Rapid Scoping Study on Global Clinical Trials Infrastructure

Final Report (December 2021)

CONTENT

1 EXECUTIVE SUMMARY

This rapid scoping report is part of a set of actions by the UK Department of Health and Social Care (DHSC) and the World Health Organization (WHO) to take forward agreements reached at the G7 Health and Leaders meetings, to improve international collaboration on clinical trials, as reflected in the G7 Clinical Trials Charter and the 100 Days Mission documents. The WHO is responsible, supported by DHSC, to scope out how an international network of clinical trial platforms could be implemented to enable a coordinated and efficient approach to testing of relevant products and interventions including VTDs *(Recommendation #9:100 Days Mission Document)*. The report attempts to provide an answer to the question of whether it is feasible to deliver more effective global clinical trials through enhanced co-ordination of existing clinical trials infrastructure, as available in international, regional, and national clinical trial networks, scattered across the world.

Clinical trials infrastructure refers to the structures through which the varied range of required capabilities for the implementation of clinical trials are organized and coordinated to enable the successful conduct of trials. This usually comprises clinical research networks within and across countries through which an organized group of clinicians and researchers share infrastructure that enables them to collaborate to conduct both small and large multiple, multi-centre clinical trials. A clinical trial network enables these clinicians and researchers to implement a clinical trial using the same protocols across multiple geographically dispersed sites. The core constituent parts of a clinical trials network are the sites that enroll patients into trials, the investigators that plan, conduct, analyze and report trials, and central trial coordination and data management. The key conclusions reached on the study are outlined in summary herewith.

A systematic effort to understand global clinical trials infrastructure is needed

There appears to have been no systematic attempt to develop a global inventory or a global heat map of clinical trial infrastructure or clinical trial networks for the purpose of enhancing their coordination towards global public health outcomes. Consequently, critical information needed to gain better understanding about these networks, to guide thinking on how networks may be coordinated to deliver better global clinical trials is largely unavailable publicly. These include information on how/why networks have formed, their existing research assets and capabilities, where they operate, types of membership models, their organisational structures and approach to central administration, their sources and type of funding, details on their research activities, the extent of their links with communities and healthcare authorities etc. A systematic approach to obtaining this data should be anchored on information obtainable from networks that are currently active in conducting or facilitating multi-country clinical research.

Preliminary mapping indicates knowledge gaps in Latin America, and Asia-Pacific regions

Based on information gathered from scanning international public health data sources and key expert interviews, this study identified eighty-nine (89) networks that are currently organized to conduct international clinical trials for VTDs involving sites spread across multiple countries and/or regions, and could *potentially* be mobilized to collaborate in VTD clinical trials during global public health emergencies. This included 11 multi-country, multi-centre clinical trial networks associated with clinical trial/research

sites in the Africa region, 11 in Asia-Pacific, 4 in Latin America/Caribbean, 13 in Europe, 24 in the Western Pacific Region, 20 in North America, and 6 global networks. Public data appears to be more limited about clinical research sites in Asia-Pacific and Latin America & the Caribbean Region.

Most of these networks (57), are *coordinating networks*, that take on the role of coordinating clinical trials and providing direct project management for trial conduct. The rest (32) are facilitating networks, which focus on enabling collaborative development and funding of clinical trials but have limited or no direct role in the management or coordination of specific trials. Majority (70) of the networks identified are focused on clinical research and trials in a specific discipline (e.g., Malaria) or a group of related disciplines (e.g., gynecologic oncology) and their research capabilities within that discipline may span multiple interventions (vaccines, therapeutics, diagnostics). A lower number of networks (18) specialize in a given area that is agnostic to any specific discipline (e.g., intensive/emergency care, anesthesiology).

Requirements for networks to be effectively leveraged for VTD trials are largely generic

The second objective of this scoping study was to provide an understanding of what networks require to be effective within a system that is optimized to enable effective coordination of VTD trials globally. The key requirements outlined by respondents include the network's ability to function as a community with shared goals centered on improving quality of patient care through the systematic use of evidence. They also highlighted as key requirements, the network's ability to sustain a collective workforce of trained clinical research personnel with sufficient knowledge to undertake sequential trials and work across multiple projects, and their capacity to collectively recruit the required number of patients from the range of locations in which the trial results would be implemented in practice. Also critical is their ability to maintain shared intellectual infrastructure, such as standardized tools, templates and procedures associated with the design, conduct, analysis, and reporting of clinical trials; and their ability to develop and maintain an array of relationships that enhance its effectiveness and efficiency. Key experts indicate that the above requirements apply similarly for vaccines, therapeutics, and diagnostics trials, highlighting a few specific capabilities that are particularly vital to certain type of trials such as community engagement/relationships, which is particularly vital to successful implementation of vaccine trials.

Delivering more effective global clinical trials will require both trial-specific and ecosystem-specific investments

The final objective of this scoping study was to provide a perspective on the biggest challenges faced by the existing infrastructure and efforts to co-ordinate it. The information presented in this regard was derived largely from the set of key expert interviews, which sought to elicit expert perspectives on the challenges faced by networks, pertaining to their potential to function effectively in the context of better coordinated global clinical trials. Experts highlighted four (4) considerations that are critical to ensuring the feasibility of delivering more effective global clinical trials through enhanced co-ordination of existing clinical trials infrastructure:

1. *Scaling up the use of pre-approved template protocols to standardize practice across networks:* This involves the use of pre-approved master protocols to encourage collaborations to generate scientific evidence in a timely manner, promote rigorous standards between clinical research networks across the different regions of the world, and create resilient capacity against a range of possible future infectious disease outbreaks.
2. *Navigating the benefits and risks of innovative clinical trials (such as platform trials):* This entails recognizing the pros and cons of platform trials, and ensuring that they are sufficiently adapted

such that existing, established networks are at their core, and that participating networks retain a degree of autonomy over certain elements of the trials while staying connected and contributing to the collective goals of such collaborative trials.

3. *Achieving better alignment between clinical trials research prioritisation, funding, and sustaining infrastructure:* This entails commitment to coordinated funding for clinical research, and ensuring that coordinated funding for clinical research is pursued in a manner that aims to grow and support networks of competent research groups by dedicating long-term funding for infrastructure and professional development, while ensuring that trials that aim to provide answers to local priorities have precedence. This will involve exploring the concepts of ongoing, jointly funded, globally-connected perpetual trials that are adapted to answer questions with both local and global relevance.
4. *Taking critical actions to strengthen core capabilities that enable effective research enterprise:* This includes advancing and accelerating actions to drive the adoption and usage of common metrics for assessing clinical research and critical trial capacity, improving interoperability, and sharing of clinical trial data, achieving better synergy in the governance and administration of clinical trials, and standardizing clinical trial human resource competency frameworks.

Experts strongly indicate that these actions must be underpinned by a recognition that ***clinical trial capacity cannot be optimized within weak health research ecosystems***, and that achieving high quality clinical trials is highly dependent on the strength of research infrastructure and capacity that already exists or has been developed within a given clinical trial/research network. Consequently, the approach to delivering better coordinated multi-national VTD trials through networks ***must not be narrowly focused on improving clinical trial conduct alone, but also be designed to enable capacity strengthening within networks, and the broader health research systems within which these networks undertake trials and conduct health research more broadly.***

Next Steps

To advance this effort, three key recommended next steps are summarily outlined in the appendix of this report. First is a ***systematic mapping of global clinical research networks*** with a view to obtain valuable operational data necessary to identify gaps in global coverage and develop necessary recommendations with respect to new sites, new networks, or new connections. Secondly, a concerted effort to explore whether ***collectively funded, globally-connected, autonomous perpetual trials delivered through networks*** are a feasible approach to achieving better coordinated clinical trials in a way that leverages innovative clinical trials while strengthening research infrastructure globally, and improving global preparedness and resilience against potential infectious disease outbreaks. Thirdly the need ***to accelerate ongoing actions on key enablers to improve global coordination on trials*** is highlighted as a key next step. This entails identifying opportunities to speed up action on clinical trial data sharing and interoperability, progressing the use of a common set of metrics and indicators for assessing and characterizing clinical trial capacity, improving synergy in the governance and administration of multi-national trials, and standardizing human resource competency definitions for clinical trials. The idea is to build on ongoing work by several organizations in the above areas.

2 GLOBAL CLINICAL TRIALS INFRASTRUCTURE: CURRENT SITUATION

2.1 CONTEXT

Clinical trials enable the testing of hypotheses that are concerned with evaluating the effectiveness, efficacy, or cost-effectiveness of a biomedical intervention (including preventive measures, treatments, clinical strategies, and diagnostics) in patients[i]. They are the primary way to generate the level of actionable evidence needed to reliably inform clinical practice or healthcare policy, hence they form the basis of global or national guidelines that inform high-quality health care.

