patients are young adults in the age group of 15-30 years. In the reported case series, children account for 30% of patients. Predominantly, the distal lower limb is affected.
New cases/ death rate (per 100,000/year)	The prevalence estimates for countries such as Mauritania and Sudan is 3.5 and 1.8 cases per 100,000 population, respectively. High numbers of cases are also reported annually from Mexico, India and Senegal. The actual number of cases is likely to be significantly higher.
WHO control strategy	The objectives of the WHO Mycetoma Control Strategy 2021-2030 are: (i) Development of rapid tests for diagnosis and effective treatment, as well as the introduction of surveillance for the detection and reporting of cases; (ii) Develop a standardized manual for diagnosis and treatment and ensure adequate training of health workers; (iii) Accessible diagnostic measures and treatment methods.
Status of therapy (side effects)	Systemic antibiotic or antifungal treatments over longer periods of time are effective in combination with a possible surgical intervention as standard. These are often not available in endemic areas. Regular clinical and laboratory checks are necessary due to side effects and pathogen resistance. Patient compliance is at risk due to the longer treatment periods and side effects.
Available vaccinations	No vaccinations available.
Diagnostics available	Biopsies, microscopic examination, cultural cultivation and PCR, which are often not available in endemic areas.

STATUS QUO, PROBLEMS AND SETBACKS

Exact data on the prevalence, incidence and geographical distribution of the disease are lacking. The disease primarily affects the poor rural population. Microbiological diagnosis is crucial for the choice of therapy. However, it requires special clinical as well as microbiological (diagnostics) expertise. Mycetoma leads to disability in young adults. Wearing sturdy shoes reduces transmission through microtrauma in the area of the feet. The treatment of mycetoma is lengthy and requires a high level of compliance as well as regular clinical and laboratory checks. The Global Mycetoma Working Group consists of: WHO Department of Control of Neglected Diseases, the United States Centers for Disease Control and Prevention, the Erasmus University Medical Centre (Netherlands) and the University of Khartoum (Sudan).

RESEARCH IN GERMANY 2018-2022

Funding & Sponsors German projects	Public funding	Private funding
Funding in euro	Not reported	Not reported
Sponsors	Not reported	Not reported

Publication & Authorship	Overall publications (% Change 2013-2017)	German publications ¹ (% Change 2013-2017)	German affiliations (Leading position) ²
Publications	246 (+20%)	3 (-70%)	10 (4)

¹ An overview of the included German publications can be found in the appendix,

² Total number of all German researchers named in publications, multiple naming of individual researchers by inclusion in different publications, as well as multiple affiliation possible; leading authors are first- last- or corresponding authors Positions

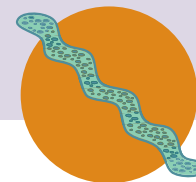
Scientific transfer of German research	Number of German trials (international)/ patents
Clinical trials	No German studies, 2 studies without German participation
Patents	5 German patents, 1 Mycetoma specific

ASSESSMENT OF THE GERMAN RESEARCH CONTRIBUTION

- ▶ In international comparison with research on other NTDs and with regard to the worldwide importance of mycetoma, the German contribution is very small.
- ▶ In Germany, mycetoma is classified as a rare infectious disease and belongs to the Orphanet classification. Research in Germany is very limited.
- ▶ Occasional publications in international journals.

NEEDS ASSESSMENT AND CONCLUSION

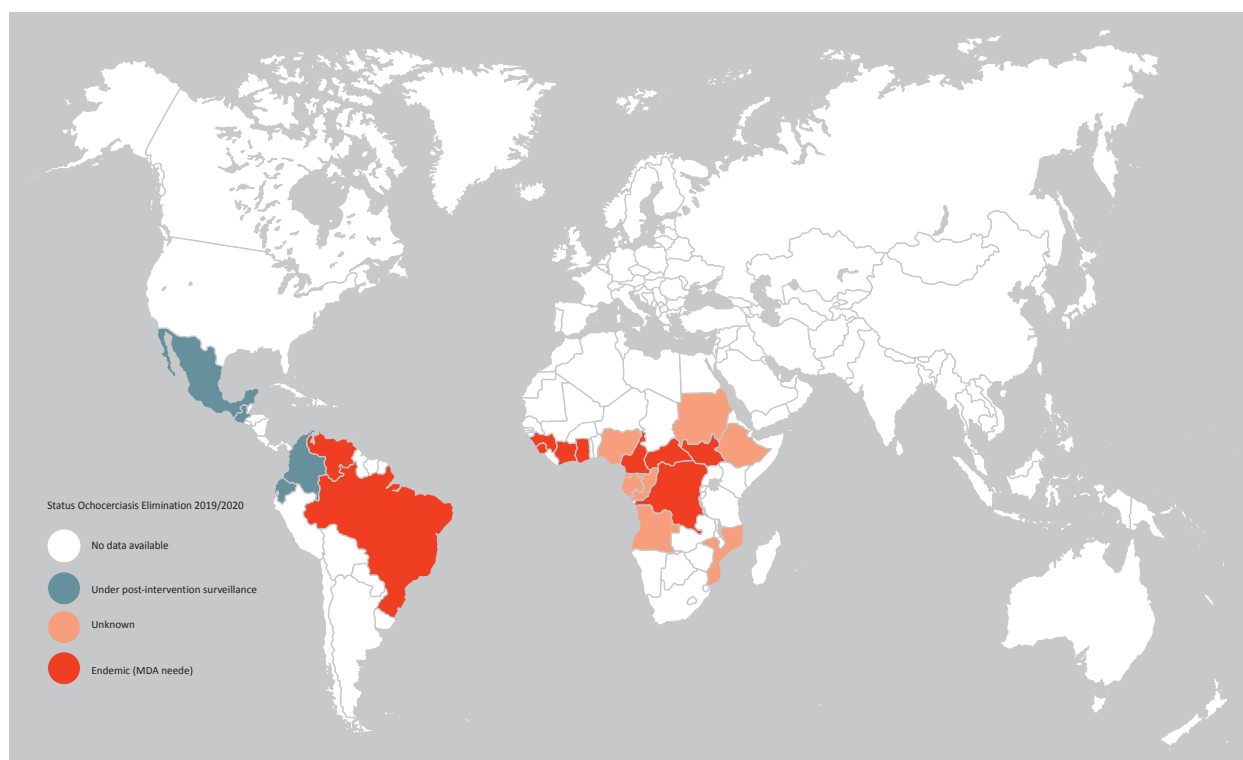
Collection of epidemiological data on the incidence, prevalence and geographical distribution of mycetoma. Implementation of prevention strategies and improvement of knowledge and awareness of mycetoma. Development of networks worldwide for data collection. Access to point-of-care tests for a sensitive and specific diagnosis of the causative microorganisms. Rehabilitation strategies for affected patients as well as adherence programs for those affected during treatment. Development and access of new drugs and their combinations for pathogen-specific therapy of mycetoma. Integration of diagnostics, therapy and rehabilitation for those affected in national programs and in health policy.



SHORT SUMMARY

Onchocerciasis is caused by the filariae *Onchocerca volvulus* and is called river blindness, as blindness may occur and the transmitting black fly *Simulium* only occurs near flowing waters. Adult filariae live in worm nodules (onchocercomas) and released larvae (*microfilariae*) migrate in the skin and occasionally into the eye and can cause skin diseases or blindness when they die. About 21 million people are infected, mainly in Sub-Saharan Africa. Ivermectin mass treatments and vector control have reduced the number of infected people and largely eliminated transmission in Latin and Central America. New adult worm-killing drugs are currently being tested in onchocerciasis patients.

DISTRIBUTION



EPIDEMIOLOGY AND OPTIONS FOR CONTROL

Population affected	21 million affected, 220 million under risk.
New cases/ death rate (per 100,000/year)	Approx. 0.5 -1% new cases/year (i.e. 1,000 per 100,000).
WHO control strategy	In the African Programme for Onchocerciasis Control (APOC), between 1995 and 2015, mass ivermectin treatments were carried out 1-2 times a year in 20 African countries. As a result, the microfilariae are eliminated from the skin for months, skin inflammation and blindness have been reduced, and 17 million DALYs (Disability Adjusted Life Years) have been prevented. The APOC program has been replaced by the Extended Special Programme for the Elimination of NTDs (ESPEN). The new goal of the WHO Roadmap 2021-2030 is to eliminate the transmission of onchocerciasis in 31% of endemic countries, including hypoendemic countries. This requires new adult worm-eliminating (macrofilaricidal) drugs and improved diagnostics.
Status of therapy (side effects)	Individual therapy with doxycycline for 4-6 weeks is effective against adults. Mass treatment with single dose ivermectin (1-2x per year), alternatively moxidectin (1x per year), kills microfilariae, but not adults. Skin itching, dizziness, fever, edema mild after 2nd treatment.
Available vaccinations	No vaccinations available.
Diagnostics available	Clinical diagnosis and detection of microfilaria in the blood. Serology (e.g., Ov16) can inform about exposure and is helpful for assessing how quickly infections spread in children (can be used as epidemiological marker for prevalence).

