Secondary Supporting Background Material for Working Papers 1 & 2:

Working Paper 1: Priority Research Areas for Basic Science and Product Development for Neglected Diseases. Sue J. Goldie[1,2], Jennifer S. Edge[1], Christen Reardon[1], Cherie L. Ramirez[1,2] *

Working Paper 2: An Initial Scan of Priority Research Areas for Public Health, Implementation Science and Innovative Financing for Neglected Diseases. Jennifer S. Edge[1] **, Steven J. Hoffman[1,2,3], Cherie L. Ramirez[1,2], Sue J. Goldie[1,2]

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Table of Contents for Working Papers 1 & 2 Secondary Supporting Background Material:

**To keep supporting materials from all five disease areas together for this Secondary package, we have included "Part 3: Bundled Disease-Specific Reports for Malaria" from Working Paper 1 & 2 Supplementary Material, here entitled "Part 1: Bundled Disease-Specific Reports for Malaria."*

Disease-specific R&D priority setting

MALARIA

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
1. Program for Appropriate Technology in Health (PATH). Staying the Course? Malaria Research and Development in a Time of Economic Uncertainty. Seattle: PATH; 2011. *The paper provides an overview of the current R&D landscape for products related to malaria treatment and control, including drugs, vaccines, vector control products, and diagnostics. It also presents a detailed breakdown of the types of R&D funding, such as type of research, source of funding, and institution type.*	The status of malaria funding was assessed using investment data for 2004 from the Malaria R&D Alliance report29 and investment data for 2007 to 2009 from the G-FINDER survey. In the sections referring to vector control products, G-FINDER data were supplemented by expert estimates of industry investment (noted in each case). The 2004 data presented in the Malaria R&D Alliance report were collected via an online survey completed by 79 organizations globally in May 2005. Three categories of organisations were surveyed (funders, funding managers and researchers and developers), and funding was captured in six R&D categories: basic research, antimalarial drug discovery and	A. Basic science • None identified B. Diagnostics • Enhance the quality and stability of currently available rapid diagnostic tests (RDTs) C. Drugs • Develop new, shorter-regimen therapies • Explore formulations that are more appropriate for vulnerable populations • Accelerate the development of new drugs to combat resistance D. Preventative vaccines • Identify more effective vaccine candidates E. Therapeutic vaccines • None identified F. Vector control • Determine ways to reduce reliance on pyrethroids for vector control due to the risk of resistance • Develop new active vector control ingredients	A. Basic science • None identified B. Diagnostics • Improve RDTs' ability to detect non-*falciparum* parasites • Develop new and improved tools for field detection of very low-density parasitaemia, including non-*falciparum* parasites • Identify ways to enhance screening for enzymatic deficiency, i.e. G6PD deficiency • Scale up research on future targets that include automated microscopy and non-invasive sampling through analysis of saliva or urine • Develop tests to detect non-malarial febrile disease pathogens or markers of infection requiring specific treatment C. Drugs • Develop a single-dose cure to replace the current three-day drug regimen • Identify ways to enhance the safety and suitability of treatment regimens for children • Develop more treatment options for pregnant women • Focus on a radical cure for *P. vivax* • Create novel compounds to tackle artemisinin resistance and transmission-blocking antimalarials D. Preventative vaccines

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	development, vaccine development and vaccine trials, vector control research, development of malaria diagnostics and implementation research. R&D categories overlap considerably with the product R&D categories used in G-FINDER and were assumed to be fully comparable. The only exception was implementation research that is not included in the G-FINDER survey and was therefore excluded from analysis. Furthermore, the Malaria R&D Alliance report did not break the six R&D categories into sub-areas (such as discovery and development), which meant authors were unable to include the 2004 data in analysis of which organisations are conducting which types of research and product development.	G. Epidemiology • None identified H. Health systems/public health research • Develop monitoring systems to detect possible resurgence of malaria I. Innovative financing • Identify ways to encourage and secure investment in malarial vaccine development and severely underfunded pools for diagnostic R&D • Determine how investments in malaria R&D can be more evenly distributed across product portfolios	• Develop a more effective second-generation *P. falciparum* vaccine and new vaccine candidates targeting *P. vivax* E. Therapeutic vaccines • None identified F. Vector control • Explore new paradigms in insecticide delivery, including novel active ingredients for bednets and indoor residual spraying (IRS) G. Epidemiology • None identified H. Health systems/public health research • Determine how to adapt screening and monitoring strategies so that a possible resurgence of malaria can be picked up rapidly I. Innovative financing • Investigate ways to make R&D funding, particularly in the public sector, more flexible and responsive to global portfolio developments and goals • Identify ways in which funders can be given improved information and tools to allow them to better coordinate funding and portfolio decisions; this includes the public, philanthropic and private sectors • Find ways to engage more funders in malaria R&D, including more economically advanced countries (G8/G20/Organisation for Economic Co-operation and Development), and research and science and technology agencies in both existing

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			and new donor countries • Determine how to maintain PDP funding since PDPs account for nearly half of the current product pipeline and virtually all new malaria products delivered in the past five years • Identify ways to ramp up funding to $220–230 million per year from 2016 and beyond to fund late-stage trials of the anticipated second-generation *P. falciparum* vaccine, as well as early preclinical work associated with transmission-blocking vaccines, vaccines for pregnant women and candidate vaccines targeting both *P. vivax* and *P. falciparum*
2. Moran M, Guzman J, Ropars A, Jorgensen M, Potter S, Selassie H. The Malaria Product Pipeline: Planning for the Future. Sydney: The George Institute for International Health/Global Forum for Health Research; 2007. *The report summarizes the findings of a study investigating the clinical development of malaria products and aims to quantify the resources needed for clinical development of the global malaria drug and vaccine portfolio over the five years to 2012,*	Data on vaccine candidates from 1984 to end 2006 was collated through a literature search of major databases; for example, NCBI Entrez-Pubmed, Cochrane review, and ClinicalTrials.gov. Candidates were deemed to be in pre-clinical development if testing in animals was reported (primate or rodent models), or in clinical development if testing in human subjects had commenced. As not all clinical trials are published in the year that they are completed, reviews (from 1997 onwards) and expert interviews relating to historical vaccine development were also assessed.	A. Basic science • Determine the role of antigen diversity for developing vaccine candidates B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • Develop more potent vaccine candidates • Promote research into new technology platforms that could increase vaccine potency • Find ways to ensure that vaccines meet batch-to-batch reproducibility E. Therapeutic vaccines • None identified	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • Create and standardize assays, reagents and protocols used at each stage of malaria vaccine product development • Develop a shared set of vaccine ranking criteria based on safety, type of immune response induced, ability to generate a functional antigen, potential formulations and manufacturability • Integrate new technologies or technologies not previously used for malaria vaccines into the research process e.g. adenovirus vectors, prime boost approaches and synthetic peptides • Evaluate technical feasibility during preclinical

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including funding for clinical trials and associated manufacturing and toxicology, and demand for malaria licensure trial sites.	For the historical vaccine snapshots, data was collated using the NCBI Entrez-Pubmed search engine with the keywords MALARIA AND VACCINE for the years 1984-1986 for the 1985 candidates, and 1994-1996 for 1995 candidates. To be included in the snapshot, the vaccine candidates had to be active (either in or between trials) in the years examined. Data relating to malaria clinical trials was collected by conducting desk research on all published clinical trials, with enrolment start and finish dates recorded. Clinical trial registries (e.g. ClinicalTrials.gov) were also sourced to determine actual or expected start and finish dates for past, current, and future trials. This data was cross-referenced with Clinical Development Plans and other trial data collected via on-site visits with product developers and through telephone interviews.	F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Determine how to ensure that trials, including phase IV trials, are allocated to avoid site competition and to maximise site progress along the development trajectory • Identify ways to build on the Malaria Vaccine Technology Roadmap • Determine how to improve the coordination of global R&D and reach agreement on a challenge model for blood-stage vaccine candidates • Clarify and codify a streamlined regulatory pathway to allow the global portfolio to move forward more quickly I. Innovative financing • Provide a clearer picture of the malaria funding gap • Find ways to increase funding for basic malaria vaccine research to avoid shrinkage of the clinical portfolio over time • Identify ways to direct investments	development to successfully scale-up a candidate to a stable, reproducible product E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Identify ways to ensure that all product development sites have an on-site staff training programme • Explore a formal mentoring system and a linked proposal of formal training attachments between younger sites and experienced African licensure sites, Western clinical trial institutions and/or Western pharmaceutical firms • Identify appropriate means to set up/build on a centralised information source on all upcoming licensure and phase IV trials • Determine ways to develop an agreed minimum site audit template and/or develop a shared Trial Site Audit service • Develop an African-based CRO to provide contract staff for clinical trials, including experienced staff and a pool of more junior staff, to mitigate large employment swings at sites I. Innovative financing • Design a donor coordination exercise to collate

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		towards novel malaria technology platforms • Investigate how immunogenic adjuvants can be made more accessible to all malaria vaccine developers	information on their collective forward funding commitments and assess against likely costs • Determine ways to encourage greater pairing of industry innovators with public malaria researchers to develop joint projects • Research incentives or policies to encourage relationships between public and academic vaccine developers and industrial facilities to cut learning curve times, ensure expertise is maintained and facilitate technology transfer • Investigate biotech-relevant policy and incentive options for groups trying high-risk, high-innovation approaches • Design incentives to encourage biotechs wishing to test out novel technologies or constructs to collaborate with well-established product-developers who have the technical skills and experience to make the technology feasible • Explore ways to enhance public-private collaborations to improve manufacturers' access to potent adjuvants • Investigate possible funding streams for contracted industry input to public candidates, e.g. by leveraging the existing manufacturing expenditures through the proposed Industry R&D Facilitation Fund
3. World Health Organization. World Malaria Report 2012. Geneva: World Health Organization; 2012. *The World Report*	Standard reporting forms were sent in March 2012 to the 99 countries with ongoing malaria transmission and two countries that recently entered the prevention of reintroduction phase.	A. Basic science • Improve understanding of artemisinin resistance and how to best manage it • Curtail the transmission of malaria by reducing the human parasite reservoir	A. Basic science • Prioritize in vitro studies to measure the intrinsic sensitivity of parasites to antimalarial drugs • Conduct molecular marker studies to identify genetic mutations and subsequently confirm the presence of mutations in blood parasites • Perform pharmacokinetic studies to characterize

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summarizes the current status of malaria control in all affected countries; it provides a critical analysis and interpretation of data provided by national malaria control programs, and also reviews progress towards internationally agreed targets and goals, describes trends in funding, intervention coverage and malaria cases and deaths on a region and country-specific basis.	Information was requested on (i) populations at risk (ii) vector species (iii) number of cases, admissions and deaths for each parasite species (iv) completeness of outpatient reporting (v) policy implementation (vi) commodities distributed and interventions undertaken (vii) results of household surveys, and (viii) malaria financing. Surveys provide information on the percentage of the population that sleeps under a mosquito net, and of children with fever who are treated and the medication they receive. Information on malaria financing was obtained from the Organisation for Economic Co-operation and Development (OECD) database on foreign aid flows and directly from the Global Fund and the US President's Malaria Initiative (PMI).	B. Diagnostics • None identified C. Drugs • Routinely conduct therapeutic drug efficacy studies • Confirm and better characterize drug resistance • Prioritize research products that reduce morbidity and mortality by ensuring rapid, complete cure of *Plasmodium* infection, thus preventing the progression of uncomplicated malaria to severe and potentially fatal disease, as well as preventing chronic infection that leads to malaria-related anaemia D. Preventative vaccines • Prioritize the development and distribution of a licensed malarial vaccine E. Therapeutic vaccines • None identified F. Vector control • Identify ways to reduce the intensity of local malaria transmission at the community level by reducing vector longevity, human-vector contact and density of the local vector mosquito population • Consolidate all available data on	drug absorption and drug action in the body B. Diagnostics • None identified C. Drugs • Measure the clinical and parasitological efficacy of medicines and the detection of small changes in treatment outcome over time D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • Find means to ensure that decisions regarding the choice of insecticide are supported by adequate and up-to-date information on resistance among local anopheline vectors • Determine the extent to which chloroquine-resistant *P. vivax* has spread • Develop new insecticides appropriate for use on insecticide-treated nets G. Epidemiology • None identified H. Health systems/public health research • Determine how to develop resistance monitoring using both bioassay (susceptibility) tests and genetic methods • Determine why discrepancies between urban and rural areas, and between wealth quintiles,

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		vector resistance • Develop new insecticidal agents and other interventions that do not rely on insecticides G. Epidemiology • Investigate how to improve malaria surveillance systems for better case detection, particularly in high-burden settings H. Health systems/public health research • Investigate how to intensify resistance monitoring • Investigate why there are discrepancies in access to treatment for vulnerable groups such as infants and pregnant women • Investigate how diagnosis and treatment can be provided at the community level through a programme of community case management in under-resourced settings • Find ways to scale-up intermittent preventative treatment (IPT) for pregnant women (IPTp) and infants (IPTi) • Learn how to expand universal diagnostic testing in the public and private sectors • Investigate how to scale up universal access to long-lasting insecticidal nets (LLINs)	exist in the uptake of intermittent preventative treatment (IPTp) among pregnant women in some countries, and how the approach for a more equitable scale-up of IPTp can be replicated in other countries • Determine how to expand the new strategy targeting the diagnosis and treatment of malaria, pneumonia and diarrhoea at community levels termed integrated community case management (iCCM) of childhood illness • Develop information systems that link diagnostic testing and treatment data I. Innovative financing • None identified

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		I. Innovative financing • Examine new ways to make existing funds stretch further by increasing the value for money of malaria commodities and the efficiency of service delivery	
4. World Health Organization Global Malaria Programme. Global Plan for Insecticide Resistance Management in Malaria Vectors. Geneva: World Health Organization; 2012. *The WHO's Global Plan for Insecticide Resistance Management in Malaria Vectors provides an overview of the threat of insecticide resistance, its impact on malaria control, and available / future strategies for managing resistance. The report also presents an overview of the results of the WHO Malaria Rapid Diagnostic Test (RDT) Product Testing.*	The RDT evaluations summarized in the report were performed as a collaboration between WHO, TDR, FIND, the US Centers for Disease Control and Prevention (CDC) and other partners. All companies manufacturing under Quality System Standard were invited to submit a limited number of products (2–3) for evaluation under the programme. Of these 168 total products, 164 progressed to testing against panels of patient-derived P. falciparum and P. vivax parasites, and a parasite-negative panel. Thermal stability was assessed after two months of storage at elevated temperature and humidity, and a descriptive ease of-use assessment was recorded. The evaluation is designed to	A. Basic science • Investigate how to fill existing gaps in knowledge about insecticide resistance mechanisms • Better understand the fundamental genetic processes of the spread of resistance • Develop new methods to assess the impact of resistance on malaria transmission B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • Identify new active ingredients for insecticides with different modes of action	A. Basic science • Identify clear genetic markers for important oxidase-mediated forms of resistance to pyrethoids • Discover genetic mutations responsible for metabolic resistance to pyrethoids in different geographical settings • Utilize high-throughput DNA-based methods to identify resistant genes • Find ways to colonize a range of vector strains resistant to different insecticides in different locations • Better understand genetic dominance, fitness cost, cross-resistance, linkage, disequilibrium, drivers of selection pressure and behavioural resistance B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines

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	provide comparative data on the performance of the submitted production lots of each product. Such data will be used to guide procurement decisions of WHO and other UN agencies and national governments. Product testing is part of a continuing programme of work to improve the quality of RDTs that are used, and to support broad implementation of reliable malaria diagnosis in areas where malaria is prevalent. A fifth round of product testing will begin in January 2013.	• Find ways to reduce reliance on insecticides in controlling malaria transmission G. Epidemiology • Gather epidemiological evidence that supports the development of new, innovative vector control paradigms • Assess current epidemiological methods to inform decision-making globally and nationally H. Health systems/public health research • Investigate how to effectively manage insecticide resistance • Create a defined system for evaluating the evidence for new forms of vector control I. Innovative financing • None identified	• None identified F. Vector control • Develop innovative, non-insecticide-based vector control tools (e.g. spatial repellents, area-wide treatments, traps and targets, and animal treatments) G. Epidemiology • Conduct epidemiological testing for durable wall lining to complement IRS for wide-scale implementation • Revise epidemiological malaria models to include insecticide resistance • Create an aggregated global database to provide global direction on insecticide resistance monitoring H. Health systems/public health research • Investigate how to measure the impact of resistance on the effectiveness of vector control • Conduct small-scale trials to assess the relative effectiveness of resistance management strategies in delaying the emergence of resistance and killing resistance vectors • Explore the formation of the WHO's proposed "vector control advisory group" for making recommendations on new vector control tools for public health purposes I. Innovative financing • None identified

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5. PLOS Medicine. malERA: a Research Agenda for Malaria Eradication. Barcelona: The Barcelona Centre for International Health Research; 2011. *The PLOS Research Agenda for Malaria Eradication Report is a compilation of publications that address the research agenda to eradicate malaria globally. This report is sponsored by The Malaria Education Research Agenda (malERA), an initiative that complements the current research agenda by identifying key knowledge gaps and defining the strategies and tools that will result in malaria eradication.*	Funded by the Bill and Melinda Gates Foundation, malERA aims to define the critical knowledge base, strategies, and tools required to reduce the basic reproduction rate (R0 or the number of secondary cases arising from a single case) to less than one. Scientists involved in malaria research were challenged to develop a multidisciplinary, global research and development agenda that would be actionable by research and public health agencies and funders/sponsors and available for discussion and debate through publication in a readily accessible format. The process engaged more than 250 scientists in a series of 20 consultations around the world (Figure 2) and was managed by a three-tier governance structure (Figure 3). This report briefly introduces the work undertaken by the various malERA Consultative Groups.	A. Basic science • Transition research away from "parasite-first" approaches to an examination of host-parasite-vector population interactions • Better understand the stage-specific biology of the parasite. • Define desired target product profiles, incorporating new approaches from different fields • Investigate how basic research can inform future strategies for the development of next-generation interventions and therapeutics • Identify roadblocks that prevent the scale-up of genetic manipulation and functional analysis of essential genes B. Diagnostics • Develop stable tests for case management in low-training, low technology settings with sensitivity sufficient for community level case management • Identify tools that can rapidly detect and monitor unexpectedly high transmission that lead to outbreaks and that can identify reintroduction of infections that may be asymptomatic C. Drugs • Optimize research on currently available malaria drugs	A. Basic science • Examine the entire parasitic life cycle-based approach to better understand transitions from one host to another • Distinguish essential metabolic pathways through systematic mutagenesis on a genome-wide scale • Investigate how new technology platforms can permit deep characterization of the metabolome • Design research studies aimed at understanding the epidemiology of the gametocyte • Develop an efficient, inexpensive P. Vivax blood-stage culture system • Create in vitro systems to understand P. Falciparum, P. Vivax and hypnozoite biology as it relates to liver-stage biology • Conduct mechanism of action studies for drugs and vaccines in the current pipeline to inform future strategies • Find ways to improve technologies for the manipulation of Plasmodium • Learn how to implement systems-based approaches in order to incorporate cutting-edge technology (e.g. metabolomics) • Utilize technologies from physical, chemical, and biomedical engineering sciences to improve molecular understanding of parasite development biology • Introduce new technologies to address roadblocks, such as: low frequency of homologous recombination in Plasmodium, difficulties associated with the manipulation of large fragments of AT-rich and repetitive genomic DNA, and the lack of robust and scalable systems for conditional gene expression

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		• Develop new, innovative drugs for malaria eradication • Produce drugs that can be administered in a single encounter at infrequent intervals, and that result in radical cure of all parasite stages (Single Encounter Radical Cure and Prophylaxis) • Design safer, more efficient drugs for pregnant women • Find ways to address the emergence of artemisinin resistance D. Preventative vaccines • Create a vaccine that targets both the sexual and mosquito stages (transmission-blocking) and the pre-erythrocytic and asexual stages • Develop a vaccine that targets multiple malaria parasite species • Explore novel approaches to elicit longer-lasting protective efficacy • Understand the dynamics between the multiplication of asexual stage parasites, gametocytogenesis, and malaria transmission rates at population level E. Therapeutic vaccines • None identified F. Vector control • Understand the ecology, behaviour, and genetic population structure of malaria vectors	B. Diagnostics • Design antigen-detecting RDTs with greater consistency in P. Falciparum detection and stable tests to detect non-P. Falciparum parasites • Discover a robust, sensitive, and specific standardized method for assessment of transmission intensity in the intervening period when transmission continues at low levels • Create tests that can detect resistance to artemisinins and ACT partner drugs • Standardize low-cost positive controls for antigen-detecting RDTs suitable for field use • Create sustainable tools for quality control of RDTs at the country level • Investigate non-blood sampling to determine the potential for detecting recoverable antigen in samples. • Develop consistent, reliable staining methods for microscopy • Map and identify G6PD deficiency (if 8-aminoquinolones are to be used) and create tools for field G6PD detection • Develop tools to standardize and improve microscopy interpretation • Create tools for hypnozoite detection and further research hypnozoite biology and biomarkers • Develop field applicable tools for minimally invasive, rapid detection of low-density parasitemia in a high-throughput manner • Identify improved assessment methods (e.g. better serological tests, minimally invasive biomarkers)

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		• Find ways to maintain sustained commitment to the long-term development of novel vector control approaches • Create a coherent research agenda for discovering and developing a broader range of insecticides G. Epidemiology • Create surveillance tools with potential for major operational impact H. Health systems/public health research • Develop a toolkit that allows for effectiveness decay analysis for identifying bottlenecks for effective coverage of malaria interventions and decisions on the degree of integration of interventions into existing and strengthened health systems • Integrate new approaches into the planning of elimination, surveillance, monitoring, and evaluation, and to create appropriate interfaces for different user communities. • Develop an essential platform for studying the biology of the liver stages and sexual forms of parasites • Conduct systems analyses of transcription, proteome, and metabolome libraries, rapid screening of drug libraries, high-	C. Drugs • Perform pharmacology studies to optimize dosing regimens of 8-aminoquinolines for gametocytocidal and anti-relapse efficacy and safety • Develop rapid and robust point-of-care glucose-6-phosphate dehydrogenase (G6PD) test to improve safety of 8-aminoquinoline use • Determine gametocytocidal and anti-relapse activity of current drugs and those in the pipeline • Develop drugs that prevent transmission by killing or preventing development of gametocytes, or blocking sporozoite development in the mosquito • Design drugs that cure liver stages of vivax (and ovale) malaria • Design sustained or pulsed release formulations and safe schizonticidal drugs for curing asymptomatic falciparum infection • Develop new, safe and effective drugs that block the infectivity of mature sexual forms of P. Falciparum gametocytes and/or dormant hepatic forms of P. Vivax • Create innovative drugs for intermittent preventive treatment during pregnancy • Explore long-acting formulations (e.g. repository formulations, oil-based depot injections cycloguanil pamoate) • Accelerate research into potential new drugs for first-line treatment to address artemisinin resistance D. Preventative vaccines • Expand vaccine development efforts to cover Plasmodium species other than P. Falciparum,

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		throughput approaches to antigen identification, and the functional definition of gene products • Evaluate health systems' readiness to optimize novel programs, systems, tests, or other interventions, and their continuing performance • Develop a decision-making framework to guide the move from control to elimination I. Innovative financing • None identified	especially P. Vivax. • Develop new, innovative vaccine delivery approaches and/or adjuvants • Create robust assays to study functional immune response at individual level to predict effect on population level transmission • Develop tools to measure malaria transmission rates to facilitate clinical development of vaccines • Explore anti-vector vaccines, highly effective pre-erythrocytic or erythrocytic stage vaccines, and vaccines targeting parasite antigens of sexual and mosquito stages of infection E. Therapeutic vaccines • None identified F. Vector control • Perform large-scale, long-term population-based field studies to understand human host and vector factors • Explore the genetic manipulation of natural vector populations that can reduce high vectorial capacities in high-risk areas • Develop an analytic framework that consolidates existing and new information on malaria transmission. • Research novel modes of action that can circumvent emerging resistance to insecticides, particularly pyrethoid-based insecticides • Create new technologies that address vectors that do not rest or feed indoors that escape current vector control tools • Develop technologies that can simply and rapidly measure transmission

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			• Educate the community effectively and engage the consumer market • Research improved choice of insecticides and methods to reduce the risk of resistance • Design a public portal to facilitate decision-making by the malaria research, control, and tool development communities G. Epidemiology • Investigate the performance of surveillance, monitoring, and evaluation by new and old technologies and to evaluate optimal strategies for implementation of surveillance as an active responsive intervention to further reduce transmission • Conduct research to develop biomarkers such as DNA-based methods or serology as monitoring and evaluation and surveillance tools • Develop information systems to monitor malaria infections, facilitate timely local program decisions and responses to reduce transmission • Develop methods, indicators, and shareable databases for parasite strain information to better track transmission • Develop methods for accessing and tracking population movements and quantifying their contribution and risk of malaria transmission • Explore how maps can be constructed to: o Show the probability of a threshold of transmission being exceeded; o Incorporate a wider range of metrics such as serological and entomological data; and o Assess cost-effectiveness of national stratification initiatives based on remotely sensed satellite data

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			H. Health systems/public health research • Update the malaria monitoring and evaluation framework to include transmission reduction • Develop key data elements for a surveillance system from a systematic review of previous elimination attempts • Identify appropriate program time points for introduction of malaria infection detection in active or passive modes • Perform a systematic review to assess and compare metrics of malaria transmission at near zero transmission levels, research the validity of novel metrics to measure transmission at near zero levels, and to measure transmission potential within areas where transmission has been eliminated • Assess the precision, bias, feasibility, and cost-effectiveness of novel sampling methods for routine monitoring of present and past infections in target populations, including mobile populations I. Innovative financing • None identified
6. European Commission. Final Report: Challenges for the Future Research on HIV/AIDS, Malaria, and Tuberculosis. Luxembourg: European Communities; 2009. *The European Commission's Final*	On 13 and 14 November 2008, the European Commission (DG Research) brought together a large number of stakeholders in an International Conference on Poverty-Related Diseases (PRDs) with the aim of increasing the impact of EU-funded research on controlling PRDs. Leading scientists,	A. Basic science • Identify reliable markers for immune protection against malaria. • Address major knowledge gaps in biology and pathogenesis of P. vivax. • Identify new potential targets for drug and/or vaccine development. • Improve understanding of the mechanisms of transmission-blocking immunity.	A. Basic science • Research the respective roles of innate and acquired immune response, antigen-presentation pathways, receptor binding, longevity of immune response, etc. • Conduct studies on transmission-blocking immunity through high-throughput antibody assays. • Perform immunogenicity testing of malaria vaccine candidates in outbred or humanized

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Report on the Challenges for the Future Research on HIV/AIDS, Malaria and Tuberculosis provides a summary of the 2008 European Commission Conference for research priorities on HIV/AIDS, Malaria, and Tuberculosis. Providing an update on the progress that has been achieved, the panel of speakers also provide detailed insight into current gaps and future research priorities.	research managers, decision-makers, funding agencies and relevant international NGOs attended (over 350 representatives from 63 countries), with significant participation from disease-endemic countries. The goals of the conference were to: i) regain political momentum for continuing and intensifying research addressing the "big three" global killer diseases; ii) set the scene by reporting on research efforts supported by the EC since 2002, when HIV/AIDS, malaria and TB first became a separate research focus under the EU's 6th Framework Programme (FP6); iii) gather input from relevant stakeholders (scientists from Europe and disease-endemic countries, industry, funding agencies, global partners, etc.) in order to set research priorities on PRDs for the remainder of the 7th Framework Programme (FP7) and beyond. After a plenary session on day 1, separate breakout sessions	B. Diagnostics • None identified C. Drugs • Design new drugs for the treatment and control of malaria. • Identify new molecular targets for antimalarial drugs D. Preventative vaccines • Develop an effective vaccine that combines antigens expressed during the different stages of the parasite's lifecycle. • Create a malaria vaccine, specifically for women in child-bearing age. • Enhance immunogenicity through vectored vaccines or new adjuvants that trigger immunity. E. Therapeutic vaccines • None identified F. Vector control • Develop novel vector control interventions and tactics. • Improve surveillance and management of insecticide resistance. • Create new insecticides and tools for resistance diagnosis and management. G. Epidemiology	rodent systems. • Use genomics, systems biology, and targeted molecular approaches to identify new drug candidates. • Utilize traditional or natural resources, in addition to synthetic compounds, for drug discovery. • Conduct long-lasting immuno-epidemiological studies to develop assays or surrogate markers to assess protection. • Create functional assay platforms for the identification of drug candidates. • Develop a convenient laboratory animal model for routine evaluation of P. falciparum and P. vivax. B. Diagnostics • None identified C. Drugs • Develop antimalarials that simultaneously target multiple development stages of the parasite and possibly the early insect stage. • Research potential drugs suitable for pregnancy and P. vivax. • Explore drugs that can block sexual or fertilized stages of the parasite in the mosquito. • Develop new drug delivery systems (e.g. slow release) • Explore alternative drug regimes (e.g. population-wide IPT). D. Preventative vaccines • Identify new functional antigens with immunogenic potential using systems-biology

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	for the three diseases were organized. On day 2 conclusions of the breakout sessions were presented and discussed. This report summarises deliberations and recommendations of the HIV/AIDS, Malaria and TB working groups.	• None identified H. Health systems/public health research • Build research capacity in endemic countries. • Conduct focused research effort on methods, technologies and associated platforms. • Leverage resources from different industries for drug development purposes. • Develop bio-informatic tools and databases for vectors and transmission. • Develop relevant platforms for functional annotation and validation of vector gene sequences. • Aim research at novel applications of currently available tools. • Improve monitoring and surveillance systems. • Scale up interventions for large-scale impact, accommodating for regional / local considerations. • Monitor cost-effectiveness of interventions. I. Innovative financing • None identified	approach. • Explore use of attenuated whole parasites for a natural multi-antigen vaccine. • Research antigenic variation and immune evasion of the parasite to identify potential targets for vaccine development. • Understand variable antigens with extensive polymorphism for vaccine development consideration. • Assess the potential of specific antigens for inclusion in a multi-component vaccine candidate, particularly P. vivax. E. Therapeutic vaccines • None identified F. Vector control • Understand the range of ecological parametics, including species biology and behaviour, ecological adaptation to climate and environment, and underlying genetic factors. • Research the metabolic pathways and immune responses that affect insecticide resistance. • Fill knowledge gaps for non-An. gambiae mosquitoes for the development of new vector control tools. • Conduct research to better understand host seeking, biting, resting, mating, egg-laying behaviour. G. Epidemiology • None identified H. Health systems/public health research

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
			• Expand research capacity through training, research and laboratory infrastructure, GCP standards, general institutional capacities, and strong national regulatory environments. • Create an open access library of compounds with known parasitic activity for academic research purposes. • Develop systems for recombinant expression of malarial proteins for structural and functional analysis. • Promote infrastructures or centres of excellence, accessible to academic bodies, with state-of the art facilities • Promoting interdisciplinary research including academia, industry and Public Private Partnerships • Promote collaboration between regulatory agencies to bring antimalarial drugs to market quicker. • Create natural product depositories, recombinant protein and production facilities, and processing facilities for support of molecular target specific screening programs. • Perform studies to address operational issues (e.g. detection of asymptomatic malaria carriers; the effective and timely elimination of the parasites by ACT; ensuring access to ACTs to all community members; optimal combination of ITNs and IRS; social and economic developments needed to improve crucial sanitation and housing conditions; the development of leadership for malaria control, building on trust, values and local empowerment. • Determine how to integrate strategies into regular health services or other public health

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
			programs. • Perform studies to address the impact of malaria interventions on the performance and sustainability of community-based health care systems to be recruited for scale-up for all age groups. I. Innovative financing • None identified
7. Evidence to Policy Initiative. Maintaining the Gains in Global Malaria Control: the Health and Economic Benefits of Sustaining Control Measures. San Francisco: University of California San Francisco; October 2011. *The Evidence to Policy Initiative's Maintaining the Gains in Global Malaria Control report provides an update on the global effort to control malaria recently. Focusing on the need for long-term, sustainable financing for malaria control efforts, the report provides a number of recommendations to donors and countries to maintain continued*	A number of methods were used to model the health impacts of sustained malaria control, including the Lives Saved Tool and Okiro and Snow's Method. Data on malaria morbidity and mortality in focus regions were analyzed to estimate the number of clinical cases and deaths that could be averted each year through the continued implementation of current control programs. Data from 2000-2010 on the annual number of suspected malaria cases and deaths from the WHO 2010 World Malaria Report and data reported by health facilities to the national malaria control program. The trends apparent in this data over time were useful for	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Better understand the link between malaria and other industries	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Conduct research to better understand timing for scaling back of prevention efforts. • Determine the economic benefits of sustaining malaria control to the agricultural sector and

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
progress in malaria control.	evaluating impact, but adjustments were required to account for underreporting and healthcare-seeking behaviours and results were compared with other published resources where possible.	I. Innovative financing • Explore Identify ways to ensure sustained, predictable financing for malaria Identify alternatives to donor financing and diversify the funding pool by broadening the number of donors	tourism. I. Innovative financing • Determine ways to foster novel domestic resource streams for malaria control, e.g. tourist taxes, community health insurance schemes, prize-linked savings, modifications to national tax codes, endowment funds, and National Health Solidarity Funds. • Create new mechanisms to improve the predictability and quality of financial resources, e.g. trust funds • Evaluate and consider widely adopting the Cash on Delivery (COD) aid approach wherein donors reward countries by tying continued financing to the maintenance of low malaria prevalence • Define the most cost-effective mix of interventions between surveillance and targeted prevention (ITNs and IRS) • Examine ways to reduce the prices of ITNs and insecticides through more effective procurement and negotiation
8. Policy Cures. Saving Lives and Creating Impact: EU Investment in Poverty-Related Disease. London: Policy Cures London; October 2012. *Policy Cures' Saving Lives and Creating Impact report assesses the impact of EU funding for poverty-related and neglected diseases*	The scope for PRND R&D and primary financial investment data in this report was extracted from the G-FINDER databases. Financial data was reported in 2007 euros to make the data comparable across the four years and to avoid conflating real year-on-year changes with changes due to inflation. Other specific datapoints were	A. Basic science • Conduct high quality basic research to contribute to the development of products targeted at malaria. B. Diagnostics • Develop new tools to accurately, rapidly diagnose malaria in developing countries. C. Drugs • Create new, innovative antimalarial drugs to combat resistance	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • Explore combination therapies to address emerging antimalarial drug resistance. • Conduct research on sufadoxine-pyrimethamine for intermittent preventative treatment for pregnant women.