During the COVID-19 pandemic, rapid, robust, and randomized clinical trials have played a critical role in informing public health and clinical decisions, pertaining to the safety and effectiveness of vaccines, therapeutics, and diagnostics (VTDs). A number of large, innovative multi-country trials have been credited with informing major public health decisions that have cumulatively saved millions of lives. However, the pandemic has also highlighted fissures in the prevailing systems for conducting large multi-country clinical trials for VTDs. Many therapeutic trials were inadequate in size, design, and conduct, and failed to generate valuable evidence to drive practice change[ii]. Vaccine trials used different laboratory testing methods and reagents, and different trial testing methodologies, creating difficulties in comparing immune responses, among other issues. More effective international collaboration on trials would have made better use of scarce resources and may have saved lives. Improving international collaboration on clinical trials to strengthen global health research and pandemic preparedness will entail investing in clinical trials infrastructure (such as clinical trial networks) in which efficient trial designs can be deployed to address global health priorities, and which can pivot rapidly to new priorities in the event of an impending pandemic.

This rapid scoping report is an outcome of actions taken by the UK Department of Health and Social Care (DHSC) and the World Health Organization (WHO) to take forward agreements reached at the G7 Health and Leaders meetings, to improve international collaboration on clinical trials, as reflected in the G7 Clinical Trials Charter and the 100 Days Mission documents. The WHO is responsible, supported by DHSC, to scope out how an international network of clinical trial platforms could be implemented to enable a coordinated and efficient approach to testing of relevant products and interventions including VTDs *(Recommendation #9:100 Days Mission Document).*

The report attempts to provide an answer to the question of whether it is feasible to deliver more effective global clinical trials through enhanced co-ordination of existing clinical trials infrastructure, as available in international, regional, and national clinical trial networks, scattered across the world. It provides an outline of what infrastructure already exists, how these networks operate both during pandemics and in peace time, and the key challenges that impact enhanced coordination.

2.2 MAPPING GLOBAL CLINICAL TRIALS INFRASTRUCTURE

Clinical trials can be broadly categorized into two groups – trials conducted by commercial entities such as pharmaceutical companies or clinical research organisations which have a financial interest in the intellectual property of the intervention being tested (commercial trials), as distinct from trials conducted

by clinical investigators and/or academic researchers working within the healthcare system or public academic institutions to improve healthcare policy or practice (investigator-initiated trials).

Investigator-initiated trials are designed to provide a public good, the outcomes of which could influence widely adopted components of standard care for many diseases, or lead to changes in clinical practice that transcend city, state, or national boundaries. They are therefore complex and require considerable expertise and training. They may also require a large number of patients to participate in a clinical study in order to identify relatively small but significant health gains. Clinical trials infrastructure refers to the structures through which the varied range of required capabilities for the implementation of clinical trials are organized and coordinated to enable the successful conduct of trials. This usually comprises clinical research networks within countries through which an organized group of clinicians and researchers share infrastructure that enables them to collaborate to conduct both small and large multiple, multi-centre clinical trials. A clinical trial network enables these clinicians and researchers to implement a clinical trial using the same protocols across multiple geographically dispersed sites. The core constituent parts of a clinical trials network are the sites that enroll patients into trials, the investigators that plan, conduct, analyze and report trials, and central trial coordination and data management.

2.2.1 Identifying previous attempts at mapping global clinical trials infrastructure

Clinical trial networks exist throughout the world and their numbers are increasing progressively. While some networks are restricted to within a city or state, others are national, international, or global in scope and reach.

The first objective of this scoping study was to provide an understanding of what infrastructure (such as clinical research networks) to co-ordinate clinical trials of VTDs across countries already exists globally. To do this, this study commenced with a scanning of international public health data sources to first identify previous attempts to map clinical trials networks globally for the purpose of enhanced coordination or collaboration between networks, and for the advancement of global health research more broadly. This was complemented by interviews with a set of key experts during which a question was asked on their familiarity with previous global clinical trial network mapping attempts.

The key findings from this effort are as follows:

- There appears to have been no systematic attempt to develop a global inventory or a global heat map of clinical trial infrastructure or clinical trial networks for the purpose of enhancing their coordination towards global public health outcomes. Whilst it is possible that similar mapping efforts for other purposes may have been undertaken at global or regional level, the data from such efforts have not been widely disseminated and are therefore not publicly available. National level mapping reports are also not available with the exception of Australia, in which a detailed systematic mapping report on clinical trials networks in Australia was developed by the Australian Clinical Trials Alliance, for the National Health and Medical Research Council of Australia, and published in November 2015.
- There are a few online platforms that have been established to provide greater visibility for clinical trial networks, sites and researchers in specific countries or regions, with a view to enabling greater access and utilization of these infrastructure. These platforms primarily present data

indicating the experience and capabilities of these sites or networks, albeit at a high level. Two such platforms identified in the course of this study include:

- *Clinical Trials Community Africa:* a platform of the African Academy of Sciences which maintains an information portal on African clinical trialists, research sites and country-specific regulatory/ethics information to inform decision making by trial sponsors.
- *Directory of Clinical Research Networks:* an online listing maintained by the Singapore Clinical Research Institute of Clinical Trial Units and groups organized as clinical research networks in Singapore, and across the Asia-Pacific region.

- The lack of previous systematic mapping efforts coupled with the nature of the data presented on online platforms limit the utility of publicly available data on global clinical trials infrastructure for the purpose of improving coordination. Information needed to gain better understanding about these networks, to guide thinking on how networks may be coordinated to deliver better global clinical trials are not available. These include information on how/why networks have formed, types of membership models, organisational structures, approach to central administration, funding, details on research activities, links with communities, links with healthcare authorities etc.
- There have been a number of efforts to develop a shared understanding of the existing landscape of Longitudinal Population Studies (LPS) across many regions of the world. For example, there has been a recent effort to map existing LPS in Africa – which mapped large surveillance and survey studies (including HDSS and living standard surveys) as well as large population-based cohorts on the continent. While these reflect non-clinical trial sites, they reflect valuable assets and capacity that could form the basis of new clinical trial sites and networks. This data is already being aggregated regionally and globally by entities like the African Population Cohorts Consortium (APCC) and the International Journal of Epidemiology Cohort Profiles, among others.

2.2.2 High-level indicative mapping of existing global clinical trials infrastructure

Overview of mapping approach

Based on information gathered from scanning international public health data sources and key expert interviews, this study provides an indicative mapping of the clinical trial infrastructure that exists globally. The focus of this effort is on clinical trial networks that are organized to conduct international clinical trials for VTDs involving sites spread across multiple countries and/or regions, and similar regional mechanisms that could be mobilized to coordinate VTD clinical trials during global public health emergencies.

Of the core constituent parts of a clinical research network, (sites that enroll patients into trials, the investigators that plan, conduct, analyze and report trials, central trial coordination and data management), sites and their associated human resources are at the very foundation, being the primary location where core data relevant to the research is obtained. The capacity of a network to conduct high quality clinical trials is therefore directly correlated with the capacity (of investigators, researchers, research support personnel and trial participants) that exists at different specific sites that make up the network, without prejudice to the capacity for coordination and data management that the network might have, and the research ecosystem within which the site or network operates. This mapping effort is therefore anchored on understanding the distribution of sites that are part of multi-centre, multi-country

clinical trial networks as these would form the foundation or 'skeleton', of a coordinated global clinical trials infrastructure.

For the identification of regional or global networks in scope for this mapping effort, this study adopts the classification of Clinical Trial Networks in use by the Australian Clinical Trials Alliance which broadly classifies networks into two types: Facilitating or Coordinating:

- *Facilitating Networks:* These networks facilitate collaborative development and funding of clinical trials but has little or no direct role in the management or coordination of specific trials. The role of management and coordination of clinical trials is allocated to one or more specialist trial coordinating centres. These centres can be based in either medical research institutions or university departments but have governance that is independent of the network. A facilitating network will not act as study sponsor.
- *Coordinating Networks:* These networks take on the role of coordinating clinical trials and providing direct project management for trial conduct (regulatory compliance, site liaison and management, protocol development, recruitment, monitoring, data management, statistical analysis, report development etc.). The institution that hosts the trial coordinating centre will act as the sponsor for investigator-initiated clinical trials or the CTN develops the capability to sponsor individual trials.

This mapping effort also highlights sites where longitudinal population studies are being undertaken or large population based cohorts exist - where these have been previously mapped. As previously stated, these reflect valuable assets and capacity that could form the basis of new clinical trial sites and/or networks.

Outcome of indicative mapping: Summary of findings

A summary of the findings for each respective region is presented in this section.

1. Africa Region

We identified 17 multi-country, multi-centre clinical trial networks associated with clinical trial/research sites in the Africa region, 8 of which are Africa-focused networks, 3 are interregional networks with sites in Africa & Europe, and 6 are global networks with sites in Africa.

The majority of these networks (15) are facilitating networks, involved primarily with collaborative development and funding of clinical trials, and strengthening capacity for clinical research more broadly, as distinct from coordinating networks that provide direct management of trial conduct. 10 of the networks are multi-disciplinary, with focus on Malaria, HIV, TB, Ebola, NTDs, and emerging infectious diseases broadly. There are also 4 disease specific networks similarly focused on infectious disease, with the remaining 3 networks involved in specialized research in Pediatric Trials, Pediatric Community Acquired Pneumonia, and Pregnancy Care.

Whilst publicly available data on the 17 networks is not sufficient to assess the number and distribution of sites, the Clinical Trials Community Platform hosted by the African Academy of Sciences identifies 1,242 trial centre/ sites as part of clinical research infrastructure in Africa. The platform does not indicate the clinical trial networks that these sites belong to or participate in, but it in itself, provides a number of network benefits to the sites and trialists that are registered on the platform.