STATUS QUO, PROBLEMS AND SETBACKS

Elimination before 2050 is unlikely without additional measures. Moxidectin, which has been registered since 2018, eliminates microfilariae for a longer period of time compared to ivermectin, but is not available free of charge for mass treatment. Doxycycline eliminates endosymbiotic *Wolbachia* bacteria and kills the adult worms. Because of the long duration of therapy, it is mainly used individually, except for remaining hot-spots in Venezuela and Brazil, as well as in Cameroon. Macrofilaricidal candidates with shorter duration of therapy are in phase 2 trials: flubentylisin (AbbVie), emodepside (Bayer), oxfendazole; or about to enter clinical phase: Coralopyronin A (DZIF/Eisai). New medicines are important for the transition from annual mass treatment (co-treatment of non-infected persons) over many years, to test and treat procedures (curative therapy) as well as for co-endemic areas with *Loa loa* in Central Africa. People with high *Loa loa* microfilariae loads can develop fatal encephalitis when ivermectin is administered.

RESEARCH IN GERMANY 2018-2022

Funding & Sponsors German projects	Public funding	Private funding
Funding in euro	1.652.337 €	3.690.115 €
Sponsors	DFG, DZIF, BMBF, European commission	The Task Force for Global health, EDCTP, DNDi. Bill & Melinda Gates Foundation, Industry

Publication & Authorship	Overall publications (% Change 2013-2017)	German publications ¹ (% Change 2013-2017)	German affiliations (Leading position) ²
Publications	563 (+54.2%)	55 (+106.3%)	144 (34)

¹ An overview of the included German publications can be found in the appendix,

² Total number of all German researchers named in publications, multiple naming of individual researchers by inclusion in different publications, as well as multiple affiliation possible; leading authors are first- last- or corresponding authors Positions

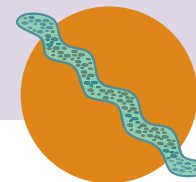
Scientific transfer of German research	Number of German trials (international)/ patents
Clinical trials	2 German studies, 18 studies without German participation (Phase 1-3)
Patents	8 German patents, 0 Onchocerciasis specific

ASSESSMENT OF THE GERMAN RESEARCH CONTRIBUTION

- ▶ The German contribution is internationally competitive, in the development of new drugs it occupies a leading, visible position with very good networking (DNDi, Gates Foundation, industrial partners, EDCTP).
- ▶ Through continuous funding, Germany can maintain this visibility.
- ▶ One German researcher is a member of the WHO DTAG commission aimed at identifying diagnostic solutions for onchocerciasis and lymphatic filariasis.

NEEDS ASSESSMENT AND CONCLUSION

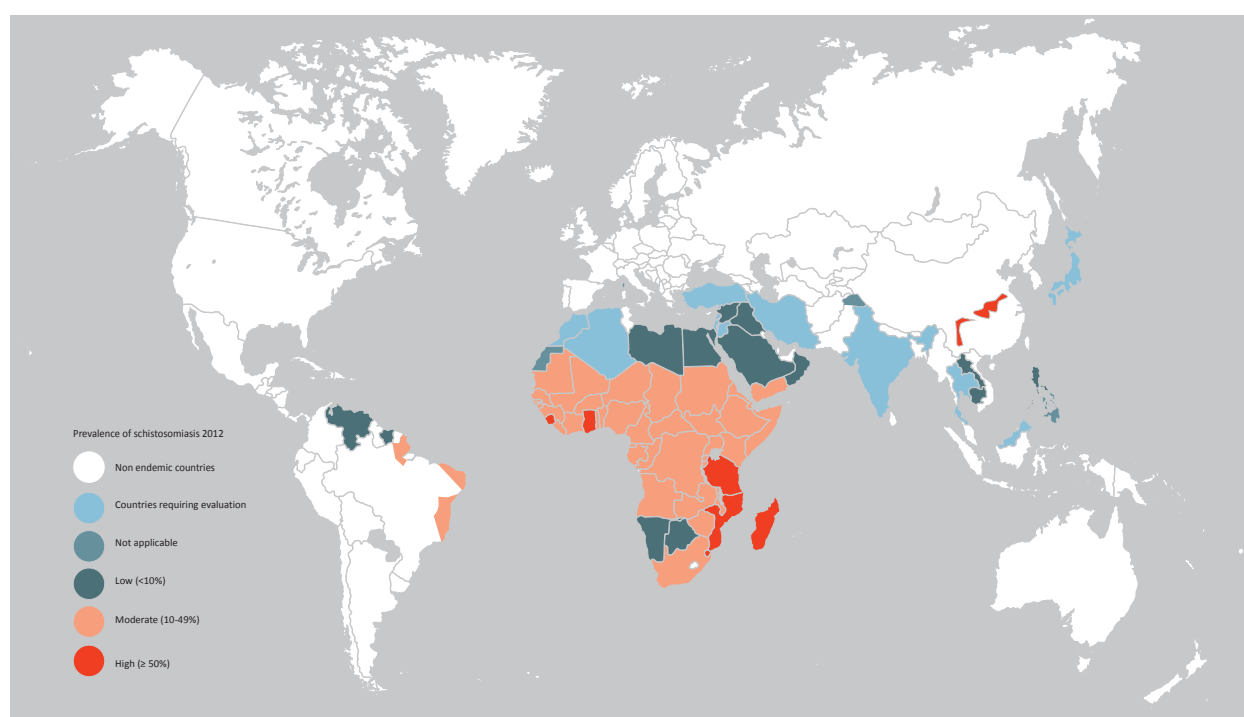
- ▶ Identification of remaining active transmission foci requires epidemiology and better diagnostics.
- ▶ New adult worm-eliminating therapeutics are being developed, e.g. in collaboration with DNDi. These programs must be continued and funded until successful (Phase 3 trials).
- ▶ ESPEN (the WHO's Extended Special Project for the Elimination of NTDs) urgently needs to be better equipped for the elimination programs, especially in economically weak regions of the world.
- ▶ Support for endemic countries (e.g. CEMAC) in bilateral and regional programs (BMZ) needs to be continued.



SHORT SUMMARY

Schistosomiasis is, after malaria, the second most important parasitic disease worldwide. Mostly prevalent in tropical and sub-tropical regions, 90% of all cases occur in Africa, schistosomiasis became endemic in Corsica since 2014. Infection is caused by fresh water contact. Schistosomes released from freshwater snails penetrate the human skin maturing into adult worms. They reside in the portal or mesenteric veins releasing hundreds of eggs per day into the surrounding tissue excreted via urine or stool. Urogenital and intestinal schistosomiasis is caused by *S. haematobium* and (mainly) *S. mansoni*, respectively. Acute inflammation and serious chronic disease including liver fibrosis and female genital malformations and bladder cancer may occur.

DISTRIBUTION



EPIDEMIOLOGY AND OPTIONS FOR CONTROL

Population affected	More than 770 million people are at risk of infection, 90% in Africa.
New cases/ death rate (per 100,000/year)	<i>Schistosoma</i> infections and deaths are not routinely registered, thus incidence and death rates are unknown and probably considerably underestimated. A surrogate for new cases/year could be the estimated number of individuals who required preventive schistosomiasis treatment that reached 251 million for 2021. Disease burden is further reflected by the Disability-adjusted Life Years (DALY) estimated at 2.5 million (for 2016).
WHO control strategy	Mass drug administration with praziquantel (PZQ) once per year; now suggested for everyone above 5 years of age living in endemic areas with >10% prevalence.
Status of therapy (side effects)	Only Praziquantel. PZQ is safe and well tolerated. A paediatric PZQ formulation is in the process of regulatory approval (EMA EU-M4all). PZQ is only efficacious against the adult worms requiring repeated treatment to achieve cure.
Available vaccinations	No vaccinations available.
Diagnostics available	Gold standard is the detection of <i>Schistosoma</i> eggs by microscopy in stool or urine. This method is specific but not sensitive and low-intensity infections (e.g. in travellers) are often not detected. Within 6 to 8 weeks after infection, the diagnosis is false negative. Serological tests are available but are not standardised and not useful in endemic countries. The detection of <i>Schistosoma</i> antigens (CAA, CCA) tests are currently developed as improved rapid diagnostic tests but specificity questionable. Sensitive methods for identifying young and adult schistosomes need to be developed. Molecular tests are available but only amenable in research or control activities. The chronic conditions require additional medical investigations or more sophisticated diagnostics (i.e. PCR) since the parasite might not be found in the conventional biological specimens.