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
(PRND) R&D, highlighting the return on investment for both developing countries and the EU. Focusing on the EU's role in funding PRND R&D, the report highlights the gains made by various EU research institutions, partnerships, and private industry.	provided by the EC, the European and Developing Countries Clinical Trials Partnership (EDCTP), European Vaccine Initiative (EVI), Tuberculosis Vaccine Initiative (TBVI), the Bill & Melinda Gates Foundation and Thomson Reuters, including: Member State and 3rd-party contributions to EDCTP, number of publications on neglected tropical diseases in 2011, and government funding commitments to EVI and TBVI. Qualitative policy data was obtained through desk-based research, and supplemented by communications with specific institutes or organisations mentioned in the report.	• Develop fixed-dose paediatric formulations for antimalarial drugs. • Develop antimalarial drugs for pregnant women. D. Preventative vaccines • Develop an effective vaccine for the prevention of malaria. E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Integrate the private sector into the poverty-related neglected disease R&D landscape. • Improve coordination efforts funders and researchers. • Identify the right balance of funding between product development and basic science. • Encourage collaboration amongst researchers to jointly develop product development portfolios. • Align efforts of aid organizations and science and technology agencies. I. Innovative financing	D. Preventative vaccines • Estimate the potential epidemiological benefit of an effective vaccine. E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Identify key product development partnerships (PDPs) to engage talented researchers in private industry. I. Innovative financing • Reduce restrictions on funding requirements to ensure that the best research candidates are prioritized (under the EU 7th Framework Programme). • Streamline administrative processes to expedite funding flows to reach researchers. • Explore pooled funding mechanisms to encourage collaboration.

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		• Improve financing coordination efforts amongst various stakeholders.	
9. Berger, M; Murugi, J; Buch, E; IJsselmuiden C; Kennedy, A; Moran, M; Guzman, J; Devlin, M; Kubata, B. Strengthening pharmaceutical innovation in Africa. Council on Health Research for Development (COHRED); New Partnership for Africa's Development (NEPAD) 2009. *COHRED's Strengthening Pharmaceutical Innovation in Africa report focuses on the agenda to promote pharmaceutical innovation in Africa by African countries. This report suggests different mechanisms and tools to support African countries moving forward, specifically advocating for a systems and evidence-based approach.*	The geographical scope of the study is Africa. It focuses on diseases that disproportionately affect Africa, including neglected tropical diseases. The method used was keyword internet searches, key informant interviews and discussions review of literature and documentation3, participation and consultation in a number of international meetings and consultations on pharmaceutical in several low income countries. The data obtained was analyzed manually along main emerging themes. The draft report was externally peer reviewed. Step 1: Identifying and categorising projects and programmes contributing to the improvement of access to medical products in Africa. Global, regional and national examples were considered. Step 2: examination of a minimum set of conditions, policies; human, structural and	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Leverage African strengths in pharmaceutical innovation (e.g. African Ministerial Council on Science and Technology). I. Innovative financing • Utilize innovative financing mechanisms across industries and stakeholders.	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Create policies to encourage local production of medicines to treat neglected diseases. • Utilize technology transfer and licensing agreements to promote local drug production. I. Innovative financing • Create new product development public-private partnerships (PDPPPs). • Engage companies in using preferential pricing arrangements.

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
	financial resources to identify initiatives most likely to be successfully implemented in any African country.		• Leverage philanthropic donations to strengthen national pharmaceutical innovation systems. • Expand access to treatment through intergovernmental organization-sponsored buyer co-payments. • Raise funds through solidarity taxes on airlines. • Engage venture capital to invest in neglected disease R&D.
10. The George Institute for International Health. Registering New Drugs: The African Context. London; The George Institute for International Health, January 2010. *The Registering New Drugs report reviews the various mechanisms and strategies available to support the registration of new drugs for neglected tropical diseases (NTDs) in developing countries. It addresses the development and strengthening of the capacity of national regulatory authorities to monitor quality, safety, and efficacy of health products, since regulatory issues are often obstacles*	A select group of experts from various organizations (including: World Health Organization, US Food and Drug Administration, European Medicines Agency, etc.) were consulted for the purposes of this analysis. The International Expert Advisory Group (EAG) played a substantial role in reviewing this report and shaping the final analysis and recommendations. The draft report was also work-shopped at a regional meeting in Nairobi, attended by many African regulators, including representatives from Angola, Democratic Republic of Congo, Ethiopia, Uganda, Tanzania and members of the HAT (human African trypanosomiasis) and LEAP (leishmaniasis) platforms.	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • Assess the safe interaction of malaria drugs in patients with TB coinfection. D. Preventative vaccines • Identify promising candidates for a new preventative malaria vaccine. E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Develop new mechanisms and	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Create centers of regulatory excellence in African subregions. • Provide automatic WHO prequalification for novel neglected disease products. • Include regulators from endemic countries in

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
to access.		pathways to ensure the urgent approval of neglected tropical disease drugs in developing countries. I. Innovative financing • None identified	regulatory reviews of neglected disease products. • Select Western medicines regulatory agencies to review prequalification decisions. I. Innovative financing • None identified
11. Moran, Mary; Ropars, Anne-Laure; Guzman, Javier; Diaz, Jose; Garrison, Christopher. The New Landscape of Neglected Disease Drug Development. London: The London School of Economics and Political Science; 2005. *The New Landscape of Neglected Disease Drug Development report provides an overview of health outcomes for developing country neglected disease patients and presents recommendations to increase the quality and number of drugs available. It also presents policies and incentives that Western governments could implement to achieve this*	An empirical approach was used for this report, covering known neglected disease drug R&D from 1975 to end 2004. All findings and conclusions are based on a review of existing knowledge, supported by original research and interviews with stakeholders involved in the development and use of new drugs. Using a multidisciplinary approach, this report consults groups from various fields (government, public health, industry. Etc.) Analysis and conclusions relate only to neglected disease drug R&D and cannot be automatically translated across to vaccines and diagnostics. Drug development activity was included only as it relates to the ten neglected diseases listed by the World Health Organization Special Programme for Research and Training in Tropical Diseases	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • Develop new, innovative antimalarial drugs suitable for developing country use. • Identify new classes of malaria products that can "outwit" parasites to avoid drug resistance. • Develop drug adaptations that make treatment compliance easier (e.g. paediatric syrups, simpler formulations, etc.). D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • Conduct research on synthetic peroxides in the development of new antimalarials. • Explore ease-of-use considerations for patients and health care workers (e.g. dosing intervals, total length of treatment, oral formulations, etc.). • Consider appropriateness of product to country health systems (e.g. cold chain issues, hospital-based admin, etc.). • Create products targeted at various populations (e.g. children, adults, pregnant women, severely ill patients, etc.). D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified

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objective.	(WHO/TDR). A number of areas of activity were excluded from the scope of this report. Developing country drug development was not considered as it is unlikely to be amenable to Western government incentives. Additionally, basic exploratory research that is not compound-based and country infrastructure, implementation, and human resource considerations were also not included in this report.	• None identified H. Health systems/public health research • Create a central clearinghouse for information regarding: targets or compounds related to neglected disease research, funding sources, and services and skills offered. I. Innovative financing • Identify new, innovative public-private partnerships (PPPs) for drug development, and create policies to encourage PPPs. • Provide shared platform services to PPPs (e.g. legal, human resources, etc.) • Offer support to PPPs in negotiating industry deals. • Create an industry R&D fund (IRFF) to underwrite industry participation in PPPs. • Provide PPP-sponsored start-up funds to new small companies. • Sell "fast-track" regulatory review of commercial drugs to finance neglected disease R&D. • Award prizes to multinationals who invest in neglected disease drug development. • Reduce financial obligations on patent and maintenance fees.	G. Epidemiology • None identified H. Health systems/public health research • Generate neglected disease data that can be cross-applied to core commercial compounds. • Upgrade clinical trial sites in developing countries I. Innovative financing • Identify PPPs that are willing to commit to a long-term funding mechanism (entirety of R&D process). • Collaborate with industry partners that will contract with PPPs to develop drugs for neglected diseases. • Garner funds from G8 countries to create the IRFF.

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
12. UNITAID. Malaria Diagnostic Technology Landscape. World Health Organization; Dec 2011. *This report describes the role of malaria diagnostic tests, unmet needs in malaria diagnosis, and factors considered in diagnostic test selection, followed by a review of existing malaria diagnostic tests and new technologies in the development pipeline. The technologies described include those for patient management, as well as those that may be more suitable for surveillance, especially in the context of elimination.*	In general, the material in this landscape was gathered by the author from publicly available information, published and unpublished reports and prospectuses, and interviews with developers and manufacturers. With regards to the technology review, significant prior work (reports, literature etc.) has been done to describe existing malaria diagnostic technologies and this is summarized below. For existing technologies, the methodology largely involved review of existing reports supplemented by expert interviews and targeted literature searches. In contrast to existing technologies, very little in-depth work has been done previously on the malaria diagnostic pipeline. Key informant interviews, along with literature and internet searches were used to identify new technologies actively being developed and commercialized. (Due to the nature of this work and the timeframe for the report, a totally exhaustive search was not possible.)	A. Basic science • None identified B. Diagnostics • Develop screening tests for detection of malaria in pregnancy, tests that measure low-level transmission, and tests that detect asymptomatic malaria infections for use in elimination campaigns • Develop tests that assist with the differential diagnosis of fever and management of non-malaria fever • Develop tests related to the diagnosis and treatment of the liver stage of P. vivax malaria • Enhance the robustness of tests to withstand extreme heat and humidity • Develop tests that are affordable, widely deployable, easy to use, rapid and accurate C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified	A. Basic science • None identified B. Diagnostics • Create a test sensitive enough to detect all cases of placental malaria as today's case management tests (microscopy and RDTs) are not sensitive enough • Develop a low-cost, high-throughput screening test is to conduct large population surveys that are used to monitor progress over time and to identify hot-spots (i.e. foci) of continued transmission • Develop test for these situations a test that has a low limit of detection, and that is highly sensitive, rapid, and portable, to screen high-risk populations, e.g. migrant workers • Design a multiplex point-of-care (POC) test that detects several common causes of fever at one time (e.g. malaria, dengue, and influenza) • Develop a POC test that serves as a triaging tool providing information on management of the patient rather than pinpointing the exact cause of fever, e.g. it would include a malaria test and biomarkers for severity of disease, information that helps differentiate broadly between bacterial versus viral infections C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines

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	Once products were identified, detailed information on these new technologies was obtained primarily through conversations with technology developers, as well as through publications, where they exist. In some instances, technologies were identified but the developers were not available to provide additional information. Because these products are in the development phase, the ultimate performance and operational characteristics may change by the time the product is launched. Similarly, projections of market launch will shift as time goes by, as will price estimates.	G. Epidemiology • None identified H. Health systems/public health research • Learn how to increase access to malaria diagnostics • Investigate how to strengthen the management of fever more broadly to maximize the public health impact of tests • Develop strategies for rapidly interpreting malarial surveillance data and translating it into public health action I. Innovative financing • None identified	• None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Determine ways to overcome factors that obstruct access to testing, e.g. unaffordable prices, limited awareness, little incentive for the private sector to offer testing, local regulatory and policy issues, and a need for extremely user-friendly test formats and packaging appropriate for the private sector • Revisit existing protocols for fever management, commence studies to investigate the common causes of fever, review treatment options for non-malaria fever, and possibly demand new diagnostic technologies that assist with the differential diagnosis of fever • Develop and refine new technologies that incorporate data storage and remote transmission capability, e.g. those that focus on surveillance data capture and analysis I. Innovative financing • None identified
13. UNITAID. Malaria Diagnostics Market Landscape. World Health Organization; Dec 2012. *This Landscape Report*	This report is based upon: • Desk review of literature and published and unpublished reports • Review of existing market data and reports	A. Basic science • None identified B. Diagnostics • None identified	• Basic science • None identified • Diagnostics • None identified

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
reflects an initiative within UNITAID to describe and monitor the malaria diagnostics landscape, including disease trends, technologies, and market characteristics. This report focuses on the market for malaria diagnostic tests, and on rapid diagnostics tests (RDTs) in particular.	• Identification of existing sources of aggregate data on the market, and analysis of data when it was available • Key informant and expert interviews, including representatives from industry, programs, donors, and academia. Research for this report was conducted from February-April 2012, and information is up to date as of April 2012.	C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • None identified I. Innovative financing • Develop means to increase the availability of information on the quality of malaria diagnostics (including development of technologies to simplify quality control testing), reinforce competition around quality, ensure consistency during manufacturer scale up, and assure the integrity of tests in the field • Identify strategies to stabilize prices of RDTs and improve predictability of demand • Find ways to draw funding for interventions that support RDT	• Drugs • None identified • Preventative vaccines • None identified • Therapeutic vaccines • None identified • Vector control • None identified • Epidemiology • None identified • Health systems/public health research • None identified • Innovative financing • Develop quality control technologies for use at all levels of the supply chain from manufacturer to point of service • Find ways to support the WHO Product and Lot Testing program and their transition to a less costly and more sustainable business model • Develop stronger incentives for upstream quality assurance, e.g. site visits, stepped-up lot testing, or changes to the WHO Product Testing program • Find ways to encourage buyers to focus on quality and product characteristics, as opposed to price alone • Strategize how interventions can be structured with frequent evaluations and flexibility to incorporate new learning • Reinforce the data on the availability of testing

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		implementation, e.g. health worker training, supervision • Develop the private sector market for malaria RDTs and determine how to expand access to testing and improve targeting of ACTs in the private sector • Identify ways to increase funding for product development for underserved populations, including pregnant women, populations living in low transmission settings, and populations affected by *P. vivax* • Develop mechanisms to strengthen market knowledge	and use of results • Improve the completeness of data on RDT procurement • Determine how to enhance efforts to collect and synthesize information on the private sector markets
14. UNITAID. Malaria Diagnostics Technology Landscape: Semi-Annual Update. World Health Organization: Dec 2012. *The Malaria Diagnostics Technology Landscape is published annually and is prepared as part of a broad and on-going effort at UNITAID to understand the technology landscape for malaria diagnostics. This document is a semi-annual update, focused on updates to the diagnostic pipeline first described in the Malaria Diagnostics Technologies*	The Malaria Diagnostics Technology Landscape Update is compiled by Jennifer A. Daily with support from UNITAID. The updates in this document were provided by the developers of these diagnostic technologies. If technologies that appear in the Malaria Diagnostics Technologies Landscape do not appear in this update, it is either because the developer did not provide an update or indicated that there were none at this time.	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
Landscape.		H. Health systems/public health research • None identified I. Innovative financing • None identified	H. Health systems/public health research • None identified I. Innovative financing • None identified
15. World Health Organization/Foundation for Innovative New Diagnostics/Centers for Disease Control/Special Programme for Research and Training in Tropical Diseases. Malaria rapid diagnostic test performance: results of WHO product testing of malaria RDTs: round 4. Geneva: World Health Organization; 2012. *This report's goal is to discuss the results of WHO's tests on the efficacy and usefulness of various Malaria Rapid Diagnostic Test Performance. The report is fourth in an ongoing series and overall found improvements/upward trends in all areas among RDTs that were resubmitted for testing. It*	Product Testing Is part of the WHO-FIND Malaria RDT Evaluation Programme. This Programme develops methods for evaluation and provides relevant data on antigen-detecting malaria rapid diagnostic tests. The programme is a collaboration of many institutions in malaria-endemic and non-endemic countries, with the global specimen bank maintained, and the testing performed, at CDC. The results provide comparative data on two lots of products against a panel of parasite samples diluted to a low parasite density (200 parasites/µl), considered close to the threshold that tests must detect to reliably identify clinical malaria in many settings (6), and a higher parasite density (2000 (or 5000) parasites/µl).	A. Basic science • None identified B. Diagnostics • Develop screening tests for detection of malaria in pregnancy, tests that measure low-level transmission, and tests that detect asymptomatic malaria infections for use in elimination campaigns • Develop new tests with a high rate of antigen detection combined with a low false-positive rate, good heat (thermal) stability and robustness against humidity for use in endemic countries C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified	A. Basic science • None identified B. Diagnostics • Find ways to enhance tests' sensitivity to detect infection among vulnerable individuals who may develop illness at low parasite densities, e.g. young children, pregnant women, immigrants, those well protected by bed nets) • Develop storage and shipping products to ensure test stability and sensitivity in high temperatures with high humidity C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
provides guidelines on how to approach parasite based diagnostics– recommending national programs use results from these reports to select the most appropriate RDTs based on local climate and characteristics of the malaria endemic to the area.		G. Epidemiology • None identified H. Health systems/public health research • Develop strategies to ensure quality preparation and interpretation of RDT results in field settings I. Innovative financing • None identified	H. Health systems/public health research • Design training programs for health workers with limited training and supervision in endemic countries • Investigate how to plan beyond rational procurement to ensure consistent supplies of all necessary materials (including gloves, sharps disposal containers, and supplies required for further case management), training of end-users, community sensitization, and monitoring of diagnostic quality and results • Identify ways to improve the management of other febrile diseases and health service delivery systems with an integrated approach with other health programmes impacting on the management of febrile illness I. Innovative financing • None identified

Disease-specific R&D priority setting

TUBERCULOSIS

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
1. New diagnostics working group of the Stop TB Partnership. Pathways to better diagnostics for tuberculosis: a blueprint for the development of TB diagnostics. Geneva: World Health Organization; 2009. *The blueprint offers a structured guide through the different phases of diagnostic development to help identify the most promising TB tests, push them toward alignment with the needs and requirements of the areas where tuberculosis is most prevalent, and help determine why some tests are held up in development.*	Peer-reviewed contributions from some 30 different authors with experience in TB diagnostics from academia (universities and research institutions), industry and NGO sectors Key challenge: find ways to adapt promising new diagnostic tools for use in high-burden settings and to open a pipeline for their development, marketing, distribution and widespread use in the places where they are needed most	A. Basic science • Validate TB-specific biomarkers for active TB disease in children and adults to assist in the production of diagnostic tests for clinical use B. Diagnostics • Develop a low-cost, accurate, user-friendly, specific and highly sensitive test • Simplify and improve detection of TB cases (including smear-negative, extra-pulmonary and childhood TB) • Determine ways to reliably identify latent TB infection and determine the risk of progression to active disease to enable the rational use of preventative therapy • Determine how to rapidly identify drug resistance to both first- and second-line anti-TB medicines • Design tests that can be performed at the point-of-care level of the health care system and that produce quick results on the same day • Develop cost-effective, patient-centred applications on common technology platforms appropriate to different tiers of developing country health systems	A. Basic science • Identify a group of biomarkers that could be used for a simple diagnostic test within five years • Pursue proteomics research to identify a set of proteins or biomarkers specific for TB that could lead to a serum-based antigen detection assay for the diagnosis of TB metabolomics B. Diagnostics • Identify way to improve specificity of tuberculin skin tests for use in endemic countries • Develop IFN-gamma release assays that can distinguish between latent and active TB • Determine how to improve sputum sample treatment procedures for all new methods of direct assay microscopy • Design an improved sputum preparation process for Antigen detection, point-of-care tests and 16S rRNA testing • Learn how to adapt liquid chromatography methods for use in TB diagnostics • Identify how to simplify nucleic acid amplification tests to reduce technicians' workloads • Design tools that utilize molecular assays to detect gene mutations • Identify ways to extend line probe assays

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		C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Identify ways to perform crucial needs assessments to measure the extent and nature of the problems faced by the people on whom the tests will be performed • Determine how to ensure technology is adaptable to local laboratory infrastructure • Find ways to maximize access to TB diagnostics I. Innovative financing • Determine ways to increase funding levels to adequately support TB R&D, with dedicated investments in diagnostics development; overall TB R&D stands at only 20% of what is	towards the detection of quinolone resistance and made more user-friendly • Develop a simple and inexpensive test with at least as good a detection limit as direct microscopy 1x 104 bacteria/ml for Antigen detection, point-of-care tests and 16S rRNA testing to reduce the workload of laboratory personnel • Develop successful "E-nose," urinalysis and breath analysis technologies for use in detecting TB • Explore a low-cost, accurate, rapid and non-invasive technique (e.g. analysis of breath or exhaled breath condensate) to greatly assist in the TB diagnosis among children • Develop an indirect assay antibody detection point-of-care test that uses a simple ELISA or lateral flow format as an ideal test C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified

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		needed	H. Health systems/public health research • Determine how to integrate regular needs assessments early in the diagnostic R&D process • Identify ways to produce *user requirements documents* as part of the needs assessments that capture detailed information on the expected performance in real-life conditions, time to results (and preferably time to treatment initiation), technical requirements, users' skills, medical algorithms within which the test is to be used and a clear description of the setting where the test is to be implemented • For impact assessment research, compare impact-related data to historical data recorded prior to the implementation of the new test in routine clinical practice I. Innovative financing • Identify ways to expand financing approaches beyond market incentive mechanisms that rely on high prices to fund R&D as they do not result in creating advanced diagnostics in the areas of highest need
2. World Health Organization/Stop TB Partnership. An international roadmap for tuberculosis research: towards a world free of tuberculosis. Geneva: World Health Organization; 2011.	Authors defined TB research priorities by identifying strategic objectives and activities established through: a systematic review of the research agendas of various groups and institutions over the	A. Basic science • Understand the stages of TB disease progression and identify markers of progression • Better characterize the transitions between stages of human TB and the bacterial or host markers that	A. Basic science • Identify the respective components of the host's immune system and of the pathogen that are responsible for elimination of *M. tuberculosis* or for preventing reactivation of latent TB infection • Understand mechanisms leading to

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The research roadmap defines the essential research questions that provide a common framework for scientific disciplines to work concurrently and collaboratively for better TB control towards the elimination of TB.	past decade; a series of expert group meetings; broad consultations with TB stakeholders; and a systematic review of priority research questions in recent reviews on new TB control tools An initial list of research priorities was prepared on the basis of those identified by the various expert group meetings, and was then compared with those identified in a thorough literature review, including previous TB research agendas, so as to select the most appropriate questions. It was then reviewed by an Expert Advisory Group with wide representation of multidisciplinary TB stakeholders Five criteria for prioritization of research questions were used: Efficacy and Effectiveness; Necessity; Deliverability; Equitability; and Answerability. A web-based consultation was organized to involve the larger TB scientific community willing to participate in defining high-priority research questions	indicate the stage of disease and predict which individuals will progress from one phase to the next • Better understand host–pathogen interaction B. Diagnostics • Increase TB case detection with new and improved diagnostics to detect active disease at the point of care, diagnose latent TB infection, predict disease progression, and rapidly screen and diagnose MDR- and XDR-TB, HIV-associated TB and paediatric TB • Simplify and validate novel tools for diagnosis at the point of care C. Drugs • Develop shorter TB regimens to cure all forms of TB that are safe, compatible with ART, suitable for children, effective against latent tuberculosis infection, affordable, easily managed in the field and that remain effective by limiting the development of drug resistance D. Preventative vaccines • Develop a safe, effective, affordable vaccine to prevent all forms of TB in all age groups and that is safe for people with HIV and other forms of immunosuppression	persistence or elimination of bacilli in various conditions (e.g. according to age or HIV infection) for the identification of drug targets • Characterize interaction of *M. tuberculosis* with the immune system during the phases of progression from infection to disease • Investigate role of mucosal lung immunity in addition to systemic immunity • Identify biomarkers (or combinations of biomarkers) that will help distinguish the stages of TB and will allow accurate identification of patients at various levels of the spectrum • Elucidate the design of systems biology models of *M. tuberculosis* metabolism and physiology to facilitate modern cell and target-based drug discovery B. Diagnostics • Investigate how to combine existing and new diagnostics to optimize the detection of various forms of TB, including drug-sensitive, drug-resistant and latent TB infection, in diverse population settings • Identify combinations of methods for collecting useful specimens from children • Identify a systemic marker of bacterial load in TB C. Drugs • Determine optimal dosage, safety and efficacy of new drugs and their interaction with other TB and non-TB drugs • Identify optimal treatment regimens for all

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		E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • Improve knowledge of the distribution and natural history of TB, especially the roles of its various determinants, to improve control activities, influence policy-making and ensure more efficient and effective methods of service delivery H. Health systems/public health research • Determine how to improve TB control programme performance and design interventions that result in improved policy-making, better implementation in health systems and more efficient and effective methods of service delivery • Identify ways to improve TB case-finding and screening, access to diagnostics, treatment access and delivery, TB-HIV programme interactions and infection control in both the general context of health services and for specific high-risk groups	TB patient types, including TB-HIV co-infection and infected children • Investigate the interaction between first- and second-line drugs and antiretroviral agents • Identify new anti-TB drugs that are fully compatible with ART for the treatment of HIV–TB co-infection • Determine the best methods to test and identify optimal combinations of drugs early enough in overall drug development D. Preventative vaccines • Determine the immune-dominant antigens associated with different metabolic states of *M. tuberculosis* to be added to vaccines to increase protection • Identify novel model systems for preclinical and clinical testing of TB vaccines, including pre- and post-exposure models and models that mimic reactivation • Determine the respective roles of innate and adaptive immunity in preventing *M. tuberculosis* infection and reactivation of latent disease and better understand immune responses against different metabolic stages of the pathogen in different populations • Develop improved vaccines for prime–boost vaccination strategies and determine their optimal conditions of use, e.g. duration of intervals, boosting dose and number of boosts • Better understand the immune response to BCG and new vaccines

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		I. Innovative financing • None identified	• Identify and standardize assays to assess vaccine-induced immunogenicity to allow better comparison of candidate vaccines E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • Conduct measurements of the burden of disease and of variations in the dynamics of TB according in specific settings • Identify the causes of low case detection and treatment, especially in certain high-risk groups and settings • Study variations in the dynamics of TB according to setting, and identify the effect of the germ, the host and the environment on *M. tuberculosis* transmission • Understand the relative contributions of different foci of TB transmission (e.g. household, community, nosocomial transmission) at population level • Identify various biological, environmental, population-based and social drivers of *M. tuberculosis* transmission • Better understand the interaction between the pathogen, the host and social determinants on *M. tuberculosis* transmission in specific settings and in high-risk populations (including TB–HIV co-infected and MDR- and XDR-TB patients)

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			H. Health systems/public health research • Define and evaluate the performance of new diagnostic tests in terms of feasibility, cost-effectiveness, reduced diagnostic delay and impact on clinical decision-making and patient benefit • Investigate methods and means to optimize TB case-finding and measure impact of intensive case-finding on mortality and other outcomes, particularly among HIV-infected populations, infants and children • Identify the most effective TB screening algorithms • Develop means to scale up isoniazid preventive therapy under field conditions and in HIV clinics delivering ART • Develop strategies to strengthen the links between TB and HIV control programmes at all levels of health care, with optimal integration of interventions • Identify strategies to scale-up access to MDR- and XDR-TB treatment in resource-limited settings and improve treatment outcomes, whether or not associated with ART • Study how to best integrate TB care with that of chronic diseases, with particular emphasis on diabetes • Develop methods to expand access to treatment for vulnerable and marginalized groups by making use of private or alternative health care providers • Determine the efficacy of individual TB infection control measures in resource-

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			limited settings and strategies to implement, monitor and evaluate TB infection control in health facilities, communities and households I. Innovative financing • None identified
3. World Health Organization. Global Tuberculosis Report 2012. Geneva: World Health Organization; 2012. *The Global Report provides a comprehensive and up-to-date assessment of the TB epidemic and progress made in prevention, care and control of the disease at global, regional and country levels, in the context of global targets and WHO's recommended strategy for achieving these targets.*	The report is based primarily on data compiled in annual rounds of global TB data collection in which countries are requested to report a standard set of data to WHO; a total of 204 countries and territories that account for over 99% of the world's estimated cases of TB reported data in 2012. Data were reviewed, and followed up with countries where appropriate, by a team of reviewers from WHO (headquarters and regional offices) and the Global Fund. Validation of data by respondents was also encouraged via a series of inbuilt and real-time checks of submitted data Data were collected on the following topics: TB case notifications and treatment outcomes, including	A. Basic science • Intensify TB-specific biomarker research • Improve understanding of the interaction between the bacillus and the human host • Better characterize *M. tuberculosis* to refine understanding about the transition from latent to active TB • Understand why prolonged antibiotic treatment is needed B. Diagnostics • Design tools to improve the diagnosis of drug-susceptible and drug-resistant TB • Develop urgently needed accurate and rapid point-of-care tests C. Drugs • Enhance and shorten treatment regimens for all forms of TB D. Preventative vaccines • Develop a more effective vaccine to supersede the BCG vaccine	A. Basic science • Identify novel biomarkers for treatment response and sterilizing activity • Determine why certain individuals infected with *M. tuberculosis* are resistant to TB disease • Identify biomarkers and bio-signatures relevant to new TB diagnostics • Identify new targets for anti-TB drugs and early indicators of protective immunity for vaccine efficacy B. Diagnostics • Develop second- generation Xpert assays and possible alternative molecular technologies C. Drugs • Determine how to improve the efficacy and tolerability of treatment for MDR-TB • Enhance the treatment of TB among people living with HIV • Investigate how to treat latent TB infection in people without active TB disease D. Preventative vaccines • Identify much-needed markers and

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	breakdowns by case type, age, sex, HIV status and drug resistance status; an overview of services for the diagnosis and treatment of TB; laboratory diagnostic services; drug management; monitoring and evaluation; surveillance and surveys of drug-resistant TB; management of drug-resistant TB; collaborative TB/HIV activities; TB infection control; engagement of all care providers in TB control; the budgets of national TB control programmes (NTPs) in 2012 and 2013; utilization of general health services (hospitalization and outpatient visits) during treatment; and NTP expenditures in 2011	E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • Conduct epidemiological research to close the gap between notified cases and estimated TB incidence • Investigate ways improve the measurement and estimation of TB incidence and mortality among children • Determine whether the number of MDR-TB cases is increasing, decreasing or stable H. Health systems/public health research • Determine how to best treat people with latent TB infection on a massive scale, especially in high-risk populations • Ascertain how to best achieve mass vaccination • Identify ways to transform sophisticated laboratory technologies into robust yet accurate point-of-care platforms I. Innovative financing • Increased investment in R&D for new TB diagnostics remains imperative	correlates of immune protection to assist in the selection of next generation vaccine candidates • Determine whether TB vaccines can effectively reduce the transmission of *M. tuberculosis* E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • Conduct systematic literature reviews of existing data on incident childhood TB, under-reporting of TB in children and misdiagnosis • Determine ways to expand case-based electronic recording and reporting systems that would facilitate compilation and analysis of aged is aggregated data • Design nationwide inventory surveys to measure under-reporting of childhood TB • Collect age-specific data from sample VR systems and mortality surveys in high-burden countries including China, India and Indonesia • Provide a definitive assessment of trends in MDR-TB globally and/or regionally H. Health systems/public health research • None identified I. Innovative financing

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			• None identified
4. UNITAID. Tuberculosis Diagnostic Technology Landscape. Geneva: World Health Organization; 2012. *The purpose of this report is to: 1) describe existing TB diagnostics and the pipeline of expected future methods and tools; 2) characterize unmet needs and the extent to which the pipeline may address these; and 3) highlight areas of persisting market shortcomings and potential opportunities for market-based interventions.*	This report was prepared by David Boyle (PATH, Seattle) and Madhukar Pai (McGill University, Montreal) with support from UNITAID. The material in this landscape is current through February 2012. In general, the material in this landscape was gathered from an extensive review of publicly available information, published and unpublished reports, WHO policies and systematic reviews, corporate prospectuses, and developer web sites, as well as meetings and interviews with technology developers. In addition to this broad approach, specific targeted analyses were carried out in areas where little information was publically available, such as a survey of Chinese diagnostics developers to identify current pipeline products.	A. Basic science • Better understand host biomarkers to identify stage-specific progress of the disease B. Diagnostics • None identified Develop urgently needed POC TB diagnostic tools that can be used in peripheral health-care settings • Develop tools that can diagnose TB in children C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Identify ways to improve TB case-finding and screening, access to diagnostics, treatment access and	A. Basic science • Identify bacterial and/or host biomarkers (or combinations of biomarkers) that will help distinguish the stages of TB and allow accurate identification of patients at various levels of the disease spectrum between latent and active TB B. Diagnostics • Investigate ways to combine existing and new diagnostics to optimize the detection of various forms of TB, including drug-sensitive, drug-resistant and latent TB infection, in diverse population settings • Identify combinations of methods for collecting useful specimens from children • Identify a systemic marker of bacterial load in TB C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified

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		delivery, TB-HIV programme interactions and infection control in both the general context of health services and for specific high-risk groups • Determine how to decentralize and scale-up use of the automated nucleic acid amplification test (NAAT) for TB diagnosis • Develop mechanisms to ensure that product development efforts meet the real needs of TB control programs I. Innovative financing • Find ways to reduce the cost and time taken for sufficient evidence to be gathered on diagnostic tools prior to their review and endorsement by WHO's STAG-TB, particularly for smaller companies	H. Health systems/public health research • Define and evaluate the performance of new diagnostic tests in terms of feasibility, cost-effectiveness, reduced diagnostic delay and impact on clinical decision-making and patient benefit • Find ways to integrate Ministries of Health and the public and private health-care sectors in informing developers as to the appropriate specifications that a product must meet to warrant effective and widespread sustained use I. Innovative financing • Strategize how to ensure competition for market share is tempered with collaboration for product development, especially between academic and commercial groups • Determine how to engage biotech start-ups from emerging economies in developing diagnostic tools to meet target product profiles • Identify how to increase developers' access to well-characterized specimen panels with which to guide their product development and provide initial evaluation data • Determine how to create harmonized study protocols and permit accurate comparison in multiple settings in order to facilitate more rapid diagnostic uptake by country programs once a WHO STAG-TB endorsement is made