From the APCC LPS mapping study, 49 HDSS sites in 16 African countries were identified, 37 of which are part of INDEPTH, a global network of health and demographic surveillance systems (HDSSs), 20 large population based cohorts were also identified across 11 African countries.

2. Asia-Pacific Region

17 multi-country, multi-centre clinical trial networks associated with clinical trial/research sites in the Asia Pacific region were identified, 11 of which are networks specific to the region, while 6 are global networks with sites in the region.

Of the 11 region focused networks, 7 are coordinating networks, primarily involved with the direct management and execution of trials. Eight (8) of the networks are either disease-specific or specialized, with disciplines including Hepatocellular Carcinoma, Thoracic Oncology, Pediatric Inflammatory Bowel Disease, Liver Transplantation, Resuscitation Outcomes, Pediatric Acute & Critical Care, Gynecologic Oncology and Renal Asian Genetics. The multi-disciplinary networks conduct research in HIV, Malaria Resistance, Severe Acute Respiratory and other emerging Infectious diseases

3. Latin America & The Caribbean Region

Publicly available information about multi-country, multi-centre clinical trial networks associated with clinical trial/research sites in this region is quite limited. 10 networks were identified, 4 of which are networks specific to the region, while 6 are global networks with sites in the region.

The four region focused networks are equally split between coordinating and facilitating networks, and are primarily involved with research in HIV, HIV/HPC Cancers, Zika and epidemic preparedness.

4. Europe

19 multi-country, multi-centre clinical trial networks associated with clinical trial/research sites spread across the European continent, 13 of which are networks specific to the region or inter-regional networks with sites in the region. Six (6) are global networks with sites in the region.

Of the 13 region focused networks, 10 are facilitating networks, involved primarily with collaborative development and funding of clinical trials, and strengthening capacity for clinical research more broadly. Ten (10) of the 13 region focused networks are either disease-specific or specialized, conducting research in Pediatric Clinical Trials, Anesthesiology & Intensive Care, Cystic Fibrosis, Neuro-Muscular Disease, Autism, Huntington's Disease, Gynecologic Oncology and Pediatric Community Acquired Pneumonia and TB. Two (2) of the three multi-disciplinary networks are concerned with epidemic preparedness, with the third being a multi-purpose network focused on supporting the conduct of clinical trials and the development of clinical trials infrastructure across the region.

5. Western Pacific Region

30 multi-country, multi-centre clinical trial networks associated with clinical trial/research sites largely in Australia and New Zealand were identified, 24 of which are networks specific to the region, while six are global networks with sites in the region.

Based on data from the aforementioned mapping conducted by the Australia Clinical Trials Alliance, 23 of the 24 region focused networks are coordinating networks, directly involved in the conduct and management of trials. All 23 networks are either disease-specific or specialized, conducting research in a broad range of disciplines including, diagnostic devices, Stroke, Anesthesia, Epilepsy, Multiple Sclerosis,

Kidney Disease, Sleep Health, Maternal & Perinatal, Emergency Medicine, Gastro-Intestinal Cancer, Lung & Thoracic Cancer, Sarcoma, Breast Cancer, Melanoma, Gynecological Oncology, Children's Hematology & Oncology, Urogenital/Prostate Cancers, Musculoskeletal, Neuro-Oncology, Primary Care – Cancer, HIV and Radiation Oncology.

6. North America

26 multi-country, multi-centre clinical trial networks associated with clinical trial/research sites largely in the United States and Canada, 20 of which are networks specific to the region, while six are global networks with sites in the region.

23 of the 24 region focused networks are coordinating networks, directly involved in the conduct and management of trials. All 23 networks are either disease-specific or specialized, conducting research in a broad range of disciplines including, HIV/HPV Cancers, Sickle Cell, Imaging, AIDS, HIV Vaccines, Drug Abuse, Spinal Cord Injury, Blood & Marrow Transplant, Emergency Care Clinical Trials, Cancer Immunotherapies, Pediatric Cancer, Exercise Clinical Trials, Pediatric Drug Trials, Neuromuscular and HIV Transmission Prevention

2.3 Assessing the requirements of clinical trial networks for VTDs

2.3.1 Context

The second objective of this scoping study was to provide an understanding of what networks require to be effective within a system that is optimized to enable effective coordination of VTD trials globally. These requirements are summarily outlined in the preceding section. An attempt is also made to clarify how these requirements may differ for vaccines, therapeutics, and diagnostics trials respectively.

2.3.2 Key Findings

Baseline requirements for networks that can be leveraged for globally coordinated VTD trials:

- Have evolved into a community with a critical mass of clinicians and other researchers that share a common mission to improve quality of patient care, in one of more fields of medicine, through the systematic use of evidence to inform practice.
- Have developed the capacity to sustain within it, a collective workforce of trained clinical research personnel that have built sufficient knowledge to work across multiple projects, and sufficient experience to limit the level of recruitment or training required for each trial.
- Have developed the capacity to undertake patient recruitment to support trials with large sample sizes and sufficient statistical power to generate clinically relevant evidence. This entails the capacity to coordinate several geographically dispersed sites that can collectively recruit thousands of patients from the range of locations in which the results would be implemented in practice, and having the ability to significantly scale up recruitment with relative speed.
- Have developed the administrative capacity to enable sites to work virtually if sites are affected by crises and to coordinate across sites and networks both during and outside of pandemics and public health emergencies.

- Have evolved shared intellectual infrastructure – where knowledge and expertise associated with the design, conduct, analysis, and reporting of clinical trials is available broadly across the network, and capabilities necessary for central management of trials have been developed within the network including project management, data management, and statistical analysis. These are usually captured in a set of standardized tools and templates that researchers across the network are familiar with.
- Have established an array of relationships that greatly enhance their effectiveness and efficiency. Key partnerships include relationships with academic organizations such as universities and medical research institutes, colleges that undertake training of medical specialists, societies that represent the interest of clinicians, and consumer advocacy groups associated with specific health conditions. These networks also have established relationships with ethical committees and regulators, to enable rapid approvals. While independent of industry, networks also have established relationships with industry that allow for sharing of resources expertise and infrastructure to conduct trials.

Do network requirements differ for vaccines, therapeutics, and diagnostics?

Respondents indicate that the requirements for networks to successfully conduct trials for vaccines, therapeutics and diagnostics are broadly similar. Three key requirements were highlighted however, as particularly essential for specific types of trials: These are summarized briefly below:

1. Deep community engagement to build trust between the community and researchers. This is especially important for vaccine trials which recruit from the community, and variability of settings in terms of sites (in hospital) out of hospital)
2. Implementation science to understand how to scale up effective interventions. This applies to both vaccines and therapeutic trials.
3. Long-term surveillance capacity to assist teams with spotting health issues as they arise as well as predicting where the pandemic or crisis will move next. This is relevant to vaccine and therapeutic trials, given its link with the recruitment capacity of the network.

2.4 Coordinating Global Clinical Trial Networks: Challenges and key areas to explore

2.4.1 Context

The final objective of this scoping study was to provide a perspective on the biggest challenges faced by the existing infrastructure and efforts to co-ordinate it. The information presented in this regard was derived largely from the set of key expert interviews conducted as part of this rapid study. The relevant questions in the interviews sought to elicit expert perspectives on the challenges faced by networks, pertaining to their potential to function effectively in the context of better coordinated global clinical trials.

2.4.2 Key Findings

Experts highlighted a set of key considerations that are critical to ensuring the feasibility of delivering more effective global clinical trials through enhanced co-ordination of existing clinical trials infrastructure. These are discussed in this section.

1. *Scaling up the use of pre-approved template protocols to standardize practice across networks*

One of the key lessons from the research response experience on COVID-19 has been the value of template or master protocols in strengthening evidence generation and enabling resilient, portable, trial capacity. A master protocol generally refers to a single overarching protocol designed to answer multiple interventional questions that would otherwise require several separate clinical trials[iii]. For instance, before the COVID-19 pandemic occurred, a platform trial had already been prepared for a respiratory disease pandemic. The Randomized, Embedded, Multifactorial Adaptive Platform Trial for Community-Acquired Pneumonia (REMAP-CAP) is a platform trial that commenced in 2016 for the evaluation of multiple treatments in the event of a respiratory pandemic resulting in critical illness, and was already enrolling patients being admitted to the intensive care unit (ICU) for community-acquired pneumonia. It had as part of its master protocol a pre-written appendix for inclusion of an influenza-like population should a pandemic occur. This existing infrastructure and protocol enabled REMAP-CAP to be rapidly adapted in the event of the COVID-19 outbreak.

Experts suggest that pre-written, and pre-approved master protocols can be leveraged to encourage collaborations to generate scientific evidence in a timely manner while promoting rigorous standards between clinical research networks across the different regions of the world, creating infrastructure that can be extended to other research questions, and importantly providing resilient capacity against a range of possible future infectious disease outbreaks.