STATUS QUO, PROBLEMS AND SETBACKS

Schistosomiasis is targeted for elimination as a public health problem within 2030. So far, strategies to plan more targeted interventions are being evaluated. Morbidity control needs to be tackled in order to cope with the consequences of chronic forms of the disease. Adapted diagnostic tools for community-based prevalence assessment and individual diagnosis in endemic settings remain a big barrier to elimination. Schistosomes with reduced susceptibility to praziquantel have been reported and young worms that are left unaffected reduce the effectiveness of control measures. Therefore, additional treatment options are becoming urgent.

RESEARCH IN GERMANY 2018-2022

Funding & Sponsors German projects	Public funding	Private funding
Funding in euro	6.717.197 €	1.702.786 €
Sponsors	DFG, DZIF, BMBF, GIZ, European commission	Volkswagen Foundation, EDCTP, COR-NTD, Fresenius Foundation, Merck, DAHW

Publication & Authorship	Overall publications (% Change 2013-2017)	German publications ¹ (% Change 2013-2017)	German affiliations (Leading position) ²
Publications	2.892 (+1.2%)	165 (-3.6%)	989 (198)

¹ An overview of the included German publications can be found in the appendix,

² Total number of all German researchers named in publications, multiple naming of individual researchers by inclusion in different publications, as well as multiple affiliation possible; leading authors are first- last- or corresponding authors Positions

Scientific transfer of German research	Number of German trials (international)/ patents
Clinical trials	5 German studies, 40 studies without German participation (Phase 1-4)
Patents	7 German patents, 1 Schistosomiasis specific

ASSESSMENT OF THE GERMAN RESEARCH CONTRIBUTION

- ▶ Germany provides an active contribution to schistosomiasis research with an average of 40 publications per year since 2017. Germany is among the leading countries in Europe publishing on the disease. Activities include diagnostic and treatment development and operational and implementation research contributing to policies and guidelines of endemic countries.
- ▶ Schistosomiasis is present on the funding lines of several German donors including the government (i.e. BMG and BMBF) and private organizations (i.e. EKFS).
- ▶ Two German researchers are member of the WHO DTAG commission aimed at identifying diagnostic solutions for Female Genital Schistosomiasis.

NEEDS ASSESSMENT AND CONCLUSION

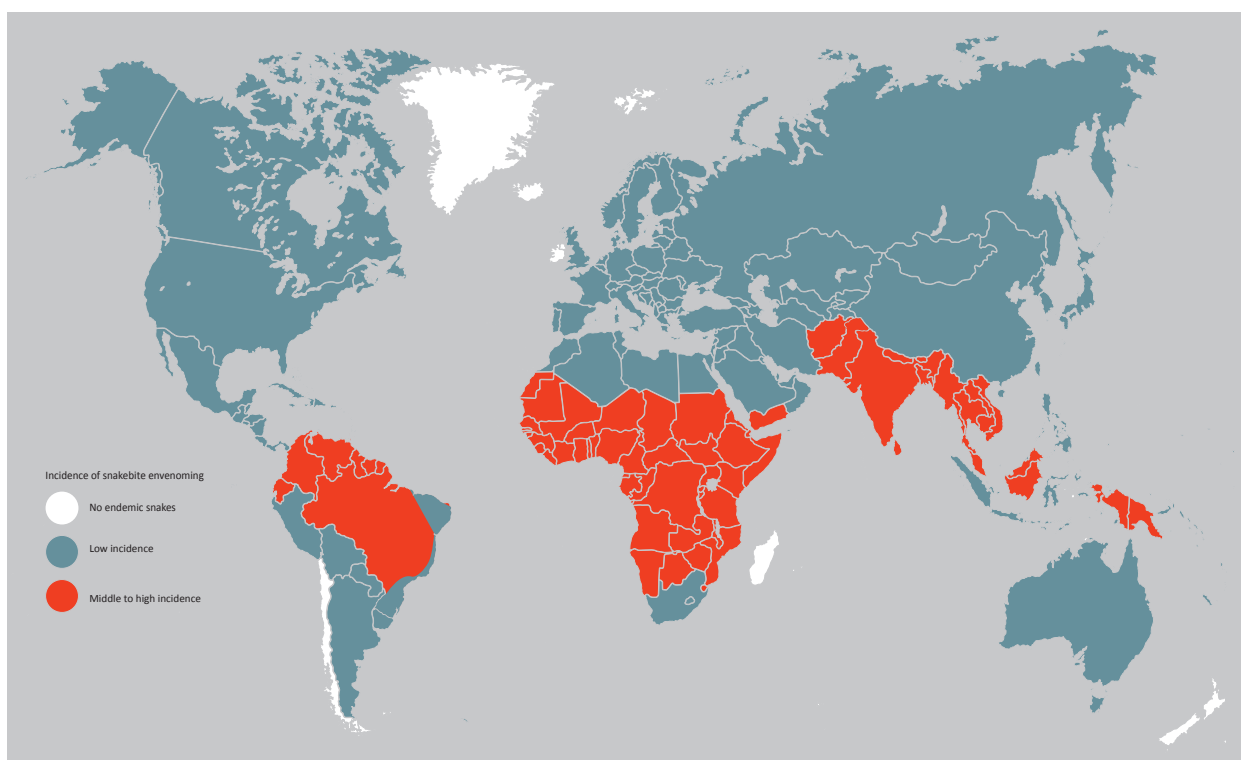
The engagement in terms of research on schistosomiasis in Germany can be considered as relatively good, but more efforts are required to align with the NTD Roadmap to support elimination of the disease as a public health problem within 2030. Major needs to address: (i) Improve diagnostics for endemic settings; (ii) Promote the identification of new therapeutic solutions; (iii) Support strategies for case management of chronic disease; (iv) Contribute to policies and public health strategies for the control of the disease in endemic countries; (v) Support training and continuous education on the different aspects of the disease.



SHORT SUMMARY

Snakebite envenoming has been on the WHO list of NTDs since 2017, and as a result, it has received more attention along with the prevention and control strategy launched by WHO in 2019. The highest disease burden is found in low- and middle-income countries in South and Southeast Asia and sub-Saharan Africa, where weak health systems and the lack of effective antivenoms, make adequate treatment difficult or impossible. Estimates put the number of snakebites at 5 million per year, with 1.8 to 2.7 million envenoming's and 80,000 to 140,000 deaths. Approximately 400,000 people must live with permanent disabilities after a snakebite.

DISTRIBUTION



EPIDEMIOLOGY AND OPTIONS FOR CONTROL

Population affected	About 5 million people are affected each year. About 3.5 billion people live with relevant risk.
New cases/ death rate (per 100,000/year)	Based on 3.5 billion people at risk for snakebite, estimates are as follows, real numbers may be even higher. <ul style="list-style-type: none"> • Snakebites 140/100,000 per year • Envenoming's 70/100,000 per year • Death rate 2/100,000 per year
WHO control strategy	WHO launched a strategy for the prevention and control of snakebite envenoming in 2019 with the goal of reducing mortality and disability by 50% by 2030. Four goals focus on: (i) Engaging and empowering the population; (ii) Providing safe and effective treatment; (iii) Strengthening health systems; (iv) Fostering partnerships and pooling resources.
Status of therapy (side effects)	Treatment of snakebite envenoming with antivenom is well established and effective. Life-threatening anaphylactic shock must be considered during administration.
Available vaccinations	Not applicable.
Diagnostics available	Laboratory diagnosis of systemic envenoming is well established. However, it is often not available in resource-poor regions. Point-of-care tests for rapid detection of snake venom in serum are usually not available.