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
5. UNITAID. Tuberculosis: Diagnostic Technology Landscape: Semi-Annual Update. Geneva: World Health Organization; Dec 2012. *This document is a semi-annual update, focused mainly on nucleic acid amplification test (NAAT) technologies, specifically roll-out of the Xpert® mycobacterium tuberculosis (MTB)/rifampicin (RIF) resistance test, and a review of fast-follower NAATs that are on the market or will be on the market by early 2013. This report also provides an update on the ongoing work to assess the market size for TB diagnostics and develop target product profiles (TPPs) for new TB diagnostics. Challenges for point-of-care (POC) testing and market dynamics and barriers for roll-out of new TB diagnostics are also reviewed.*	The Tuberculosis Diagnostic Technology Landscape: Semi-Annual Update 2012 was compiled by Madhukar Pai (McGill University, Montreal) and David Boyle (Program for Appropriate Technology in Health [PATH], Seattle) with support from UNITAID. The material in this landscape report was gathered by the authors from publicly available information, published and unpublished reports and articles, and interviews with test developers and manufacturers. The material in this landscape is current through December 2012.	A. Basic science • None identified B. Diagnostics • Develop a rapid low-cost, accurate, user-friendly, specific and highly sensitive point-of-care (POC) diagnostic test • Simplify and improve detection of TB cases using rapid, non-sputum based POC test for the diagnosis of extra-pulmonary TB (EPTB), smear-negative and childhood/pediatric TB • Determine ways to reliably identify latent TB infection and determine the risk of progression to active disease to enable the rational use of preventative therapy • Develop a simple-to-perform, improved rapid molecular DST assays for first- and second-line drug resistance • Design tests that can be performed at the point-of-care level of the health care system and that produce quick results on the same day • Develop urgently needed POC TB diagnostic tools that can be used in peripheral health-care settings{ • Develop tools that can diagnose TB in children • Develop a rapid 'rule-out' or triage test, especially for TB-HIV co-	A. Basic science • None identified B. Diagnostics • Investigate the performance of all fast follower NAATs to better understand the potential application of these tools for TB diagnosis in low-resource settings • Develop methods to ensure that the performance of highly-sensitive NAATs is not compromised by manufacturing, transport, storage, the environment, or the user • Develop urgently needed standardized external quality assurance (EQA) devoted to the Xpert® MTB/RIF and fast-follower NAATs to ensure adequate performance of equipment and users via uniform standards • Find ways to ensure that EQA panels for Xpert® MTB/RIF assay seek fulfillment of the following elements: o (i) testing material must contain whole *M. tuberculosis*; o (ii) transportation of EQA material must be safe; o (iii) testing procedures must be compatible with the current Xpert® MTB/ RIF testing protocol; o (iv) health care workers who do not have laboratory skills must be able to perform the EQA testing in non-laboratory settings; and o (v) the EQA program must be cost-effective and sustainable

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		infection in high burden settings • Find ways to gain consensus on which target product profile (TPP) attributes will have the biggest impact on reducing the incidence of TB in disease-endemic countries, and which meet clinical and practical needs C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Identify ways to improve TB case-finding and screening, access to diagnostics, treatment access and delivery, TB-HIV programme interactions and infection control in both the general context of health services and for specific high-risk groups • Determine how to decentralize and	• Determine whether new fast follower NAAT tests fit with current TB diagnostic algorithms and if they can be successfully implemented in peripheral microscopy laboratories in high burden countries • Identify which types of sample preparation/processing methods allow for truly decentralized implementation at the microscopy center level • Determine the acceptable trade-off between higher throughput and lower cost NAATs vs. more manual involvement on the other as compared to partially integrated assays with higher cost per test but reduced needs for user input • Determine how appropriate quality control procedures for test integrity can be developed for and maintained in peripheral facilities with minimal oversight from National Tuberculosis Programs (NTPs) • Determine the tolerance of test hardware to excessive heat, humidity, and dust • Identify if the fast-follower NAATs can be made more affordable and cost-effective compared to the Xpert® MTB/RIF assay given the recent price reduction of the GeneXpert® technology • Conduct case studies of successfully scaled-up tests and pragmatic trial results, incorporating their features into new test TPPs • Utilize patient, clinical and user assessments to identify tests that meet perceived needs

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		scale-up use of the automated nucleic acid amplification test (NAAT) for TB diagnosis I. Innovative financing • Determine market potential and market barriers for new TB diagnostic tests, after accounting for the roll-out of Xpert® MTB/RIF • Conduct market analyses to support new product development that will: o (i) convince industries and investors that investments in new TB tools are needed, o (ii) inform target product profiles (TPPs) that can guide product development and scale-up, and o (iii) guide donor/funder decisions	• Investigate mathematical modeling to explore the likely impact of various TPPs on reducing TB incidence • Find ways to ensure that the most critical elements evaluated in POC testing are rapid turn-around and communication of results to guide clinical decisions and completion of testing and follow-up action in the same clinical encounter (or at least on the same day) • Determine how POC testing can fit within real-world workflow patterns and economic/incentive structures to ensure use and sustainability • Determine whether Xpert® MTB/RIF implemented in centralized/reference laboratories will have an impact on reducing diagnostic and treatment delays • If Xpert® MTB/RIF is mostly used for drug-resistance screening or for smear-negative TB, determine if it will have an impact on TB transmission and incidence • Investigate whether implementation of Xpert® MTB/RIF and newer NAATs in a passive case detection approach reduce patient delays in seeking care, and the role of these technologies in intensified and active case finding • Determine whether NAATs be successfully implemented at the point-of-care to enable same-day TB diagnosis and treatment (i.e. a “test and treat” approach C. Drugs • None identified

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			D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • None identified Identify ways to support the implementation of GeneXpert instruments and Xpert cartridges • Investigate how to accelerate access to Xpert® MTB/RIF in countries with a high prevalence of TB/HIV co-infection • Consider how to train staff in peripheral microscopy centres to implement and use viable new fast follower NAATs • Develop processes to ensure quality assurance (QA) of NAAT performance is conducted before testing begins to demonstrate appropriate functionality • Identify how the performance of minimally-supervised NAAT users can be monitored via routine proficiency testing • Determine the appropriate regulatory and policy pathway for country-level adoption and scale-up of fast follower NAAT technologies • Conduct clinical and public health impact

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			evaluations of Xpert MTB/RIF at different health care levels • Conduct operational research and cost-effectiveness evaluations of MTB/RIF{E} • Determine the optimal positioning of MTB/RIF in diagnostic algorithms • Conduct qualitative and quantitative research to better understand patient health-seeking and provider behaviors in the community and elsewhere to design diagnostic technologies where early diagnosis is likely to succeed • Find ways to scale-up operational research to map out where individuals in the population seek health care, where health care services are available, what resources (including lab capacity) exist at each level of health care, what fraction of patients with suspected TB access each level of health care (patient volumes), where TB treatment services are available, and where technology deployment is likely to capture the largest fraction of patients with TB early in the infectious period • Utilize implementation science to understand the most important barriers to POC testing to use such data to design TPPs that can overcome delivery obstacles and health system limitations • Determine how to best design systems for rapid reporting of diagnostic test results to care providers, and a mechanism to link test results to appropriate counseling and treatment • Determine the best strategy for deploying

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			new diagnostics at the first point of contact among informal and private sector health providers I. Innovative financing • Identify how fast follower NAAT scan receive sufficient donor or investor support to undergo validation and demonstration studies that are required for WHO review and endorsement • Determine how much of the diagnostic TB market is addressed with Xpert® MTB/RIF, and problems/needs that have yet to be addressed • Create detailed TPPs necessary for product-specific needs in order to guide investments and engage industries and donors in meeting unmet needs
6. UNITAID. Tuberculosis: Medicines Technology Landscape. Geneva: World Health Organization; 2012. *The goal of this report is to provide TB stakeholders with an assessment of the TB medicines landscape so as to identify opportunities to improve market dynamics and ensure accessibility of safe and effective TB treatment.*	Findings from peer-reviewed literature and policy documents were combined with a survey of key institutions focused on improving TB treatment and the accessibility and rational use of TB medicines. The key informant survey does not capture the work of all institutions addressing TB treatment research and accessibility issues, though key informants were asked to identify other relevant institutions working on these issues. Most agencies identified were already surveyed for this	A. Basic science • Intensify TB-specific biomarker research, and validate TB-specific biomarkers for active TB disease in children and adults to assist in the production of diagnostic tests for clinical use • Identify biomarkers that can predict cure, treatment efficacy and failure, and relapse • Develop new molecules with novel ways of inhibiting or killing the TB bacteria B. Diagnostics • Develop a rapid low-cost, accurate, user-friendly, specific and highly	A. Basic science • Identify biomarker(s) that measures medicine activity in real time or can predict whether a medicine or regimen will result in a stable cure for a patient B. Diagnostics • None identified C. Drugs • Investigate how to reduce side effects and pill burden for patients co-infected with HIV • Conduct more randomized, controlled clinical studies to explore options that enhance cure rates for MDR-TB and XDR-TB

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	analysis, indicating that the survey for this analysis reached most key institutions. Research for this report was conducted in 2012; information presented is up to date as of August 2012.	sensitive point-of-care (POC) diagnostic test • Develop tools that can diagnose TB in children C. Drugs • Develop shorter TB regimens to cure all forms of TB that are safe, compatible with ART, effective against latent tuberculosis infection, affordable, easily managed in the field and that remain effective by limiting the development of drug resistance • Develop pediatric medicine formulations for children of all ages • Find ways to obtain better data on how best to use current medicines, especially in patients co-infected with HIV and in children • Investigate the drug-drug interactions of TB medications with treatments for other diseases or conditions, particularly with ART and opioid substitution therapy (OST) for drug-resistant TB (DRTB) • Conduct urgently needed research into whether delamanid and bedaquiline can be safely and effectively co-administered, as they are the two novel TB medicines furthest in development to treat people with MDR- or XDR-TB D. Preventative vaccines	• Determine how to obtain research evidence that can guide clinicians in determining appropriate TB treatment for children under five, especially for those with DR-TB • Tailor pediatric fixed-dose combination (FDC) formulations to deliver the dosages suitable to treat DS-TB in children • Determine how to include children in studies of second-line medicines (SLMs) so clinical trial data are able to inform the use of these medicines in children • Determine whether self-administered once-weekly rifapentine and isoniazid regimens with shortened duration actually improve adherence and cut costs by reducing patient visits, staff time, and number of pills in practice, particularly in high-burden countries • Develop second-generation compounds with better activity and better safety profiles than their predecessors • Develop child-friendly treatment formulations so pharmacokinetics (PK) studies of new compounds and SLMs can be initiated • Conduct pediatric PK studies to identify the therapeutic dose needed based on the absorption, metabolism, distribution, and excretion of the medicine based on child age and stage of development • Clarify the data and regulatory pathway on how best to combine more than one new compound to come up with a new regimen in a clinical trial

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		• None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Determine how to improve TB control programme performance and design interventions that result in improved policy-making, better implementation in health systems and more efficient and effective methods of service delivery • Find ways to ensure that TB programs adequately address preventing and treating the disease among high-risk populations, e.g. drug users and persons suffering from malnutrition, marginal housing, and poor housing conditions like overcrowding and bad ventilation • Examine how to expand the integration of IPT with ART and place responsibility for IPT on national AIDS programs (NAPs) so TB treatment is essential to HIV management and services become	D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Define and evaluate the performance of new diagnostic tests in terms of feasibility, cost-effectiveness, reduced diagnostic delay and impact on clinical decision-making and patient benefit • Develop means to scale up isoniazid preventive therapy under field conditions and in HIV clinics delivering ART • Develop strategies to strengthen the links between TB and HIV control programmes at all levels of health care, with optimal integration of interventions • Determine ways to scale up the implementation of isoniazid prevention therapy to treat latent TB infection (LTBI), and to get persons with LTBI to seek care • Identify ways to strengthen laboratory infrastructure and mentor new investigators for TB research in mid- to high-burden countries, e.g. by developing detailed manuals translated into local

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		more integrated • Identify ways to support the paradigm shift towards drug regimen development, as opposed to individual medicine development, that will require regulatory agencies, research institutions, funders, policy makers, and advocates to work more collaboratively to ensure that the efficient testing and approval of new regimens is safe and maximizes resources • Identify ways to harmonize regulatory requirements for TB treatment approval across agencies to expedite the review process • Identify ways to increase the effectiveness of procurement mechanisms for the uptake of quality assured medicines • Explore ways to engage civil society in greater advocacy around TB medicines to potentially positively impact forecasting efforts, the regulatory environment and procurement and distribution I. Innovative financing • Determine ways to increase funding levels to adequately support TB R&D, particularly for investments in diagnostics development and quality clinical trials • Determine market potential and	languages, training, and standardization exercises to qualify the laboratories in accordance with international guidelines • Determine how to develop capacity for regulatory authorities to ensure that they are able to respond to trial sponsors and provide timely feedback on protocols and medicine applications, e.g. by streamlining the process for submitting dossiers to health authorities • Find ways to reduce administrative delays in the application process that hinder implementation, raise the cost of studies, and may deter companies from investing in developing treatments for TB • Determine how to achieve better national planning for medicines stockouts in the public sector I. Innovative financing • Determine how to improve coordination between the leading funders of TB medicine procurement • Find ways to consolidate the fragmented public sector market for TB medicines • Determine how to obtain better data on the quality of medicines and their appropriate use in the private sector to allow a more accurate assessment of the total global market • Determine how to fully roll out the public-private mix to ensure rational use of medicines in line with global treatment standards and to harness the private-sector demand to further strengthen the

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		market barriers for new TB diagnostic tests, after accounting for the roll-out of Xpert® MTB/RIF • Conduct market analyses to support new product development that will: o (i) convince industries and investors that investments in new TB tools are needed, o (ii) inform target product profiles (TPPs) that can guide product development and scale-up, and o (iii) guide donor/funder decisions • Improve poor market forecasting for TB medicines to better anticipate demand, reduce risk and incentivize more manufacturers to enter the field of TB medicines development • Develop consistent and coordinated procurement practices to achieve the lowest sustainable price for quality assured TB medicines • Learn how to accurately size the market for TB medicines	market for QA TB medicines • Develop strategies that can further efforts to accurately anticipate demand, increase purchasing power through pooled procurement to reduce prices, or provide incentives to increase robust competition to ensure accessibility of quality TB treatment • Investigate ways to coordinate external donor funding and country-based public-sector funding to demonstrate actual demand and strengthen market forecasting of QA products
7. Lawn S, Mwaba P, Bates M, Piatek A, Alexander H, Marais B, et al. Advances in tuberculosis diagnostics: the Xpert MTB/RIF assay and future prospects for a point-of-care test. Lancet Infect Dis. 2013;13:349-361.	Lawn et al. searched PubMed and Google Scholar (Jan 1, 1995, to Dec 24, 2012), the Cochrane library (Jan 1, 2001, to Dec 24, 2012), and Embase (Jan 1, 2001, to Dec 24, 2012) for reports published in English with the terms “tuberculosis”,	A. Basic science • Intensify TB-specific biomarker research, and validate TB-specific biomarkers for active TB disease in children and adults to assist in the production of diagnostic tests for clinical use	A. Basic science • Identify a group of biomarkers that could be used for a simple diagnostic test within five years B. Diagnostics • Develop a protocol whereby sputum samples are pretreated to prevent the DNA

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
Lawn et al. review the rapidly growing body of scientific literature and discuss the advantages and challenges of using the Xpert MTB/RIF assay in areas where tuberculosis is endemic. They also review other prospects within the developmental pipeline.	"*Mycobacterium tuberculosis*", "TB diagnostic tests", "TB diagnosis", "clinical trials", "Xpert MTB/ RIF assay", "GeneXpert", "Cepheid", "accuracy", "sensitivity", and "specificity". The authors also searched the website of the STOP TB Partnership's New Diagnostic Working Group. They reviewed studies cited by articles identified by this search strategy and selected those we identified as relevant.	B. Diagnostics • Develop a rapid low-cost, accurate, user-friendly, specific and highly sensitive point-of-care (POC) diagnostic test • Develop a simple-to-perform, improved rapid molecular DST assays for first- and second-line drug resistance • Investigate the clinical and programmatic effects and cost-effectiveness of the Xpert MTB/RIF assay C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Identify ways to increase global capacity for drug susceptibility testing (DST)	in non-viable organisms being amplified during PCR • Assess the ability of the Xpert MTB/RIF assay to diagnose HIV-associated tuberculosis through urine sample testing on different populations • Investigate whether the Xpert MTB/RIF assay might enable active tuberculosis screening to be done within antenatal clinics in high tuberculosis burden settings • Investigate whether Xpert MTB/RIF assay's new software and cartridge combination, G4, improves line-probe assays concordance with rifampicin resistance • Explore the potential for fully automated NAAT systems that use isothermal amplification and operate at lower temperatures to be used outside the laboratory environment • Investigate the clinical effect and accuracy of the new point-of-care immune-chromatographic (dip-stick) assay that detects mycobacterial lipoarabinomannan in urine in different settings C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		I. Innovative financing • Determine ways to increase funding levels to adequately support TB R&D, particularly for investments in diagnostics development and quality clinical trials • Find ways to reduce the cost and time taken for sufficient evidence to be gathered on diagnostic tools prior to their review and endorsement by WHO's STAG-TB, particularly for smaller companies	• None identified G. Epidemiology • None identified H. Health systems/public health research • Identify strategies to scale-up access to MDR- and XDR-TB treatment in resource-limited settings and improve treatment outcomes, whether or not associated with ART • Consider how to train staff in peripheral microscopy centres to implement and use viable new fast follower NAATs • Identify ways to strengthen laboratory infrastructure and mentor new investigators for TB research in mid- to high-burden countries, e.g. by developing detailed manuals translated into local languages, training, and standardization exercises to qualify the laboratories in accordance with international guidelines • Conduct urgently needed operational research on the clinical outcomes and effects of programmatic implementation efforts for Xpert MTB/RIF • Determine the potential benefits from reduced morbidity, mortality, and disease transmission associated with appropriate delivery of TB treatment and lower rates of inappropriate therapy • Strategize how national ministries of health can take a step-wise approach to introduction and scale-up of Xpert MTB/RIF, beginning with the establishment

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
			of an in-country coordination mechanism, e.g. an Xpert MTB/RIF assay technical working group or advisory team • Develop Xpert MTB/RIF implementation plans that consider the local epidemiology, available diagnostic services and laboratory systems, first-line and second-line drug treatment capacity and align with relevant strategic plans (eg, national tuberculosis and AIDS control programmes and national laboratory strategic plans) • Conduct embedded research studies and enhance monitoring and assessment of the South African success with Xpert MTB/RIF assay implementation • Find ways to match increased diagnosis of drug-sensitive tuberculosis and MDR tuberculosis with expanded capacity to effectively treat these cases, including a scale-up in quality MDR tuberculosis treatment facilities and trained staff • Design rigorous quality assessment programmes for TB treatment and diagnosis to ensure results are accurate, e.g. following the South African model that used dried culture spots of inactivated *M tuberculosis* on filter paper I. Innovative financing • Determine how the donor assistance that has heavily subsidised the implementation of Xpert MTB/RIF in resource-limited settings will affect the development and entry of newer diagnostic assays to the marketplace

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
8. Wallis R, Kim P, Cole S, Hanna D, Andrade B, Maeuer M, et al. Tuberculosis biomarkers diversity: developments, needs and challenges. Lancet Infect Dis. 2013;13:362-372. *Wallis et al. review progress in tuberculosis biomarker development and efforts being made to harness resources to meet future challenges.*	Wallis et al. searched in PubMed and Google Scholar (Jan 1, 1980–Dec 31, 2012), the Cochrane Library (Jan 1, 2001–Dec 31, 2012), and Embase (Jan 1, 2001–31 Dec, 2012) for English language publications with the terms "tuberculosis", "*Mycobacterium tuberculosis*" plus "biomarker", "vaccine", "gene expression", "micro-RNA", "proteomics", "metabolomics", "positron", "interferon gamma release", or "clinical trial". They also reviewed studies cited by articles identified by this search strategy and selected those that we identified as relevant. Some review articles are cited to provide readers with more details and references than this review can accommodate.	A. Basic science • Intensify TB-specific biomarker research, and validate TB-specific biomarkers for active TB disease in children and adults to assist in the production of diagnostic tests for clinical use • Identify biomarkers that can predict cure, treatment efficacy and failure, and relapse • Identify specific single biomarkers or combinations of biomarkers that can distinguish latent tuberculosis infection versus subclinical versus active tuberculosis disease; identify those who are at highest risk for progression to disease; and predict protective immunity • Better understand the interaction between the bacillus and the human host • Delineate the specific mechanisms of protective immune networks between people (host) and *M. tuberculosis* (pathogen) • Better characterize *M. tuberculosis* to refine understanding about the transition from latent to active TB and identify the biomarkers of disease progression • Better define the profile of desired characteristics (ie, target product profile) for key biomarker research areas • Strategize how to maximise and	A. Basic science • For biomarkers that are non-culture-based, find ways to increase the availability of well characterised biobanks containing bio-specimens from patients who have had adequate follow-up to establish long-term treatment outcome and better qualify biomarkers as a surrogate for a clinical endpoint • Conduct full synthesis studies on the role of month 2 culture status as a biomarker predictor of required duration of treatment • Determine the optimum methods for specimen collection (pooled over 12–16 h *vs* spot) and processing (decontamination with sodium hydroxide variably decreases mycobacterial viability) for automated liquid culture systems used in biomarker development • Conduct studies on the ability to resuscitate or recognise live but dormant non-replicating bacilli and mechanisms behind relapse to improve existing culture-based detection systems • Conduct further studies of lipoarabinomannan as a candidate biomarker • Explore changes in tuberculosis-specific gene and protein expression profiles (transcriptomics) as potentially viable in assessing of the early response to tuberculosis treatment • Investigate the prognostic significance of resuscitation-promoting factors in the

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		optimise biomarker research through coordination and increased collaborations between basic scientists, clinical triallists, pharmaceutical industry and end users • Determine how to validate new biomarker discoveries and translate new biomarker discoveries into functional point-of-care use B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Explore ways to scale-up central biobanks for the provision well-characterised samples for the validation of biomarkers research	detection of otherwise non-culturable mycobacteria in sputum • Explore the measurement of host gene expression profiles as biomarkers of treatment efficacy, and if this method could provide more information about clinical outcome than would quantitative sputum microbiology • Conduct prospective longitudinal studies of MicroRNA and metabolomic patient profiles as potential indicators of TB cure and reactiviation • Conduct further studies of bactericidal or viral neutralisation assays after vaccination in people in tuberculosis-endemic regions to assess the potential correlation with clinical outcomes • Pursue cross-sectional studies of close tuberculosis contacts without HIV with minimally symptomatic subclinical disease that could provide important information about candidate biomarkers B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		I. Innovative financing • None identified	F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • None identified I. Innovative financing • None identified
9. Wells W, Boehme C, Cobelens F, Daniels C, Dowdy D, Gardiner E, et al. Alignment of new tuberculosis drug regimens and drug susceptibility testing: a framework for action. Lancet Infect Dis. 2013. Available from: http://dx.doi.org/10.1016/S1473-3099(13)70025-2. *Wells et al. examine how surveillance data and modelling can help country stakeholders to design appropriate DST algorithms and to decide whether to change drug regimens. They assess how the development of practical DST assays can be used to guide clinical decisions for individual patients. If combined judiciously during both*	This Series paper draws on material from a meeting of the Tuberculosis Diagnostics Research Forum sponsored by the Bill & Melinda Gates Foundation and the US National Institutes of Health held on Oct 1–2, 2012, in Arlington, VA, USA. Additionally, we identified references for this review by searching PubMed with a focus on articles published between January, 2008, and November, 2012. Search terms included, but were not restricted to, "tuberculosis", "drug susceptibility testing", "drugs", "diagnostics", "drug resistance", "surveillance", and "point-of-care testing". We did not apply language restrictions. Additional information came from our personal collections of peer-reviewed papers, from the	A. Basic science • Find ways to obtain better data about the molecular immune mechanisms of resistance —and the correlation of those mutations with clinical outcomes—for the development of drug susceptibility testing (DST) assays and vaccines B. Diagnostics • Find ways to gain consensus on which target product profile (TPP) attributes will have the biggest impact on reducing the incidence of TB in disease-endemic countries, and which meet clinical and practical needs C. Drugs • Develop pediatric medicine formulations for children of all ages • Find ways to ensure joint development and implementation of new tuberculosis regimens and	A. Basic science • Determine how to scale up the translational science needed to provide the basis for molecular diagnostics development • Find ways to link gene mutations to phenotypic resistance (ie, the amount of drug needed to inhibit bacterial growth) using translational sciences research • Develop strain collections (preferably sequenced) that will assist with the testing of new diagnostic assays and the development of genomic databases that would predict drug susceptibility phenotypes B. Diagnostics • Determine whether new fast follower NAAT tests fit with current TB diagnostic algorithms and if they can be successfully implemented in peripheral microscopy laboratories in high burden countries • Test the viability of the rifampicin DST to diagnose MDR tuberculosis

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
development and implementation, new tuberculosis regimens and new DST assays have enormous potential to improve patient outcomes and reduce the burden of disease.	reference lists of identified papers, and from reviewers.	new DST assays for enhanced clinical performance D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Determine how to best utilize surveillance data and mathematical modelling to help country stakeholders design appropriate DST algorithms and decide whether to change drug regimens • Determine how to establish existing or emerging resistance levels via surveillance data I. Innovative financing • Determine market potential and market barriers for new TB diagnostic tests, after accounting for the roll-out of Xpert® MTB/RIF • Conduct market analyses to support new product development that will:	• Investigate isoniazid DST as a means to detect isoniazid-resistant, rifampicin-susceptible strains, whose patients have reduced treatment success • Study DST to detect susceptibility to rifampicin and fluoroquinolones for implementation of 4-month regimens, especially in countries that already do DST for rifampicin • For the PaMZ regimen, develop a rapid test for moxifloxacin and pyrazinamide because clinically significant resistance to PA-824 has not yet been shown • Develop DST for PA-824 and other new drugs for use in surveillance as resistance to them develops and their use becomes more widespread • Better characterize silent mutations by standardised and validated culture-based pyrazinamide resistance assays and incorporate findings into a molecular testing algorithm C. Drugs • Identify optimal treatment regimens for all TB patient types, including TB-HIV co-infection and infected children • Determine optimal dosage, safety and efficacy of new drugs and their interaction with other TB and non-TB drugs • Conduct post-marketing studies to identify treatment failures and resistance mechanisms of new TB drugs D. Preventative vaccines

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		o (i) convince industries and investors that investments in new TB tools are needed, o (ii) inform target product profiles (TPPs) that can guide product development and scale-up, and o (iii) guide donor/funder decisions	• None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Find ways to obtain nationally representative data on moxifloxacin and pyrazinamide resistance • Identify how to scale up surveillance to monitor the development of resistance to bedaquiline, delamanid and others • Find ways to inspire research collaboration within a country undertaking a drug resistance survey to pilot new DSTs and develop monitoring systems linked with treatment outcomes and patient care; such a study could provide the proof of principle and the data to validate new integrated monitoring system • Determine where DST should be placed in treatment algorithms for various epidemiological and economic contexts{l} • Determine what different DST assays—with different speed, accuracy, price, and technical specifications (ie, which drugs, how many mutations)—would achieve in terms of a population-level effect and cost-effectiveness, and what the trade-offs are

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
			between these various specifications • Determine the population-level effect and cost-effectiveness of different DST algorithms (eg, DST for all, DST for only patients who are being re-treated or in whom previous treatment had failed, or use of new regimens without DST) as a function of baseline drug resistance and rate of emerging resistance • Determine whether DST is better bundled into case-detection assays (as with the Xpert MTB/RIF assay), or if should it be a reflex test that is done only after tuberculosis is diagnosed • Determine how to simplify the patient protocol for DST to improve follow-up should non-centralised DST remain the leading public health strategy I. Innovative financing • Develop a mechanism to ensure that private laboratories pass along any savings from assays purchased at concessionary prices toward private sector procurement of new DST assays • Find ways to provide diagnostic companies with greater information to predict user needs (where the user is often a national tuberculosis programme) and market demand to reduce the risk associated with DST investments
10. Brennan P, Robertson B. Tuberculosis vaccines: a strategic blueprint for the next decade. Elsevier. 2012.	The Tallinn meeting was distinguished by the exceptional prior preparation and organization. Most	A. Basic science • Intensify TB-specific biomarker research, and validate TB-specific biomarkers for active TB disease in	A. Basic science • Determine why certain individuals infected with *M. tuberculosis* are resistant to TB disease

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
92(1):S1-S35. *This special Supplement to Tuberculosis is distinguished by the presentation of the important document Tuberculosis Vaccines: A Strategic Blueprint for the Next Decade. The authors acknowledge the sources of funds that facilitated the convening of the Tallinn meeting and the subsequent shaping of the document, and also those others who contributed to its final structure. In this supplement the Blueprint itself is complemented by several key papers that capture the outcomes of discussions from Workshops held at the Tallinn forum.*	important were the pre-conference surveys distributed to the relevant community – researchers, clinicians, pharmaceutical companies, government and non-government agencies, donors and other stakeholders involved in the global TB vaccine development efforts. Out of these efforts arose a consensus definition of the priority areas, the essentials for progress, the critical research and discovery activities to be followed, and the hallmark decision points in selection of TB vaccine candidates for clinical trials. All of these aspects provide the framework of this *Blueprint*, a document in itself is a model in clarity, decisiveness and presentation.	children and adults to assist in the production of diagnostic tests for clinical use • Identify specific single biomarkers or combinations of biomarkers that can distinguish latent tuberculosis infection versus subclinical versus active tuberculosis disease; identify those who are at highest risk for progression to disease; and predict protective immunity • Find ways to obtain better data about the molecular immune mechanisms of resistance —and the correlation of those mutations with clinical outcomes—for the development of drug susceptibility testing (DST) assays and vaccines B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • Develop a more effective vaccine to supersede the BCG vaccine • Develop a safe, effective, affordable vaccine to prevent all forms of TB in all age groups and that is safe for people with HIV and other forms of immunosuppression • Identify correlates of immunity and biomarkers for TB vaccine	• Identify new targets for anti-TB drugs and early indicators of protective immunity for vaccine efficacy • Learn what constitutes protective immunity in different age groups and populations against TB • Identify the respective components of the host's immune system and of the pathogen that are responsible for elimination of *M. tuberculosis* or for preventing reactivation of latent TB infection • For biomarkers that are non-culture-based, find ways to increase the availability of well characterised biobanks containing bio-specimens from patients who have had adequate follow-up to establish long-term treatment outcome and better qualify biomarkers as a surrogate for a clinical endpoint • Identify correlate or surrogate endpoints of protective immunity • Gain a more thorough understanding of the very earliest events of infection with Mtb and their consequences • Better understand and characterize the antigens involved in Mtb host immune evasion mechanisms • Conduct genome-wide host gene expression profiling studies that can point to novel host biomarker signatures of both protective immunity and disease activity, identify potential correlates of protection, and also unravel cellular pathways involved in the pathogenesis of and resistance to Mtb

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		development • Design a vaccine that elicits a response that is superior to natural immunity induced by infection with Mtb • Explore the potential for developing a transmission-blocking TB vaccine • Determine how to build and engage in collaborative efforts to advance the use of novel adjuvants for TB vaccines • Determine how to establish comprehensive, measurable and globally acceptable criteria for selecting, assessing and advancing the best vaccine candidates in human clinical studies • Find ways to increase the profile of TB vaccine research at global, national and community levels in order to generate support and political will, to increase investment in TB vaccine research, to create an enabling and supportive environment for clinical trials, and to lay the groundwork for acceptance and adoption of new TB vaccines once licensed • Determine if vaccines can prevent infection and provide sterilizing immunity E. Therapeutic vaccines • None identified	• Explore novel (high risk) approaches using immunological, transcriptional and other biological state-of-the-art technologies to identify correlates of immunity for tuberculosis B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • Develop new animal and human challenge models and objective criteria for down selecting vaccines for the various target profiles, especially vaccines preventing reactivation of latent *Mycobacterium tuberculosis* (Mtb) infection • Utilize innovative research approaches to gain a better understanding of TB immunology, microbiology, pathology, molecular biology and vaccinology{j} • Integrate creativity in R&D via the following strategies: o Use out-of-the-box approaches and advanced technologies to identify mechanisms of protective immunity for tuberculosis o Expand the antigenic vaccine repertoire and introduce new antigen combinations to prevent infection and provide sterilizing immunity o Facilitate translational research, comparative preclinical studies and