2. Navigating the benefits and risks of innovative clinical trials (such as platform trials)

As with master protocols, the COVID-19 pandemic response experience has yielded lessons for innovative clinical trials, including the prospect of better integrated research efforts through platform trials. Platform trials are multi-arm perpetual clinical trials that allow comparison between all active drugs and, on the basis of interim evaluations, allow arms to be dropped or added mid-trial to improve efficiency. The WHO-coordinated SOLIDARITY trials are examples of platform trials setup to inform the use of a range of therapies for COVID-19 hospitalizations. These trials facilitated collaboration across sites (mainly hospitals) in different countries, by providing streamlined processes for patient enrolment, centralized web-based randomization procedures with minimal paperwork, centralized data capture system, harmonized statistical support, and a number of other services to minimize the burden of research duties in participating, under a core master protocol.

While this approach has been successful in establishing large trial networks with common infrastructure, and rapidly creating a research system that can potentially generate high-quality data to answer multiple research questions, it is important to note that the degree of centralization involved in these trials portend significant risks to the very aim of better coordination as it limits the extent of technical input from local investigators at participating sites, and the potential for capacity to be retained locally.

To deliver better coordinated global clinical trials, platform trials will need to be sufficiently adapted such that existing, established networks are at their core, and that participating networks retain a degree of autonomy over certain elements of the trials while staying connected and contributing to the collective goals of such collaborative trials.

3. Achieving better alignment between clinical trials research prioritisation, funding, and sustaining infrastructure

In order to build and sustain the capacity to conduct high quality clinical trials and research, networks need to be consistently engaged in activity that utilizes and strengthens the shared infrastructure and

capacity that has been developed within the network. A key feature of strong state, national or regional networks is the ability to generate core funding to drive these activities that keep the network active and 'warm' in between trials. On the flip side, lack of core funding for network activities is one of the biggest challenges that impact their ability to build and sustain their intellectual and physical infrastructure, and their ability to stay relevant to members of the network.

From a global perspective, fragmented funding of clinical trials research serves to worsen the funding issue and creates a situation where core funding of networks is disproportionately inequitable. For the existing network infrastructure to deliver more effective global clinical trials, and better support global public health preparedness, better coordination in the funding of clinical research will need to be achieved. Improving coordination in clinical trial research funding, however, is not a goal that should be pursued in isolation. Efforts to coordinate funding for clinical trial research should aim to create long-term support for clinical research networks, especially for networks in LMICs, where the funding constraints are more debilitating to the growth of these networks. These coordinated funding efforts should aim to grow and support a large network of competent research groups by dedicating long-term funding for infrastructure and professional development, while ensuring that LMIC investigator-initiated or institution-initiated trials that aim to provide answers to local priorities have precedence.

Experts interviewed indicate that the COVID-19 pandemic has increased latent support for the idea of globally connected perpetual clinical trials, wherein funders and governments collaborate to provide ongoing funding for networks to engage on clinical trials that are asking locally and globally relevant research questions on an ongoing basis, thereby building sustained infrastructure (including in low resource environments) that provides the capacity that can speedily pivot to tackle emergency research at a global level when needed. Coordinated funding of large-scale long-term platform trials can help to ensure long-term collaboration between networks, providing their members with the opportunities to develop skills and gain experience, ultimately strengthening capacity within the network. A complex but critical element of this approach is evolving a structure that allows for prioritisation of trials to be decided at country level (or significant country level input into the prioritisation process), to ensure more evaluation of affordable and scalable interventions in low-resource settings, while also expanding capacity development associated with these trials to key country-dependent elements of infrastructure such as the capacity of regulatory and ethical oversight review committees.

The COVID-19 Solidarity Response Fund which was set-up to allow donations to help fund the Solidarity trials, could be considered as a pilot for a model of coordinated trial funding that helps achieve alignment between research prioritisation, funding and sustaining infrastructure, in the context of delivering better and more coordinated global clinical trials.

4. Taking critical actions to strengthen core capabilities that enable effective research enterprise

Key experts interviewed as part of this scoping study highlighted a set of capabilities that are critical to the emergence of a global clinical trial ecosystem, where clinical research networks can be effectively galvanized to respond in a coordinated way to future global health emergencies and/or pandemics. These capabilities are highlighted along with imperative potential action(s):

a) *Adoption of common metrics for assessing clinical research and critical trial capacity*: There is need for global health stakeholders to adopt a common set of metrics for the evaluation, and description of research capacity at the level of national health research systems, but also at the

level of networks, institutions, and clinical research sites. Consensus around the use of metrics will make it easier to better target capacity building efforts, and also make it operationally easier to coordinate various networks and sites for global clinical trials. The ESSENCE for Health Research initiative has made significant progress on a basic set of metrics and indicators that can be further developed, leveraging on data aggregated by the WHO's Global Observatory for health R&D and the NIH's World RePORT platform. The Global Health Security Agenda (GHSA) is also working to develop metrics specific to clinical trial capacity.

b) *Improving interoperability and sharing of clinical trial data:* There is need for better coordination to enable clinical trial data from multiple platforms, institutions, and geographies to be collated and analysed with minimal effort. The adoption of the FAIR (Findable, Accessible, Interoperable and Reusable) to global clinical trial data management is essential to delivering better coordinated global clinical trials. Several ongoing efforts in this direction need to be given priority and accelerated, preferably under the leadership and steer of the WHO, with the cooperation of, and commitment from large global funders of health research, who can significantly influence data sharing principles within their respective domains. Some of the work of the Special Programme for Research and Training in Tropical Diseases (TDR), and platforms like the International COVID-19 Data Alliance (ICODA) and the Global Partnership for Sustainable Development Data (GPSSD) can be leveraged to advance this objective.

c) *Synergy in the governance and administration of clinical trials:* There needs to be a coordinated effort to simplify the ethical administrative, regulatory, and logistical challenges faced by networks in the conduct of trials. The lack of a common set of rules, procedures, and research ethics board configurations adds significant cost and inefficiency through approval delays. Shared application of standards will simplify and expedite regulatory and ethical processes. In Europe, efforts toward centralization have been initiated through the European Clinical Research Infrastructure Network (ECRIN) and European Network of Research Ethics Committees (EUREC) to address the heterogeneity and complexity of existing regulatory requirements in European Union (EU) nations. However, different countries interpret the regulations differently when transforming them into law, with the attendant adverse effect on trials conducted in the region. These challenges affect the conduct of trials globally, so a global solution is required. The idea of a central regulatory entity, with global representation, that is responsible for comprehensive regulatory approval for multinational trials has been suggested, and could be explored. In the interim, more support for platforms like the Clinical Trial Community (CTC Africa) and others that aim to reduce the procedural and administrative burden associated with conducting trials in certain regions, or support global collaborative research more broadly need to be encouraged.

d) *Standardizing human resource competencies for clinical trials:* There needs to be synergy in the definition of the defines the knowledge, skills, and attitudes necessary for conducting safe, ethical, and high-quality clinical research. Multiple frameworks have been developed to define professional roles, support performance evaluations, define education and training requirements, and facilitate regulatory compliance. A conscientious effort towards a degree of harmonization that can inform usage and application by clinical research networks across all geographies will further strengthen the global research infrastructure and make globally coordinated clinical trials more feasible.

3 APPENDIX

3.1 FOR FURTHER SCOPING

1. *Systematic mapping of global clinical trial networks*
    a. *Develop detailed definition of network archetype to be mapped*
    b. *Define active non-clinical trial sites to be included*
    c. *Identify key data sources and develop global shortlist*
    d. *Issue comprehensive survey to obtain details for full characterization of networks (site/site location, human resources, key activities, operating model, funding, core capabilities et.c)*
    e. *Collate and undertake geo-spatial analysis, develop geo-coded maps*
    f. *Undertake detailed analysis and identify gaps, and opportunities for new sites, networks, or connections*
2. *Exploring the potential for collectively funded, globally-connected, autonomous perpetual trials delivered through networks*
    a. *Develop detailed concept note and value proposition*
    b. *Develop detailed design of alternative models exploring various*
        i. *Funding approaches*
        ii. *Coordination structure (configuration of participating networks)*
        iii. *Administration/governance arrangements*
        iv. *Approach to prioritisation of research/trials*
        v. *Trial designs*
        vi. *Roll-out strategy*
    c. *Undertake analysis of strategic alternatives*
    d. *Facilitate multi-stakeholder engagement to drive implementation*
3. *Accelerating ongoing actions on key enablers to improve global coordination on trials*
    a. *Undertake landscape scanning to identify ongoing initiatives across the identified key areas:*
        i. *Clinical trial data sharing and interoperability*
        ii. *Metrics and indicators for assessing clinical trial capacity*
        iii. *Synergy in the governance and administration of multi-national trials*
        iv. *Standardizing human resource competency definitions for clinical trials*
    b. *Analyze opportunities for supporting accelerated actions building on ongoing work in the above areas*
    c. *Develop and implement action plan*

3.2 Summary Profiles of Clinical Trial Networks Identified

3.2.1 Africa Region

1. The Trials of Excellence for Southern Africa (TESA) Network

This is a regional research network of Southern Africa Countries, with the objectives to build clinical trials' capacity and infrastructure for the identification, treatment, and prevention of poverty-related infectious diseases, including emerging and re-emerging diseases in the Southern Region of Africa by mentoring and training the existing capacities among the researchers, clinicians, and laboratory technicians to conduct trials in line with ethical guidelines and Good Clinical Practices. It was launched in 2009, during the European and Developing Countries Clinical Trials Partnership (EDCTP) phase 1. At this stage, nine institutions from six different countries from Southern Africa were part of this consortium whose aim was to creating a framework for collaboration, capacity building and training among member institutions. Currently, TESA II, incorporating thirteen institutions from eight Southern African and four European countries, which are predisposed to strengthen clinical research capacities in Southern Africa, as well as to increase North-South South- South networks among member institutions. Countries participating in this network are Botswana, Malawi, Mozambique, South Africa, Zambia and Zimbabwe.