STATUS QUO, PROBLEMS AND SETBACKS

Despite progress since 2017, three core problems remain: (i) too few financial resources, (ii) too little data, and (iii) too little effective antivenom. First, there is a lack of funding opportunities and advocacy, as snakebite envenomation is neither an infectious disease nor a traditional non-communicable disease and thus falls through the cracks in many funding programs. Second, more scientific evidence is needed due to the lack of resources as well as integration of snakebite into other NTD programs. Third, there is a lack of regulation and production capacity for antivenom, data on antivenom efficacy, and country ownership and coordination.

RESEARCH IN GERMANY 2018-2022

Funding & Sponsors German projects	Public funding	Private funding
Funding in euro	115.100 €	99.112 €
Sponsors	GIZ	Else Kröner-Fresenius Foundation

Publication & Authorship	Overall publications (% Change 2013-2017)	German publications ¹ (% Change 2013-2017)	German affiliations (Leading position) ²
Publications	2.357 (+10.6%)	77 (-12.5%)	303 (80)

1. An overview of the included German publications can be found in the appendix,

2. Total number of all German researchers named in publications, multiple naming of individual researchers by inclusion in different publications, as well as multiple affiliation possible; leading authors are first- last- or corresponding authors Positions

Scientific transfer of German research	Number of German trials (international)/ patents
Clinical trials	0 German studies, 15 studies without German participation (Phase2-4)
Patents	No registered German patents

ASSESSMENT OF THE GERMAN RESEARCH CONTRIBUTION

German research focuses mainly on epidemiology and management of snakebite envenoming, training of medical personnel and community engagement in Southeast Asia, South America and since 2021 also in Africa. In addition, some basic laboratory research, especially in the field of venom analysis is conducted.

NEEDS ASSESSMENT AND CONCLUSION

Effective antivenom must be produced in sufficient quantities and available free of charge. Medical personnel must regularly participate in further training. Alternative treatments with improved efficacy and side effect profile must be developed.

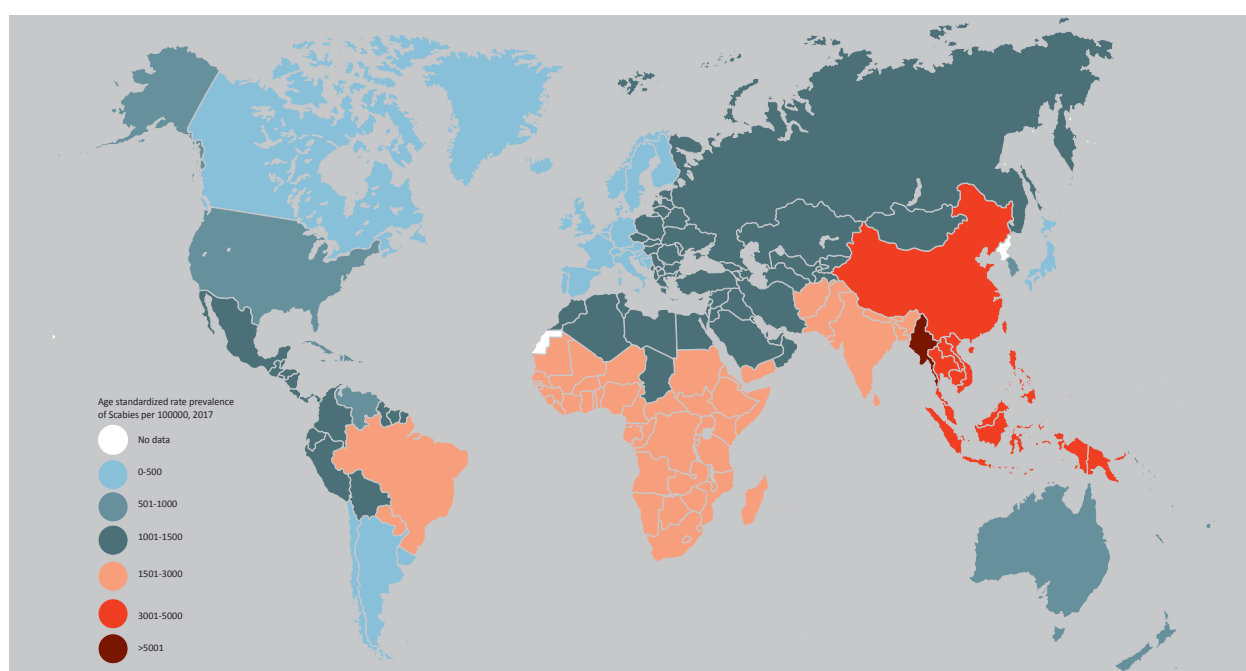
In the last five years, snakebite envenoming has received much more attention and new projects involving German scientists have been initiated. However, much more financial and human resources are needed to achieve a significant reduction in morbidity and mortality by 2030. The availability of effective antivenom and training of medical personnel are top priorities.



SHORT SUMMARY

Scabies is a worldwide dermatological condition, estimated by the WHO to affect >200 million people. *Sarcoptes scabiei var homini* burrows and lays eggs in the top layer of the skin. The transmission is through skin contact. After hatching in 3-4 days, the eggs develop into adult mites within a couple of weeks. Patients develop inflammatory reactions to the presence of mite proteins and faeces after 4-6 weeks, causing intense itch and rash. Scabies associated skin infection is a common risk factor for kidney disease and possible rheumatic heart disease. Diagnosis of a scabies is made based upon the customary appearance and distribution of the rash and the presence of burrows. The treatment of scabies involves topical scabicide or oral ivermectin.

DISTRIBUTION



EPIDEMIOLOGY AND OPTIONS FOR CONTROL

Population affected	Relatively common infestation that can affect individuals of any age and socioeconomic status; the worldwide prevalence is estimated to be more than 200 million infested at any given time, particularly prevalent among children and older adults and immunocompromised people, with wide variation in prevalence among individual geographic regions.
New cases/ death rate (per 100,000/year)	Prevalence estimates in the recent scabies-related literature range from 0.2 to 71%. Up to 10% of children in resource-poor areas are affected. It is not a fatal disease; however, it can cause severe morbidity and poor quality of life.
WHO control strategy	Repeated Mass Drug Administration (MDA) over several years. Aim is the regular examination, particularly of those living at close quarters, in order to prevent mass infestation.
Status of therapy (side effects)	Topical scabicide: 5% permethrin, 0.5% malathion in aqueous base, 10-25% benzyl benzoate emulsion or 5-10% sulphur ointment. Oral ivermectin: Itch commonly intensifies with effective treatment for 1-2 weeks. Ivermectin: no data for pregnant women and children < 15kg body weight. Treatment of the whole household at the same time and repeated treatment might be more effective.
Available vaccinations	No vaccination available.
Diagnostics available	Diagnosis of a scabies usually relies on clinical assessment based upon the customary appearance and distribution of the rash and the presence of burrows. Visualization using dermatoscopy is common. There are no accurate, objective tests. Microscopy of skin scrapings can confirm the diagnosis, but it is insensitive, invasive and often impractical.

STATUS QUO, PROBLEMS AND SETBACKS

Since 2017, scabies has been recognized by the WHO as one of the most important neglected tropical diseases. In 2018, the WHO NTD Global Working Group on Monitoring and Evaluation recommended that the global burden of scabies should be established, diagnostic criteria be produced, and interim guidelines for public health interventions be introduced. The International Alliance for the Control of Scabies (IACS) generated criteria for the diagnosis of scabies in 2018, with further development in 2020. It was proposed that the diagnosis can be made at one of three levels of certainty: confirmed, clinical, or suspected scabies.

RESEARCH IN GERMANY 2018-2022

Funding & Sponsors German projects	Public funding	Private funding
Funding in euro	Not reported	Not reported
Sponsors	Not reported	Not reported

Publication & Authorship	Overall publications (% Change 2013-2017)	German publications ¹ (% Change 2013-2017)	German affiliations (Leading position) ²
Publications	646 (+54.2%)	33 (+106.3%)	144 (38)

¹ An overview of the included German publications can be found in the appendix,

² Total number of all German researchers named in publications, multiple naming of individual researchers by inclusion in different publications, as well as multiple affiliation possible; leading authors are first- last- or corresponding authors Positions

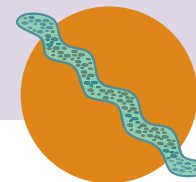
Scientific transfer of German research	Number of German trials (international)/ patents
Clinical trials	2 German studies, 30 studies without German participation (Phase 1-4)
Patents	8 German patents, 4 Scabies specific

ASSESSMENT OF THE GERMAN RESEARCH CONTRIBUTION

- ▶ There is no known research project on scabies conducted by German university institutions nor funded projects.
- ▶ More efforts are necessary from German funding bodies and researchers and university institutions from Germany for the control and elimination of scabies.