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		F. Vector control • None identified G. Epidemiology • Determine which sources of data should be used to establish TB incidence rates H. Health systems/public health research • Investigate how to expand upon efforts to raise awareness of the role of new TB vaccines as part of a comprehensive response to the global TB epidemic, and build support at all levels I. Innovative financing • Determine ways to increase funding levels to adequately support TB R&D, particularly for investments in diagnostics development and quality clinical trials • Find ways to expand financing to provide sufficient resources to advance and sustain research on TB vaccines • Identify new funders and determine how to establish new partnerships and collaborations for TB R&D • Identify opportunities for cost-sharing across sectors and better utilization of existing resources • Explore new innovative financing models	animal models that mimic human TB disease • Explore antibody-mediated mechanisms for transmission blocking vaccines development • Explore and expand the glycolipid and polysaccharide repertoire of Mtb vaccine development • Investigate the use of non-conserved, sequence variable antigens of Mtb which could prove to be conformationally conserved in the design of vaccines, particularly live whole cell vaccines{J} • Investigate the use of stage specific, less dominant, and more sequence variable antigens recruiting novel populations of immune cells for use in adjuvant development • Identify new or better animal models that enable assessment of protective responses for specific human target populations (including natural infection) and for defining correlates of protection, e.g. promising cattle and pig transmission models • Determine how to standardize existing animal models • Explore applications of new technologies for measuring vaccine responses in animal models such as modern imaging technologies • Identify ways to utilize circulating human clinical isolates as challenge strains in preclinical models • Develop and adapt models for vaccine

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		• Identify ways to broaden the base of advocates, allies and champions for TB and vaccine R&D • Find ways to establish and fund trusted global organizations or consortia that can broker partnerships, coordinate meetings, establish useful websites and offer venues that solve problems in a timely manner	submissions to regulatory agencies to address issues of safety, immunogenicity and effectiveness required for regulatory approvals • Find ways to learn from experimental failures by publishing data or making it available through information sharing mechanisms • Develop methods to learn from the successes and failures of others, especially those researching malaria, HIV and cancer vaccines • Discover biomarkers that predict vaccine efficacy, that serve as useful markers of vaccine success, that correlate with natural protection and susceptibility, as well as markers that correlate with disease risk following infection • Further investigative and identify biomarkers that are associated with disease progression or remission, e.g. longitudinal assessment of a range of clinical markers can provide a sensitive and specific indicator of vaccine effects through modulation of the disease state{J} • Find ways to introduce novel assays into vaccine trials to establish a surrogate of protective immunity • Identify signatures of efficacy that can be used as readouts for induction of protective responses in TB vaccine studies • Find ways to improve clinical capabilities for testing novel TB vaccines in all age groups, in individuals infected with Mtb and/or HIV and in BCG vaccinated persons

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
			in a cost effective manner in difficult environments in endemic countries • Find ways to develop innovative partnerships, sharing of sites, harmonization of endpoints and other clinical trial parameters and mechanisms for acquiring efficient regulatory review of trials • Determine TB prevalence and incidence, select trial sites and choose target populations for TB vaccines that result in the greatest reduction in disease • Design clinical trials with appropriate endpoints for determining an acceptable efficacy for TB vaccines in different target populations • Determine ways to address regulatory and ethics issues and plan for post-licensure sustainability in developing countries • Conduct efficacy trials that target HIV negative adolescents/adults given that they have higher rates of TB, they are important targets for mass vaccination campaigns and clinical endpoint definitions will likely be much clearer • Define large, global networks that would aim to conduct specific types of trials for promising vaccine candidates to overcome barriers of testing in a single location • Determine how organizations performing clinical studies in areas endemic for infectious diseases can best share trial site infrastructure to expedite clinical trials of vaccines • Target infants for replacement and prime-

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
			boost vaccine development, and conduct accurate assessments of efficacy in this group • Explore adaptive trial designs that can drop ineffective or reactogenic candidates, or modify group sizes based on predefined criteria to accelerate the clinical development of a vaccine • Develop creative strategies for obtaining timely regulatory approvals while assuring the quality of the review and protecting clinical subjects • Identify how to engage regulatory authorities early in the development process so that sponsors can receive advice from regulators on clinical trial design, endpoints and ethical issues • Conduct post-marketing surveillance to assess the potential for rare adverse events • Determine ways to establish mechanisms for assuring the sustained quality of TB vaccines following marketing authorization and distribution • Determine how to perform head to head candidate comparisons within agreed upon model systems to help decision making in the candidate selection process • Develop robust critical assessment of vaccine product characteristics • Explore standardizing assays among laboratories evaluating clinical specimens or use of a centralized laboratory to enable comparison among different candidates • Find ways to obtain consensus within the

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
			TB community on stage-specific criteria for moving new candidates through various stages of development from research to preclinical and through subsequent phases of clinical trial testing • Determine can investigators can cooperate to combine new Mtb antigens with novel adjuvants to develop the best TB vaccines • Determine if antibody responses to TB vaccines are relevant to protection • Identify the best clinical strategies for showing that vaccines can effectively prevent the reactivation of latent TB disease • Identify the best strategies for studying therapeutic TB vaccines E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • Determine how to gather good quality data through epidemiological studies that can serve as a guide for planning vaccine efficacy trials, and determine how to fund such work H. Health systems/public health research • Gain a greater understanding of the complexities of global control of TB, as well as the shortcomings of the currently available BCG vaccine to stimulate demand

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
			for new TB vaccines from communities, national level policymakers, decision makers and international leaders who set global health priorities and action • Find ways to broadly communicate and disseminate the findings of recent public health impact modeling and expand cost-effectiveness modeling for TB vaccines • Fully investigate linkages between TB and other global health and development issues, such as HIV/AIDS and maternal and child health, the threat of MDR and XDR-TB and the contributions that new TB vaccines could make to advance the global health and development agenda • Identify ways to inform and engage the media, government officials, NGOs, affected communities and other key stakeholders at the community, regional and country level about the value of TB vaccine development efforts and clinical trials in order to ensure transparency, generate a supportive environment and reduce the probability of misinformation or negative public response to clinical trials • Find ways to link to organizations developing similar products for neglected global diseases other than TB so that lessons learned and solutions to common problems can be effectively communicated to the TB community • The organizations developing new diagnostics and drugs for TB should work closely together with the vaccine community to effectively reduce TB

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
			disease in at risk communities • Determine the best criteria for measuring the public health impact of vaccines I. Innovative financing • Find ways to engage emerging economies, and particularly the "BRICS" countries (Brazil, Russia, India, China and South Africa), as important partners in global efforts to develop new TB vaccines • Determine ways to provide donors, policymakers, health care providers, civil society and other key stakeholders with information and evidence to support investment in TB vaccines • Determine how to engage with the broader global health community, emphasizing the alignment between TB research and global health and development • Find ways to link the TB advocacy and research communities that operate independently of one another to promote the need for continued and expanded investment in global health research

Disease-specific R&D priority setting

HIV/AIDS

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
1. Joint United Nations Programme on HIV/AIDS (UNAIDS). Global report: UNAIDS report on the global AIDS epidemic 2012. Geneva: UNAIDS; 2012. *The UNAIDS Report on the Global AIDS Epidemic provides the latest data on numbers of new HIV infections, numbers of people receiving antiretroviral treatment, AIDS-related deaths and recommendations to overcome challenges to reach the targets set forth in the 2011 Political Declaration.*	In 2012, 186 countries submitted comprehensive reports on progress in their national AIDS response (equivalent to 96% of the 193 United Nations Member States). The report summarizes the current situation in the effort to reach the 2015 targets set forth in the 2011 Political Declaration and identifies key trends. Using a scorecard approach on key indicators, the report allows individual countries to compare their own achievements with those of others. Regional breakdowns enable comparison of progress between different parts of the world. As part of global AIDS response monitoring, countries have completed extensive surveys on national AIDS policy frameworks. The National Commitments and	A. Basic science • Develop new anti-microbicidal agents to prevent transmission B. Diagnostics • Design testing services that are simple and easy to access C. Drugs • Investigate ways to improve results at each stage of the treatment continuum • Learn how to improve the efficiency and effectiveness of treatment programmes for high-risk groups D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • Find ways to ensure that testing programmes are reaching the age and population cohorts at highest risk, particularly those co-infected with tuberculosis (TB) and HIV	A. Basic science • Develop rectal microbicides to prevent sexual transmission of HIV among men who have sex with men (MSM) B. Diagnostics • Continue to develop a broad array of new testing strategies • Focus on enhancing provider-initiated testing and counselling, rapid testing technologies and home-based testing methods C. Drugs • Determine whether to maintain lifelong triple antiretroviral therapy for pregnant women living with HIV who initiate treatment at CD4 counts above 350 per ml, whether to include efavirenz in combination regimens for pregnant women and the type and duration of recommended infant-feeding practices to maximize prevention benefits for the child • Evaluate and refine joint treatment drug regimens for co-infection of TB and HIV • Prioritize research into treatment options that reduce the risk of HIV transmission among children D. Preventative vaccines • None identified E. Therapeutic vaccines

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
	Policies Instrument obtains information on the process of national strategizing on AIDS, engagement of civil society and other key constituencies as well as policy approaches for HIV prevention and treatment.	H. Health systems/public health research • Investigate how to improve retention rates for people enrolled in HIV care and treatment • Consult and engage communities in planning how to best scale up access to treatment • Identify ways to make health systems more responsive to the needs of vulnerable populations • Accelerate the next phase of HIV treatment by prioritizing implementation research on existing interventions • Identify ways to expand joint treatment programmes for co-infection of TB and HIV I. Innovative financing • Identify means to further reduce the cost of antiretroviral medicines and per-person treatment costs through better program management • Develop innovative funding mechanisms to spur additional health research and development for HIV and other health problems confronting low- and middle-income countries, with particular emphasis on developing affordable new tools to address priority issues • Strategize how to cultivate emerging economies as international AIDS donors within a framework of global	• None identified F. Vector control • None identified G. Epidemiology • Identify ways to strengthen health reporting systems to monitor treatment retention by age and sex • Identify ways to strengthen case reporting and the tracking of progress of the collaborative HIV and TB activities by HIV stakeholders through harmonized indicators and globally recommended patient monitoring systems • Learn how to improve the reporting of sex-aggregated epidemiological and HIV service coverage data for injection drug users • Produce reliable national estimates of the total number of people who inject drugs • Investigate how to reach out to, and monitor, a higher proportion of MSM H. Health systems/public health research • Strategize how to link HIV-positive persons to easily accessible care that where they can be swiftly evaluated • Find new ways to improve treatment coverage among children, especially those who are youngest and most vulnerable • Develop methods to reach more men earlier with HIV testing and treatment services in high-prevalence settings • For MSM, investigate how combining prevention efforts on HIV-related behaviour, access to antiretroviral therapy for MSM who are HIV-positive, and the potential use of pre-exposure

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		solidarity and shared responsibility	prophylaxis in a coordinated and accelerated programme can reduce the sexual transmission of HIV • Involve people living with HIV and affected communities in planning, implementing and evaluating high-quality, rights-based care and treatment programmes to improve retention rates • Produce consistent nationwide data that permit retention rates to be tracked over time, and continue reporting for people who transfer to new treatment centers • Research how to scale-up the three I's for HIV and TB (intensified TB case- finding; isoniazid preventive therapy and infection control for TB) I. Innovative financing • Identify ways to reduce the cost of antiviral medications, particularly second- and third-line regimens • Develop strategies to manage intellectual property that are oriented towards public health goals, such as the full use, as required, of flexibilities permitted under international regulations such as the Agreement on Trade-Related Aspects of Intellectual Property Rights administered by the World Trade Organization • Identify ways to build-up local pharmaceutical capacity and take full advantage of the flexibilities permitted under the Trade-Related Aspects of Intellectual Property Rights (TRIPS) agreement • Develop a monitoring system to ensure that national HIV spending is focused on effective investment and increases in domestic spending, including developing innovative and sustainable AIDS funding sources

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
			• Determine how to improve the efficiency of AIDS spending through such means as capturing productivity gains, further reducing the costs of antiretroviral medicines, integrating services and improving service delivery
2. Joint United Nations Programme on HIV/AIDS (UNAIDS). World AIDS Day Report 2012. Geneva: UNAIDS; 2012. *The report provides an update on the HIV/AIDS epidemic, outlines some of the significant progress made in the AIDS response in recent years, and includes information on declining HIV infections in children, reduced AIDS-related mortality, and the need for continued investing both domestically and internationally to overcome pressing challenges in order to reach the targets set by the 2011 Political Declaration by 2015*		A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • Gather better data on service needs and coverage among vulnerable groups H. Health systems/public health research • Determine how to increase population-based HIV testing to reach persons at highest risk • Determine how to increase access to antiretroviral therapies to all eligible persons, particularly sex workers,	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • Estimate service needs and coverage among women and children at highest risk of HIV in countries with concentrated epidemics H. Health systems/public health research • Identify means to provide HIV discordant couples with greater access to antiretroviral therapies, and use antiretroviral therapy as a prophylaxis for people at high risk of HIV infection • Strategize how to actively engage community members in providing care to raise treatment

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		MSM and people who inject drugs • Improve retention rates for people enrolled in HIV treatment programmes I. Innovative financing • Identify ways to reduce the cost of HIV treatment to maintain the treatment bottom line • Investigate ways reduce dependency on overseas development assistance for national-level AIDS responses	retention rates • Investigate ways to overcome human resource constraints on service delivery • Determine why despite improving access to health care, pregnant women are not starting, or being reported to start, antiretroviral therapy • Develop combined behavioural, biomedical and structural strategies, both intensively in specific populations in concentrated epidemics and across the whole population in generalized epidemics • Understand and resolve the gender gap in services for drug users whereby women who inject drugs have even poorer access to HIV services I. Innovative financing • Identify ways to reduce the cost of second and third line treatment regimens • Better leverage opportunities to link treatment to other services like couples counselling and testing or opioid substitution therapy • Determine how to shift from international to domestic production of drugs
3. European Commission. Final Report: Challenges for the Future Research on HIV/AIDS, Malaria, and Tuberculosis. Luxembourg: European Communities; 2009. *The European Commission's Final*	On 13 and 14 November 2008, the European Commission (DG Research) brought together a large number of stakeholders in an International Conference on Poverty-Related Diseases (PRDs) with the aim of increasing the impact of EU-funded research on controlling PRDs. Leading	A. Basic science • Conduct research on approaches to eliminate viral latency and associated reservoirs of persistent infection. • Explore how to induce broadly reactive neutralising antibodies, as well as how to induce and maintain mucosal immunity. • Determine methods to exploit innate immunity and how to control infection with cell-mediated	A. Basic science • Explore the utilization of immune modulation, gene therapy, and therapeutic vaccines to address viral latency. • Conduct basic research into B-cell biology as it relates to the induction and maintenance of effective antibodies, and better understand the mechanisms of B cell impairment. • Determine how innate immunity can be engaged to enhance immunity of vaccines as applied to the rational development of novel adjuvant

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
Report on the Challenges for the Future Research on HIV/AIDS, Malaria and Tuberculosis provides a summary of the 2008 European Commission Conference for research priorities on HIV/AIDS, Malaria, and Tuberculosis. Providing an update on the progress that has been achieved by the European Commission's Seventh Framework Programme, the panel of speakers also provide detailed insight into current gaps and future research priorities.	scientists, research managers, decision-makers, funding agencies and relevant international NGOs attended (over 350 representatives from 63 countries), with significant participation from disease-endemic countries. The goals of the conference were to: i) regain political momentum for continuing and intensifying research addressing the "big three" global killer diseases; ii) set the scene by reporting on research efforts supported by the EC since 2002, when HIV/AIDS, malaria and TB first became a separate research focus under the EU's 6th Framework Programme (FP6); iii) gather input from relevant stakeholders (scientists from Europe and disease-endemic countries, industry, funding agencies, global partners, etc.) in order to set research priorities on PRDs for the remainder of the 7th Framework Programme (FP7) and beyond. After a plenary session on day 1, separate breakout sessions	responses. • Explore the interactions between effective microbicides (or oral PREP) and potential prophylactic vaccines. B. Diagnostics • None identified C. Drugs • Expand the current microbicide pipeline beyond the use of antiretroviral microbicides. • Develop microbicides that are combination products that reduce the potential for resistance. • Identify drug leads directed against known targets but also against novel viral (i.e. structural and regulatory proteins) or cellular targets. • Design new drugs that target highly conserved molecular and functional areas or epitopes on their target and that show minimal, if any, cross-resistance to other classes of existing antivirals. • Create new drugs with less long-term side effects. • Explore pharmacological and mechanistic insights in drug-action and drug/drug interaction to define and select the most optimal drug combinations. • Build upon the successful results of oral pre-exposure prophylaxis results.	strategies. • Explore how innate immunity might be utilized to accelerate amnestic vaccine responses following viral exposure. • Determine whether microbicide-vaccine interactions could boost or modify vaccine responses • Explore whether microbicides (or PREP) could be used during immunization to cover any period of potential enhanced susceptibility induced by potent immunogens, adjuvants or vectors. • Research whether a combination of vaccines and microbicides can prevent viral breakthrough that might be seen with either intervention strategy if used alone. • Conduct studies to understand the risk of resistance for next generation microbicides. B. Diagnostics • None identified C. Drugs • Invest resources in novel target identification, engagement of innate immunity, and the possible use of gene therapy to express protective factors. • Create microbicide formulations that maximize subject adherence and give sustained release to reduce compliance burden. • Develop better biomarkers of safety and efficacy for microbicides. • Elucidate the molecular events leading to infection to support rational targeting of microbicide strategies. • Determine whether antiretrovirals acting later in the viral cycle (integrase, protease inhibitors etc)

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	for the three diseases were organized. On day 2 conclusions of the breakout sessions were presented and discussed. This report summarises deliberations and recommendations of the HIV/AIDS, Malaria and TB working groups.	D. Preventative vaccines • Develop a neutralizing antibody-based vaccine that prevents HIV infection. • Explore non-classical routes to antibody-mediated protection for vaccine development. • Create a T-cell based disease-modifying vaccine. • Understand the role of mucosal immunity in the development of a preventive HIV vaccine. E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Determine methods to address the management of long-term toxicity in treated patients. • Understand correlates or surrogates of HIV protection and/or viral containment. • Continue the ability to perform para-clinical studies in non-human primates and small human clinical trials for safety and immunogenicity. • Determine the optimal time to initiate clinical antiretroviral therapy. • Perform research to facilitate	have a role to play in prevention. • Understand how new technology (multi-plex cytokine analysis, proteomics, transcriptomics, etc.) can be best applied to safety monitoring. • Assess vaginal and penile safety. • Develop markers of drug pharmacokinetics and pharmacodynamics as potential predictors of efficacy. • Conduct parallel studies in human and nonhuman primates to determine whether ex-vivo viral challenge of mucosal biopsies following in vivo application of microbicides may provide a surrogate marker of protection. • Gather scientific criteria to determine the potential window of protection for microbicides (time from application to intercourse). • Assess the efficacy of intermittent dosing for oral pre-exposure prophylaxis. • Identify drugs that are endowed with a high genetic barrier (i.e. multiple mutations in the target are required to afford significant phenotypic resistance) from the very beginning in the drug development process. • Utilize pharmacokinetics and genetics during drug treatment to predict the emergence of potential side-effects. • Perform research to optimally use old as well as new drugs, in particular in rational combinations. • Utilize non-classical combinations such as NRTI-sparing regimens, and including a role for new agents like IN or entry inhibitors. • Address potential viral reservoirs during novel drug development using various approaches (i.e. immunotherapy).

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		diagnosing the infection early in its course and reduce infectiousness. I. Innovative financing • None identified	D. Preventative vaccines • Increase molecular understanding of the HIV envelope spike structure and its interaction with broadly neutralizing antibodies (bNAbs) that may support NAbs induction. • Explore additional functional antibody activities (including ADCC, ADCI, macrophage inhibition, transcytosis inhibition and viral aggregation) to determine their potential contribution to protection. • Conduct research related to inducing antibodies to the chemokine coreceptors and/or providing broadly neutralizing antibodies passively via a viral vector or stem cell transformation. • Define the antigens and appropriate vectors that elicit the most potent inhibition of virus replication. • Research insert and vector design in order to maximize breadth and magnitude of CD8 responses. • Develop novel CD8 inhibition assays. • Define the role of virusspecific CD4 T helper cell responses (both positive and negative attributes) in durable HIV containment. • Increase the availability of mucosal adjuvants. • Develop technologies to better assess mucosal responses. • Develop effective heterologous prime-boost strategies. • Design mucosal delivery strategies for DNA, proteins, and vectors. • Evaluate competing concepts and candidates using standardized methodologies. E. Therapeutic vaccines

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			• None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Study individuals who appear to be protected from HIV despite high-risk behavior in order to facilitate the design of immunogens able to elicit the corresponding protective responses in non-infected individuals. • Maintain non-human primate facilities for clinical trials. • Utilize relevant ADMET models (Absorption-Distribution-Metabolism-Excretion- Toxicity) during the drug discovery/ development process for safety purposes. • Create accurate monitoring and interpretation systems to identify drug resistance selection and virus tropism. • Improve insights in clinical markers identifying when a patient has a biological failure, and how to combine the (new) available drugs accordingly. • Develop a database that contains information, including: patient HIV samples (i.e. genetics, mutations), treatment history, and immunological parameters • Explore immunotherapeutic approaches, particularly in combination with chemotherapy. • Monitor incidence rates rigorously (e.g. type of virus and recent infections). • Identify social and cultural factors that deter at-

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
			risk people from being tested. • Perform research to better understand the pathogenesis and possible excess risk of HIV-infected populations contracting age-related comorbidities. • Conduct studies to quantify the benefits and risk from using (and not providing access to) antiretroviral therapy and other biomedical interventions. • Perform research on the impact of TB co-infection and how they are most optimally managed. I. Innovative financing • None identified
4. HIV Vaccines & Microbicides Resource Tracking Group. Investing to End the AIDS Epidemic: A New Era for HIV Prevention Research and Development. HIV Vaccines & Microbicides Resource Tracking Group; 2012. *The Investing to End the AIDS Epidemic Report provides an overview of global HIV R&D investments, specifically for prevention therapies and interventions. The report provides a snapshot of some of the major advances in HIV*	The HIV Vaccines and Microbicides Resource Tracking Working Group (the Working Group) consists of Global Advocacy for HIV Prevention, the International AIDS Vaccine Initiative, the International Partnership for Microbicides, and UNAIDS. Data collection by the Working Group involved accessing both public information and collecting information through direct appeals to funding agencies. The Working Group: 1) identified key funding agencies; 2) collected publicly available information; 3) contacted the funding	A. Basic science • Identify new broadly neutralizing antibodies for vaccine development. B. Diagnostics • None identified C. Drugs • Explore next generation approaches to HIV prevention through continued investment in drug discovery. D. Preventative vaccines • None identified E. Therapeutic vaccines • Build upon the progress of multiple potential vaccines currently in the pipeline. • Design vaccines that stimulate broadly neutralizing antibodies against HIV.	A. Basic science • Research the structures of antibodies, how they evolve, and how they are produced by the immune system. • Perform research regarding mutations in the CCR5 gene or removal of the CCR5 protein for cure research. B. Diagnostics • None identified C. Drugs • Perform trials to assess the safety and effectiveness of new microbicides and rectal microbicides (e.g. tenofovir gel 1%). • Conduct research for dapirivine-based vaginal rings that combine antiretrovirals with contraceptive hormones. • Continue research into pre-exposure prophylaxis and treatment as prevention using different dosing strategies amongst various populations.

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
prevention R&D, a number of the key financial inefficiencies related to HIV R&D, and general existing R&D gaps.	agencies identified and 4) reviewed, checked and analyzed the information collated. For each of the funders identified, the publicly available information was reviewed for data on annual investment levels. Information sources consulted included: government reports, annual reports, US Securities and Exchange Commission (SEC) filings, published studies and articles, scientific presentations and website postings. The financial information received from each funder was reviewed against the project inclusion criteria and cross-checked. Any issues or questions were followed up with the funder. The estimates for each sector were then reviewed for consistency to ensure that similar definitions were used and to eliminate double counting. The categories used to describe different R&D activities for vaccines and microbicides were derived from those developed by the	F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Assess the effectiveness of new prevention technologies and tools. I. Innovative financing • None identified	• Research HSV-2 prevention in HIV-negative individuals using various therapeutic and prophylactic methods (e.g. acyclovir) D. Preventative vaccines • None identified E. Therapeutic vaccines • Conduct follow-up studies to RV144 results to better understand immunoglobulin IgG antibodies that bind to V1/V2 variable loops and plasm IgA antibodies that bind to the HIV envelope. • Perform studies to evaluate an extended prime-boosting mechanisms. • Utilize two research approaches: (1) a sterilizing cure that would eradicate HIV from the body (2) a functional cure that would keep the patient healthy without drugs but not eliminate the virus from the body. • Explore complementary strategies that target CD4 cells and other locations that are resistant to antriretrovirals and can attack latent HIV once it becomes active. • Develop an HSV-2-specific vaccine. F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Invest substantially in theoretical, qualitative and quantitative behavioural and social research. • Research implementation of male circumcision

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
	US National Institutes of Health with the addition of a category for policy and advocacy.		and non-surgical circumcision for HIV prevention. • Improve research and development efforts for female condoms, as well as community education and advocacy efforts. • Refine current strategies and develop new strategies for preventing vertical transmission to infants at birth and during breastfeeding. I. Innovative financing • None identified
5. Smelyanskaya, Marina. Global Investments in HIV Treatment Research and Development in 2010 and 2011. New York: Treatment Action Group; March 2013. *This Treatment Action Group's (TAG) report on Global Investments in HIV Treatment Research and Development collects investment data on HIV treatment research and development in 2010 and 2011. In collaboration with UNAIDS, TAG analyzes HIV treatment R&D investment trends and also distinguishes a number of remaining*	In 2012, TAG surveyed key HIV treatment R&D funders to assess the state of global investments in the development of innovative strategies to treat and control HIV. For this report, TAG solicited data for years 2010 and 2011. Electronic surveys were sent to 171 potential contacts, including the comprehensive database of 140 key HIV R&D treatment donors developed in 2009, and an additional 31 contacts acquired through desktop research or recommended by AVAC and other participating funders. A new reporting template was developed that invited participants to report the 2010 and 2011 research disbursements, funding trends, and the HIV treatment	A. Basic science • None identified B. Diagnostics • Develop new, innovative diagnostic tools for resource poor settings. C. Drugs • Improve the current antiretroviral medication landscape through drug discovery investment. D. Preventative vaccines • None identified E. Therapeutic vaccines • Divert resources to explore cure research and development. F. Vector control • None identified G. Epidemiology • None identified	A. Basic science • None identified B. Diagnostics • Develop diagnostic tools capable of detecting early stages of infection. • Research tools that will simplify and accelerate HIV testing (rapid point-of-care tests). C. Drugs • Create more efficient, less toxic antiretroviral medications. • Develop simpler, longer lasting formulations. D. Preventative vaccines • None identified E. Therapeutic vaccines • Develop therapeutic vaccines that can exhibit substantial viral-load reduction. F. Vector control • None identified G. Epidemiology

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
gaps.	R&D funding priorities they considered of utmost importance. 2010 and 2011 investment data was collected for seven research categories, including: basic science, applied / infrastructure/ unspecified, drugs, HIV diagnostics, therapeutic vaccines, treatment as prevention, and operational and implementation science.	H. Health systems/public health research • Research the public health implications of antiretroviral utilization in HIV-positive patients. I. Innovative financing • None identified	• None identified H. Health systems/public health research • Conduct research to evaluate the effectiveness of early treatment of antiretrovirals on HIV-positive individuals. • Investigate methods to determine antriretroviral levels in blood to assess resistance and adherence. I. Innovative financing • None identified
6. Policy Cures/DSW. Saving Lives and Creating Impact: EU Investment in Poverty-Related Disease. London: Policy Cures London; October 2012. *Policy Cures' Saving Lives and Creating Impact report assesses the impact of EU funding for poverty-related and neglected diseases (PRND) R&D, highlighting the return on investment for both developing countries and the EU. Focusing on the EU's role in funding PRND R&D, the report highlights the*	The scope for PRND R&D and primary financial investment data in this report was extracted from the G-FINDER databases. Financial data was reported in 2007 euros to make the data comparable across the four years and to avoid conflating real year-on-year changes with changes due to inflation. Other specific datapoints were provided by the EC, the European and Developing Countries Clinical Trials Partnership (EDCTP), European Vaccine Initiative (EVI), Tuberculosis Vaccine Initiative (TBVI), the Bill & Melinda Gates Foundation and Thomson	A. Basic science • Conduct high quality basic research to contribute to the development of products targeted at HIV B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • Develop an effective vaccine for the prevention of HIV E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • Continue modeling efforts to understand the potential impact of an HIV vaccine with at least 50% efficacy E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
gains made by various EU research institutions, partnerships, and private industry.	Reuters, including: Member State and 3rd-party contributions to EDCTP, number of publications on neglected tropical diseases in 2011, and government funding commitments to EVI and TBVI. Qualitative policy data was obtained through desk-based research, and supplemented by communications with specific institutes or organisations mentioned in the report.	• None identified H. Health systems/public health research • Find ways to improve coordination efforts between funders and researchers I. Innovative financing • Find ways to improve financing coordination efforts amongst various stakeholders • Find ways to increase funding	H. Health systems/public health research • Identify key product development partnerships (PDPs) to engage talented researchers in private industry • Find ways to integrate the private sector into the poverty-related neglected disease R&D landscape • Investigate how to encourage collaboration amongst researchers to jointly develop product development portfolios • Strategize how to align efforts of aid organizations and science and technology agencies I. Innovative financing • Identify ways to reduce restrictions on funding requirements to ensure that the best research candidates are prioritized (under the EU 7th Framework Programme) • Learn how to streamline administrative processes to expedite funding flows to reach researchers • Explore pooled funding mechanisms to encourage collaboration • Identify the right balance of funding between product development and basic science
7. Berger M, Murugi J, Buch E, IJsselmuiden C, Kennedy A, Moran M, et al. Strengthening pharmaceutical innovation in Africa. Council on Health Research for Development (COHRED)/New Partnership for Africa's	The geographical scope of the study is Africa. It focuses on diseases that disproportionately affect Africa, including neglected tropical diseases. The method used was keyword internet searches, key informant interviews and discussions review of	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • None identified	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • None identified

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
Development (NEPAD); 2009. *COHRED's Strengthening Pharmaceutical Innovation in Africa report focuses on the agenda to promote pharmaceutical innovation in Africa by African countries. This report suggests different mechanisms and tools to support African countries moving forward, specifically advocating for a systems and evidence-based approach.*	literature and documentation3, participation and consultation in a number of international meetings and consultations on pharmaceutical in several low income countries. The data obtained was analyzed manually along main emerging themes. The draft report was externally peer reviewed. Step 1: Identifying and categorising projects and programmes contributing to the improvement of access to medical products in Africa. Global, regional and national examples were considered. Step 2: examination of a minimum set of conditions, policies; human, structural and financial resources to identify initiatives most likely to be successfully implemented in any African country.	E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Learn how to leverage African strengths in pharmaceutical innovation (e.g. African Ministerial Council on Science and Technology) I. Innovative financing • Find ways to increase investment in African pharmaceutical innovation and neglected disease R&D	E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Investigate how policy changes can encourage local production of medicines to treat neglected diseases • Find ways to utilize technology transfer and licensing agreements to promote local drug production I. Innovative financing • Support the creation of new product development public-private partnerships (PDPPPs) • Learn how to engage companies in using preferential pricing arrangements • Investigate how to leverage philanthropic donations to strengthen national pharmaceutical innovation systems • Find ways to expand access to treatment through intergovernmental organization-sponsored buyer co-payments • Investigate how to raise funds through solidarity taxes on airlines Learn how to engage venture capital to invest in neglected disease R&D

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
8. Drugs for Neglected Diseases Initiative (DNDi)/The George Institute for International Health. Registering New Drugs: The African Context. London: The George Institute for International Health; January 2010. *The Registering New Drugs report reviews the various mechanisms and strategies available to support the registration of new drugs for neglected tropical diseases (NTDs) in developing countries. It addresses the development and strengthening of the capacity of national regulatory authorities to monitor quality, safety, and efficacy of health products, since regulatory issues are often obstacles to access.*	A select group of experts from various organizations (including: World Health Organization, US Food and Drug Administration, European Medicines Agency, etc.) were consulted for the purposes of this analysis. The International Expert Advisory Group (EAG) played a substantial role in reviewing this report and shaping the final analysis and recommendations. The draft report was also work-shopped at a regional meeting in Nairobi, attended by many African regulators, including representatives from Angola, Democratic Republic of Congo, Ethiopia, Uganda, Tanzania and members of the HAT (human African trypanosomiasis) and LEAP (leishmaniasis) platforms.	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • Identify potential TB drugs that can be safely administered to HIV-positive TB patients D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Develop new mechanisms and pathways to ensure the urgent approval of neglected tropical disease drugs in developing countries • Develop ways to manage scarce regulatory resources in the short term to fill the capacity gap while African medicines regulatory agencies (MRAs) move through their growth period • Find ways to strengthen African MRAs in the medium to long-term so they	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • Confirm the safety and efficacy of various TB drugs for HIV-positive TB patients D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Strategize how to create and fund centers of regulatory excellence in African sub-regions • Provide automatic WHO prequalification for novel neglected disease products that meet WHO treatment recommendations and that are approved by stringent MRAs • Include regulators from endemic countries in regulatory reviews of neglected disease products (i.e. formal twinned review in all cases) • Find ways to improve Article 58's attractiveness to product developers by allowing Automatic WHO drug prequalification of products given a