Reference Links: https://tesa.tghn.org/, http://www.tesanoe.org/,*http://www.edctp.org/networks-excellence/#*

2. The West Africa Network for TB, AIDS, and Malaria (WANETAM)

It was set up in 2009. It is one of the four networks established by the European and Developing Countries Clinical Trials Partnership (EDCTP) to combat poverty-related diseases such as malaria, tuberculosis HIV/AIDS, and other diseases. It included 14 institutions in 7 countries namely The Gambia, Burkina Faso, Nigeria, Mali, Ghana, Guinea Bissau and was coordinated by Senegal. The network was further strengthened within the last two years by the contribution of EU member-states (Belgium and UK) initiated research project (WANETAM-plus), which allowed the inclusion of other African institutions. The objective of WANETAM was capacity building and technology transfer to prepare West African institutes for the successful conduct of clinical trials and to create a network for sub-regional scientific collaborations.

Reference Links: https://wanetam.org/gv/, *http://www.edctp.org/networks-excellence/#*

3. The East Africa Consortium for Clinical Research (EACCR)

EACCR3 is an Eastern African-led network established in 2009 and comprises of 23 regional partners from Ethiopia, Kenya, Rwanda, Sudan, Tanzania, and Uganda, and 5 Northern partners from Belgium, Netherlands, Norway, Sweden, Switzerland, and United Kingdom. It aims to strengthen the capacity to conduct internationally acceptable health research with specific focus on clinical trials on poverty related diseases (HIV, TB, Malaria) and neglected Infectious emerging and re-emerging diseases) in the region.

Reference Links: http://www.eaccr.org/, http://www.edctp.org/networks-excellence/#

4. The Central African Network on TB, HIV/AIDS, and malaria (CANTAM)

In Central Africa, the Central African Network on TB, HIV/AIDS, and malaria (CANTAM) is the first regional network of excellence supported by EDCTP in Sub-Saharan Africa for the conduct of clinical trials on HIV/AIDS, malaria, and tuberculosis in compliance with ICH/GCP standards. It was created in 2009 with

the major aim to build capacity in seven institutions in the three countries Cameroon, Gabon and the Republic of Congo (RoC) for the conduct of clinical trials. The strategy for achieving this goal was to select institutions with the lowest capacities to conduct clinical research in Cameroon and RoC and to drive them to a higher level through participation in multicentre clinical research involving the highly experienced center in Gabon.

Reference Links: http://www.cantam.org/, http://www.edctp.org/networks-excellence/#

5. The Malaria Clinical Trials Alliance (MCTA)

This is a programme of the International Network for the Demographic Evaluation of Populations and Their Health (INDEPTH) network of demographic surveillance centres. It was launched in 2006 with two broad objectives: to facilitate the timely development of a network of centres in Africa with the capacity to conduct clinical trials of malaria vaccines and drugs under conditions of good clinical practice (GCP); and to support, strengthen and mentor the centres in the network to facilitate their progression towards self-sustaining clinical research centres. This was done in partnerships with the Malaria Vaccine Initiative (MVI) and the Medicines for Malaria Venture (MMV) with support from the Bill & Melinda Gates Foundation. Countries participating in this network are Burkina Faso, Gabon, Ghana, Kenya, Malawi, Mozambique, Nigeria, Tanzania, Senegal and The Gambia.

Reference Links: https://malariajournal.biomedcentral.com/articles/10.1186/1475-2875-9-103

6. Clinical Trials Community (CTC) online platform

This is a project run by the Alliance for Accelerating Excellence in Science in Africa (AESA) in partnership with the African Union Development Agency (AUDA-NEPAD) and funded by the Bill & Melinda Gates Foundation. The goal of this programme is to increase the level of clinical trial investments in Africa by increasing the visibility of the African clinical trialists and sites with the possibility of contributing to COVID-19 clinical trials, with a final objective of promoting the progression of intra-African collaboration around clinical trials and making transparent and accessible individual country regulatory and ethics procedures to inform decision making by sponsors and funders.

Reference Links: https://www.aasciences.africa/aesa/programmes/clinical-trials-community

7. African coalition for Epidemic Research, Response and Training (ALERRT)

This is a clinical research and response network for epidemic infections in sub-Saharan Africa. The overall goal of ALERRT is to build a sustainable clinical and laboratory research preparedness and response network in Sub-Saharan Africa (SSA) to reduce the public health and socio-economic impact of (Re-) emerging and Epidemic-Prone Infectious Diseases (REPID) in SSA.

Reference Link: https://alerrt.tghn.org/

8. The Pan-African Network for Rapid Research, Response, Relief and Preparedness for Infectious Disease Epidemics (PANDORA-ID-NET)

This is a novel multidisciplinary 'One Health' initiative that supports broad themes addressing response to emerging infections in Africa and supporting this through capacity development and training. This project is funded by the European and Developing Countries Clinical Trials Partnership (EDCTP), led by Prof Francine Ntoumi (Republic of Congo), Sir Alimuddin Zumla (UCL) and Prof Giuseppe Ippolito (INMI, Italy)

and includes partners from 13 African Institutions and 9 European Institutions. The PANDORA consortium aims to develop and strengthen effective outbreak response capacities across all geographical regions in sub-Saharan Africa, in partnership with national governments and other international stakeholders.

Reference Link: https://pandora.tghn.org/about/

9. PediCAP:

This is a research project focused on antibiotic therapy of severe and very severe childhood community acquired pneumonia. Through a collaboration between African and European partners it aims to provide data on optimal duration and oral step-down therapy for paediatric community acquired pneumonia. Its primary objective is to optimize antibiotic treatment for childhood pneumonia in low middle-income countries by a randomized trial using an innovative duration - response design. PediCAP aims to establish an active community of practice between the research teams and collaborators which will ensure the skills are in place to deliver a high-quality trial and associated sub-studies. Furthermore, PediCAP's long-term goal is to equip the participating teams in the South and the North with lasting capability to run, lead and design their own studies beyond this project.

Reference Link: https://pedicap.tghn.org/about/

10. Pregnancy Care Integrating translational Science, Everywhere (PRECISE):

The PRECISE Network is a broadly-based group of research scientists and health advocates working in collaboration to investigate placental disorders in sub-Saharan Africa. The broad objectives of this network cover all strategic areas of the programme; research capacity building, global maternal and child health research, partnership building and advocacy. One of the objectives is to develop a unique cohort of biologically and contextually characterised pregnant and non-pregnant women of reproductive age in East (Kenya), West (The Gambia) and Southern (Mozambique) sub–Saharan Africa to support research into placental disorders (hypertension, fetal growth restriction and stillbirth) in the region.

Reference Link: https://precisecommunity.tghn.org/about/

11. PanACEA

This consortium brings together a group of scientists from 11 countries and 16 institutions with skills in clinical trials design and implementation, pulmonology, mycobacteriology, pharmacokinetics, statistics, and delivery of clinical service. Its mission is to shorten and simplify treatment of uncomplicated pulmonary Tuberculosis, to increase the Tuberculosis clinical trial capacity in Africa and develop sustainable Tuberculosis clinical trials network in Africa. This project is part of the European Developing Clinical Trial Partnership (EDCTP) programme supported by the European Union.

Reference Link: http://panacea-tb.net/about-us/mission/

3.2.2 Asia-Pacific Region

1. The Asia-Pacific Hepatocellular Carcinoma (AHCC) Trials Group

This is a collaborative research group formed in 1997 by clinicians from major medical centres in the Asia-Pacific region. The mission of the AHCC network is to conduct preventive and therapeutic trials in (HCC), carry out translational research in this field and develop training and educational programs pertaining to

HCC. The first randomized controlled trial of the group was initiated by the Singapore General Hospital as a single-centre prospective HCC clinical trial, which went on to expand rapidly into a multi-centre trial in the Asia-Pacific region. The Trials Group has since completed 8 prospective, multi-centre clinical studies in HCC that has involved more than 50 participating centres from 17 countries including Singapore, South Korea, China, Japan, Indonesia, Hong Kong, New Zealand and Malaysia and has enrolled more than 3,000 patients.

Reference Link: https://www.scri.edu.sg/crn/asia-pacific-hepatocellular-carcinoma-ahcc-trials-group/about-ahcc/

2. The Cancer Therapeutics Research Group (CTRG)

It was formed in October 1997 as part of the drive to develop Singapore into a life sciences hub and centre for drug development and clinical trials. Since then, the Group has expanded to 8 member institutions from Singapore, Hongkong, Korea, Australia and Taiwan. One of its objectives is to provide high quality data through ICH-GCP compliant clinical trials for rapid registration and licensing of new compounds in Asia. The need for high quality and well-coordinated clinical trial groups in Asia-Pacific has provided many opportunities for the CTRG in clinical trials and translational research, having established itself as a leader in this region. The institutions forming the CTRG collectively bring extensive experience in oncology drug development.