NEEDS ASSESSMENT AND CONCLUSION

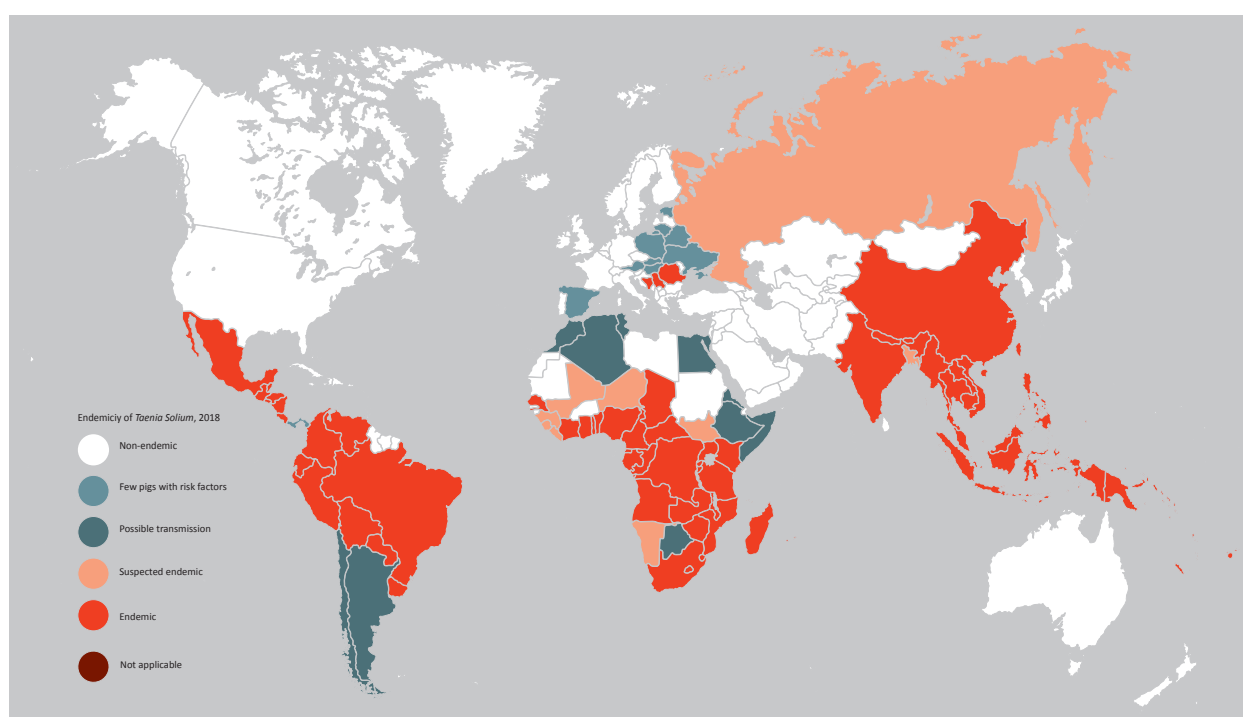
Increasing numbers of scabies cases have been reported from various countries in the past two decades. The COVID-19 pandemic has seen additional increased scabies transmission. Scabies commonly remains unrecognized and is therefore not treated accordingly despite available treatment options. There is a need for synergistic action from all stakeholders including healthcare professionals, government institutions, and non-governmental organizations. A goal to be set for every country when developing strategic plans for the control of community spread scabies may be the proper education of whole populations and the accurate data and proper disease reporting.



SHORT SUMMARY

Taenia solium taeniasis/(neuro)cysticercosis (TSCT) is the most important food-associated parasitic disease and occurs mainly in sub-Saharan Africa, Latin America and Southeast Asia. Humans become infected through undercooked, cyst-infected pork. The cysts develop into adult tapeworms (taeniasis) in the human intestine. Humans excrete parts of tapeworms (proglottids) and infectious eggs. These are ingested by pigs (intermediate host) through coprophagy or by humans themselves (accidental host) due to poor hygiene. The result is cysticercosis (porcine and human), which most times manifests as neurocysticercosis (NCC) in humans. Intestinal taeniasis is often asymptomatic. Combination anthelmintic therapy for symptomatic NCC appears to be superior to monotherapy, however, side effects have not been well established so far; diagnosing TSCT is often complex.

DISTRIBUTION



EPIDEMIOLOGY AND OPTIONS FOR CONTROL

Population affected	<i>T. solium</i> : 5.5 million people infected worldwide; NCC: the most common parasitic cause of epilepsy in endemic countries (up to 30% of all epilepsies; 2.8 million DALYs); Taeniasis: 2-6% in TSCT endemic areas.
New cases/ death rate (per 100,000/year)	New cases not reliably known; deaths from NCC approx. 28,000 per year.
WHO control strategy	Mass drug administration with anthelmintic drugs (MDA) for taeniasis; vaccination and drug treatment of pigs; slaughter with meat inspection; improvement of sanitary facilities and compliance with hygiene rules after using the toilet and before food preparation; health education with involvement of affected populations; evidence-based treatment of NCC; application of the One Health approach.
Status of therapy (side effects)	NCC: praziquantel/albendazole + steroids; side effects: perifocal cerebral edema with potential neurological signs/symptoms, gastrointestinal symptoms; Taeniasis: praziquantel, niclosamide; side effects for praziquantel as under NCC, especially in patients with asymptomatic NCC cysts in the brain; NCC treatment guidelines by WHO, MDA guidelines for taeniasis by PAHO; lack of systematic/controlled studies and meta-analyses.
Available vaccinations	Only for porcine cysticercosis (e.g. TSO18).
Diagnostics available	NCC: serology (serum and cerebrospinal fluid), magnetic resonance imaging, cerebral computed tomography, PCR from cerebrospinal fluid; Taeniasis: microscopy/antigen ELISA of stool samples Serological diagnostics not yet optimal in terms of sensitivity and specificity; first indications of suitability of a cysticercosis rapid test for the diagnosis of active, symptomatic NCC.

STATUS QUO, PROBLEMS AND SETBACKS

TSCT is a public health problem, especially in Africa, and an important zoonosis. The three pillars of the NTD Roadmap 2030 include acceleration of programmatic measures; intensification of cross-sectoral approaches, e.g. One Health concept; promotion of national responsibility. In detail, these are: development of diagnostics, planning, governance, project management and evaluation, access and logistics, as well as advocacy and financing; for TSCT this means: improvement of diagnostics, therapy and prevention, e.g. vaccines in the veterinary field; intensified TSCT control in hyperendemic areas in the human field; increased engagement by governments; more lobbying by the WHO, FAO and WOAHA necessary.

RESEARCH IN GERMANY 2018-2022

Funding & sponsors German projects	Public funding	Private funding
Funding in euro	4.431.293 €	Not reported
Sponsors	DFG, BMBF	Not reported

Publication & Authorship	Overall publications (% Change 2013-2017)	German publications ¹ (% Change 2013-2017)	German affiliations (Leading position) ²
Publications	953 (-8.3%)	53 (+70.9%)	182 (55)

¹ An overview of the included German publications can be found in the appendix,

² Total number of all German researchers named in publications, multiple naming of individual researchers by inclusion in different publications, as well as multiple affiliation possible; leading authors are first- last- or corresponding authors Positions

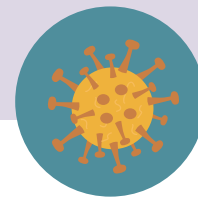
Scientific transfer of German research	Number of German trials (international)/ patents
Clinical trials	1 German study, 9 studies without German participation (Phase2-4)
Patents	6 German patents, 0 Taeniasis / Cysticercosis specific

ASSESSMENT OF THE GERMAN RESEARCH CONTRIBUTION

- ▶ In international comparison, in comparison to research on other neglected diseases and in view of the global importance of TSCT, the German contribution is clearly underrepresented.
- ▶ In recent years, Germany has been involved in large-scale epidemiological, diagnostic and therapeutic TSCT studies in collaboration with African partners.
- ▶ In particular, there are no research activities in Germany in the development of a human vaccine against taeniasis and/or cysticercosis as well as prognostic and diagnostic biomarkers, especially in basic sciences.