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		can conduct their own regulatory reviews of novel neglected disease drugs I. Innovative financing • None identified	positive opinion under Article 58, a positive Art.58 opinion to be converted to EMEA approval with a single European bridging study *OR* a positive Art.58 opinion to provide automatic EU Orphan approval • Find ways to select Western MRAs to review prequalification decisions on behalf of the WHO Investigate how the WHO can conduct at strategic review of its own drug prequalification priorities to identify priority diseases for inclusion I. Innovative financing • None identified
9. Moran M, Ropars A, Guzman J, Diaz J, Garrison C. The New Landscape of Neglected Disease Drug Development. London: The Wellcome Trust; 2005. *The New Landscape of Neglected Disease Drug Development report provides an overview of health outcomes for developing country neglected disease patients and presents recommendations to increase the quality and number of drugs available. It also presents policies and*	An empirical approach was used for this report, covering known neglected disease drug R&D from 1975 to end 2004. All findings and conclusions are based on a review of existing knowledge, supported by original research and interviews with stakeholders involved in the development and use of new drugs. Using a multidisciplinary approach, this report consults groups from various fields (government, public health, industry. Etc.) Analysis and conclusions relate only to neglected disease drug R&D and cannot be automatically translated	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • Develop new, innovative HIV drugs suitable for developing country use. D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • Explore ease-of-use considerations for patients and health care workers (e.g. dosing intervals, total length of treatment, oral formulations, etc.). • Consider appropriateness of product to country health systems (e.g. cold chain issues, hospital-based admin, etc.). • Create products targeted at various populations (e.g. children, adults, pregnant women, severely ill patients, etc.). • Develop adaptations that make treatment compliance easier (e.g. paediatric syrups, simpler formulations, etc.) D. Preventative vaccines • None identified

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
incentives that Western governments could implement to achieve this objective.	across to vaccines and diagnostics. Drug development activity was included only as it relates to the ten neglected diseases listed by the World Health Organization Special Programme for Research and Training in Tropical Diseases (WHO/TDR). A number of areas of activity were excluded from the scope of this report. Developing country drug development was not considered as it is unlikely to be amenable to Western government incentives. Additionally, basic exploratory research that is not compound-based and country infrastructure, implementation, and human resource considerations were also not included in this report.	H. Health systems/public health research • Create a central clearinghouse for information regarding: targets or compounds related to neglected disease research, funding sources, and services and skills offered I. Innovative financing • Find ways to increase the affordability of industry-developed drugs • Identify new, innovative public-private partnerships (PPPs) for drug development, and create policies to encourage PPPs • Find ways to provide shared platform services to PPPs (e.g. legal, human resources, etc.) • Find ways to support PPPs in negotiating industry deals • Find ways to provide PPP-sponsored start-up funds to new small companies	E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Generate neglected disease data that can be cross-applied to core commercial compounds. • Upgrade clinical trial sites in developing countries I. Innovative financing • Investigate ways to lower the cost of lead compounds, active pharmaceutical ingredients and/or formulation costs for developing countries • Identify PPPs that are willing to commit to a long-term funding mechanism (entirety of R&D process) • Collaborate with industry partners that will contract with PPPs to develop drugs for neglected diseases • Create an industry R&D fund (IRFF) to underwrite industry participation in PPPs • Find ways to garner funds from G8 countries to create the IRFF • Learn how to sell “fast-track” regulatory review of commercial drugs to finance neglected disease R&D • Award prizes to multinationals who invest in neglected disease drug development. • Find ways to reduce financial obligations on

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
			patent and maintenance fees
10. UNITAID. HIV/AIDS Diagnostic Technology Landscape. 2nd Edition. Geneva: World Health Organization; 2012. *This report reviews the current technology landscape for HIV diagnostics, including (i) the algorithms and tests required in HIV/AIDS care and treatment, both before and after treatment initiation; (ii) the platforms used and price points of that testing; and (iii) the ways in which testing is delivered. The report then reviews the current technologies and diagnostic platforms in three key testing areas: CD4 and viral load testing for adults and children, as well as EID (including EID run on viral load platforms)—all of which are today typically accessed through sophisticated*	The material in this landscape was gathered by the author from publicly available information, published and unpublished reports and prospectuses, and interviews with developers and manufacturers and is current through March 31, 2012. This report therefore examines the new diagnostic technologies in the pipeline—most of which are designed for use at or near the point of patient care—and considers to what degree they meet the World Health Organization's (WHO's) "ASSURED" criteria, meaning that they are (or will be): Affordable, Sensitive, Specific, User-friendly, Robust/Rapid, Equipment-free, and Deliverable to those who need the test.	A. Basic science • None identified B. Diagnostics • Further develop a broad range of new testing strategies and services that are simple to use and easy to access • Develop new, innovative diagnostic tools for resource-poor settings • Find ways to improve efficiency of CD4, viral load, and early infant diagnosis (EID) RDTs • Focus on quality improvements at all levels of diagnostic testing for HIV/AIDS C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Determine how to improve access to robust, high-quality CD4, viral load,	A. Basic science • None identified B. Diagnostics • Develop high-quality, cost-effective point of care (POC) CD4 testing options to reduce loss to follow-up for rural patients • Develop viral load testing methods that could be conducted at the point of patient care with assays meeting WHO's ASSURED criteria and reduce the need for infrastructure and training for use • Explore disposable CD4 testing models to replace device-based systems in resource-limited settings • Develop more tests that can be used at POC and that deliver same-day results, e.g. using mobile technologies • Develop more viral load assays that can detect and quantify all known HIV-1 subtypes (like the Cavidi ExaVir assay), as well as inter-subtype recombinants and emerging variations • Design more viral load tests with the ability to use dried blood samples (DBS) to greatly simplify the transport of samples and ease of use for health workers • Explore applications of DBS used in laboratory-based viral load platforms for use in EID testing C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
laboratory-based testing platforms, even in resource-limited settings.		and early infant diagnosis (EID) RDTs at the point of patient care, particularly in hard-to-reach places, to enhance ART staging and monitoring • Determine the appropriate country-specific mix of high-volume laboratories and POC testing • Develop ways to improve systems for sample referral and results distribution for central labs • Map barriers to, and foster the acceleration of, new technology introduction, especially for POC technologies I. Innovative financing • None identified	• None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Investigate ways to reduce costs, improve training of laboratory technicians, enhance the quality of laboratory instruments and well-functioning sample transport systems for CD4, viral load and EID RDTs • Identify ways sample transport networks can enable access to testing for patients in peri-urban and rural settings • Determine how cost effectiveness and access can be enhanced via the consolidation of centralized testing facilities in high volume centers (e.g., super-labs) • Examine how factors like urban/rural split of the country, the expected volume of each category of testing, the comparative all-in cost of centralized versus decentralized testing and the ability to effectively transport samples between collection sites and laboratories affects the high-volume laboratory and POC testing mix • Determine how to upgrade patient management algorithms to accommodate the effective use of viral load information I. Innovative financing • None identified

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
11. UNITAID. HIV/AIDS Diagnostic Technology Landscape: Semi-Annual Update. Geneva: World Health Organization; Oct 2012. *The HIV/AIDS Diagnostics Technology Landscape is published annually and is prepared as part of a broad and on-going effort to understand the technology landscape for HIV/AIDS. This document is a semi-annual update on the point-of-care (POC) technologies for CD4, viral load, and early infant diagnosis (EID) testing, as well as the diagnostic pipeline.*	The HIV/AIDS Diagnostics Landscape is compiled by Maurine M. Murtagh with support from UNITAID. The material in this landscape was gathered by the author from publicly available information, published and unpublished reports and prospectuses, and interviews with developers and manufacturers. The updates in this document were provided by the developers of these diagnostic technologies. If technologies that appear in the HIV/AIDS Diagnostics Technology Landscape do not appear in this update, it is either because the supplier did not provide updates or indicated that there were none at this time.	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • None identified I. Innovative financing • None identified	A. Basic science • None identified B. Diagnostics • Investigate ways to accelerate the launch of POC testing platforms dedicated to EID and viral load technologies C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • None identified I. Innovative financing • None identified
12. Murtagh M. UNITAID Technical Report: HIV/AIDS Diagnostic Landscape. Geneva: World Health Organization; July	None provided	A. Basic science • None identified B. Diagnostics • Further develop a broad range of new testing strategies and services that are	A. Basic science • None identified B. Diagnostics • Explore disposable CD4 testing models to replace device-based systems in resource-limited settings

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
2011. *This report reviews the current landscape for HIV diagnostics, including the algorithms and tests required in the care and treatment of the HIV/AIDS patient, both before and after treatment initiation; the price points of that testing; and the ways in which testing is delivered, including the technology platforms in use today.*		simple to use and easy to access • Develop new, innovative diagnostic tools for resource-poor settings • Focus on quality improvements at all levels of diagnostic testing for HIV/AIDS C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Determine how to improve access to robust, high-quality CD4, viral load, and early infant diagnosis (EID) RDTs at the point of patient care, particularly in hard-to-reach places, to enhance ART staging and monitoring • Map barriers to, and foster the acceleration of, new technology introduction, especially for POC technologies • Better understand the testing continuum required for the HIV	• Develop more tests that can be used at POC and that deliver same-day results, e.g. using mobile technologies C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Investigate ways to reduce costs, improve training of laboratory technicians, enhance the quality of laboratory instruments and well-functioning sample transport systems for CD4, viral load and EID RDTs • Identify ways sample transport networks can enable access to testing for patients in peri-urban and rural settings • Determine how cost effectiveness and access can be enhanced via the consolidation of centralized testing facilities in high volume centers (e.g., super-labs) • Examine how factors like urban/rural split of the country, the expected volume of each category of testing, the comparative all-in cost of centralized

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		patient I. Innovative financing • Better understand the current diagnostic market dynamics and trends	versus decentralized testing and the ability to effectively transport samples between collection sites and laboratories affects the high-volume laboratory and POC testing mix I. Innovative financing • None identified
13. UNITAID. 2011 HIV/AIDS Diagnostic Technology Landscape: Semi-Annual Update. Geneva: World Health Organization; Oct 2011. *The HIV/AIDS Diagnostic Landscape is published annually and is prepared as part of a broad and ongoing effort to understand the technology landscape for HIV/AIDS. This document is a semi-annual update on the point-of-care (POC) technologies for CD4, viral load, and early infant diagnosis (EID) testing, as well as the diagnostic pipeline.*	The HIV/AIDS Diagnostic Landscape is compiled by Maurine M. Murtagh with support from UNITAID. The material in this landscape was gathered by the author from publicly available information, published and unpublished reports and prospectuses, and interviews with developers and manufacturers. The updates in this document were provided by the developers of these diagnostic technologies. If technologies that appear in the HIV/AIDS Diagnostic Landscape do not appear in this update, it is either because the supplier did not provide one or indicated that there were none at this time.	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • None identified I. Innovative financing • None identified	A. Basic science • None identified B. Diagnostics • Investigate ways to accelerate the launch of POC testing platforms dedicated to EID and viral load technologies C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • None identified I. Innovative financing • None identified

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
14. UNITAID. Diagnostic market analysis: HIV simple/rapid, enzyme immunoassay (EIA) and supplemental tests: available data and implications for future funding. Geneva: World Health Organization: July 2011. *The purpose of this document is to characterize the market for diagnostic products for the detection of HIV, with a focus on HIV simple/rapid, enzyme immunoassay (EIA), and supplemental tests. This document is intended to provide: 1) An overview of technologies that were purchased during the time period analyzed in the report; 2) Analysis of available procurement data and information gaps; and 3) Discussion of issues related to market dynamics for HIV simple/rapid, EIA, and supplemental tests.*	None provided	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Determine how to improve access to robust, high-quality CD4, viral load, and early infant diagnosis (EID) RDTs at the point of patient care, particularly in hard-to-reach places, to enhance ART staging and monitoring I. Innovative financing • Better understand the current diagnostic market dynamics and trends • Utilize available procurement data to inform future funding and	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • None identified I. Innovative financing • Utilize information on price variation by country and by test to improve cost-effectiveness of procurement • Find ways to better account for market consolidation in procurement decisions to balance competition with market stability • Determine ways to support improved accuracy of GPRM procurement data • Identify methods to address and resolve potential overlap in Global Fund PQR and UNICEF

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		procurement strategy • Find ways to improve the quality and completeness of data collection and data analysis for procurement	procurement data • Identify methods to encourage more complete reporting in Global Fund PQR • Strategize ways to overcome inconsistent or insufficient data entry for procurement, e.g. using drop-down lists • Determine how to account for funding timeframes in reporting procurement data • Further analyse direct-from-manufacturer procurement to procurement through suppliers, agents, or intermediaries to assess potential for improved cost-effectiveness • Determine the activities needed to complement procurement of HIV simple/rapid, EIA and supplemental tests, e.g. positive and negative controls
15. Fauci A, Johnston M, Dieffenbach C, Burton D, Hammer S, Hoxie J, *et al*. HIV vaccine research: the way forward. Science. 2008; 321: 530-532. *In light of a level budget for biomedical research at the U.S. National Institutes of Health (NIH), Fauci et al. emphasize that HIV/AIDS vaccine research efforts need to be carefully prioritized such that resources to energize HIV vaccine*	None provided.	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • Develop a neutralizing antibody-based vaccine that prevents HIV infection • Determine why the STEP vaccine trial failed and its implications for the T-cell concept and future vaccine development • Develop better immune-monitoring assessment tools • Pursue new avenues and explore	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • Develop immunogens that induce antibodies to neutralize a broad array of primary isolates of HIV • Develop a vaccine that successfully contains both antibodies and T-cells that recognize diverse strains of HIV and that reach the site of infection very quickly before infection becomes irreversibly established • Design and conduct more studies that test the T-cell vaccine concept

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
discovery can be identified. The authors summarize progress and challenges in HIV vaccine research, the priorities arising from a recent summit at NIAID, and the actions needed, some already under way, to address those priorities.		cross-fertilization from genetics, structural biology, systems biology, cell biology, and peptide chemistry (among others) to generate knowledge useful in vaccine design and evaluation E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • None identified I. Innovative financing • None identified	• Determine how and whether insufficient T-cell response or other qualities of the cellular immune response (such as the balance between HIV-specific CD4+ T cell and CD8+ T cell responses, or the polyfunctionality, proliferative capacity, specificity, avidity, and the location or kinetics) played a role in the failure of the STEP vaccine • Examine the genomic sequences of infecting HIV strains to demonstrate whether immunization resulted in early immunologic pressure on the incoming HIV virus in the STEP trial, and potentially suggest which HIV genes or epitopes should be included in subsequent vaccines • Conduct studies with mucosal and biopsy specimens to explore whether activation of cells at the mucosal sites were different between vaccine and placebo recipients in the STEP trial • Determine whether the Ad5 vaccine elicited T-cell or antibody-mediated responses that could have enhanced HIV acquisition in the STEP trial • Design whole-genome studies that may reveal associations between host genetic background, baseline Ad5 titer, and HIV acquisition • Evaluate immunity to vectors, including at the tissue level • Develop better NHP models, and more closely link them to clinical research, e.g. via parallel studies, and the exchange of researchers, including young investigators, between the clinic and NHP facilities so that common questions in HIV vaccine discovery can be identified and addressed using common tools • Investigate whether a specific vaccine such as Ad5 induces the same immune responses and degree of cell activation at mucosal sites in non-human

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
			primates (NHPs) as in humans • Determine whether the use of heterologous gene inserts increases the breadth of immune responses • Investigate whether electroporation of DNA alters the qualitative or quantitative nature of induced immune responses • Develop and validate additional assays that measure proliferative capacity, mucosal recruitment, cytotoxic capacity, or other immune functions that may provide a more robust indication of functional antiviral activity • Further define the first events leading to HIV and SIV's entering the gut-associated lymphoid tissue • Determine the rate and mechanisms by which immune cells are mobilized to the site of infection and whether innate responses can alter the course of infection • Characterize the cellular and humoral immune responses needed to control viral replication through modulation and/or elimination of specific cell subsets in the SIV model and studies of HIV-infected populations • Determine the 3D structure of the HIV envelope trimer • Determine why broadly neutralizing antibodies are uncommon and how they can be elicited{O} • Define the specificities of antibodies that neutralize diverse primary HIV isolates • Develop more relevant animal models (and challenge viruses) to explore protection or enhancement of infection or disease, especially heterologous challenge models • Determine why SIV is apathogenic in some NHP studies

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
			• Identify correlates of vaccine-induced immune protection, especially the mechanisms whereby non-pathogenic (e.g. attenuated) SIV's prevent infection by pathogenic virus E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • None identified I. Innovative financing • None identified

Disease-specific R&D priority setting

NEGLECTED TROPICAL DISEASES

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
1. World Health Organization. Research Priorities for Helminth Infections. Technical Report of the TDR Disease Reference Group on Helminth Infections (DRG4). Technical Report Series No. 972. Geneva: World Health Organization; 2012. *This report comprehensively summarizes current helminth research issues and opportunities for improving disease control and reducing poverty. It identifies research gaps and challenges, and presents recommendations to inform public health policy, guide implementation programmes, and focus the research community on the dire needs and the opportunities for advancing disease control and improving human welfare.*	This part of the report sets out the methods used to identify the research priorities in relation to helminth infections. These included the identification of which helminthiases to consider, conceptualization and preparation of white papers on specific topics, prioritization of research areas and recommendations, and validation of the prepared annual report. A multistage process as set out below was used to arrive at the final product: i) Identification of the helminth infections to be considered ii) Identification of the research gaps to be considered iii) The first DRG4 meeting iv) Prioritization of themes v) Underlying values vi) Criteria for ranking vii) The second DRG4 meeting viii) Ranking of priority research areas by experts in DRG4 ix) Stakeholders consultation meetings and other external contributions x) Two stakeholder consultations	A. Basic science • Investigate how helminth parasites modulate host–parasite interactions at the within-host levels • Determine programme end-points for elimination of helminth infection • Identify the mechanisms of host immune responses to helminths, and translate knowledge of these mechanisms into rational strategies for vaccine development B. Diagnostics • Find ways to improve available diagnostic tests, specifically their sensitivity, specificity, multiplex capacity, and ability to measure infection intensity, and detect drug resistance for helminth infections • Determine how to standardize and validate methodologies and cost-effective protocols for diagnosis in the process of monitoring and evaluation (M&E) • Improve existing/develop novel diagnostic assays M&E of the impact of control programmes on helminth infection and associated	A. Basic science • Examine the impact of helminth parasites on the host immune response of concurrent infection with other helminth and non-helminth pathogens, the impact of parasite control interventions on such host–parasite interactions, and how concurrent infections affect clinical outcomes and the host's ability to seroconvert upon vaccination • Identify how to annotate parasite genomes and transcriptomes, and to develop new tools for parasite functional genomics in key species • Define the determinants and mechanisms of helminth-induced pathologies, including carcinogenesis, and excess human mortality • Define parasite (and vector/intermediate host) population and ecological genetic structures in the contexts of genetic responses to interventions within and between parasite populations, parasite transmission, and epidemiology • Conduct studies on the pathogenesis, genetics, population structure, vector–parasite–host(s) interactions and immunology to further support the basis for translating basic research into operations/implementation of existing or

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
	xi) Publication of the DRG4 report	morbidity, and for supporting decisions towards control/ elimination end-points C. Drugs • Assess drug efficacy and promptly detect the development of drug resistance D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • Develop and refine mathematical models to investigate relationships between infection and morbidities to aid programmes aiming to reduce the burden of disease (elimination of public health problem) • Determine how to increase the use and application of epidemiological models to aid M&E and surveillance, the design of cost-effective sampling protocols and the monitoring of intervention efficacy including drug resistance • Identify how to produce updated	improved control measures B. Diagnostics • Find ways to encourage the convergence of epidemiological and laboratory approaches to develop tools optimal for control programmes that are facilitated by the recognition that parasitological diagnosis at the individual level is not appropriate for implementing and monitoring such interventions • Determine how to apply modern laboratory techniques to diagnosis development, particularly the use of PCR and molecular techniques to produce parasite recombinant proteins as reagents for serodiagnostic tests • Better understand the performance characteristics of currently available tools for diagnosis for each of the human helminth infections, and identify critical gaps in diagnostic technology • Find ways to overcome key challenges in diagnostic development for helminth infections, including quantifying intensity of infection, response to anthelmintic chemotherapy, (including detection of anthelmintic resistance), disease mapping and surveillance, elimination and the need to collect data amenable to use in mathematical modelling of infection • Develop new diagnostic tests using biomarkers of infection that reflect infection intensity

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		helminth disease prevalence maps • Develop tools and systems for post-control surveillance • Determine how to optimize existing/ develop novel instruments for effective surveillance, including prompt detection of resistance, pharmacovigilance, and post-intervention surveillance systems H. Health systems/public health research • Find ways to optimize the deployment of existing intervention tools to maximize impact (including impact against polyparasitism) and sustainability, with focus on pharmaceuticals, vaccines, vector control and ecohealth approaches (sanitation, clean water, improved nutrition, education) • Develop strategies incorporating delivery of multiple interventions at various levels to maximize sustainability of control programmes in general, and of integrated neglected tropical diseases (NTD) control in particular • Examine community-directed intervention successes, issues, challenges and needs for NTDs • Develop strategies (taking gender	• Develop and validate clinical, phenotypic and molecular methods for monitoring of drug efficacy and resistance • Develop and validate questionnaire-based methods for diagnosis of helminth infections • Find ways to link measures of diagnostic performance for the diagnostic tests optimized or developed with statistical/mathematical tools to support monitoring and evaluation of helminth control programmes C. Drugs • Develop new drugs and treatments for onchocerciasis and lymphatic filariasis D. Preventative vaccines • Explore anti-helminth vaccines as part of the solution to control helminthic infections of poverty E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • Find ways to ensure mathematical models take into account cumulative effects of chronic disease for evaluation of disease burden and the impact on such burden of control interventions

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		issues into account) to increase awareness of ill-health processes, community participation, ownership and empowerment, as well as equity in access to health services for communities and risk groups • Find ways to build adequate research capacity for the management of helminthiases and other infectious diseases of poverty • Identify ways to steer intervention from disease control towards permanent elimination I. Innovative financing • Find ways to advance political will and commitment to increase the capacity of helminth disease research in disease-endemic countries • Determine how to generate investments in South–South collaborations for helminth R&D	• Determine how to link epidemiological models to cost-effectiveness analyses of NTD interventions and their alternatives • Find ways to monitor the progress of control interventions and quantify changes in incidence of infection and disease • Develop maps of helminth infection and co-infection as well as of intermediate hosts' and vectors' distribution to enable accurate assessment of distribution and burden of disease • Assess the contribution of systematic non-compliant persons as well as of migrants and refugees, pregnant/lactating women and under five-year olds to the maintenance of transmission • Identify and evaluate climate and environmental changes that impact helminth infections • Develop and refine models to investigate relationships between infection and transmission thresholds to aid programmes aiming to eliminate the infection reservoir • Develop metapopulation and spatially-explicit parasite transmission models • Develop and validate mathematical models for co-infections H. Health systems/public health research • Develop surveillance systems for monitoring the sub-optimal response by *Onchocerca volvulus* to ivermectin • Conduct operations research to address challenges and needs to help fill

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
			programmatic gaps in *O. volvulus* and lymphatic filariae control • Investigate how helminth parasites modulate host–parasite interactions at the population level • Determine how to incorporate environmental considerations and health education into helminth control programs to facilitate programme integration and sustainability • Identify the social and environmental structures that contribute to the maintenance of helminth infection (including polyparasitism) for developing multi-disciplinary interventions • Develop strategies incorporating delivery of multiple interventions at various levels to maximize sustainability of control programmes in general and of integrated NTD control in particular • Determine how to strengthen understanding of the sociological, behavioural, political and economic drivers of helminth infection and control to improve community knowledge/education, achieve empowerment/equity/gender, participation and ownership; and increase intervention coverage, compliance and sustainability • Find ways to continuously update and share data platforms to optimize data management, analysis, and (mathematical/statistical/ geographical/climate change) modelling,

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
			integrating scientists, stakeholders and end-users • Develop appropriate health research policies and capacity building in disease-endemic countries to provide conducive environment and adequate expertise for sustained disease control efforts I. Innovative financing • Determine how to encourage Member States of the African, American (Latin America and Caribbean Islands), and South-East Asia Regions to promote and support the development of regional policies supporting the development of effective linkages and partnerships with international health research agencies • Find ways to gain regional commitment and strong advocacy to strengthen policies on health research aimed at providing evidence to justify health actions and practices that are flexible and responsive to the short- and long-term national needs • Find ways to encourage African countries to put in place research-friendly legislative reforms that facilitate exchange of expertise and data whilst ensuring protection of intellectual property rights • Develop comprehensive policies and strategies for supervision across all sectors in the regional and national innovation sector to foster transparency in terms of funding and its disbursement, strategic planning, priority-setting, knowledge

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
			management and demand creation
2. World Health Organization. Sustaining the drive to overcome the global impact of neglected tropical diseases. Second WHO report on neglected tropical diseases. Geneva: World Health Organization; 2013. *In January 2012 the World Health Organization (WHO) published a roadmap (1) setting targets for the prevention, control, elimination and eradication of 17 neglected tropical diseases or conditions: Buruli ulcer, Chagas disease, taeniasis/cysticercosis, dengue, dracunculiasis, echinococcosis, endemic treponematoses, foodborne trematodiases, human African trypanosomiasis, the Leishmaniases, leprosy, lymphatic filariasis, onchocerciasis, rabies, schistosomiasis, trachoma and soil-transmitted helminthiases. This report further elaborates on concepts discussed in the*	None provided	A. Basic science • None identified B. Diagnostics • Develop new NTD diagnostics that can be used in remote/difficult settings C. Drugs • Assess drug efficacy and promptly detect the development of drug resistance • Develop and deliver preventive chemotherapy as an integrated package for co-endemic NTDs • Discover safe and effective medicines that are simpler to administer, can be easily used in remote areas and cheaper than those currently available D. Preventative vaccines • Develop new models for preventive immunization against NTDs E. Therapeutic vaccines • None identified F. Vector control • Concentrate on developing innovations in vector control for dengue, Chagas disease, lymphatic	A. Basic science • None identified B. Diagnostics • Determine how to improve the specificity of leprosy diagnosis using clinical or other investigations C. Drugs • Complete a clinical trial of oral antibiotic therapy (using rifampicin and clarithromycin) by 2014 to achieve intensified control of Buruli ulcer • Find new low-cost treatment regimens for African trypanosomiasis, or investigate how to reduce the cost of melarsoprol-free treatment • Develop improved chemotherapy for Taeniasis/Cysticercosis infection in humans and pigs • Develop new or refined preventative chemotherapy options for lymphatic filariasis, onchocerciasis, schistosomiasis, soil-transmitted helmnithiases and blinding trachoma D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
roadmap, describes the need for sustainable progress, and examines the challenges in implementation encountered by Member States, WHO and their partners.		filariasis, the Leishmaniases and onchocerciasis to reduce transmission • Develop safe and effective products for vector control that do not rely on insecticide • Find ways to reduce the time needed to bring new products to market by as much as possible • Find ways to achieve a collaborative approach among sectors for agriculture, health and the environment to achieve the sound management of pesticides • Learn how to better integrate veterinary public health services into the control of neglected zoonotic diseases G. Epidemiology • Determine how to optimize existing/ develop novel instruments for effective surveillance, including prompt detection of resistance, pharmacovigilance, and post-intervention surveillance systems • Collect epidemiological data that shows the differential impact of NTDs according to a patient's sex and age in order to better inform policies, and guide targeted interventions for sustainable control	• Identify ways to strengthen national capacities in medical entomology, entomological surveillance and operational research • Develop career paths and incentives for entomologists to pursue public-health entomology instead of academic research • Prioritize studies on multi-disease packages and host approaches for selected neglected zoonotic diseases in order to improve and sustain the cost effectiveness of efforts to control these diseases • Develop ways to control vectors by treating potential sources of unsafe water with temephos (Abate) and distributing filters to strain water • Identify how to improve environmental sanitation against NTDs e.g., storm water drainage (leptospirosis), land drainage (fascioliasis) and community-led total sanitation (cysticercosis) G. Epidemiology • Find ways to fill gaps in the knowledge about the burden of Leishmaniasis and its incidence in most endemic countries • Find ways to ensure that assessments of the burden of zoonoses take into account their dual burden on the health of humans and of livestock, and thus their total cost to society H. Health systems/public health research • Determine how national programmes can

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		H. Health systems/public health research • Find ways to optimize the deployment of existing intervention tools to maximize impact (including impact against polyparasitism) and sustainability, with focus on pharmaceuticals, vaccines, vector control and ecohealth approaches (sanitation, clean water, improved nutrition, education) • Develop strategies incorporating delivery of multiple interventions at various levels to maximize sustainability of control programmes in general, and of integrated neglected tropical diseases (NTD) control in particular • Find ways to combine five public-health strategies and deliver them locally to overcome NTDs: (i) preventative chemotherapy; (ii) innovative and intensified disease-management; (ii) vector control and pesticide management; (iv) safe drinking-water, basic sanitation and hygiene services, and education; and (v) veterinary public-health services • Determine how to change paradigms of reactive approaches to disease outbreaks and instead	develop a culture of integrated and coordinated planning and NTD programme management to enable programmes to scale up effectively and encourage commitment from governments • Find ways to achieve universal coverage of prevention and control interventions for neglected tropical diseases • Find ways to increase access to essential medicines of assured quality at affordable prices and a well-trained and motivated work force to delivery NTD treatment services • Determine ways to involve sectors other than health, including finance, education, agriculture and veterinary public health, water and sanitation, and environmental management in NTD research and control • Develop methods to overcome obstacles and risks to implementation, e.g. the effects of natural disasters and human conflicts that result in the displacement of millions of people, and disrupt public-health interventions and disease surveillance • Investigate how to build sufficient human-resources capacity (both technical and managerial) required to support the scaling up of interventions at all levels of national health-care systems as well as to mobilize resources • Develop closely coordinated programme planning, service delivery and shared indicators for monitoring and evaluation of

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		implement sustainable preventive measures that are guided by entomological and epidemiological surveillance • Develop procedures and alternative strategies that can be used if drug resistance is detected I. Innovative financing • Identify how to expand support from Member States and their partners to ensure that new products are developed for preventing, diagnosing and controlling NTDs, and to ensure that access to services continues to expand • Find ways to advance political will and commitment to increase the capacity of helminth disease research in disease-endemic countries	the control of lymphatic filariasis and onchocerciasis • Identify opportunities to implement control measures for Buruli ulcer together with other public health programmes • Identify how to implement advocacy and awareness campaigns that will be followed by intensified leprosy detection and treatment at the local level in countries that report more than 1 000 new cases annually • Find ways to coordinate operational research to increase early diagnosis and the quality of leprosy services • Intensify leprosy research by investing in the development of diagnostics and treatment, and working to prevent neuritis • Find ways to ensure control and research efforts for African trypanosomiasis are based on sustainable public health objectives, not only on the actual burden of the disease • Develop and validate standard methodology for Taeniasis/Cysticercosis intervention in endemic communities • Determine how implement combined strategies for Taeniasis/Cysticercosis elimination, including achieving routine vaccination of pigs in endemic areas, better management of pig farms and pork production practices, improved sanitation, and health education • Design and identify ways to scale-up innovative and intensified disease-

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			management for Buruli ulcer, Chagas disease, both forms of human African trypanosomiasis, the Leishmaniases (cutaneous, mucocutaneous and visceral forms), leprosy and yaws • Determine how to improve individual case management by finding ways to diagnose cases early, provide treatment to cure or reduce infection and morbidity, manage complications, and adopt strategies to respond appropriately to different levels of endemicity and health-system capacity • Find ways to scale up interventions for control and elimination of neglected zoonotic diseases when feasible in select geographical and epidemiological settings • Find ways to strengthen advocacy for control of neglected zoonoses among stakeholders via informing them about the societal burden of these diseases, and providing education to affected populations to create demand for control at all levels of society • Develop integrated approaches to eliminate Dracunculiasis by learning to improve surveillance, intensify case-containment measures, provide access to improved drinking-water sources and promote behavioural change and awareness via information dissemination and education • Determine ways to maintain and generate needed expertise at the national level and to improve programmes' abilities to adapt

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			to local conditions • Develop methods to align improvements in sanitation together with delivering preventive chemotherapy and health education as a basis for sustaining reductions in the prevalence of helminthes • Find ways to scale-up environmental interventions for NTDs • Determine how to improve husbandry practice and upgrade abattoirs and meat inspection, particularly for echinococcosis, cysticercosis and bovine tuberculosis I. Innovative financing • None identified
3. World Health Organization. Research Priorities for Zoonoses and Marginalized Infections. Technical Report of the TDR Disease Reference Group for Zoonoses and Marginalized Infections. Technical Report Series No. 971. Geneva: World Health Organization; 2012. *The report emphasizes that the diseases discussed are diverse and cover the spectrum of infectious agents, from viruses to worms. The infections*	The purpose of DRG 6 was to systematically review research evidence and evaluate its relevance to control needs, assess challenges in control and highlight new and significant scientific advances. It was also to provide independent advice and guidance on priority areas and critical research gaps as a contribution to the Global Report. It is recognized that there are many ways to identify priorities based on expected outcomes. DRG 6 followed a sequential strategy, starting with initial informal consultation, semiquantitative prioritization exercises by members followed by a further stakeholders'	A. Basic science • Better understand the full spectrum of disease symptoms for NTDs B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • Develop more animal vaccines against transmission of NTDs E. Therapeutic vaccines • None identified	A. Basic science • Conduct detailed studies to elucidate the spectrum of symptoms for cysticercosis and taeniasis, including stroke associated with NCC to inform burden of disease studies • Investigate the impact of schistosomiasis on malnutrition and cognition in relation to single infections and polyparasitism B. Diagnostics • Develop immunological tests for diagnosis and biomarkers of infection status/exposure and for differentiation of *T. solium* and *T. saginata* • Develop more sensitive and specific diagnostics for early detection of *Echinococcus* infection including:

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display a variety of transmission patterns, have a global geographical distribution throughout the tropics and subtropics, and exist in different ecological environments and in different health system settings. However, this complexity is compounded, compared with non-zoonotic infections, by the need to involve other sectors (for example livestock services, education, environment, water and sanitation, and wildlife) when decisions on policy for control, financing for control across sectors, defining research priorities and implementing research findings are made.	consultation, proceeding to the development of a series of matrices based on specific indicators of identified research priorities. The DRG also drew on authoritative reports, some of which were convened under the auspices of WHO and TDR, which had also identified priorities for some of the diseases discussed.	F. Vector control • Learn how to better integrate veterinary public health services into the control of neglected zoonotic diseases G. Epidemiology • Find ways to gather more accurate estimates of the global disease burden for NTDs • Determine how to optimize existing/ develop novel instruments for effective surveillance, including prompt detection of resistance, pharmacovigilance, and post-intervention surveillance systems • Conduct small-scale focused epidemiological studies on zoonoses to gather basic information for the design of control programmes and awareness generation and to support advocacy • Determine how to re-attribute the burden of morbidity and mortality attributed to diseases and conditions (cancers, neurological conditions, injuries) to the neglected parasitic/zoonotic diseases • Re-evaluate the societal burden of disease for zoonoses	o methods (imaging, serology) to assess parasite viability and/or progression of both cystic and alveolar disease; o comparison of the efficacy, sensitivity and specificity of copro-DNA tests to establish strain-specific detection for *E. granulosus* in dogs • Find ways to improve diagnostics so they are effective at detecting schistosomiasis in low-prevalence populations, and so they can be used as surveillance tools in order to determine whether effective control has been achieved • Develop new, safe diagnostic techniques for acute infection during pregnancy to detect toxoplasmosis in the mother and fetus • Develop cost-effective diagnostic and management protocols for CNS toxoplasmosis in high-risk HIV-seropositive patients • Develop appropriate and effective methods for the collection of samples for diagnosis of rabies in humans both post mortem (e.g. periorbital biopsies) and antemortem (e.g. nuchal skin biopsies) • Find ways to encourage more widespread use of existing techniques for field collection and storage of samples and tests for rabies diagnosis and surveillance, such as the direct rapid immune-histochemical test, and use of preservatives/specialized paper for stabilization of virus and RNA • Develop inexpensive, robust and reliable

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		H. Health systems/public health research • Find ways to expand the surveillance for zoonotic diseases in humans and animals • Develop guidelines for implementing integrated surveillance to better define the problem of zoonoses • Develop plans for prevention and control activities for zoonoses • Conduct, maintain and report inventories of control activities and tools currently being deployed for zoonotic diseases • Conduct more extensive studies on the costs of zoonotic intervention, the cost−benefits and cost−effectiveness I. Innovative financing • None identified	diagnostic tests for bacterial zoonoses that can be used in field and hospital settings • Establish locally appropriate cut-off points for acquisition of valid data to inform disease burden studies e.g. the single comparative intradermal test for bovine tuberculosis and serological tests for brucellosis • Design diagnostic strategies to differentiate brucellosis vaccinated animals from naturally infected animals in order to prevent unnecessary livestock slaughter • Develop inexpensive and reliable brucellosis diagnostic tests for use in local hospital and field settings C. Drugs • Conduct field-based randomized clinical trials to evaluate the efficacy of oxfendazole and its effectiveness with recombinant vaccines against porcine cysticercosis • Find ways to scale-up multicentric prospective evaluations of available clinical treatment options, including surgery, ultrasound, drug regimens (albendazole, flubendazole and ivermectin, including dosages and combinations) for echinococcosis • Continue to explore new drug candidates for use in the immune-compromised *Cryptosporidium* host • Evaluate and find ways to implement new

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			biological regimens for humans, including use of monoclonal antibodies as a cost-effective replacement for rabies immunoglobulin • Conduct clinical research on optimal drug treatment regimens for etiologically confirmed *M. bovis* and non-tuberculous mycobacterial infections • Evaluate the effectiveness of the standard DOTS regimen administered in cases of tuberculosis caused by *M. bovis* and non-tuberculous mycobacterial infections, as few cases are differentiated on the basis of culture results D. Preventative vaccines • Further assess different vaccine strategies/options/combinations for echinococcosis, e.g. a vaccine for ovine echinococcosis and development of a vaccine for use in definitive canine hosts{C} • Develop animal vaccines for toxoplasmosis • Develop a livestock vaccine to block animal infection and consequently reduce the excretion of infectious cysts into the environment and transmission of infection to humans • Establish reliable, economical and harmonized *in vitro* laboratory tests to ensure the quality and in particular the potency of rabies vaccines • Develop combined approaches to dog rabies vaccination and immuno-

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
			contraception • Develop effective livestock vaccines and vaccination strategies for *M. bovis* that are feasible in most developing countries • Critically assess the immunogenic properties of currently available brucellosis vaccines and their effectiveness in areas of high endemicity • Find ways to improve the safety and immunogenicity of the current vaccines against *Brucella melitensis* and *Brucella abortus* • Develop multivalent, low-cost, locally produced vaccines for enteric diseases that are sufficiently effective to interrupt transmission cycles E. Therapeutic vaccines • None identified F. Vector control • Conduct studies of disease burden in both humans and animals in both urban and rural settings in a manner that brings the human and veterinary health communities together • Determine the role of the variety of animals in transmission as reservoirs for *Schistosoma japonicum* and *S. mekongi* (buffalo or others such as dogs, cats or rats) • Determine the precise role of carabao (water buffalo) in the transmission of *S. japonicum* in the Philippines

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
			• Identify agricultural practices that reduce the exposure of livestock to cryptosporidiosis infection in order to interrupt transmission to humans G. Epidemiology • Develop and validate transmission dynamics models to assess the cost−effectiveness and cost−benefits of alternative control strategies for cysticercosis and taeniasis, echinococcosis • Find ways to measure the health and economic burden of echinococcosis caused by both *E. granulosus* and *E. multilocularis*, including productivity losses in humans and animals and cost−effectiveness of current control approaches • Determine how to estimate the global burden of foodborne trematodiases (FBT) • Evaluate national FBT disease surveillance, and its effectiveness in tracking FBT infections • Find ways to quantify the impact of improved water quality and sanitation on toxoplasmosis infection • Find ways to quantify the proportion of chronic abortions globally that are attributable to toxoplasmosis • Determine how to document the burden of cryptosporidiosis in young children in developing countries • Determine the extent of livestock as source of *Cryptosporidium* infections in humans in the developing world

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
			• Develop and evaluate new technologies for integrated, real-time rabies surveillance and response (e.g. mobile computing technologies) • Develop cross-sectoral assessments of the bacterial zoonoses disease burden to allow for realistic evaluation of the cost−effectiveness of disease interventions • Construct a common measure of zoonotic disease burden that incorporates human health indices, costs to the public health sector, monetary burden for the livestock sector and costs to the private sector • Better understand the human disease burden of zoonotic tuberuclosis, and how and why the prevalence of human *M. bovis* and non-tuberculous mycobacterial infections varies in different communities • Identify animal-related risk factors for human infection with different mycobacterial species of zoonotic TB, including potential factors associated with small ruminants • Generate data and develop methodologies to allow an accurate estimation of the societal burden of brucellosis, focusing primarily on burden of disease in livestock and human populations • Develop better methods for surveillance of human enteric infections, including syndromic classification and etiology if possible, based in representative community settings, both urban and rural, and across the whole age range

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
			• Clarify the reservoirs for animal and human enteric infections and the pathways of transmission among animals, from animals to humans, from humans to humans and from humans to animals • Determine how to implement ongoing surveillance for enteric disease drug resistance and determine the most effective means to disseminate this information • Measure the effectiveness of Community-Led Total Sanitation (CLTS) on incidence and prevalence of zoonotic and marginalized diseases through epidemiological studies and community-based randomized trials • Assess the DALY burden borne by individuals affected by zoonotic diseases • Assess the monetary impact of zoonoses to livestock and human productivity • Study risk factors in both people and animals with a view to successfully targeting at-risk groups for high-priority intervention of zoonoses • Investigate methods for quantifying the rate of underreporting of zoonotic diseases in humans • Develop transmission dynamics models to predict the effectiveness of alternative control measures for zoonoses • Conduct cohort studies on several zoonoses in which the symptoms in humans appear several years after infection

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
			• Conduct randomized trials to estimate the effectiveness of alternative control strategies, including integrated/combined strategies for zoonoses H. Health systems/public health research • Determine the economic cost of neglected zoonoses for both the human and animal populations involved • Study the efficacy of integrated interventions that address more than one zoonotic disease and/or agent at the same time, and determine the cost effectiveness of these interventions • Investigate promotion of health literacy and social mobilization to ensure maximal engagement of the affected populations in the selected interventions • Develop audience-specific health education and behaviour change interventions for cysticercosis and taeniasis, and assess their effectiveness together with gender-related correlates in intervention studies • Conduct operational research on the cost−effectiveness of integrated control for Asian schistosomiasis to establish optimum approach at scale in different geographical settings, including the value of transmission-blocking vaccines for use in buffalo or other mammalian hosts • Conduct studies on the problems of coverage and compliance related to access to mass treatment in the Philippines

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
			(Samar province) for Asian schistosomiasis in relation to animal reservoir diversity to define which zoonotic sources have an impact on the incidence of human infections • Develop appropriate and gender-sensitive tools and methods to assess the health and socioeconomic impact of control programmes on individuals and households for Asian schistosomiasis • Find ways to increase interest in the discovery and development of new diagnostic tools, vaccines and new trematocidal drugs for foodborne trematodiases • Determine how to improve access to clean water, adequate sanitation and sewage treatment, and enhanced food safety measures to have an impact on foodborne trematodiases • Develop integrated control approaches and intersectoral collaboration between public health and veterinary medicine for foodborne trematodiases, including collaboration on considerations of feasibility, efficacy and cost−effectiveness • Conduct operations research on integrated control (mass treatment, education and behaviour change communication, community-directed/led strategies for health, sanitation and aquaculture management) in endemic communities and intersectoral collaboration between public health and veterinary medicine and

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			public and private sectors in planning implementation, including food safety issues for foodborne trematodiases • Analyze gender (male and female) differentials on access to and compliance with FBT treatment for foodborne trematodiases (FBT) • Develop appropriate and gender-sensitive tools and methods to assess the socioeconomic impact of FBT on individuals, households, communities and societies • Assess the impact of FBT and its control into the health education programmes for communities and schools, and its effect on the knowledge and practice of endemic communities to prevent and control FBT • Assess the cost−effectiveness of integration of existing serological test regimes for toxoplasmosis into antenatal care programmes in low-income settings • Develop culturally acceptable health education programmes to improve food hygiene in the home, especially for pregnant women, to prevent toxoplasmosis infection • Find ways to enhance the surveillance of cryptosporidiosis infection prevalence in humans and livestock, and determine the short- and longer-term health and economic consequences for both populations • Assess the impact of community-level water and sanitation improvements on the

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
			prevalence of human cryptosporidiosis infection in both urban and rural settings • Find ways to strengthen laboratory capacity for the diagnosis and surveillance of rabies to generate accurate data on incidence and guide control strategies and estimates of disease burden • Find ways to establish prioritization and cooperation of rabies control between health, veterinary and wildlife agencies • Evaluate the cost−effectiveness of different WHO-recommended pre and post-exposure regimens or rabies, including indirect costs associated with hospital visits • Investigate the economics of dog oral vaccination strategies and identify appropriate settings for implementing oral vaccination campaigns in dogs • Conduct ethnographic and participatory research to design relevant and understandable criteria for measuring the impact of bacterial zoonoses, and that incorporates a broader consideration of burden with consideration of the value of livestock for human well-being and development • Design and evaluate cost−effective brucellosis livestock vaccination strategies and advocate “One Health” approaches to implementation at the policy-maker level through ministries of health and agriculture • Develop approaches to raise awareness

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
			among physicians of the need for differential diagnosis of *Brucella* in cases of non-specific febrile illness • Conduct applied research on the development, implementation and evaluation of appropriate preventive health educational measures that are likely to provide a cost−effective means of reducing the burden of a wide range of bacterial zoonotic infections • Develop infrastructure and capacity to identify zoonotic enteric pathogens in the relevant animal populations • Determine the economic burden resulting from infections in livestock, including illness and loss of markets and income from animals and the direct and indirect economic costs of foodborne illnesses • Develop ways to improve the communications between veterinary and human health professionals, to include integrated training modules and mechanisms for exchange of information • Identify how to create joint veterinary/human health outbreak investigation teams, with access to quality laboratory capacity for diagnosis allied to enhancement of veterinary and human grassroots public health educational services (educational extension model) to improve animal and human health outcomes • Develop strategies to control the delivery of drugs used for enteric infections

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
			without restricting access when these medications are urgently needed in order to increase appropriate use and delay the emergence and spread of drug resistance • Identify the optimal investments in livestock animal and human primary health care capacity to ensure appropriate treatment as well as the use of effective prevention modalities • Create new approaches to community sanitation measures and the provision of clean water supplies • Estimate the duration of "open defecation free" (ODF) status following CLTS • Estimate the cost−benefit of CLTS as compared with other approaches • Study the human-animal interface to clarify the social, cultural, behavioural, economic and gender dimensions of improving community access to proper sanitation through CLTS • Evaluate the impact of CLTS on specific communities dependent on equines and camelines, smallholder pig farmers and those dependent on aquaculture • Further study mechanisms for coordinated public and animal health action within national government systems that comprise both the public health and animal health systems as a single entity on an equal partner basis • Find ways to increase the level of priority accorded to zoonotic diseases by increasing advocacy and undertaking

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
			research to underpin the importance of zoonotic infections as drivers of poverty • Find ways to extend the concept of zoonoses to cover diagnosis, data-sharing, monitoring and surveillance systems, training, interventions and delivery • Conduct long-term (longitudinal) studies assessing health education "multipacks", i.e. for diseases with similar or overlapping bio-social determinants • Find ways to integrate a gender-sensitive approach to health education/promotion and behaviour change, e.g. the role of women, as they more often tend to be small livestock keepers • Organize and conduct comparative studies on traditional versus participatory research for zoonoses and marginalized infections • Conduct evaluation research (assessment of methodologies for programme/project evaluation) for zoonotic diseases • Assess the specific contribution of educational components within integrated interventions • Expand systems research to determine how best the different sectors can interact • Find ways to integrate animal and human disease expertise with social science perspectives • Find ways to scale up research training to increase human resources in the area of public health, including veterinary and livestock services, for addressing zoonoses

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
			• Create opportunities to evaluate and modify zoonotic control strategies as experience is gained in implementation • Determine how to combine interventions allied to improved water and sanitation, and health education and promotion, and deploy them for the human and animal diseases in parallel • Expand research on the use of new communication technologies such as smart phones to enhance surveillance, reporting and evaluation of zoonoses I. Innovative financing • None identified
4. World Health Organization. Research Priorities for Chagas Disease, Human African Trypanosomiasis and Leishmaniasis. TDR Disease Reference Group for Chagas Disease, Human African Trypanosomiasis and Leishmaniasis. Technical Report Series No. 975. Geneva: World Health Organization; 2012. *The report identifies research gaps and opportunities where research activities can provide knowledge and*	DRG3 consisted of 14 academic or public health leaders in the areas of Chagas disease, human African trypanosomiasis (HAT) and/or leishmaniasis, as mentioned in the introduction. The members came from research institutions, international organizations, health and medical organizations, governmental and inter-governmental organizations worldwide. The chair and co-chairs were selected on the basis of their internationally-recognized research and long-term experience in research and control related to these diseases, and their experience working in disease endemic countries. The reference	A. Basic science • Assess the importance of asymptomatic infection for Chagas disease (CD), Human African Trypanosomiasis (HAT) and Leishmaniasis B. Diagnostics • Develop new diagnostics for case detection and characterization, including drug resistance and tests of cure for Chagas disease, Human African Trypanosomiasis and Leishmaniasis • Develop improved means to identify specific disease states: from asymptomatic and chronic to cured conditions for CD, HAT and Leishmaniasis	A. Basic science • Conduct studies that investigate the process of HAT entry into the central nervous system (CNS) and subsequent pathogenesis that produces a debilitating and lethal second-stage of the disease B. Diagnostics • Develop diagnostics for infants of *T. cruzi*-infected mothers, second-stage human African trypanosomiais, and visceral leishmaniasis in different global regions C. Drugs • Develop new drugs for Chagas' disease that provide a shorter treatment course with fewer side-effects than nifurtimox and benznidazole, and devise paediatric formulations

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
tools that can lead to interventions to alleviate or prevent disease. Finally, the report identifies priority areas on which to focus research activity and investment to advance the understanding of these diseases and contribute to health improvement.	group was hosted by Sudan and Brazil, in partnership with the WHO country and regional offices. A multi-stage interactive process was used to identify promising areas for research; this entailed assembling, evaluating, ranking, and reducing the number of priorities identified. The aim was to enable researchers, funding agencies, policymakers and other public health stakeholders to integrate relevant information and expert views and avoid conflict of interest as they consider various options for making decisions.	C. Drugs • Investigate new safe therapeutics to avoid drug resistance, including exploring combinations of approved anti-kinetoplastid drugs, repurposing of existing approved drugs and developing new drugs for Chagas disease, Human African Trypanosomiasis and Leishmaniasis • Develop drugs for chronic Chagas disease, second stage human African trypanosomiasis, visceral leishmaniasis, and cutaneous leishmaniasis • Develop new, effective, safe and affordable drugs, preferably oral, for all the trypanosomiases and leishmaniases D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • Concentrate on developing innovations in vector control for dengue, Chagas disease, lymphatic filariasis, the Leishmaniases and onchocerciasis to reduce transmission	• Find ways to overcome current problems of toxicity, efficacy, administration and length of treatment for CD, HAT and leishmaniases • Discover and develop new drugs for kinetoplastid pathogens using the foundation laid by genome sequencing projects and the identification of potential drug targets • Determine ways to confirm chemically validated drug targets and rigorously assess new drugs for chances of success by ranking against additional criteria such as druggability, assay feasibility, toxicity, and potential for the emergence of drug resistance for CD, HAT and leishmaniases • Improve the usability of currently registered drugs, including a shortened 10-day course (rather than 21–35 days) of melarsoprol that followed pharmacokinetic studies and a clinical trial with a 3-day course of pentamidine for HAT • Identify new drug candidates for HAT, particularly new molecules with trypanocidal activity that can penetrate the blood brain barrier • Find ways to preserve the utility of drugs for CL and VL forms of leishmaniasis • Determine how to overcome challenges of drug resistance, limited efficacy for different strains and species, and cost for VL pentavalent antimonials and lipid amphotericin B formulations • For CL, focus on preserving the potency of

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		• Find ways to achieve a collaborative approach among sectors for agriculture, health and the environment to achieve the sound management of pesticides • Investigate new vector control technologies, including markers of successful vector control for Chagas disease, Human African Trypanosomiasis and Leishmaniasis • Research vector population characteristics, including insecticide resistance for Chagas disease, Human African Trypanosomiasis and Leishmaniasis G. Epidemiology • Find ways to gather more accurate estimates of the global disease burden for NTDs H. Health systems/public health research • Conduct operational research on integrated disease and vector control for Chagas disease, Human African Trypanosomiasis and Leishmaniasis I. Innovative financing • Determine how to increase R&D funding available for trypanosomatid diseases so that it is comparable with malaria,	pentamidine, fluconazole, azithromycin, itraconazole used as systemic therapy for cutaneous, mucocutaneous, diffuse cutaneous and post kala-azar dermal leishmaniasis, and heat therapy, cryotherapy, and intralesional antimony drugs used for cutaneous forms of the disease D. Preventative vaccines • Investigate vaccines to prevent *Leishmania* infection and disease, and vaccines to block transmission of *Leishmania* • Develop prophylactic or therapeutic vaccines for Leishmania and assess the importance of asymptomatic infection in CD, HAT and leishmaniases • Examine the host-pathogen relationship when developing prophylactic, therapeutic or transmission-blocking vaccines for CD, HAT and leishmaniasis • Develop a vaccine protocol that could be used to reduce transmission of *T. cruzi* to humans for Chagas disease; this is a practical and achievable goal within a short time frame • Develop a live vaccine that could be delivered orally to larger groups of animals against *T. cruzi* infection; the vaccine not need to be 100% effective in preventing infection since reducing the level of infectiousness of dogs for insects could impact transmission

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		tuberculosis and HIV/AIDS	• Test the efficacy of a human vaccine for CD and its potential integration with other control mechanisms • Develop a HAT vaccine that blocks initial infection given the repertoire of surface antigens produced by the metacyclic parasites that are transmitted by the tsetse fly is much more limited than the repertoire of the bloodstream forms • Determine how to utilize the findings from basic science studies of HAT to identify targets for vaccine development that would prevent CNS entry or pathogenesis • Develop a transmission-blocking vaccine for HAT that would prevent establishment of the parasite in the tsetse vector • Develop a prophylactic vaccine for leishmaniasis based on the strong naturally acquired resistance that develops following a primary infection as well as demonstrated protection seen in a variety of animal models • Investigate and validate the possibility that no non-living vaccine will be able to generate, and more importantly maintain, the level of cell-mediated immunity necessary to protect against sandfly-transmitted infections in humans • Develop animal models and test leishmaniasis vaccines in dogs as they can be evaluated using natural exposure • Explore killed whole cell vaccines for their low cost, ease of production, have prophylactic and therapeutic potential for

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
			leishmaniasis E. Therapeutic vaccines • None identified F. Vector control • Assess vector infestation in Chagas disease • Delineate target vector populations of human African trypanosomiasis • Define cost-efficient insecticidal targets for control of human African trypanosomiasis as a prevention strategy • Understand the factors that influence house invasion by sylvatic Triatominae and why some bugs may succeed in colonizing a house while others do not • Determine how to produce more cost-effective, target-based control technologies for HAT that will impact the *gambiense* reservoir of parasites in the *gambiense* form of disease that resides in humans • Determine the effective reservoir of parasites in the *rhodesiense* form of disease resides in domestic or wild animals • Develop vector source reduction for leishmaniasis using environmental measures that could include: o rendering soil unsuitable for sandfly larvae, thereby reducing the numbers of emerging sandflies o spraying of flowering trees

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
			o indoor residual spraying, insecticide treated nets and vector repellents G. Epidemiology • Investigate surveillance methods for Chagas disease and human African trypanosomiasis, and economic analysis of treatment and vector control methods for CD, HAT and leishmaniasis H. Health systems/public health research • None identified I. Innovative financing • Develop a highly efficient and collaborative environment to optimize effort and the use of funding for trypanosomatid diseases that engages the academic community, public institutes and the pharmaceutical/biotech sector in a unified effort
5. Burki T. Ticks and Turkey. Lancet. 2012; 380:1897-98. *With more countries expected to detect Crimean-Congo haemorrhagic fever in the coming years, Talha Khan Burki takes a closer look at the risk factors and reach of this zoonotic disease.*	None provided	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • None identified	A. Basic science • None identified B. Diagnostics • Develop an on-site diagnostic dipstick to test for Crimean-Congo haemorrhagic fever (CCHF) C. Drugs • Conduct much needed double-blind clinical trials of ribavirin to determine whether ribavirin is improving the survivor

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • Find ways to gather more accurate estimates of the global disease burden for NTDs H. Health systems/public health research • None identified I. Innovative financing • None identified	rate Crimean-Congo haemorrhagic fever D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • Determine how to provide more accurate estimates of the distribution of the *Hyalomma* spp tick responsible for Crimean-Congo haemorrhagic fever • Determine optimal regimens to control *Hyalomma* spp ticks using insect repellent and livestock insecticidal sprays • Identify ways to enlist experts to map the behaviour of the *Hyalomma* spp tick, particularly in response to population and ecological changes G. Epidemiology • Determine how to provide a more accurate estimate of global Crimean-Congo haemorrhagic fever (CCHF) prevalence and distribution using improved surveillance methods • Investigate why the burden of CCHF is higher in Turkey than elsewhere so that other countries can draw conclusions about their own risks, e.g. whether it is due to the environment, the virus, a genetic factor, or something to do with the tick vector

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
			H. Health systems/public health research • Find ways to ensure at-risk communities take precautions against CCHF by wearing protective clothing and getting health professionals to ensure that safety measures are adhered to within hospitals, most crucially when they encounter haemorrhaging patients I. Innovative financing • Develop strategies to increase the diagnostic and vaccine market for Crimean-Congo haemorrhagic fever
6. Karesh W, Dobson A, Lloyd JO, et. al. Ecology of zoonoses: natural and unnatural histories. Lancet. 2012; 380:1936-45. *Karesh et al. review how zoonotic diseases result from natural pathogen ecology, and how other circumstances, such as animal production, extraction of natural resources, and antimicrobial application change the dynamics of disease exposure to human beings. In view of present anthropogenic trends, the*	Karesh et al. selected high-quality references that showed rigorous scientific methodologies in their research and analyses. We searched Web of Science for reviews and research articles published between Jan 1, 1990, and June 1, 2012, with the search terms "zoonotic disease" and "antimicrobial resistance", and filtered results for "animals", "wildlife", or "wild animals". The authors chiefly selected publications from the past decade but did not exclude commonly referenced or highly regarded older publications. They also searched reference lists of articles identified by this search and selected those	A. Basic science • Investigate the complex ecology of antimicrobial resistance and foodborne zoonoses B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • Find ways to achieve a	A. Basic science • Better understand the zoonotic microbiome from people and that of the animals they contact, and what causes zoonotic microbes to proliferate in some conditions • Study the effects of the use of antibiotics in animal production, and find ways to enhance the translation of this science by involving physicians, veterinarians, and ecologists in the design and interpretation of studies • Explore the use of alternatives such as probiotics, diets to promote healthy or protective gastrointestinal flora, new methods of immune-system modulation, bacteriophages, bacterial cell wall hydro lases, and anti-microbial peptides to help reduce the need for antimicrobial use in

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
authors advocate for a more effective approach to zoonotic disease prevention and control that requires a broad view of medicine that emphasises evidence-based decision making, and integrates ecological and evolutionary principles of animal, human, and environmental factors.	we judged relevant. Review articles and book chapters are cited to provide readers with more details and more references. Non-peer-reviewed sources such as reports from the World Organization for Animal Health, the Food and Agriculture Organization, and WHO were also reviewed to provide direct information or additional supporting references. Additional references and materials were suggested by anonymous reviewers and additional reviewers invited by the authors.	collaborative approach among sectors for agriculture, health and the environment to achieve the sound management of pesticides • Learn how to better integrate veterinary public health services into the control of neglected zoonotic diseases • Develop bold new approaches to gauge the risk of zoonotic pathogens spreading from their natural reservoirs to humans, and their potential to become new human infectious pathogens G. Epidemiology • Better understand how changes in the environment affect zoonotic disease trends, and how these changes affect microbial dynamics across the system • Utilize combined public health and ecology approaches to drive advances in predicting the emergence and spread of novel zoonoses • Understand the relation between environmental changes, wildlife population dynamics, and the dynamics of their microbes to forecast risk of human infection with enzootic or endemic zoonoses • Investigate the dynamics of	people and animals B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • Conduct long-term multicentre studies to improve understandings of natural variation, changes with time, interspecies transfer and the dynamics of antimicrobial resistance in wildlife, both naturally occurring and arising from anthropogenic influences • Conduct observations studies and experimental work with wildlife that could provide valuable insights into understanding the population and community effects of antimicrobial use and persistence of changes G. Epidemiology • Find ways to encourage collaboration between public health scientists, who normally use epidemiological techniques with human case data, and disease

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		zoonotic pathogens in their wildlife reservoir to learn if potential early warning systems can be developed to better inform the risk of an outbreak in livestock or people, and ultimately reduce the number of cases of human disease • Determine how to standardize data collection and find ways to increase long-term monitoring and risk assessment for the development of multidrug resistance or multi-bacterial infections in human beings resulting from antimicrobial use in food animals and from wildlife H. Health systems/public health research • Determine how to promote the One Health perspective to understand the ecology of zoonotic diseases at the human being–animal interface, and integrate knowledge of animal and human medicine, agriculture, ecology, sociology, microbial ecology, and evolution, and the underlying issues that drive increased transmission of pathogens in humans, wildlife, and livestock • Find ways to enhance multi-	ecologists who often work with wildlife or livestock data to model risk in human beings H. Health systems/public health research • Design and evaluate cost−effective brucellosis livestock vaccination strategies and advocate "One Health" approaches to implementation at the policy-maker level through ministries of health and agriculture • Determine how to enhance international disease-prevention efforts by identifying ways to advance implementation of WHO's International Health Regulations and international standards for animal health and zoonoses produced by the World Organization for Animal Health • Investigate how to improve veterinary services in many low-income and middle-income countries to increase detection, quantification, reporting and prevention of zoonotic infection in animals • Find ways to enhance the role ecologists play in zoonotic control programmes to produce more accurate mathematical model outputs via collaboration with clinicians with real-time data, participation in both prospective and retrospective study design, and field studies to identify key risk factors to target surveillance and interventions • Develop guidelines for safe or best practices that include ecological knowledge

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		sectoral collaboration in prevention and response efforts for zoonotic diseases, and in the elimination or mitigation of transmission routes to prevent their emergence • Find ways to encourage collaboration between ministries of health, environment and agriculture, and inter-governmental agencies involved in health, trade, food production, and the environment on zoonotic control efforts given that zoonoses affect developed and developing countries alike and spread readily across national boundaries I. Innovative financing • None identified	to reduce the risk of zoonotic disease emergence or occurrence among industries based on the extraction of natural resources, and find ways to mandate these guidelines through the funding mechanisms that support large-scale development projects or find ways for mandated guidelines to be required by financial insurers I. Innovative financing • None identified
7. Kilpatrick A, Randolph S. Drivers, dynamics, and control of emerging vector-borne zoonotic diseases. Lancet. 2012; 380:1946–55. *Kilpatrick et al. draw attention to key differences between vector dynamics and disease burden that result from increased pathogen transmission after habitat change and introduction into new*	Kilpatrick et al. searched PubMed and ISI Web of Knowledge with the terms "emerging infectio*", "vector-borne diseas*", "zoonos*" or names of specific vector-borne infections, in combination with "control", "exotic", "climate change", "socio-econom*", "land use", or "evolution" for reports published in any language before July, 2012. Searches were done at all stages, from the initial drafting of the paper to submission of the revised and final version. Authors	A. Basic science • None identified B. Diagnostics • Develop diagnostics for point-of-care use for infection and exposure to allow for proper assessments of case fatality ratios and disease burden for vector-borne pathogens C. Drugs • None identified D. Preventative vaccines	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
regions. The authors describe challenges inherent in the control of vector-borne zoonotic diseases and propose some emerging non-traditional strategies that could be effective in the long term.	also relied on our own familiarity with the scientific literature. We largely selected reports from the past 6 years, but did not exclude older publications that were informative and useful. The authors also searched the reference that we judged to be relevant. Reviews and book chapters are cited to provide readers with comprehensive sources of references, but primary research is also included where possible within the space allowed. The reference list was modified on the basis of comments from peer reviewers.	• None identified E. Therapeutic vaccines • None identified F. Vector control • Explore new techniques to develop vectors resistant to pathogens by infecting them with naturally occurring intracellular insect parasites (eg, *Wolbachia*) • Find ways to attempt to control many vector-borne pathogens that are zoonotic and have transmission intensity in vectors driven primarily by wildlife reservoirs G. Epidemiology • Acquire a robust understanding of how all aspects of climate and climate change affect rates of the processes involved in transmission of vector-borne pathogens • Develop collaborative models that include researchers, public health agencies, the government, and the public to identify the causes of increases in incidence and subsequent targeting with appropriate control measures to reverse the ecological drivers of vector-borne disease emergence, e.g. risk related to specific types of land use could be ameliorated by	F. Vector control • None identified G. Epidemiology • Determine how to expand the breadth of analyses investigating the relationship between climate and vector-borne pathogens to include all potential factors affecting incidence of infection and prevalence of disease, both biological and non-biological • Develop vector-borne disease predictions based on climate that are truly cross-disciplinary, evidence-informed collaborations, marrying biologists' pursuit of improved models of vector abundance, infection prevalence, and pathogen evolution (eg, drug resistance) with understanding from medical and social scientists about developments in treatment and interventions, land-use change, and human societal factors H. Health systems/public health research • Design and evaluate cost−effective brucellosis livestock vaccination strategies and advocate "One Health" approaches to implementation at the policy-maker level through ministries of health and agriculture • Investigate correlations that exist between land use and disease incidence or measures of risk, and develop rigorous and

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		urban planning and management of host and vector communities through landscaping, hunting, or restoration of ecological communities H. Health systems/public health research • Find ways to encourage collaboration between ministries of health, environment and agriculture, and inter-governmental agencies involved in health, trade, food production, and the environment on zoonotic control efforts given that zoonoses affect developed and developing countries alike and spread readily across national boundaries • Better understand the mechanistic processes linking land use and socioeconomic conditions with disease to enable the prediction of future trends and control or mitigation of vector-borne pathogens I. Innovative financing • None identified	mechanistic analyses that identify causal factors that are needed for intelligent urban planning to anticipate and avoid future vector-borne pathogen-based epidemics • Develop behavioural change strategies promoting personal protective behaviours to prevent the emergence of endemic or exotic pathogens I. Innovative financing • None identified
8. Morse S, Mazet J, Woolhouse M, Parrish C, Carroll D, Karesh W, et al. Prediction and prevention of the next pandemic	Morse et al. searched PubMed and ISI Web of Knowledge with the terms “emerging infectio*”, “zoonos*”, or “pathogen discovery” in combination with the terms	A. Basic science • Develop the basic research agenda to allow potential zoonotic pandemic pathogens to be distinguished from harmless	A. Basic science • Analyze zoonotic viral traits and phylogenetic relations, and how these correlate with emergence and pathogenicity after a virus spills over