Reference Link: https://www.ncis.com.sg/Research-and-Education/Haematology-Oncology-Research-Group-HORG/Pages/Cancer-Therapeutics-Research-Group-(CTRG).aspx

3. The Asian Thoracic Oncology Research Group (ATORG)

It was formed in 2016 with the vision to be the central coordinating platform for multi-centre clinical trials and translational research for thoracic malignancies in the Asia-Pacific region. ATORG's mission is to advance medical knowledge of lung cancer and improve health outcomes of patients in Asia. In the near-term, ATORG aims to form a trial coordination office for proof-of-concept trials, facilitate translational research for lung cancer across Asia and educate and train personnel in the conduct of clinical research. Its members are from Singapore, South Korea, Taiwan and Hong Kong.

Reference Link: https://www.scri.edu.sg/crn/asian-thoracic-oncology-research-group-atorg/about-atorg/

4. Asian Pediatric Inflammatory Bowel Disease (PIBD) Research Network

It was formed with a mission to create a prospective paediatric inflammatory bowel disease registry to identify disease patterns amongst the Asian PIBD cohort, and to pool valuable clinical data that would be of scientific interest to the global community managing inflammatory bowel disease. It is also a platform for multicenter studies / clinical trials/ translational research in Paediatric Inflammatory Bowel Disease. Its members are from Hong Kong, Malaysia, Philippines, Singapore, Sri Lanka, Taiwan and Thailand.

Reference Link: https://www.scri.edu.sg/crn/paediatric-inflammatory-bowel-disease-pibd-research-network/about-asian-pibd-research-network/

5. The Asian Liver Transplantation Network (ALTN)

It was established in late 2016. The ALTN comprises of prominent medical practitioners skilled in liver transplantation across Asia. The group's research interest focuses on liver transplantation in Asia looking at the indications, outcomes, adherence, etc. Its vision is to be a strategic network of key opinion leaders in Liver Transplantation from Asia, a platform for regular exchange to facilitate best clinical practice, multicenter studies / clinical trials and fill clinical / research Gaps in Liver Transplantation. Its members are from Singapore, Hong Kong, Taiwan, Japan, Korea and Indonesia.

Reference Link: https://www.scri.edu.sg/crn/asian-liver-transplantation-network/about-altn/

6. Pan-Asian Resuscitation Outcomes Study Clinical Research Network (PAROS-CRN)

The PAROS CRN is a collaborative research group formed in 2010 by dedicated Pre-hospital and Emergency Care (PEC) providers conducting PEC research in the Asia-Pacific region. Its mission is to improve outcomes from Pre-hospital and Emergency Care across the Asia-Pacific region by promoting high quality research into resuscitation. It endeavors to improve outcomes from PEC across the Asia-Pacific region through the creation of a platform to support and stimulate research into effective strategies to improve survival in PEC. By offering practical ways of monitoring and meaningful measurement of PEC outcomes, PAROS CRN has an enormous potential to contribute significantly to PEC research, regardless of whether they are epidemiological studies or clinical trials.

Reference Link: https://www.scri.edu.sg/crn/pan-asian-resuscitation-outcomes-study-paros-clinical-research-network-crn/about-paros/

7. Pediatric Acute & Critical Care Medicine Asian Network (PACCMAN)

This is a collaborative research network formed in 2015 by pediatric intensive care providers. The primary aim of PACCMAN is to promote collaboration by bringing together individuals to share experience and develop best practices for this diverse region. It serves as a platform to support and stimulate research into effective strategies to improve survival in critically ill children. This allows connectivity with all countries throughout Asia who can then participate/contribute as a community in meaningfully research whether they are observational or randomized.

Reference Link: https://www.scri.edu.sg/crn/pediatric-acute-critical-care-medicine-asian-network/about-paccman/

8. Deciphering Diversities: Renal Asian Genetics Network (DRAGON)

This is a research consortium based in National University of Singapore, set up to investigate glomerular and proteinuric diseases in Asians. The network consists of nephrologists, paediatricians, pathologists, scientists and biostatisticians. Its mission is to advance our understanding of the demographics, genetics and clinical features of primary glomerular diseases and cystic diseases in Asians. We aim to provide the basis to direct future functional work, to improve clinical management strategies and explore innovative treatment targets for glomerular diseases.

Reference Link: https://www.scri.edu.sg/crn/deciphering-diversities-renal-asian-genetics-network-dragon/deciphering-diversities-renal-asian-genetics-network-dragon/

9. Asia Pacific Gynecological Oncology Trials group (APGOT)

This group was formed in November 2019 to focus on collaborative studies in gynaecological cancer within the Asia Pacific region, strengthening capabilities and ensuring a greater range of trials are available for women. It is to focus on Phase II Clinical Trials and studies that can be co-developed with industry funders. Strong links are to be forged with ENGOT in Europe. Members can expect early access to new treatments for some of the more difficult to treat cancer subtypes through these clinical trials.

Reference Links: https://probonoaustralia.com.au/wp-content/uploads/2018/07/210212_ANZGOG_AnnualReport2020_A4_Single-page-layout.pdf , https://www.anzgog.org.au/anzgog-attends-apgot-meeting-singapore/

10. The MORU Tropical Health Network

This network conducts targeted clinical and public health research that aims to discover and develop appropriate, practical, affordable interventions that measurably improve the health of people living in resource-limited parts of the world. The core of MORU's activities is patient-centered research in the areas of Malaria, Mother and child health, Microbiology & non-malaria infections, Critical illness, Medicine quality, Statistics, data & modelling and Bioethics and Engagement. The network is geographically dispersed across 5 research units and 50 sites across Asia and Africa and hosts the 'Thailand Wellcome Africa and Asia Programme'.

Reference Link: https://www.tropmedres.ac/about

11. The Oxford University Clinical Research Unit (OUCRU)

This is a large-scale clinical and public health research unit with site offices in Viet Nam, Indonesia, and Nepal. Its vision is to have a local, regional, and global impact on health by leading a locally driven research programme on infectious diseases in Southeast Asia. Its research programme covers clinical and laboratory research with hospital and community-based patient populations, including epidemiology, immunology, host and pathogen genetics, molecular biology, microbiology and virology, mathematical modelling, bioinformatics, and biostatistics. This work is supported by an extensive clinical trials unit and data management centre compliant with national and international regulations and comprehensive management, finance, and administrative support offices with support from Wellcome Trust as part of the Africa and Asia Programmes.

Reference Link: http://www.oucru.org/about-us/

3.2.3 Western-Pacific Region

1. Australasian Radiopharmaceutical Trials Network

The Australasian Radiopharmaceutical Trials network (ARTnet) was officially launched at the 44th Australian and New Zealand Society of Nuclear Medicine (ANZSNM) Annual Scientific Meeting in Adelaide in April 2014 as a joint venture between the ANZSNM and the Australasian Association of Nuclear Medicine Specialists (AANMS). It is a new collaborative network bringing together medical specialists, technologists, scientists, and researchers from the field of Nuclear Medicine and Molecular Imaging with a shared interest in multicenter clinical trials utilizing radiopharmaceuticals for imaging or therapy. Members are Australia wide, New Zealand and International.

2. *Australasian Stroke Trials Network*

The Australasian Stroke Trials Network (ASTN) established in 1996 is the key body in promoting, facilitating, and coordinating both commercially sponsored and investigator-initiated stroke trials in Australasia. This network, which comprises 35 centres located in Australia, New Zealand, Singapore and Hong Kong, facilitates the development of coordinated strategies for involvement of the Australasian Pacific region in International Stroke Trials. The ASTN was initially set up to follow the network concept developed in North America and Europe.

3. Australian & New Zealand College of Anaesthetists Clinical Trials Network

The Australian and New Zealand College of Anaesthetists Clinical Trials Network (ANZCA CTN), which was established in 2002 (as the ANZCA Trials Group), has been conducting practice changing NHMRC-funded multicenter trials for almost a decade. The ANZCA CTN is committed to providing evidence-based practices in anaesthesia, pain, and perioperative medicine. The primary goal of the network is to improve the evidence base of anaesthesia by endorsing high quality, multicenter randomized controlled trials, and related research. Members are Australia wide, New Zealand and International.

4. Australian Epilepsy Clinical Trials Network

The Australian Epilepsy Clinical Trials Network (AECTN) was established in 2013 as a coordinating body for epilepsy clinical trial centres in Australia and New Zealand to facilitate both industry-funded and investigator driven research. It is a part of the Neuroscience Trials strategic alliance representing professional network of clinicians and other healthcare professionals committed to seeking improvement in treatment of Epilepsy and related disorders through the cooperative planning, implementation, analysis and reporting of controlled clinical trials and of other relevant research.

5. Multiple Sclerosis Research Australia Clinical Trials Network

The Multiple Sclerosis Research Australia Clinical Trials Network (MSRACTN) was established in 2010 to facilitate clinical trials for Multiple Sclerosis in Australia and New Zealand. The network aims to increase awareness of and access to clinical trials for patients with this complex and often disabling disease that is characterized by variable and unpredictable progression. Modelled on other successful clinical trials networks, the focus of the group's activity remains improvement of the opportunity to participate in trials for patients.