NEEDS ASSESSMENT AND CONCLUSION

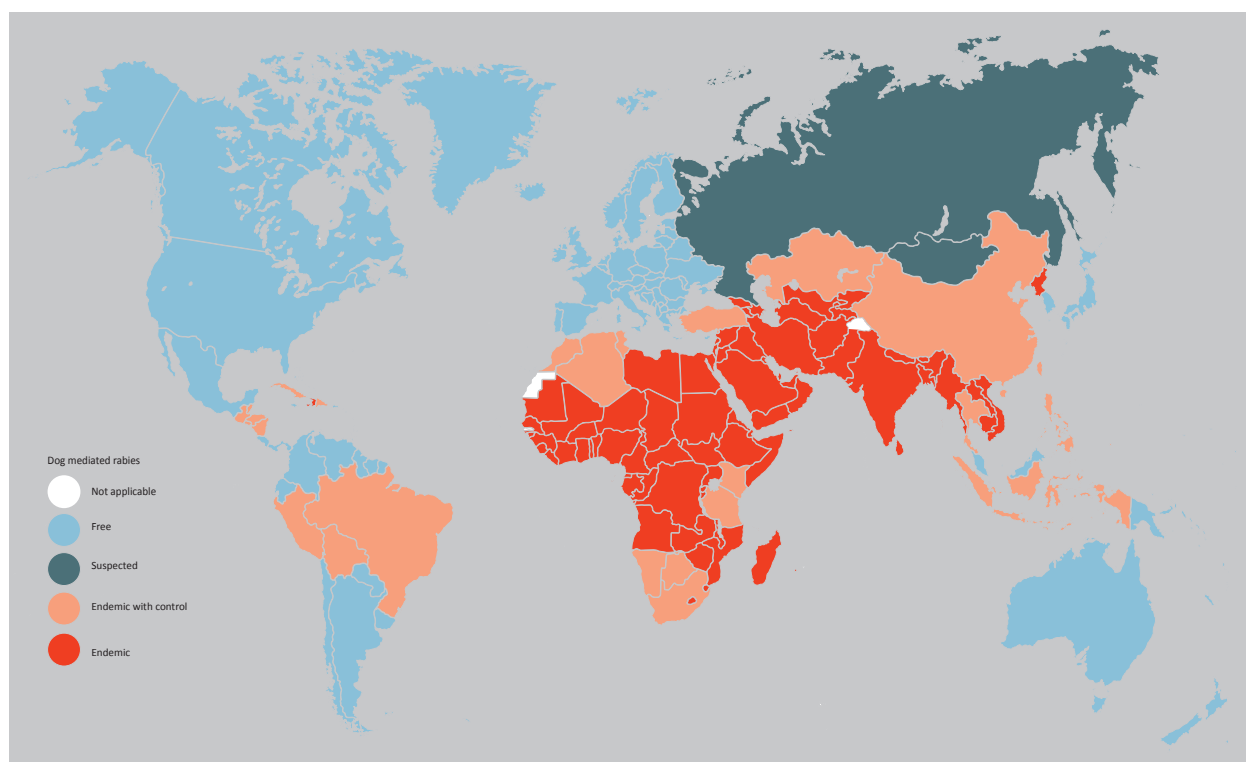
Need for field-ready rapid tests (in humans and pigs), antigen and antibody tests for both species already developed/or are under development; lack of development of biomarkers for the diagnosis of NCC complementary to radiological imaging and for therapy indications; need for clinical trial for pediatric doses and drug formulations of albendazole, praziquantel and steroids; confirmation of the superiority of combination anthelmintic therapy for the treatment of active symptomatic NCC compared to monotherapy in randomized controlled trials; development of strategies to implement the WHO NCC treatment guidelines in order to promote the acceptance by health workers including medical staff on site; need for increased networking of existing research activities and platforms from different disciplines (e.g. human medicine, veterinary medicine, nutritional sciences, etc.).



SHORT SUMMARY

Rabies is the only viral neglected zoonosis in the world and is one of the NTDs with the highest Disability Adjusted Life-Years (DALYs). It is caused by neurotropic RNA viruses of the *Rhabdoviridae* family, genus *Lyssavirus*. Canine-mediated rabies is of particular importance for human infection. People, especially children, are particularly affected in developing and emerging countries in Africa and Asia. Infection occurs through the bite of diseased animals that excrete the virus with saliva or through contact of mucous membranes with saliva containing the virus. Without immediate post-exposure prophylaxis, infection will inevitably lead to death.

DISTRIBUTION



EPIDEMIOLOGY AND OPTIONS FOR CONTROL

Population affected	Although 100% preventable, it is estimated that approximately 59,000 people die each year from rabies infection (95% CI 25,000 – 159,000). Worldwide, 3.7 million DALYs are lost due to dog-mediated rabies.
New cases/ death rate (per 100,000/year)	Unknown, geographically heterogeneous.
WHO control strategy	Elimination of canine and wild animal rabies by parenteral or oral mass vaccination of reservoir animals, preventive (PreP) and post-exposure prophylaxis (PEP) in humans; Integrated Bite Case Management. Global Strategic Plan: Eliminate Zero by 30 by 2030.
Status of therapy (side effects)	There are no established therapies, only palliative treatment with a focus on pain control, sedation, anxiolysis and convulsive suppression.
Available vaccinations	Yes. Preventive and post-exposure vaccination and treatment regimens available.
Diagnostics available	Post mortem: Antigen, RNA detection, virus isolation from brain material, commercial point-of-care (POC), rapid test can only be used to a limited extent and after prior validation. Ante mortem: Clinical symptoms, RNA detection from saliva, tear fluid (samples taken at several time points) or biopsies (neck skin, brain). Antibody diagnosis not suitable due to pathogenesis of the pathogen.

STATUS QUO, PROBLEMS AND SETBACKS

Very slow implementation of the WHO/WOAH/FAO global strategic plan “Zero by 30”. Tripartite *United Against Rabies* (UAR) Forum established to strengthen cross-sectoral approaches. Despite international efforts, rabies has not yet been taken into account by the international vaccine alliance GAVI. Availability and quality of data on rabies surveillance and global consequences of rabies regionally inadequate. Problems are (i) lack of availability of immunoglobulins for PEP in Africa and Asia; (ii) no reduced vaccination regimens or therapy available; (iii) control strategies for canine and wild animal rabies suboptimal.

RESEARCH IN GERMANY 2018-2022

Funding & Sponsors German projects	Public funding	Private funding
Funding in euro	Not reported	Not reported
Sponsors	Not reported	Not reported

Publication & Authorship	Overall publications (% Change 2013-2017)	German publications ¹ (% Change 2013-2017)	German affiliations (Leading position) ²
Publications	1.565 (+ 13.8%)	72 (-1.4%)	274 (67)

¹ An overview of the included German publications can be found in the appendix,

² Total number of all German researchers named in publications, multiple naming of individual researchers by inclusion in different publications, as well as multiple affiliation possible; leading authors are first- last- or corresponding authors Positions

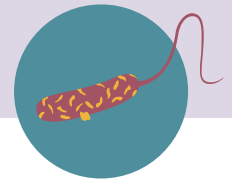
Scientific transfer of German research	Number of German trials (international)/ patents
Clinical trials	1 German study, 48 studies without German participation (Phase 1-4)
Patents	26 German patents, 14 Rabies specific

ASSESSMENT OF THE GERMAN RESEARCH CONTRIBUTION

- ▶ In an international comparison and in view of the global significance of rabies, the German contribution to both basic and applied rabies research is considerable. Within the framework of the G7 and G20, Germany is committed to international support in the fight against zoonoses, including the fight against global canine rabies, and is the largest donor to date.
- ▶ There are no national guidelines or action strategies for research priorities in the field of rabies. Research is orientated towards the recommendations of the WHO. The research mandate of the Friedrich Loeffler Institute (FLI) results from its international status and commitment as WHO CC for Rabies Surveillance and Research and WOAH (World Organisation for Animal Health) reference laboratory for rabies.
- ▶ The German contribution to scientific publications is comparatively large, but is limited almost exclusively to work by the FLI and thus to rabies in animals.