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
zoonosis. Lancet. 2012; 380:1956-65. *Morse et al. review what is known about zoonotic pathogens that emerge, the hosts that they originate in, and the factors that drive their emergence. The authors discuss challenges to their control and new efforts to predict pandemics, target surveillance to the most crucial interfaces, and identify prevention strategies. The article lays out a series of research and surveillance opportunities and goals that could help to overcome these challenges and move the global pandemic strategy from response to pre-emption.*	"modeling", "prediction", "surveillance", "evolution", "ecology", or "methodology" for papers published in any language before Sept 25, 2012. The authors did their searches when they began to develop and write the paper and again before submission of the revised, final version. Some coauthors provided references that they deemed of particular importance. We largely selected publications from the past 5 years, but did not exclude commonly referenced and highly regarded older publications. The authors also searched the reference lists of articles identified by our searches and selected those judged relevant. Reviews and book chapters are cited to provide readers with more detailed information and references than is possible in the space allowed. The reference list was modified on the basis of comments from peer reviewers.	microbes by use of molecular sequence data only, or information that can be deduced from these data—eg, structures of key proteins B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • Determine the relative importance of host relatedness versus contact frequency in the emergence of zoonotic diseases H. Health systems/public health research • Health perspective to understand the ecology of zoonotic diseases at the human being–animal interface, and integrate knowledge of animal and human medicine, agriculture,	• Further elucidate the relationship between host range and plasticity as they relate to the likelihood of pathogens transmitting between different host taxa, and develop predictive correlations for these events • Provide better estimates of a virus's ability to evolve by investigating the factors that allow a pathogen to successfully jump species, including high mutability and an absence of proofreading to correct mutations • Better understand host—receptor interactions, including understanding of the interactions for commonly expressed receptors (eg, sialic acids or heparan sulfate proteoglycans) or ease of adaptation of the virus to a new host receptor • Investigate viruses' capacity to exploit new routes of transmission, and include human behaviour as a critical component that should be integrated into any predictive model • Conduct research that allows scientists to better predict the virulence of zoonotic pathogens, and increases our ability to assess the likelihood that a wildlife or livestock virus will cause noteworthy disease if the virus does infect people • Further elucidate patterns of host–virus coevolution among related viruses and their wildlife hosts by analysing genetic sequences and improving understanding of the pathogen's opportunities for transfer

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		ecology, sociology, microbial ecology, and evolution, and the underlying issues that drive increased transmission of pathogens in humans, wildlife, and livestock • Find ways to encourage collaboration between ministries of health, environment and agriculture, and inter-governmental agencies involved in health, trade, food production, and the environment on zoonotic control efforts given that zoonoses affect developed and developing countries alike and spread readily across national boundaries • Develop a new systematic, pre-emptive risk assessment approach that aims to prevent the spread, or even the initial emergence, of pandemics of zoonotic origin I. Innovative financing • None identified	B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • None identified I. Innovative financing • None identified
9. Hotez P. New Antipoverty Drugs, Vaccines, and Diagnostics: A Research Agenda for the US President's Global Health Initiative (GHI). PLoS Negl Trop Dis. 2011;5(5): e1133.		A. Basic science • None identified B. Diagnostics • Concentrate diagnostic development efforts on products for Amebiasis, CD, Giardiasis, HAT, Leishmaniasis, Taeniasis-	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
doi:10.1371/journal.pntd.0001133.		cysticercosis, Echinococcosis, Food-borne trematodiases, Loiasis, Lymphatic filariasis, Onchocerciasis, Schistosomiasis, Ascariasis, Hookworm, Trichuriasis, Strongyloidiasis, Toxocariasis, Dengue and other flaviviruses, Rabies, Rift Valley fever, Baronellosis, Bovine tuberculosis, Buruli ulcer, Cholera, Enteric pathogens (Gram neg), Leprosy, Leptospirosis, Trachoma, Treponematoses, Mycetoma and Ectoparasitic infections C. Drugs • Investigate new safe therapeutics to avoid drug resistance, including exploring combinations of approved anti-kinetoplastid drugs, repurposing of existing approved drugs and developing new drugs for Chagas disease, Human African Trypanosomiasis and Leishmaniasis • Develop drugs for chronic Chagas disease, second stage human African trypanosomiasis, visceral leishmaniasis, and cutaneous leishmaniasis • Develop new, effective, safe and affordable drugs, preferably oral, for all the trypanosomiases and leishmaniases	D. Preventative vaccines • Focus specifically on vaccine product development for Amebiasis, Chagas disease, HAT, Leishmaniasis, Food-borne trematodiases, Onchocerciasis, Schistosomiasis, Hookworm, Strongyloidiasis, Dengue and other flaviviruses, Rabies, Rift Valley Fever, Bovine TB, Cholera, Enteric pathogens (Gram Neg), Leprosy, Leptospirosis, Rheumatic fever, Trachoma, Treponematoses and Paracoccidiomycosis E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • None identified I. Innovative financing • Find ways to incentivize greater investments in NTD product development from the GHI through a model of “vaccine diplomacy” that will inspire the next generation of poverty-reducing biotechnologies and also strengthens US foreign relations in NTD-endemic countries

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		• Develop a macrofilaricide drug • Concentrate research efforts towards drug development for Chagas disease, HAT, Leishmaniasis, Taeniasis-cysticercosis, Echinococcosis, Food-borne trematodiases, Loiasis, Lymphatic filariasis, Onchocerciasis, Schistosomiasis, Hookworm, Trichuriasis, Strongyloidiasis, Toxocariasis, Dengue and other flaviviruses, Rabies, Rift Valley Fever, Baronellosis, Bovine TB, Buruli Ulcer, Cholera, Enteric pathogens (Gram Negative), Leprosy, Leptospirosis, Treponematoses, Mycetoma, Paracoccidiomycosis and Ectoparasitic infections D. Preventative vaccines • Focus on new vaccine development for leishmaniasis, Chagas disease, hookworm infection, schistosomiasis, dengue, and enteric bacterial pathogens E. Therapeutic vaccines • None identified F. Vector control • Concentrate on developing innovations in vector control for dengue, Chagas disease, lymphatic	

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		filariasis, the Leishmaniases and onchocerciasis to reduce transmission • Research vector population characteristics, including insecticide resistance for Chagas disease, Human African Trypanosomiasis and Leishmaniasis • Focus new vector control product/transmission-blocking zoonotic animal reservoir product development on Chagas disease, HAT, Leishmaniasis, Taeniasis-cysticercosis, Echinococcosis, Food-borne trematodiases, Lymphatic filariasis, Onchocerciasis, Schistosomiasis, Ascariasis, Toxocariasis, Dengue and other flaviviruses, Rabies, Rift Valley Fever and Bovine TB G. Epidemiology • None identified H. Health systems/public health research • None identified I. Innovative financing • Determine how to fill the funding gap for NTD product development within the US President's Global Health Initiative	

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
10. World Health Organization. Global Report for Research on Neglected Diseases of Poverty. Geneva: World Health Organization on behalf of the Special Programme for Research and Training in Tropical Diseases; 2012. *The report identifies research-related actions that policy-makers, funders and researchers should focus on if the public health challenges of infectious diseases of poverty are to be met. The report details the drivers of infectious diseases in poor populations and highlights how advances in science and technology can be used to meet the challenges of controlling these diseases.*	Experts were convened from across the globe to work in ten disease-specific and thematic reference groups to carry out a review and consultation process and identify top research priorities. Each reference group was jointly led by a disease endemic country and international chair or co-chair, and each was hosted by a disease endemic country with WHO country or regional offices acting as the secretariat. The analysis and research priorities developed by these expert groups and followed by regional and national consultations with stakeholders and workshops underpins this *Global Report*. Developed over three years and in three phases, The *Global Report for Research on Infectious Diseases of Poverty* identifies research-related actions that policy-makers, funders and researchers should focus on if the public health challenges of infectious diseases of poverty are to be met. The report details the drivers of infectious diseases in poor populations and highlights how advances in science and technology can be used to meet the challenges of controlling these	A. Basic science • Identify ways to embed basic research within a superstructure of more integrated interdisciplinary and systems-based research{ • Better understand the "ecosocial" factors which facilitate resistance; determine the strategies – biological, chemical, genetic, cultural and social – that exist to better control pathogens and vectors B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • Better understand how changes in the environment affect zoonotic disease trends, and how these changes affect microbial dynamics across the system	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Determine ways to involve sectors other than health, including finance, education, agriculture and veterinary public health, water and sanitation, and environmental management in NTD research and control • Determine the economic cost of neglected zoonoses for both the human and animal populations involved • Determine the economic burden resulting from infections in livestock, including illness and loss of markets and income from animals and the direct and indirect

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
	diseases.	• Utilize combined public health and ecology approaches to drive advances in predicting the emergence and spread of novel zoonoses • Understand the relation between environmental changes, wildlife population dynamics, and the dynamics of their microbes to forecast risk of human infection with enzootic or endemic zoonoses • Investigate the dynamics of zoonotic pathogens in their wildlife reservoir to learn if potential early warning systems can be developed to better inform the risk of an outbreak in livestock or people, and ultimately reduce the number of cases of human disease • Develop collaborative models that include researchers, public health agencies, the government, and the public to identify the causes of increases in incidence and subsequent targeting with appropriate control measures to reverse the ecological drivers of vector-borne disease emergence, e.g. risk related to specific types of land use could be ameliorated by urban planning and management of host and vector communities through landscaping, hunting, or	economic costs of foodborne illnesses • Develop ways to improve the communications between veterinary and human health professionals, to include integrated training modules and mechanisms for exchange of information • Identify how to create joint veterinary/human health outbreak investigation teams, with access to quality laboratory capacity for diagnosis allied to enhancement of veterinary and human grassroots public health educational services (educational extension model) to improve animal and human health outcomes • Study the human-animal interface to clarify the social, cultural, behavioural, economic and gender dimensions of improving community access to proper sanitation through CLTS • Develop effective ways to build capacity among human and veterinary pathologists, including the integration of disease-surveillance, shared animal-human epidemiological studies, and best ways to develop health services able to deal with animal and human health • Determine the best open-access models for sharing of new knowledge and products, and the delivery of new innovations{J} • Find ways to highlight the importance of innovation by engaging key players in global networks • Develop and work towards a “one world-

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		restoration of ecological communities • Assess the utility of GIS and bioclimatic monitoring systems to measure, anticipate and plan for infectious disease outbreaks, and to build infrastructural capacity in disease endemic countries (e.g. HealthMapper, Global Health Atlas, TREES Project) • Determine the socioeconomic impact of zoonotic diseases on livestock production and the consequences that control measures of such disease have for the livestock trade • Determine zoonotic diseases' impact on wildlife populations and biodiversity • Investigate how social variables (gender, ethnicity, culture) influence human-animal interactions, the transmission of disease, cultural aetiologies of disease and patterns of health-seeking • Identify the social and mental health consequences of disability caused by infectious disease (e.g. social stigma, fear) H. Health systems/public health research • Determine how to promote the	one research" community agenda • Learn how to foster a culture of open innovation for sharing knowledge, technology and repositories (e.g. demographic and biological database, bio-banks, biomarker banks, standard libraries and databases for traditional knowledge, social science data, etc.) • Create an open innovation platform that brings together independent but cooperating agencies and consortia, including networks of researchers, community members and health workers can help progress research, monitor health indices, undertake community audits and evaluation, better manage intellectual property, and distribute financing • Create monitoring systems to track pharmacological side effects and community attitudes towards health technologies and to strengthen capability to translate technologies into local solutions • Develop methods to implement a cross-disciplinary "One Health, One World" strategy in relation to research for infectious diseases of poverty that includes champions from government, civil society, education and the private sector, particularly in disease endemic countries • Develop mechanisms through which researchers in different countries can learn from one another (e.g. the BRICS countries), possibly through regional partnerships, new networks, online

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		One Health perspective to understand the ecology of zoonotic diseases at the human being–animal interface, and integrate knowledge of animal and human medicine, agriculture, ecology, sociology, microbial ecology, and evolution, and the underlying issues that drive increased transmission of pathogens in humans, wildlife, and livestock • Find ways to encourage collaboration between ministries of health, environment and agriculture, and inter-governmental agencies involved in health, trade, food production, and the environment on zoonotic control efforts given that zoonoses affect developed and developing countries alike and spread readily across national boundaries • Better understand the mechanistic processes linking land use and socioeconomic conditions with disease to enable the prediction of future trends and control or mitigation of vector-borne pathogens • Identify ways to foster closer collaboration between government, private sector, civil society and communities – in areas such as agriculture, technology, education,	forums, exchange programmes and collaborations I. Innovative financing • Determine how public–private partnerships can be expanded and scaled-up to include not only PDPs, but also the development of more basic research in the laboratory and the delivery of sustainable innovative products into the field • Find ways to reduce duplication and improve coordination of R&D funding for priority conditions by integrating goals and reducing overlap • Find ways to reduce competition for funds as a source of wastage • Find ways to improve the coordination of priorities for action in order to harmonize approaches to R&D funding e.g. through the proposed model of the WHO Expert Working Group on Research and Development Financing • Obtain funding data on implementation research, support for capacity building, and a broader class of research activities that explore aspects of behaviour, economics, politics, trade and the environment as they apply to infectious diseases of poverty • Develop a classification system to organize data on R&D for health • Find ways to resolve the issue of separating ultimate funders from recipients of funds and from intermediaries (such as PDPs) • Develop information systems to help

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		social welfare, transport and health – to better understand complex socio-ecological drivers which contribute to ill-health and the spread of infectious diseases • Develop methods to ensure that research findings, clinical experience and learning from both human and veterinary domains are connected • Identify ways to target the education sector, especially universities, to play a bigger role in building capacity and fostering interdisciplinary learning and research among a new generation of scientists and policy-makers through encouraging interdisciplinary work • Develop research frameworks to assess the reciprocal impact of global initiatives, national health systems and intersectoral governance on infectious disease control • Develop methods to determine the optimal balance between health workforce options and requirements to attain disease control targets in the context of broader health systems strengthening • Learn how to improve access and appropriate use of quality medical	capture data on funding flows for R&D on health • Investigate methods to build new funding capacity for supporting R&D in emerging economies such as Brazil, China and India • Identify high-level actions on which policy-makers, funders and researchers should focus when developing their health research related strategies • Create and use a new index of infectious diseases of poverty to serve as a surrogate marker of national socioeconomic development o Establishment of a framework of indicators for the index, based on a series of commissioned reviews and other research{J} o Identify institutions and other stakeholders, and provide funding to support development, piloting and small scale validation, in partnership with relevant stakeholders for the index{J} o Develop a stakeholders' platform to review, agree and recommend a strategy and framework for scale-up and implementation of the index • Create platforms to engage policy-makers with research entrepreneurship in endemic countries to demonstrate commitment to health research that could allow them to fund research and, in turn, use research outputs to underpin other policies • Develop means to engage stakeholders in

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		technologies for infectious disease control • Determine how stand-alone disease control information systems be integrated into existing national health information systems and into general health decision-making processes • Investigate how to develop research frameworks to assess the interaction between Global Health Initiative-targeted services and non-Global Health Initiative-targeted services so that overall service delivery is improved • Develop leadership strategies and mechanisms to share common values of equity and the right to healt, community involvement and sustainability across diverse actors through an outcome-oriented approach • Adopt systems thinking to assess the impact of system changes as they are designed and implemented, e.g. to better understand the impact of decentralization on disease control interventions, or how the introduction of pay-for-performance schemes impacts the rest of the health system • Further investigate how health systems interact with the wider	long-term partnerships with universities, public health and research institutes and health care systems in LMICs to facilitate LMIC health research ownership • Find ways to encourage funders to provide a framework that will allow leading research institutions and policy-makers in disease endemic countries to acquire expertise and capacity for priority setting, policy formulation and monitoring and evaluation of the effectiveness of actions • To facilitate LMIC health research ownership and strengthen partnerships with international donors, LMICs could: o develop research priorities congruent with the burden of infectious diseases of poverty in their own populations; o find ways to increase their own research activity and improve research leadership; o develop regional partnerships to build research infrastructure, human resources and research capacity; o create policies and develop plans to guide national and international investments towards the identified research priorities; o develop plans to increase their national support for research and translation of research to strategies for health • Create an innovation platform to foster a culture of innovation to benefit public health

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		social system and institutions (e.g. understanding how governance and political systems, culture and globalization forces impact on the structure and functions of health systems) • Investigate critical research questions concerning the scaling-up of interventions (.e.g What is the opportunity cost of scaling-up a specific innovation on other forms of health care and disease control? How does it relate to equity and efficiency? What are the contextual determinants for success? What information is available to assess scaling-up strategies?) • Investigate the impact of product development partnerships (PDPs) and incentives on developing country innovation systems, and identify the most effective partnerships to encourage health innovation for the poor while minimizing risks • Determine the most effective ways to implement the criteria for innovation (effectiveness, affordability, acceptability and sustainability) in national and global innovation systems • Develop platforms for innovative systems in Brazil, China, Indian and South Africa to be scaled-up, better	o Develop a new paradigm of an "open innovation culture", with a broader definition of innovation, through the collaboration of research and development agencies, industry and academia – both "north" and "south" – with disease endemic countries o Find ways to strengthen the research, development and implementation capacity of disease endemic countries through the use of roadmaps for innovative development, partnerships with BRIC countries, etc. o Create and expand an "open access innovation platform" comprising of open access to research information and to raw data, and mechanisms for joint ownership and sharing of intellectual property rights through fair and legal frameworks • Create an easily accessible, online global platform that supports a database and detailed analysis of resources and financial investment in health research that can provide policy-makers, funders and researchers with information they need to guide their activities, identify funding gaps and mitigate duplicated efforts

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		integrated with other capacity building initiatives and more effectively globalized to assist smaller LMICs to create similar innovative environments • Identify strategies and social entrepreneurship models that are available for local communities to innovate in the prevention, control and treatment of infectious diseases • Find innovative methods to translate and customize health interventions and products to local settings in order to overcome cultural and social barriers (e.g. stigma, social norms) and sustain interventions over the long term • Develop systems to continually monitor and evaluate centers of excellence in LMICs to ensure their capacity in research innovation (e.g. they do not bias the national science and technology landscape) • Determine the most effective way to link the local milieu of innovation in the public and private sectors in LMICs with international partners • Develop sophisticated regulatory and intellectual policies to provide the framework for an open innovative platform I. Innovative financing • Identify how to allocate greater	

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		funding priority to research that adopts interdisciplinary approaches that encourage collaboration between government ministries and agencies, and that better incorporate ecology into disciplines – including public health, medicine, social sciences, veterinary sciences and agriculture • Determine how to inspire greater investment in human capital and knowledge systems • Determine the best mix of infectious disease control funding mechanisms to strengthen health system financing, and in what contexts • Determine how global funding can be used to build mechanisms for innovation and health R&D in the lowest income countries • Find ways to give LMICs with developing capacities more active roles in public–private PDPs that cater to long-term LMIC goals for product development • Create incentives to invest in implementation research to complement advances in product development for infectious diseases of poverty • Develop methods to avoid wastage and improve the efficiency of R&D	

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		funding for infectious diseases of poverty • Find ways to strengthen the data reservoir concerning funding flows to infectious disease R&D • Develop processes and methods to ensure that R&D funding is relevant to the needs on the ground • Find ways to ensure that research capacity building activities are seen as integral to the funding agenda • Develop a strategic approach to the funding and support of research and to the generation and use of research outputs	
11. Glassman A, Chalkidou K. Priority setting in health: Building institutions for smarter public spending. Washington: Center for Global Development; 2012. *The result of this report is a set of thoughtful, pragmatic, and actionable recommendations that can be utilized by countries and global health organizations alike. Successful examples of priority setting mechanisms, from Thailand, the UK, and*	This report was written by Amanda Glassman and Kalipso Chalkidou, informed by the discussions of the Priority-Setting Institutions for Global Health Working Group. The working group, consisting of experts and policymakers from around the world, aims to shape how countries and the global community can be more effective through improved decision-making processes that manage the complex politics of resource allocation in the health sector.	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
elsewhere, provide lessons for countries that do not currently have explicit systems to set priorities across interventions and technologies and to manage the political and other costs that typically result.		• None identified G. Epidemiology • None identified H. Health systems/public health research • Develop and refine processes to assess health interventions and technologies as inputs to budget decision making and the design of publicly subsidized health benefits I. Innovative financing • Find ways to reallocate part of public and donor monies toward the most cost-effective and equity-enhancing health interventions and technologies • Design and implement a systematic process for health priority-setting within "health technology assessment systems" at national and global levels to increase the value for money of donor investments	• None identified G. Epidemiology • None identified H. Health systems/public health research • None identified I. Innovative financing • Create a global health technology assessment facility to provide sustained technical and consultative support to global funding agencies and low- and middle-income country governments • Develop platforms to direct donor support to countries creating or developing their own health technology assessment systems • Find ways to accredit health technology assessment systems and institutions in LMICs (possibly through a self-assessment of competencies), and work to include phased accreditation requirements as conditions for external funding • Investigate ways to increase the allocative efficiency of both global health donors and national health systems • Examine the suitability of health technology assessment systems to serve as a hub of know-how, technical assistance, and knowledge brokerage on institutionalizing health technology assessment systems and on the design/adjustment of health benefits

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
			plans, defining best practices and evaluating results, at the service of LMIC governments and global health funding agencies through a practitioner-to-practitioner approach of knowledge sharing • Utilize health technology assessment systems to generate economies of scale in the generation and adaptation of evidence dossiers for specific LMICs, applying toolkits and glossaries already developed, in order to avoid duplication of effort and save money • Develop methods to benchmark and compare coverage decisions (through GDP per capita normalization, for example) on high-cost drugs and devices worldwide, as an input to decision making where local health technology assessment analysis is not possible • Build and find ways to support regional networks of policy makers and practitioners, such as HTAsiaLink • Investigate ways to maximize the consistency of the methods and evidence included in health technology assessment, in cooperation with existing networks working on harmonization, to reduce the burden to industry and to product development partnerships • Find ways to facilitate dialogue between health systems and industry to ensure that the benefits of new technology and system needs are mutually understood and

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
			reflected in price and availability • Develop methods to ensure that health technology assessment facilities are of use both to countries with health technology assessment agencies and those without them • Develop health technology assessments facilities' (HTAFs) ability to work with and mobilize expertise from health technology assessment agencies and academic institutions around the world, in order to allow for a practitioner-to-practitioner model of technical assistance and just-in-time support to decisions • Determine how HTAFs can attract and retain world-class health technology assessment experts to assist LMICs directly in accreditation or health technology assessment system development • Find ways to guarantee HTAFs' ability to ensure independence and transparency • Develop a financial model that is self-sustaining for HTAFs, although seeded by initial donations or support, ideally from health technology assessment pioneers in LMICs like Brazil, Poland, and Thailand or from countries that are investing heavily in their health care systems and are committed to evidence of return on investment, e.g. China and Turkey • Design a governance model that assures HTAFs' independence and rigor, while permitting engagement with governments and stakeholders involved in health

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
			technology assessment around the world • Develop methods to ensure HTAFs operate in close coordination with the WHO and the PAHO

Disease-specific R&D priority setting

CHILDHOOD PNEUMONIA AND DIARRHOEA

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
1. Bhutta Z, Das J, Walker N, Rizvi A, Campbell H, Rudan I, Black R. Interventions to address deaths from childhood pneumonia and diarrhea equitably: what works and at what cost? The Lancet. 2013 Apr [cited 2013 Apr 25]. Available from: http://dx.doi.org/10.1016/S0140-6736(13)60648-0. *This article assesses the effectiveness of various preventive and therapeutic interventions against childhood diarrhea and pneumonia. Using the Lives Saved Tool model, the article presents a sensitivity analysis to predict the impact of various interventions on childhood mortality and the associated costs in 75 different countries. Additionally, this article provides an overview of research priorities for new delivery platforms that could potentially have a significant impact on childhood diarrhea and pneumonia mortality.*	We undertook two expert panel methods to assess the feasibility and effectiveness of ten emerging health interventions for childhood diarrhoea and 23 for pneumonia. We undertook a method to develop research priorities in line with the CHNRI80–82 with various experts worldwide. For diarrhoea, we expanded on previous methods by identifying priorities to reduce morbidity and mortality caused by childhood diarrhoea in the next 15–20 years. For pneumonia, we used a research method to define priorities to reduce mortality caused by childhood pneumonia by 2015, including health policy and systems research. The panel shows the highest ranked research questions in these two areas. In these areas, research priorities including identification of barriers to health-care access—eg, implementation barriers to increase coverage of existing, effective interventions—and	A. Basic science • None identified B. Diagnostics • Find ways to improve point-of-care diagnostic techniques C. Drugs • Investigate new ways to treat childhood pneumonia D. Preventative vaccines • Find ways to improve efficacy of low-cost pneumococcal conjugate vaccines for childhood pneumonia E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Identify the barriers to increases in coverage and ensure that hard	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • Develop non-liquid and mucosal antibiotic paediatric formulations to treat childhood pneumonia D. Preventative vaccines • Develop common-protein pneumococcal vaccines • Find ways to improve existing vaccines (eg, measles or *Haemophilius influenzae* type b) to enable needle-free delivery and heat stability • Develop more combination vaccines and vaccines against major viral pathogens E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
	identification of drivers of care-seeking behaviour, ranked highly.	to reach populations have access to effective interventions—ie, oral rehydration solution, zinc, *Haemophilius influenza* type b and pneumococcal vaccines, WHO's seven-point plan, and WHO's strategy for acute respiratory infection • Identify contextual or cultural factors that positively or negatively affect care-seeking behaviour and which factors most effectively drive care-seeking behaviour • Identify the best indicators for measurement of uptake of interventions and effectiveness of communication strategies I. Innovative financing • None identified	H. Health systems/public health research • Investigate the effectiveness of culture-appropriate health education and public health messages on changes in health-seeking behaviour, hospital admission, and mortality, and which communication strategies are best to spread knowledge and generate care-seeking behaviour • Identify the main barriers to increase demand for and compliance with vaccination schedules for available vaccines in different contexts and settings • Determine the added effect of integrated Community Case Management or Integrated Management of Childhood Illness on early and equitable administration of appropriate treatment for acute diarrhoea and for pneumonia • Identify the effect on child health outcomes of interventions to support mothers, for example to reduce maternal depression, strengthen maternal coping, and develop problem-solving skills for child health • Determine the capacity of health systems worldwide to correctly diagnose and manage childhood pneumonia, and the obstacles to correct diagnosis and case management in developing countries • Identify how trained community health workers can be effectively trained and sustained and whether they can be trained to adequately assess, recognize danger signs, refer, and treat acute

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
			respiratory infections, including safe and effective administration of antibiotics • Find ways to evaluate the effectiveness of a community-led approach to total sanitation I. Innovative financing • None identified
2. Chan M, Lake A. Integrated action for the prevention and control of pneumonia and diarrhoea. The Lancet. 2013 Apr [cited 2013 May 4]. Available from: http://dx.doi.org/10.1016/S0140-6736(13)60692-3. *Chan and Lake introduce the Lancet Series on Childhood Pneumonia and Diarrhoea, emphasizing the need to end all preventable child deaths from pneumonia and diarrhoea by 2025. The authors emphasize the new WHO/UNICEF Integrated Global Action Plan for the Prevention and Control of Pneumonia and Diarrhoea as a landmark document guiding countries to meet this goal by establishing healthy environments to protect children from pneumonia and diarrhoea and by increasing access to cost-effective interventions for*	Not applicable; none provided.	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Identify the barriers to increases in coverage and ensure that hard to reach populations have access	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Identify and find ways to provide access to interventions for children in the most hard-to-reach places • Determine how to strengthen primary

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
both prevention and treatment.		to effective interventions—ie, oral rehydration solution, zinc, *Haemophilius influenza* type b and pneumococcal vaccines, WHO's seven-point plan, and WHO's strategy for acute respiratory infection • Determine how to best support implementation of the WHO/UNICEF *Integrated Global Action Plan for the Prevention and Control of Pneumonia and Diarrhoea* • Identify the children at greatest risk of CD&P, and who are the hardest to reach and the most neglected I. Innovative financing • None identified	care responses to CD&P • Find ways to remove or reduce financial barriers to access • Identify ways to expand the role of non-governmental providers • Determine how to best utilize new mobile technologies to achieve sustainable, quality services for CD&P • I. Innovative financing • None identified
3. Chopra M, Mason E, Borrazzo J, Campbell H, Rudan I, Liu L, et al. Ending of preventable deaths from pneumonia and diarrhoea: an achievable goal. The Lancet. 2013 Apr [cited 2013 Apr 25]. Available from: http://dx.doi.org/10.1016/S0140-6736(13)60319-0. *This report provides an assessment of the current state of interventions targeted towards childhood pneumonia and*	None provided	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
diarrhea. It also uses modeling techniques to estimate that cause-specific death rates of live births from pneumonia and diarrhea could be significantly reduced if all countries could achieve the rates of decline of regional leaders. This report also provides a series of recommendations (including increasing health policy and systems research) to achieve the goal of ending preventable pneumonia and diarrhea-related deaths by 2025.		F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Identify the barriers to increases in coverage and ensure that hard to reach populations have access to effective interventions—ie, oral rehydration solution, zinc, *Haemophilius influenza* type b and pneumococcal vaccines, WHO's seven-point plan, and WHO's strategy for acute respiratory infection • Determine how to scale-up implementation and operations research to inform progress in mortality reduction I. Innovative financing • None identified	F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Identify the main barriers to increase demand for and compliance with vaccination schedules for available vaccines in different contexts and settings • Determine the added effect of integrated Community Case Management or Integrated Management of Childhood Illness on early and equitable administration of appropriate treatment for acute diarrhoea and for pneumonia • Identify how trained community health workers can be effectively trained and sustained and whether they can be trained to adequately assess, recognize danger signs, refer, and treat acute respiratory infections, including safe and effective administration of antibiotics • Find ways to improve the acceptability and effectiveness of oral rehydration solution and zinc to treat childhood diarrhea • Determine the key barriers to health-care seeking and access for pneumonia I. Innovative financing • None identified

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
4. Fischer Walker C, Rudan I, Liu L, Nair H, Theodoratou E, Bhutta Z, et al. Global burden of childhood pneumonia and diarrhea. The Lancet. 2013 Apr [cited 2013 Apr 25]. Available from: http://dx.doi.org/10.1016/S0140-6736(13)60222-6. *This report provides an overview of the burden of disease of childhood diarrhea and pneumonia, stratified by a number of factors, including: age, gender, and region. The report also specifically provides insight into the epidemiological overlap of both pneumonia and childhood diarrhea and the risk factors for both diseases. Additionally, this report describes the two most prominent vaccine-preventable strains of diarrhea and pneumonia, rotavirus and Streptococcus pneumonia, and states that further action is needed to address the reduction in infection rates globally.*	We searched PubMed, Embase, Global Health, Scopus, Web of Knowledge, and the WHO Regional Databases with combinations of key terms and medical subject headings, including "diarrhea", "pneumonia", "respiratory tract infection", "children", "childhood", "neonates", "neonatal", "age-group 0–4 years", "epidemiology", "incidence", "prevalence", "morbidity", "mortality", "case-fatality", "severity", "sepsis", "sequelae", and "etiology", and terms for specific risk factors and specific pathogens to identify pertinent reviews. We did not restrict our search by language of publication.	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • Identify ways to scale-up global disease surveillance • Consolidate data and fill knowledge gaps about mortality attributed to CD&P H. Health systems/public health research • None identified I. Innovative financing • None identified	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • Investigate how disease burden changes as socio-demographic conditions evolve • Observe how the incidence of other diseases and changes in risk factors impact CD&P H. Health systems/public health research • Find ways to track trends in emerging diseases as new interventions are introduced I. Innovative financing • None identified
5. Gill C, Young M, Schroder K, Carvajal-Velez L, McNabb M,	A series of collaborative consultations and workshops	A. Basic science • None identified	A. Basic science • None identified

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
Aboubaker S, Qazi S, Bhutta Z. Bottleneck, barriers, and solutions: results from multi-country consultations focused on reduction of childhood pneumonia and diarrhoea deaths. The Lancet. 2013 Apr [cited 2013 Apr 25]. Available from: http://dx.doi.org/10.1016/S0140-6736(13)60314-1. *This report addresses the barriers to reducing the millions of necessary deaths due to childhood diarrhea and pneumonia. The report identifies the bottlenecks that impair access to commodities (i.e. supply chain management, insufficient funding), as well as the key programmatic barriers (i.e. lack of coordination, inadequate training). This report recommends that a solution to these problems is advocacy in order to raise awareness and raise the appropriate resources needed to prioritize childhood diarrhea and pneumonia.*	involving several hundred academic, public health, governmental and private sector stakeholders were convened to identify the key barriers to progress and to issue recommendations.	B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Explore solutions to pragmatic issues in the areas of programme management and resource allocation for CD&P I. Innovative financing • None identified	B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Determine the key barriers to health-care seeking and access for pneumonia • Find ways to track trends in emerging diseases as new interventions are introduced • Determine whether the effectiveness of IMCI and related initiatives could be improved if operationalized as a programme in the model of PEPFAR or PM • Investigate how to improve the coordination of CD&P efforts and secure sufficient access to services • Identify ways to enhance the production, distribution, and promotion of key

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
			commodities • Determine how to strengthen weak monitoring and assessment systems I. Innovative financing • None identified
6. Kikwete J. Playing our part to save children's lives. The Lancet. 2013 Apr 12 [cited 2013 May 4]. Available from: http://dx.doi.org/10.1016/S0140-6736(13)60719-9. *Kikwete emphasizes the need for greater leadership, coordination and commitment from all stakeholders involved in reducing the causes of child mortality. He identifies nine key areas where action could be taken to improve the global response to women's and children's health to reduce the number of preventable child deaths per year.*	None provided	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Identify the barriers to increases in coverage and ensure that hard to reach populations have access to effective interventions—ie, oral rehydration solution, zinc,	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Identify how trained community health workers can be effectively trained and sustained and whether they can be trained to adequately assess, recognize danger signs, refer, and treat acute respiratory infections, including safe and