6. The Australasian Kidney Trials Network

The mission of the AKTN is to deliver high quality clinical trials to improve the health and wellbeing of people with kidney disease. To achieve this, the AKTN in conjunction with global collaborators including the European Vasculitis Study Group (EUVAS) and the Canadian Kidney Knowledge Translation and Generation Network (CANN.NET) designs, conducts and supports clinical trials in Australia and New Zealand (ANZ) thereby enabling a broad range of research concerned with the prevention and treatment of kidney disease. The AKTN is also committed to fostering clinical trials expertise in ANZ and the Asia Pacific region by offering formal educational and training opportunities (higher research degree scholarships and fellowships) along with informal learning opportunities (mentoring early career researchers; research resource and knowledge sharing).

7. *The Australasian Sleep Trials Network:*

The Australian Sleep Trials Network (ASTN) is an inclusive consortium that was founded in 2005 to develop infrastructure to support Australasian multicentre trials in the field of sleep research. The network was formed to enable, facilitate, and conduct large-scale multicentre investigator driven clinical trials of national and international significance, funded by Government or industry, that have potential to have a major impact on sleep health in the Australasian region. Members are Australia wide and New Zealand.

8. *The Interdisciplinary Maternal Perinatal Australasian Collaborative Trials Network*

The Interdisciplinary Maternal and Perinatal Australasian Collaborative Trials Network (IMPACT) was formed in 1994 as part of the then Australian Perinatal Society and, in 1997, it became a subcommittee of the Perinatal Society of Australia and New Zealand (PSANZ). The network is dedicated to improving outcomes for mothers and babies through the conduct of well-designed randomized control trials coupled with subsequent dissemination and application of trial results. The core values of IMPACT are collaboration, open communication, maintaining best practice to improve health outcomes, quality, and relevance of the research, raising awareness of trials, investment in the future, trust and confidentiality, and partnership with mothers and their families. Members are Australia wide, New Zealand and International.

9. *Australasian College for Emergency Medicine Clinical Trials Group*

The Australasian College for Emergency Medicine (ACEM) is a non-for-profit organization responsible for training emergency physicians and advancement of the professional standards in emergency medicine care across a range of specialized areas in Australia and New Zealand. The Emergency Medicine Clinical Trials Group (ACEM CTG) was established as a subcommittee of the ACEM Scientific Committee with an interest in research and clinical trials in the emergency department setting. It endorses clinical trials related to various aspects of emergency medicine including but not limited to pre-hospital care, emergency department clinical care, disaster response, toxicology, medical education and training, triage, and patient flow. While it is a relatively new network, the ACEM CTG has become a peak organization for emergency medicine in Australasia focused on clinical trials and research in emergency department settings delivering education, advocacy, and member support. The members are New South Wales, Victoria, Queensland, Western Australia

10. *Australasian Gastro-Intestinal Trials Group*

The Australasian Gastro-Intestinal Trials Group (AGITG), formed in 1991, is an independent not-for-profit academic collaborative research group that develops and conducts clinical trials to test new treatments for gastro-intestinal (GI) cancer. The AGITG focuses on identifying gaps in medical knowledge and developing clinical trials that are potentially practice changing in areas of high clinical need. The AGITG continually strives to achieve better health outcomes through GI-related clinical and biological research in Australasia and internationally. Members are Australia wide, New Zealand and International.

11. *Australasian Lung Cancer Trials Group:*

Founded in 2004, the Australasian Lung Cancer Trials Group (ALTG) is a multi-disciplinary organization whose mission is to reduce the incidence, morbidity and mortality of lung and other thoracic cancers and

improve the quality of life of patients, careers and families in Australia and New Zealand through the coordination and facilitation of high-quality clinical research. Membership is available to all medical and non-medical people interested in clinical research in lung and thoracic cancer. The group conducts trials through both international collaborations and cooperative work with the NHMRC Clinical Trials Centre and Peter MacCallum Cancer Centre in Australia. Members are Australia wide and New Zealand.

12. Australasian Sarcoma Study Group

The Australian Sarcoma Study Group (ASSG), which originated in 2008, is a co-operative group of clinicians sharing interest in undertaking basic, translational, clinical, and supportive care research to develop and deliver treatments of sarcomas and related tumors to the Australian community and globally. This organization provided infrastructure enabling collaboration between multidisciplinary teams and bringing together health professionals working on development of best treatments and care for sarcoma cancer sufferers. The network is focused on initiation and maintenance of a national sarcoma research capability in Australia, formation of international clinical trials partnerships and effective collaborations across cancer research disciplines**.** Members are Australia wide, New Zealand and International.

13. Australia & New Zealand Breast Cancer Trials Group

The Australia and New Zealand Breast Cancer Trials Group (ANZBCTG) is the largest independent, oncology clinical trials research group in Australia and New Zealand. For more than 35 years, it has conducted clinical trials for the treatment, prevention, and cure of breast cancer. Breast cancer research conducted in Australia, predominantly by the ANZBCTG, has contributed to the significant improvement in breast cancer related mortality that has occurred over the last thirty years.

14. Australia & New Zealand Melanoma Trials Group

Since its establishment in 1999, the focus of the Australian and New Zealand Melanoma Trials Group (ANZMTG) has been related to skin cancers and melanoma. The network has recognized the need for central support of melanoma trials for investigators and consumers and has been actively involved in coordinating efforts of researchers, health care professionals and consumers in conducting high quality clinical research for melanoma control. Since its first successful project in designing and conducting the randomized Phase III trial in melanoma, that compared adjuvant radiotherapy to observation in patients with resected nodal disease, ANZMTG has been developing and conducting new clinical trial protocols and research projects.

15. Australia New Zealand Gynecological Oncology Group

The Australia New Zealand Gynecological Oncology Group (ANZGOG), which was established in 2000, is a not-for-profit company limited by guarantee and a health promotion charity that fundraise in all states of Australia. ANZGOG encourages and facilitates high quality national and international collaborative research dedicated to gynecological oncology such as ovarian, cervical, uterine, vulvar, and vaginal cancers. It has contributed to the initiation and successful conduct of investigator-led multicenter clinical trials recruiting across more than 51 sites throughout Australia and New Zealand. These trials and research activities provide the opportunity for women in Australia and New Zealand to participate in important clinical trials that are seeking new treatments that hold the promise of improving their outcomes.

16. Australian & New Zealand Children's Hematology/Oncology Group

Since its establishment in 1986 the Australian and New Zealand Children's Hematology/Oncology Group (ANZCHOG) has been dedicated to improving outcomes for children with cancer through conducting clinical trials as an integrated component of routine healthcare delivery. It is a national multidisciplinary, cooperative network formed to provide the infrastructure for collaboration of professionals working in the fields of pediatric blood diseases and cancer. It is an independent non-profit organization with a multi-disciplinary membership involved in national and international clinical trials, clinical and laboratory-based research. It also holds workshops, seminars, and an annual scientific meeting.

17. Australian & New Zealand Intensive Care Society Clinical Trials Group

The Australian and New Zealand Intensive Care Society Clinical Trials Group (ANZICS CTG) was established in 1994. What started as a small group of professionals, committed to seeking better clinical research and greater quality evidence in intensive care medicine, has evolved into a group with more than 500 members who are world leaders in the design and conduct of multicenter trials that define best treatment for patients with immediately life-threatening critical illness. The network is active in more than 90 adult and paediatric Intensive Care Units (ICUs) and interacts closely with the registries that are maintained by the ANZICS Centre for Outcome and Resource Evaluation.

18. Australian & New Zealand Urogenital & Prostate Cancer Trials Group

The Australian and New Zealand Urogenital and Prostate Canter Trials Group (ANZUP) is an active cancer cooperative clinical trials group, established to bring together all the professional disciplines and groups involved in researching and treating prostate and other urogenital cancers. ANZUP was established in 2008 for the purpose of conducting national and international research in these cancers. The group's focus is on the conduct of clinical trials to improve the treatment of Bladder, Kidney, Testicular and Prostate Cancers for all appropriate patients in Australia and New Zealand. Its collaboration with various professionals across multiple disciplines provides numerous opportunities for streamlined clinical research of the highest quality for the benefits of patients with urogenital cancers.

19. Australian Musculoskeletal Clinical Trials Group

The Australia & New Zealand Musculoskeletal (ANZMUSC) Clinical Trials Network is a newly established group, formed to optimize musculoskeletal health through high quality, collaborative clinical research. The focus is on all forms of arthritis and musculoskeletal conditions including osteoarthritis, rheumatoid arthritis, osteoporosis, trauma, and regional conditions (such as low back pain, neck pain, and shoulder pain).

20. Cooperative Trials Group for Neuro-Oncology

The Cooperative Trials Group for Neuro-Oncology (COGNO) was established in 2007, following identification of the need to develop a central mechanism enabling a coordinated, structured approach to the management of large-scale multi-center neurooncological trials in Australia. The group is focused on conducting investigator-initiated collaborative trials addressing important clinical questions in patients with brain tumors. It strives to achieve better health outcomes for patients and those affected by brain tumors through clinical trials research. Members are Australia wide, New Zealand and International.