NEEDS ASSESSMENT AND CONCLUSION

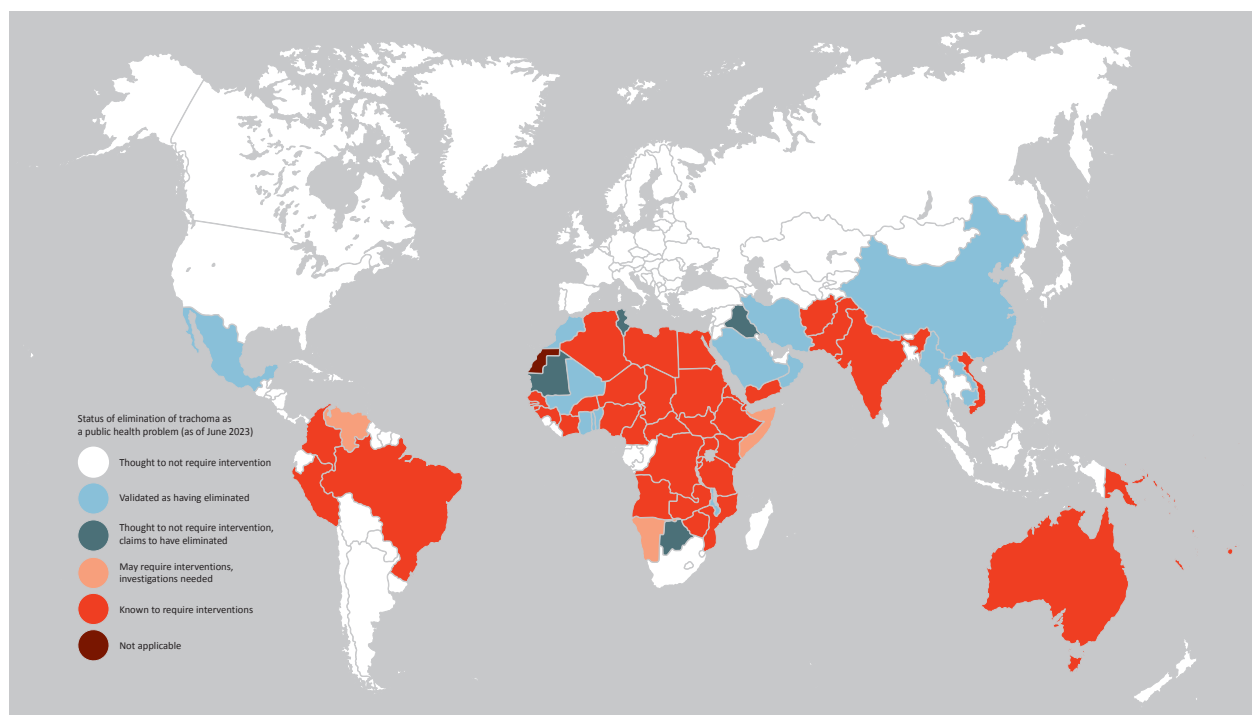
Rabies surveillance and the availability/quality of data on the disease and its global consequences urgently need to be intensified or improved. New (combination) and cross-reactive (against other lyssaviruses) vaccines for humans and universal oral vaccines for carnivorous reservoir animal species need to be developed. Due to the lack of availability of current formulations, there is an urgent need to develop alternative immunoglobulin preparations (monoclonal antibodies) for PEP. There is an urgent need for research into reduced vaccination regimens for PreP and PEP with the same long-term effect due to limited vaccine availability. There is an urgent need for operational and implementation research to improve the efficiency of established control strategies in reservoir animal species (dogs, wild animals).



SHORT SUMMARY

Trachoma is the leading infectious cause of blindness. The pathogen, serotypes of the bacterium *Chlamydia trachomatis*, is transmitted through direct contact with infectious eye or nasal secretion or eye-seeking flies. Repeated conjunctival infections lead to scarring and trichiasis, which can be corrected through a relatively simple eyelid surgery. Left untreated, the cornea becomes cloudy leading to irreversible loss of vision. Women are affected 1.8 times more often than men. Trachoma can be eliminated as a public health problem with a package of interventions known as SAFE strategy. Despite significant progress, trachoma remains a public health problem particularly in parts of Africa. The German contribution to trachoma research remains limited.

DISTRIBUTION



EPIDEMIOLOGY AND OPTIONS FOR CONTROL

Population affected	In 25th April 2023, 115.7 million people at risk, lived in districts with an active trachoma prevalence above elimination threshold (84% in Africa, incl. 52% in Ethiopia) and 1.5 million people were estimated to require surgery for potentially blinding trichiasis.
New cases/ death rate (per 100,000/year)	Not known, no direct deaths caused by trachoma.
WHO control strategy	SAFE strategy, comprising Surgery for Trachomatous Trichiasis (TT), Antibiotics to clear ocular <i>C. trachomatis</i> infection, Facial cleanliness, and Environmental improvement to reduce transmission. Eyelid surgery (S) should be offered to any individual considered to benefit. A, F and E components are recommended for populations with a prevalence of active trachoma above elimination threshold, with all eligible residents offered antibiotic treatment annually, the number of rounds depending on the prevalence.
Status of therapy (side effects)	The very few major side effects include choking and allergic reactions to antibiotics and post-operative TT. By July 2023, 17 countries have been validated by WHO as having eliminated trachoma. In 2022, 128,224 people were managed for TT; 71% were females and 73% of surgeries were done in Ethiopia. 36.2 million people received antibiotics; 52% were females and 51% of treatments were given in Ethiopia.
Available vaccinations	No vaccination available.
Diagnostics available	Defined clinical criteria to indicate when to treat; laboratory markers (PCR, serology) to confirm current or previous infection (e.g. to inform programs and for research).

STATUS QUO, PROBLEMS AND SETBACKS

Despite advances, trachoma remains a major health problem particularly in Africa. The elimination target is achievable based on country ownership, community centered approaches and global partnership. New diagnostic tools and vaccines will become relevant especially during the endgame (e.g. slower than expected progress, surveillance). There is need for research (i) to further improve the outcomes for patients with TT; (ii) on effective crosscutting collaboration e.g. with WASH, eye health, education, One Health and disability inclusion; (iii) on the safety and effectiveness of integrated interventions in populations with multiple NTDs; (iv) on adequate and sustained external and domestic funding.

RESEARCH IN GERMANY 2018-2022

Funding & Sponsors German projects	Public funding	Private funding
Funding in euro	289.779 €	Not reported
Sponsors	BMBF	Not reported

Publication & Authorship	Overall publications (% Change 2013-2017)	German publications ¹ (% Change 2013-2017)	German affiliations (Leading position) ²
Publications	1.899 (+20.8%)	77 (-10.5%)	734 (125)

¹ An overview of the included German publications can be found in the appendix,

² Total number of all German researchers named in publications, multiple naming of individual researchers by inclusion in different publications, as well as multiple affiliation possible; leading authors are first- last- or corresponding authors Positions

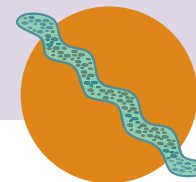
Scientific transfer of German research	Number of German trials (international)/ patents
Clinical trials	0 German study, 13 studies without German participation (Phase2-4)
Patents	1 German patent, 4 Trachoma specific

ASSESSMENT OF THE GERMAN RESEARCH CONTRIBUTION

- ▶ Relative to other major donor countries, in comparison to research for other NTDs and reflecting the importance of trachoma globally and especially in Africa, the German contribution in the area of trachoma relevant research must be considered as small.
- ▶ Since the last 2018 expertise, there has been laudable capacity development for operational research at BNITM. However, trachoma relevant research has not yet been included / addressed there.
- ▶ There is only a fragmented engagement by German institutions with global NTD research platforms such as the COR-NTDs with limited engagement in trachoma research.