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		Haemophilius influenza type b and pneumococcal vaccines, WHO's seven-point plan, and WHO's strategy for acute respiratory infection • Determine ways to ensure all children have access to life-saving vaccines and essential treatments such as amoxicillin for pneumonia and oral rehydration solution and zinc for diarrhoea I. Innovative financing • None identified	effective administration of antibiotics • Identify and find ways to provide access to interventions for children in the most hard-to-reach places • Determine how to promote awareness and accelerate action to address the social and environmental determinants of health, for example by reducing harmful indoor air pollution produced by burning firewood • Identify ways to increase demand from families and communities for quality health services • Find ways to strengthen partnerships between public and private actors to encourage innovations in, and expand the reach of, health services • Determine how to ensure that women and children know their rights to quality health care and are empowered to hold their leaders to account for any failure to deliver on their commitments • Determine how measure the results of tackling diarrhoea and pneumonia and compare the progress to the promises that have been made I. Innovative financing • None identified
7. Samarasekera U, Horton R. Continuing the child survival revival. The Lancet. 2013 Apr 12 [cited 2013 May 4]. Available from:	None provided	A. Basic science • None identified B. Diagnostics • None identified	A. Basic science • None identified B. Diagnostics • None identified

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
http://dx.doi.org/10.1016/S0140-6736(13)60718-7. *Samarasekera and Horton review global trends in the reduction of child mortality, but note that world is not on track to meet Millennium Development (MDG) Goal 4, a two-thirds reduction in child deaths between 1990 and 2015. Authors emphasize that additional progress will require targeting the leading causes of mortality: neonatal and infectious causes. Global focus must be concentrated on childhood pneumonia and diarrhoea—the leading causes of death in the post-neonatal period—and greater cooperation on the ground. The authors then outline each of the four papers in the Series.*		C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Develop integrated programmes to tackle the shared risk factors of diarrhea and pneumonia I. Innovative financing • None identified	C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Determine how integrated programs can best address common risk factors including a lack of exclusive breastfeeding of children younger than six months, under-nutrition and zinc deficiency I. Innovative financing • None identified
8. World Health Organization/The United Nations Children's Fund (UNICEF). Ending preventable child deaths from pneumonia and diarrhoea by 2025: The integrated Global Action Plan for Pneumonia and Diarrhoea (GAPPD). Geneva: World Health Organization; 2013.	The GAPPD does not present a change of direction in terms of *what* needs to be done. It simply identifies opportunities to better integrate activities as well as capture synergies and efficiencies. It proposes an integrated framework of	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
The joint WHO/UNICEF report outlines current progress in reducing the global burden of childhood pneumonia and diarrhoea, identifies existing proven interventions that can maximize mitigation efforts and outlines the Global Action Plan for Pneumonia and Diarrhoea (GAPPD). The GAPPD provides an integrated framework of key interventions to protect, prevent and treat pneumonia and diarrhoea in children less than five years of age. It offers suggestions of supporting activities to improve and accelerate the implementation of interventions of proven benefit.	interventions to control diarrhoea and pneumonia (described in section 5) and provides a range of supporting activities to improve and accelerate the implementation of these interventions (explained in section 8). Audience: The GAPPD is intended primarily for national governments and their partners, and secondarily for global organizations, donor agencies and other actors working on pneumonia and diarrhoea. The GAPPD also recognizes that community-level groups and individuals will be critical for effective implementation of the strategy.	D. Preventative vaccines • Find ways to achieve the Global Immunization Vision and Strategy targets for vaccines against measles and pertussis E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Identify the barriers to increases in coverage and ensure that hard to reach populations have access to effective interventions—ie, oral rehydration solution, zinc, *Haemophilius influenza* type b and pneumococcal vaccines, WHO's seven-point plan, and WHO's strategy for acute respiratory infection • Identify the best indicators for measurement of uptake of interventions and effectiveness of communication strategies • Identify the children at greatest risk of CD&P, and who are the	D. Preventative vaccines • Find ways to introduce pneumococcal conjugate vaccine (PCV) and Haemophilus influenzae type B (Hib) vaccines into the national immunization programmes of high-mortality countries E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Determine how to utilize current data to identify groups at greater risk or missed by services, and develop targeted approaches to reach them • Investigate the effectiveness of culture-appropriate health education and public health messages on changes in health-seeking behaviour, hospital admission, and mortality, and which communication strategies are best to spread knowledge and generate care-seeking behaviour • Determine how integrated programs can best address common risk factors including a lack of exclusive breastfeeding of children younger than six months, under-nutrition and zinc deficiency

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		hardest to reach and the most neglected • Determine ways to ensure all children have access to life-saving vaccines and essential treatments such as amoxicillin for pneumonia and oral rehydration solution and zinc for diarrhoea • Find ways to prevent children from becoming ill from pneumonia and diarrhoea by ensuring universal coverage of immunization, HIV prevention and healthy environments • Develop clear country-level strategies and work plans, with key responsibilities assigned • Find ways to scale-up implementation research and identify optimal modes of delivery for existing interventions • Find ways to adopt effective case management at the community and health facility levels • Design advocacy campaigns promoting exclusive breastfeeding and zinc supplementation to reduce rates of low birth weight and under-nutrition • Evaluate the effectiveness of	• Develop or update country-level situational analyses for pneumonia and diarrhoea • Identify areas of harmonization and collaboration between programmes and sectors, including the private sector, academia and civil society • Develop a set of common indicators for tracking progress on CD&P • Learn how to best coordinate the implementation of interventions by applying lessons from other integrated disease prevention and control efforts{H} • Develop tools and platforms to track the execution and progress of coordinated implementation efforts • Design collaborative platforms that engage and embed critical partners in overall work, including the involvement of multiple sectors and programs, private and civil society organizations, and UN agencies and development partners • Development methods to select priority interventions based on local context within national action plans • Find ways to establish better linkages between existing programmes to lead synergies and efficiencies that will maximize the benefits • Design mechanisms for close collaboration between the Ministry of Health (MoH) and other sectors, especially the ministries responsible for water, education, energy and the environment

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		new technologies that can reduce indoor air pollution and conduct additional research to demonstrate the health benefits of these interventions • Formulate new strategies to promote hand washing with soap and water, particularly among caregivers in developing countries • Develop means to ensure individuals and communities understand the value of vaccines and demand immunization as both their right and responsibility • Develop communication strategies that translate research evidence into meaningful information for communities and individuals in highest-mortality countries I. Innovative financing • None identified	• Determine how to build research capacity in the countries most affected • Prioritize community-based action research, sociocultural research on knowledge, attitudes, perceptions, cultural practices and health seeking behaviours, and research on delivery strategies, on overcoming barriers to interventions and on better ways for implementation • Countries with a high under-five mortality rate should develop and adopt plans to expand adequate case management of pneumonia at the hospital, health facility and community levels to achieve 90% coverage • Find ways to improve the management of HIV infection and increae use of *P. jiroveci* pneumonia prophylaxis to reduce the mother-to-child transmission of HIV • Create incentives to stimulate demand and improve caregiver knowledge, attitudes and practices towards immunization • Create incentives for households and health workers in favour of immunization • Conduct social research to improve the delivery of immunization services and the ability to meet the needs of diverse communities • Identify reasons for vaccine hesitancy and take steps to increase community confidence and demand for immunization • Conduct communications research to

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
			inform individuals and communities about the benefits of immunization and to hear their concerns • Conduct operational and social science research to identify successful strategies to reduce inequities and improve the quality and delivery of immunization services • Investigate the use of more effective information through modern communication technologies to improve programme efficiencies and increase coverage and impact • Identify community-based decision-makers and groups to strengthen community-based support for breastfeeding • Conduct assessments and formative research to strengthen community-based breastfeeding initiatives • Carry out national level formative research on pneumonia and diarrhoea to foster and strengthen care seeking/demand for case management and community knowledge of prevention measures • Develop generic communication messages/materials and adapt these tools to meet the needs of local communication strategies • Periodically assess implementation/impact of communication efforts • Find ways to build capacity for

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
			community-based groups, peer counsellors and community leaders to lead prevention measures I. Innovative financing • None identified
9. Huda T, Nair H, Theodoratou E, Zgaga L, Fattom A, El Arifeen S, et al. An evaluation of the emerging vaccines and immunotherapy against staphylococcal pneumonia in children. BMC Public Health. 2011; 11(Suppl 3):S27. Available from: http://www.biomedcentral.com/1471-2458/11/S3/S27. *Huda et al. review the existing literature, outlining the progress of the emerging vaccines and immunotherapy against Staphylococcus aureus at all stages of development. Authors present the evidence regarding key issues surrounding these products and assess the level of collective optimism of international experts over their priority status for receiving investment support. The paper is presented as part of a series of papers, each in turn focusing on different emerging vaccines and other interventions against pneumonia.*	We used a modified CHNRI methodology for setting priorities in health research investments. This was done in two stages. In Stage I, we systematically reviewed the literature related to emerging vaccines against *Staphylococcus aureus* relevant to several criteria of interest: answerability; cost of development, production and implementation; efficacy and effectiveness; deliverability, affordability and sustainability; maximum potential impact on disease burden reduction; acceptability to the end users and health workers; and effect on equity. In Stage II, we conducted an expert opinion exercise by inviting 20 experts (leading basic scientists, international public health researchers, international policy makers and representatives of pharmaceutical companies) to participate. The policy makers	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • Assess the potential impact of all emerging vaccines and immunotherapy against *Staphylococcus aureus* and determine an investment strategy based on key prioritization factors • Develop an essential multi-component vaccine for *S. aureus* E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • Investigate and resolve issues relating to optimal antigenic target identification, criteria for acceptable efficacy, identification of the target population in children as well as adults, commercial development limitations, optimal timing of immunization strategy, storage and cold chain requirements, cost of development and cost effectiveness for a potential *S. aureus* vaccine • Identify the right combination of, and find ways to combat, more than one virulence factor for *S. aureus* in the human host E. Therapeutic vaccines • None identified F. Vector control

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
	and industry representatives accepted our invitation on the condition of anonymity, due to sensitive nature of their involvement in such exercises. They answered questions from CHNRI framework and their "collective optimism" towards each criterion was documented on a scale from 0 to 100%.	H. Health systems/public health research • None identified I. Innovative financing • None identified	• None identified G. Epidemiology • None identified H. Health systems/public health research • None identified I. Innovative financing • None identified
10. Webster J, Theodoratou E, Nair H, Seong A, Zgaga L, Huda T, et al. An evaluation of emerging vaccines for childhood pneumococcal pneumonia. BMC Public Health. 2011; 11(Suppl 3):S27. Available from: http://www.biomedcentral.com/1471-2458/11/S3/S27. *Webster et al. present the evidence regarding key issues surrounding the first two vaccine development strategies and assess the level of collective optimism among international experts concerning the level of investment priority they feel is justified. The paper is presented as part of a series of papers, each in turn focusing on different emerging vaccines and other interventions against pneumonia.*	We used a modified CHNRI methodology for setting priorities in health research investments. This was done in two stages. In Stage I, we systematically reviewed the literature related to emerging SP vaccines relevant to several criteria of interest: answerability; efficacy and effectiveness; cost of development, production and implementation; deliverability, affordability and sustainability; maximum potential for disease burden reduction; acceptability to the end users and health workers; and effect on equity. In Stage II, we conducted an expert opinion exercise by inviting 20 experts (leading basic scientists, international public health researchers, international policy	A. Basic science • None identified B. Diagnostics • Develop means to improve diagnostic ability to identify the bacterial aetiology of pneumococcus C. Drugs • None identified D. Preventative vaccines • Develop a multivalent pneumococcal conjugate vaccine covering all serotypes and/or a cross-protective common protein vaccine to significantly reduce the burden of pneumococcal disease in children under age 5 years • Investigate the health systems and contextual factors that	A. Basic science • None identified B. Diagnostics • Find ways to use new diagnostic tools inter-alia in studies estimating burden of disease as well as vaccine effectiveness studies to accurately interpret the impact of a vaccine on IPD • Identify diagnostics that do not require samples from within the lung, yet may be more sensitive than blood culture isolation, to aid monitoring efforts of vaccine impact on invasive pneumococcal disease (IPD) C. Drugs • None identified D. Preventative vaccines • Direct pneumococcus vaccine research efforts towards developing a low cost pneumococcal protein vaccine (PPV)

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
	makers and representatives of pharmaceutical companies). They answered questions from CHNRI framework and their "collective optimism" towards each criterion was documented on a scale from 0 to 100%.	affect the distribution of vaccines E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • None identified I. Innovative financing • None identified	E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • None identified I. Innovative financing • None identified
11. Tate J, Patel M, Cortese M, Lopman B, Gentsch J, Fleming J, et al. Remaining issues and challenges for rotavirus vaccine in preventing global childhood diarrheal morbidity and mortality. Expert Rev Vaccines. 2012;11(2):211-220. *Tate et al. seek to update a previous review and describe the key remaining issues and challenges for the rotavirus vaccine in the global fight against diarrhea morbidity and mortality among children. Rotavirus vaccines have*	None provided	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • Develop strategies to improve the performance of oral rotavirus vaccines • Design approaches to monitor the safety of rotavirus vaccines and understand the relationship	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • Investigate how increasing the number of doses or alter the timing of doses given as part of the oral rotavirus primary vaccine series affects performance • Assess the role of zinc and probiotic supplementation at the time of rotavirus

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
had a dramatic impact on morbidity and mortality from diarrhea among children in high- and middle-income countries that have introduced the vaccine into their national immunization programs. Widespread introduction of rotavirus vaccine in developing countries is imminent and their full potential in reducing the global burden from severe childhood diarrhea may soon be realized. Authors describe the remaining issues and challenges in ensuring the success of the global rotavirus vaccination program and to discuss further research needed to help address them.		between rotavirus vaccines and intussusception E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • Develop approaches to monitor the long-term impact of rotavirus vaccines in resource-limited settings H. Health systems/public health research • Find ways to gather local effectiveness and impact data from developing countries in Africa and Asia currently introducing rotavirus vaccines to effectively monitoring vaccine performance and identify ways to improve impact I. Innovative financing • None identified	vaccination • Evaluate the potential interference of maternal antibody and breastfeeding in rotavirus vaccine efficacy • Investigate how adding an additional dose of vaccine at a later age may improve the duration of protection from vaccination • Find ways to establish background rates of intussusception in select countries of Africa and Asia • Examine treatment patterns for intussusception, rates of surgery and outcomes • Evaluate and validate the Brighton case definition for intussusception in a variety of settings • Conduct self-controlled case-series studies to examine if a short-term increase in risk of intussusception following rotavirus vaccination exists in other settings • Investigate the recommended age restrictions for when to give the first and last doses of the rotavirus vaccine to minimise risk of intussuseption and optimize the timeliness of vaccination in low-income countries E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
			• Conduct studies to monitor trends in diarrhea and rotavirus disease burden pre- and post-rotavirus vaccine introduction • Determine how to use surveillance platforms to conduct epidemiologic studies to estimate rotavirus vaccine effectiveness under conditions of routine use • Determine how to evaluate the total population impact of rotavirus vaccination including indirect benefits H. Health systems/public health research • Evaluate and explore options available to potentially expand developing countries' cold chain and storage capacity prior to vaccine introduction programs I. Innovative financing • None identified
12. Patel M, Glass R, Desai R, Tate J, Parashar U. Fulfilling the promise of rotavirus vaccines: how fare have we come since licensure? Lancet Infectious Dis. 2012; 12: 561-70. *Patel M et al. look at the effectiveness of the introduction of rotavirus vaccines on diarrheal related sickness and death in children and propose further steps for consideration to increase*	We searched PubMed with the primary search terms "rotavirus" and "vaccine" or "rotavirus" and "impact" between Jan 1, 2006, and Sept 1, 2011. We did not limit our search by language. We included all studies that measured the effect of rotavirus vaccination on rotavirus events, the number of people admitted to hospital for gastroenteritis, or deaths after routine use of	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • Identify modifiable factors to maximise rotavirus vaccine protection and reduce the	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • Investigate the recommended age restrictions for when to give the first and last doses of the rotavirus vaccine to

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
uptake of the vaccine and vaccine efficacy.	rotavirus vaccine. We excluded clinical trials from the pooled data.	effectiveness gap between low-income and high-income settings E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • Develop approaches to monitor the long-term impact of rotavirus vaccines in resource-limited settings H. Health systems/public health research • Find ways to generate momentum and enthusiasm for rotavirus vaccination in the least developed countries with the high mortality rates • Develop platforms for concerted action between vaccine manufacturers, financial donors and decision-makers to achieve rotavirus vaccination goals in a timely manner I. Innovative financing • None identified	minimise risk of intussuseption and optimize the timeliness of vaccination in low-income countries • Conduct research on modifiable strategies to increase rotavirus performance in under-resourced settings, e.g. changes to the age that children receive vaccine, delaying breastfeeding for a few hours after vaccination, decoupling of rotavirus vaccination from oral poliovirus vaccination, and provision of concomitant zinc and probiotics • Assess how a booster dose of rotavirus vaccine given with measles vaccination might increase protection after age 1 year in low-income settings E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • Develop means to interpret the changing ecology of rotavirus strains after vaccine introduction in the context of vaccine effectiveness studies or changes in absolute disease burden H. Health systems/public health research • Conduct communications research to inform individuals and communities about the benefits of immunization and to hear

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
			their concerns • Evaluate and explore options available to potentially expand developing countries' cold chain and storage capacity prior to vaccine introduction programs I. Innovative financing • None identified
13. United Nations Children's Fund (UNICEF). Pneumonia and Diarrhoea: Tackling the Deadliest Diseases for the World's Poorest Children. New York: UNICEF; 2012. *The report outlines the current burden of childhood pneumonia and diarrhoea, advocates for the need to focus on these issues, explores current strategies to treat them, and investigates ways to scale up treatment and prevention efforts. The report examines ways in which to child mortality from these two diseases can be reduced through several interventions, and the particular groups to target (i.e. rural, poor) with these interventions. Ultimately, the report supports the immediate scale-up of, and access to, treatment and prevention for childhood pneumonia and diarrhoea.*	Cause-specific mortality estimates, recently published for 2010, are based on the work of the Child Health Epidemiology Reference Group (see www.cherg.org).1 Prevention and treatment coverage estimates are derived from a series of public access databases compiled by UNICEF and reflect data available as of 15 April 2012. These databases are based on information from nationally representative household surveys routinely administered in low-income countries, notably UNICEF-supported Multiple Indicator Cluster Surveys and others. Some coverage estimates are derived using a combination of survey data and other sources, such as data on water supply and sanitation and on immunization. Information on community case management	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • Find ways to achieve the Global Immunization Vision and Strategy targets for vaccines against measles and pertussis • Identify modifiable factors to maximise rotavirus vaccine protection and reduce the effectiveness gap between low-income and high-income settings E. Therapeutic vaccines • None identified F. Vector control • None identified	A. Basic science • None identified B. Diagnostics • Investigate ways to accelerate the launch of POC testing platforms dedicated to EID and viral load technologies C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Investigate the effectiveness of culture-appropriate health education and public

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
	policy and implementation is based on a cross-sectional survey of 44 UNICEF country offices in sub-Saharan Africa using a structured instrument with closed and open-ended questions. The offices were first contacted in May 2010 and queried through May 2011 to ensure that information reflected the status of community case management in 2010. Of 44 country offices, 4 did not respond: Cape Verde, Gabon, Guinea-Bissau and Sao Tome and Principe.	G. Epidemiology • None identified H. Health systems/public health research • Identify the barriers to increases in coverage and ensure that hard to reach populations have access to effective interventions—ie, oral rehydration solution, zinc, *Haemophilius influenza* type b and pneumococcal vaccines, WHO's seven-point plan, and WHO's strategy for acute respiratory infection • Identify the best indicators for measurement of uptake of interventions and effectiveness of communication strategies • Determine how to best support implementation of the WHO/UNICEF *Integrated Global Action Plan for the Prevention and Control of Pneumonia and Diarrhoea* • Develop integrated programmes to tackle the shared risk factors of diarrhea and pneumonia • Find ways to adopt effective case management at the community and health facility levels • Design advocacy campaigns promoting exclusive	health messages on changes in health-seeking behaviour, hospital admission, and mortality, and which communication strategies are best to spread knowledge and generate care-seeking behaviour • Determine the added effect of integrated Community Case Management or Integrated Management of Childhood Illness on early and equitable administration of appropriate treatment for acute diarrhoea and for pneumonia • Determine how integrated programs can best address common risk factors including a lack of exclusive breastfeeding of children younger than six months, under-nutrition and zinc deficiency • Countries with a high under-five mortality rate should develop and adopt plans to expand adequate case management of pneumonia at the hospital, health facility and community levels to achieve 90% coverage • Find ways to improve the management of HIV infection and increae use of *P. jiroveci* pneumonia prophylaxis to reduce the mother-to-child transmission of HIV • Carry out national level formative research on pneumonia and diarrhoea to foster and strengthen care seeking/demand for case management and community knowledge of prevention measures • Conduct research to gather more evidence on the quality of care when

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		breastfeeding and zinc supplementation to reduce rates of low birth weight and under-nutrition • Evaluate the effectiveness of new technologies that can reduce indoor air pollution and conduct additional research to demonstrate the health benefits of these interventions • Formulate new strategies to promote hand washing with soap and water, particularly among caregivers in developing countries • Develop communication strategies that translate research evidence into meaningful information for communities and individuals in highest-mortality countries • Develop strategies to rise national coverage of pneumonia and diarrhoea interventions to levels found in the richest groups • Investigate how to best implement integrated community case management (iCCM) programmes in developing countries • Find ways to scale-up rigorous monitoring, evaluation and documentation of existing iCCM	community health workers are given increasingly complex tasks or deliver multiple interventions as part of iCCM • Determine how to recruit, retain, supervise and motivate community health workers to provide high-quality care within iCCM programs • Develop an urgently needed operations research "learning agenda" I. Innovative financing • None identified

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		programmes I. Innovative financing • None identified	
14. United Nations Children's Fund (UNICEF). Update on Work on Medicines. Presentation. New York: UNICEF IPC; Dec 2012. *The presentation represents an update on the UNICEF Work on Medicines group following the UNICEF/WHO Joint Pharmaceuticals Suppliers meeting in Copenhagen (September 2012). It outlines key product development priorities for tackling childhood pneumonia and diarrhoea, provides the latest statistics on private sector care-seeking behaviours, gives an overview of procurement trends from 2006-2011 and outlines plans for sustainable procurement.*	None provided	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • Develop Amoxicillin 250 mg dispersible tablets as the key target product for treating pneumonia D. Preventative vaccines • Investigate ways to increase the availability of high-quality zinc supply in-country • Develop tools to guide the design and implementation of high-impact demand generation programs at scale for zinc and ORS E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology	A. Basic science • None identified B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • Map the availability (registration and over-the-counter (OTC) status) of zinc in high-burden countries and conduct quality surveys of specific products to inform appropriate quality standards • Identify mechanisms to provide technical support to selected manufacturers to meet defined quality standards of zinc supplements • Design and coordinate regional regulatory activities for zinc (e.g., joint regulatory reviews for product registration and OTC status) • Determine how to best support in-country design and implementation of strategies targeting increased uptake of zinc/ORS among consumers and providers in private and public sectors • Conduct systematic reviews of existing

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		• None identified H. Health systems/public health research • Determine ways to ensure all children have access to life-saving vaccines and essential treatments such as amoxicillin for pneumonia and oral rehydration solution and zinc for diarrhoea • Find ways to advance and support sustainable procurement of medicines and medical devices • Find ways to establish guidance to governments and United Nations agencies on what are priority areas for action related to selection and supply chain of medicines procurement • Investigate opportunities for interagency collaboration through UNICEF IPC I. Innovative financing • None identified	research/evidence on consumer and provider preferences, adherence, other data to inform strategy development for zinc and ORS E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Conduct environmental impact evaluations of the production, distribution and use of medicines and medical devices (including carbon footprint and environmental toxicity), sustainability aspects related to labor and trade, and ways in which selection and procurement can reduce impact I. Innovative financing • None identified
15. Ambroggio L, Thomson J, Kurowski E, Courter J, Statile A, Graham C, et al. Quality improvement methods increase appropriate antibiotic prescribing for childhood pneumonia. Official Journal of the American Academy	At a tertiary children's hospital, QI methods were used to rapidly implement the Pediatric Infectious Disease Society/Infectious Disease Society of America guideline recommendations for	A. Basic science • None identified B. Diagnostics • None identified C. Drugs	A. Basic science • None identified B. Diagnostics • None identified C. Drugs

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
of Pediatrics. 2013; 131:e1623. doi: 10.1542/peds.2012-2635. *Ambroggio et al. demonstrate that quality improvement (QI) methods can rapidly improve adherence to national guidelines even in settings without a formal antimicrobial stewardship program to encourage judicious antibiotic prescribing for the management of community-acquired pneumonia (CAP) in children.*	appropriate first-line antibiotic therapy in children with CAP. QI interventions focused on 4 key drivers and were tested separately in the emergency department and on the hospital medicine resident teams, using multiple plan-do-study-act cycles. Medical records of eligible patients were reviewed weekly to determine the success of prescribing recommended antibiotic therapy. The impact of these interventions on our outcome was tracked over time on run charts.	• None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Develop quality improvement (QI) methods that can be used to instill appropriate stewardship of antibiotics in the absence of a formal antimicrobial stewardship programs (ASP) • Find ways to utilize QI methods to rapidly improve adherence to national guidelines on the judicious prescribing of antibiotics for community-acquired pneumonia (CAP) I. Innovative financing • None identified	• None identified D. Preventative vaccines • None identfied E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • None identified I. Innovative financing • None identified
16. Wazny K, Zipursky A, Black R, Curtis V, Duggan C, Guerrant R, et al. Setting research priorities to	The CHNRI methodology was created to assist those who develop research policy and/or	A. Basic science • Find ways to optimize the current combination of zinc and	A. Basic science • Assess whether a mixture of zinc and ORS be developed that successfully

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reduce mortality and morbidity of childhood diarrhoeal disease in the next 15 years. PLoS Med. 2013; 10(5): e1001446. doi:10.1371/journal.pmed.1001446. *Wazny et al. undertook a fresh exercise to build and expand two previous research priority-setting exercises in childhood pneumonia and diarrhoea to further elucidate the timeframe of various research options, the number of research options generated, and the number of participants. Authors employed the Child Health and Nutrition Research Initiative (CHNRI) method to identify research gaps and resource priorities to reduce morbidity and mortality caused by childhood diarrhoeal disease over the next 15 years.*	invest in health research by identifying research gaps and resource priorities systematically and transparently in a specified context. The aim is to help policy makers understand the potential risks and benefits of a range of research options. This methodology has been used previously to identify research gaps and resource priorities in areas such as birth asphyxia and childhood pneumonia. The CHNRI method has four stages: (i) the context of the problem and the criteria for priority setting are defined; (ii) technical experts generate and rank research questions; (iii) stakeholders give input regarding the weighting of the CHNRI criteria; and, (iv) research scores for the research questions are calculated and agreement between experts is analysed. Detailed information on the CHNRI methodology has been provided in previous publications. We supplemented the CHNRI method by hosting an international workshop on the identified research priorities, which is reported elsewhere.	ORS therapies B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • None identified H. Health systems/public health research • Identify the barriers to increases in coverage and ensure that hard to reach populations have access to effective interventions—ie, oral rehydration solution, zinc, *Haemophilius influenza* type b and pneumococcal vaccines, WHO's seven-point plan, and WHO's strategy for acute • Identify contextual or cultural factors that positively or negatively affect care-seeking	reduces duration and stool output • Determine whether there is a critical window for early childhood diarrhoea that can affect future physical and mental development, e.g. at 0–6 months, 6 months –2 years, or 3–5 years of age B. Diagnostics • None identified C. Drugs • None identified D. Preventative vaccines • None identified E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • Determine the extent to which the roll-out of rotavirus vaccination reduces the burden of acute dehydration as well as diarrhoea • Determine whether the community-led total sanitation approach lead to decreased diarrhoea risk • Assess whether access to, and benefits received from, nutritional supplementation programmes reduce global burden of diarrhoeal disease

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		behaviour and which factors most effectively drive care-seeking behaviour respiratory infection • Investigate how to best implement integrated community case management (iCCM) programmes in developing countries • Find ways to scale-up rigorous monitoring, evaluation and documentation of existing iCCM programmes I. Innovative financing • None identified	• Identify the risk factors for diarrhoea mortality H. Health systems/public health research • Identify and test alternative delivery strategies designed to ensure that ORS and zinc are reaching hard to reach populations and being used by the poorest of the poor (for example, home distribution of ORS and zinc) • Identify the key barriers against the appropriate use of ORT • Determine which factors drive care-seeking behaviour during childhood diarrhoeal disease and how ORS and zinc programs can be positioned to best respond to these factors • Identify the factors have led to the decline in ORS use rates in countries where rates were high and now are low • Identify which factors most effectively drive caregiver demand for ORS and zinc • Identify the attributes of successful and sustainable childhood diarrhoea programs, e.g. determine which designs and strategies were used in programs and interventions that led to drastic reductions in diarrhoeal disease burden • Determine the added impact of iCCM on early and equitable administration of appropriate treatment for acute diarrhoea • Determine how the perception of diarrhoea as an illness affects: o Key household practices like hand

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			washing o Willingness to pay for point-of-use water disinfection products o Care seeking, and o Compliance to ORS and zinc treatment • Determine how best to move caregivers from knowledge of ORS and/or zinc treatment to actual trial and eventual adoption as routine practice, and identify the stages of behaviour change in order to tailor messages accordingly • Determine whether moving from general and generic to more specific targeted messaging would influence practices, when they are best delivered, and what would this include • Determine what would be needed to move a caregiver from awareness to trial of ORS and zinc, and what the relative impact of mass media vs. group vs. one-on-one communication strategies would be • Determine whether communication strategies vary in effectiveness between rural and urban populations • Determine the individual risk effects of malnutrition, poor sanitation, low level of education, and reduced levels of vitamins and micronutrients in acquiring diarrhoea in children living in the developing world • Identify which contextual or cultural factors positively or negatively influence ORS and zinc utilization or compliance

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			• Evaluate if early initiation and exclusive breast feeding is associated with reduced burden of diarrhoea and improved growth • Determine the best indicators for measuring the effectiveness of communication messages for childhood diarrhoea and the effectiveness of different communication channels in terms of (a) awareness of, (b) readiness to try, and (c) actual use of ORS and/or zinc I. Innovative financing • None identified
17. Scott J, Brooks A, Peiris J, Holtzman D, Mulholland E. Pneumonia research to reduce childhood mortality in the developing world. J Clin Invest. 2008; 118: 1291-1300. doi:10.1172/JCI33947. *Scott et al. concentrate their Review on childhood pneumonia and specifically on research to reduce the unacceptable magnitude of child deaths from this disease. The authors highlight critical gaps in our understanding of the epidemiology, etiology, and pathophysiology of pneumonia that, if filled, could accelerate the control of pneumonia and reduce early childhood mortality.*	None provided	A. Basic science • Elucidate the causal factors leading to death from pneumonia • Conduct research to refine pneumonia classification • Identify biomarkers that can rapidly differentiate bacterial from viral pneumonia to assist in focusing diagnostic development and antibiotic therapies • Develop an adaptable research approach to the etiological investigation of pneumonia, particularly for pneumonia of unknown etiology and emerging lung infections • Elucidate the pathophysiology of pneumonia and immune regulation of the inflammatory	A. Basic science • Find ways to gather more detailed information about the etiology and pathophysiology of the disease • Find ways to refine classifications of pneumonia using clinical signs and a more sophisticated radiological interpretation • Assess and validate the diagnostic potential of IL-1 receptor antagonist, IL-1beta, IL-6, IL-8, G-CSF, TNF-alpha, and soluble triggering receptor expressed on myeloid cells (sTREM) for cases of severe bacterial infections in the developing world • Investigate the relative contribution of multiple viruses in the genesis of respiratory pathology and their interactions with bacterial pathogens • Determine why H5N1 influenza causes severe pneumonia in children, whereas the SARS-CoV causes milder disease

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		response to lung infection • Conduct research into the role of innate immunity in severe cases of childhood pneumonia B. Diagnostics • Develop a gold standard against which to test new diagnostics for childhood pneumonia • Develop a rapid, easy to use, inexpensive diagnostic test for childhood pneumonia C. Drugs • None identified D. Preventative vaccines • Develop novel vaccines against the animal coronaviruses that could be precursors of future SARS-like diseases • Develop an effective RSV vaccine to guard against pneumonia and bronchiolitis due to RSV infection E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • Better understand the	• Investigate factors that influence the control of inflammation • Better understand the balance of roles between TLRs and cytokines in modulating lung inflammation to help explain the mechanisms of action of zinc B. Diagnostics • Determine the causal attribution of organisms identified in blood or nasal secretions in the etiology of pneumonia C. Drugs • None identified D. Preventative vaccines • Find ways to overcome barriers of antigenic diversity within animal coronaviruses to identify antigens for vaccine targeting • Better understand immune responses to bacterial respiratory pathogens E. Therapeutic vaccines • None identified F. Vector control • None identified G. Epidemiology • Find ways to build-up capacity for local and regional surveillance of antibiotic resistance, particularly in settings with high levels of penicillin insensitivity

Source	Approach, Methodology, Criteria, People Involved	Identified Important Questions/Goals Needing Research	Key Findings/Priorities for Addressing these Questions/Goals
		epidemiology of fata pneumonia • Assess the impact of antimicrobial resistance on the management of childhood pneumonia H. Health systems/public health research • Conduct studies on the efficacy of simple public health measures (e.g. social distancing, masks and hand hygiene) on transmission of respiratory viruses • Elucidate the role of zinc in pneumonia treatment • Define the parameters of equity and develop systems to monitor changes (e.g. identify the main determinants of risk that might be geographic or ethnographic) • Find ways to improve the quality of inpatient pediatric care I. Innovative financing • None identified	H. Health systems/public health research • Assess the potential impact of economical oxygen concentrators on child mortality from hypoxia • Assess the use of zinc supplementation in outpatient settings where most children with pneumonia are treated • Determine the acute effects of zinc as a treatment for pneumonia I. Innovative financing • None identified