NEEDS ASSESSMENT AND CONCLUSION

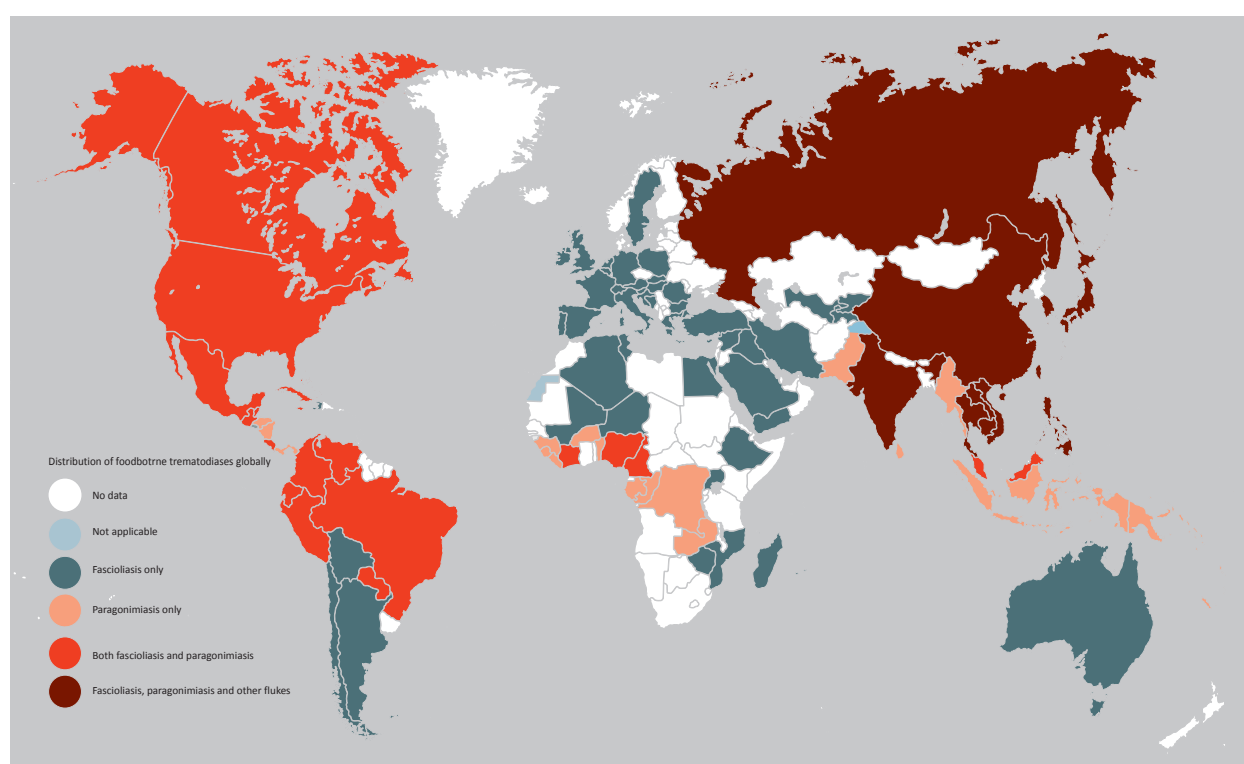
Much of the German trachoma research focus remains on basic pathogen biology. This could assist in the development of new diagnostics and vaccines especially relevant during the endgame and post-elimination period. The safety, effectiveness, efficiency and sustainability of integrated disease management need to be tested through implementation research. In order to effectively utilize existing German research expertise in areas outlined above, it is necessary to engage with local research institutions (e.g. capacity development, coordination) and global platforms such as the "Network of WHO Collaborating Centers for Trachoma". With sufficient additional resources, the WHO elimination target for trachoma is achievable.



SHORT SUMMARY

Clonorchis sinensis, *Opisthorchis viverrini* and *O. felinus* (small liver flukes); *Fasciola hepatica* and *F. gigantica* (large liver flukes) with worldwide spread. Infections via consumption of insufficiently heated fish and crustaceans (small liver flukes), direct infection with metacercariae in water (large liver flukes) or aquatic plants (*Fasciolopsis buski*). Other trematodes with lower prevalence (*Dicrocoelium* spp., *Echinostoma* spp., *Paragonimus kellicotti* and *Pseudamphistomum truncatum*). Colonization of the bile ducts (*Fasciola* spp., *Clonorchis*, *Opisthorchis* spp.), the lungs (*Paragonimus* spp.), or the intestine (*Fasciolopsis*) and long persistence. Complications such as central nervous system involvement (*Fasciola* spp., *Paragonimus* spp.). *O. viverrini* and *C. sinensis* are carcinogenic (cholangiocarcinomas), *O. felinus* as a carcinogen is discussed.

DISTRIBUTION



EPIDEMIOLOGY AND OPTIONS FOR CONTROL

Population affected	All age groups are affected. High levels of contamination when eating raw fish, crustaceans, snails and amphibians; or through water or aquatic plants.
New cases/ death rate (per 100,000/year)	WHO total annual cases: 200,000 cases/year, 7,000 deaths/year (DALYs 1.1 million/year).
WHO control strategy	Targeted treatment (incl. school children), in endemic areas (mass drug administration); improvement of hygiene, sanitation and information.
Status of therapy (side effects)	Praziquantel in children six years of age and older: dosage 75 mg/kg/day in three doses (<i>Fasciolopsis</i>); for two days (<i>Clonorchis</i> and <i>Opisthorchis</i>); 25 mg/kg/day in three doses for two days (<i>Paragonimus</i>). Triclabendazole dosage 10mg/kg/day 2x12 hours (<i>Fasciola</i> , <i>Paragonimus</i>).
Available vaccinations	No vaccination available.
Diagnostics available	Microscopic detection of eggs: in stool: <i>Fasciola</i> , <i>Fasciolopsis</i> , <i>Clonorchis</i> and <i>Opisthorchis</i> ; in sputum: <i>Paragonimus</i> . Serology (during prepatency (acute) but also chronic and ectopic infection): <i>Fasciola</i> . Ultrasound (resp. CT, MRI): Liver fluke.

STATUS QUO, PROBLEMS AND SETBACKS

Trematodes occur endemic across all continents except Antarctica, control with praziquantel and triclabendazole in animals and humans. No fight against the stages of development. Economic dependence on cattle, sheep (*Fasciola*) and pigs (*Fasciolopsis*) and thus a significant zoonosis. Mollusks, fish, shellfish and aquatic plants are important food sources in Southeast Asia and China. Active ingredients limited to praziquantel and triclabendazole.

At the moment, no new research approaches, immunological approaches or vaccines. *Fasciola* resistance to triclabendazole is known. No eradication aimed under the 2030 Roadmap, but put out to tender for control. Public health measures in the areas of governance, monitoring of intervention measures, as well as an improvement of the health care system are necessary.

RESEARCH IN GERMANY 2018-2022

Funding & Sponsors German projects	Public funding	Private funding
Funding in euro	Not reported	Not reported
Sponsors	Not reported	Not reported

Publication & Authorship	Overall publications (% Change 2013-2017)	German publications ¹ (% Change 2013-2017)	German affiliations (Leading position) ²
Publications	3.226 (-0.4%)	144 (-6.5%)	616 (138)

¹ An overview of the included German publications can be found in the appendix,

² Total number of all German researchers named in publications, multiple naming of individual researchers by inclusion in different publications, as well as multiple affiliation possible; leading authors are first- last- or corresponding authors Positions

Scientific transfer of German research	Number of German trials (international)/ patents
Clinical trials	0 German studies, 2 studies without German participation
Patents	7 German patents, 1 Trematodes specific

ASSESSMENT OF THE GERMAN RESEARCH CONTRIBUTION

- Compared to research on other NTDs and in view of the global significance of food-borne trematodes, Germany's contribution is very low globally, especially compared to endemic countries such as China and Thailand.

NEEDS ASSESSMENT AND CONCLUSION

Diagnostics: The development and evaluation of more sensitive and specific serological diagnostics and PCR, especially for *Fasciola*. The development and provision of point-of-care differential diagnostic methods (*Fasciola* and *Fasciolopsis*). One Health approach for control: Monitoring of diseases in animals and humans. Investigations into the risk to persons through surveillance and monitoring. Evaluation of best One Health measures through implementation research.

Research and development of new classes of drugs with efficacy against cestodes and trematodes in animals and humans is needed due to reported resistances against praziquantel and triclabendazole.



Appendix

The appendix contains the complete search syntax, supplementary results and a discussion of the methodology. The attachment is available via the following link:

<https://www.bnitm.de/forschung/forschungsgruppen/population/abt-infektionsepidemiologie/laborgruppe-fusco/dissemination-and-awareness-activities/ntd-expertise>

This study was made possible by the support of the Federal Ministry of Education and Research (BMBF).

The opinions included in this text are the responsibility of the authors and do not fundamentally reflect the position of the funding body.

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