21. Primary Care Collaborative Cancer Clinical Trial Group

The Primary Care Collaborative Cancer Clinical Trials Group (PC4) was established in February 2009, with support from Cancer Australia, to promote the conduct of high-quality cancer research in primary care. The vision of the Group is to prevent cancer, to improve care and outcomes for people affected by cancer, to influence health care policy, and to promote best practice cancer care. This is done by fostering collaboration among researchers, health professionals and consumers; building research capacity through Training Awards, Concept Development, and other workshops, and mentoring early career researchers; and facilitating the conduct of high-quality research by providing our trial coordinators with resources tailored to complex intervention trials. Members are Australia wide, New Zealand and International.

22. Therapeutic and Vaccine Research Program, Kirby Institute

The Therapeutic and Vaccine Research Program (TVRP) was established in 2002 following consolidation of previously arranged structures within what was then the National Centre in HIV Epidemiology and Clinical Research (NCHECR) and is now known as the Kirby Institute. Over the nearly three decades of operation the TVRP has become a recognized coordinating center for national and international research responsible for a range of clinical trials designed to assess the effectiveness of new HIV therapies, new treatment strategies or candidate vaccines for treatment and prevention of HIV and other virus diseases. The TVRP has led a large number of clinical trials supported by competitive applications (national and international) and commercially funded phase I through Iv clinical trials. The TVRP collaborates directly with nearly 100 clinical centres in 18 countries on six continents. Members are Australia wide and International.

23. Trans Tasman Radiation Oncology Group

The Trans Tasman Radiation Oncology Group (TROG) is a global leader in radiotherapy research conducting high quality controlled clinical trials focused on investigation of the effects of radiation therapy to improve outcomes and quality of life for people affected by cancer. TROG was established in 1989 by the then seven radiotherapy centres across Australia and New Zealand and has over 1000 members. Its objective is to advance the study of cancers treatable with radiotherapy (breast, lung, prostate, skin, head, and neck) and to contribute to a process of continual improvement in cancer treatment for the benefit of patients in the Trans-Tasman region and internationally. TROG has a Central Operations Office that provides full trial management from the time of initial trial concept proposal through to completion and publication in medical journals.

Reference Link: https://www.clinicaltrialsalliance.org.au/wp-content/uploads/2015/12/ACTA_Networks_Report_2004-14_online.pdf

24. Australian Partnership for Preparedness Research on Infectious Disease Emergencies (APPRISE)

This is a Centre of Research Excellence to develop research and evidence to inform Australia's capacity to prepare, respond and recover from infectious diseases. It is an Australia-wide network of leading experts, institutions and research networks involved in clinical, laboratory, public health, and ethics research. The network coordinates multidisciplinary research teams and key stakeholders to provide a national focus and international links for infectious disease research.

Reference Link: https://www.apprise.org.au/who-we-are/

3.2.4 Europe

1. Collaborative Network for European Clinical Trials for Children (c4c)

The conect4children (c4c) project will address the critical problems with the design, implementation and operational conduct of paediatric clinical trials, for example, the fragmented and redundant efforts between sponsors, sites and countries. This project will generate a sustainable infrastructure that optimizes the delivery of clinical trials in children through a) a single point of contact for all sponsors, sites and investigators; b) efficient implementation of trials adopting consistent approaches, aligned quality standards and coordination of sites at national and international level; c) collaboration with specialist networks; d) high-quality input to study design and preparation through a rigorous strategic and operational feasibility assessment and e) the promotion of innovative methodologies. The team is led by Eugenio Baraldi of the Department of Women's and Children's Health.

Reference Links: https://cordis.europa.eu/project/id/777389, https://conect4children.org/

2. European Society of Anaesthesiology and Intensive Care

ESAIC provides continuing education and advances knowledge, leads the way in patient safety, helps to elevate the anesthesiologist's practice, and creates valuable and lasting connections with our global community. In doing this, the ESAIC contributes to the growth and innovation found in the field of anesthesiology and intensive care. Through their education and exams department, and along with their annual congress, they promote the exchange of knowledge between European anesthesiologists worldwide by disseminating information related to scientific progress in anesthesiology. With grants, they carry out clinical trials in various countries across Europe. Each trial has its chief Investigator.

Reference Link: https://www.esaic.org/research/clinical-trial-network/

3. European Cystic Fibrosis Clinical Trial Network (ECFS-CTN) -

Active since 2008. The network currently provides access to 57 large and experienced CF centres, located in 17 different countries throughout Europe, caring for 21,500 adult and paediatric CF patients. The aim of the European Cystic Fibrosis Clinical Trial Network is to intensify clinical research in the area of cystic fibrosis and to bring new medicines to patients as quickly as possible.

Reference Link: https://www.ecfs.eu/ctn

4. European Network of Paediatric Research at the European Medicines Agency (Enpr-EMA)

Enpr-EMA is a network of research networks, investigators and centres with recognized expertise in performing clinical trials in the paediatric population. Members perform research with children (newborns to adolescents), in multiple therapeutic areas, and ranging from pharmacokinetics to pharmacovigilance

Reference Link: http://www.encepp.eu/publications/documents/3.1_EnprEMA.pdf

5. The European Clinical Research Infrastructure Network (ECRIN)

ECRIN supports, coordinates, and manages high-quality, independent and fully transparent multinational clinical trials. ECRIN aims at improving patients and citizens' health worldwide by means of multinational clinical research projects, to which it offers integrated support by providing: Information, consultancy, and

services. ECRIN runs two initiatives in parallel, both funded by the FP7 Infrastructure Unit: (1)ECRIN-ERIC, a legal entity whose sustainability is supported by the Member States, will be in charge of supporting the multinational clinical trials selected by the ECRIN Scientific Board. (2) ECRIN-IA (Integrating Activity, 2012-2015), will be in charge of further structuring and expanding the network, especially by promoting user communities for rare diseases, medical devices and nutrition.

Reference Link: http://ecranproject.eu/en/content/european-clinical-trials

6. European Reference Network - Neuromuscular Diseases (EURO-NMD)

Few patients with a neuromuscular condition currently benefit from effective or curative therapies, and many do not have a definite diagnosis. Uniting healthcare and research would begin to address this and is therefore in the best interests of patients. EURO-NMD members are not only specialist healthcare providers but also among the world's leading researchers in the neuromuscular field and as such recognise the value in a network like EURO-NMD. We aim to keep our patients informed about research both general and specific to their condition. We will also highlight opportunities they will have to participate in this research which could be in the form of biobanks, registries, natural history studies, clinical trials.

Reference Link: https://ern-euro-nmd.eu/research/

7. Clinical Trial Network (AIMS-2-TRIALS)

The network seeks to develop a network to reduce the barriers to running clinical trials in autism. The network will connect individuals at over 120 sites across 37 countries in Europe. It is called the Clinical Trials Network. It will conduct safe and high-quality trials of emerging therapies to support autistic people who may benefit from medical and other therapies. The Network is led by Tony Charman of King's College London and Lorraine Murtagh of Roche.

Reference Link: https://www.aims-2-trials.eu/our-research/clinical-trials-network/

8. European Huntington's Disease Network (EHDN)

The EHDN is an independent nonprofit network dedicated to advancing research, conducting clinical trials and improving care for people affected by Huntington's disease. The network is composed of clinicians, researchers and people affected by HD, working together to accomplish the set goal.
Reference Link: http://www.ehdn.org/

9. European Network for Gynaecological Trial Groups (ENGOT)

The ENGOT is a research network of the European Society of Gynaecological Oncology (ESGO). It currently consists of 21 trial groups from 25 European countries that perform cooperative clinical trials. ENGOT's goal is to bring the best treatment to gynaecological cancer patients through the best science and enable every patient in every European country to access a clinical trial.
Reference Link: https://engot.esgo.org/clinical-trials/publications/

3.2.5 Latin America and the Caribbean Region

1. US-Latin American-Caribbean HIV/HPV-Cancer Prevention Clinical Trials Network

This network focuses on developing evidence to improve and optimize approaches for the prevention of human papillomavirus (HPV)-related cancers in people living with human immunodeficiency virus (HIV)

infection. This international collaborative research network brings together institutions in the United States and counterparts in low- and middle-income countries (LMICs) in the Latin American and the Caribbean (LAC) region.

Reference Link: https://prevention.cancer.gov/major-programs/us-latin-american-caribbean-clinical-trials-network

2. *Latin American Cooperative Oncology Group*

LACOG is an Academic Research Organization that aims to support and develop cancer research in Latin America. In the last years, we have built a professional structure, the LACOG Coordinating Office, which attends to the demands of our clinical trials and intergroup studies. LACOG is a partner of Projeto CURA to promote fundraiser activities and support cancer research projects that are critical to the diverse population of Latin American patients. Working together we will improve patient care in Latin America. LACOG currently counts on more than 400 investigators members, present in 194 institutions from 16 Latin American countries.

Reference Link: https://lacogcancerresearch.org/about-lacog/

3. ReDE Research Capacity Network:

This is an international network focused on building research capacity and preparedness to tackle infectious disease outbreaks in Latin America and Caribbean. REDe is tasked with creating a regional research network that can respond to emerging infectious diseases. This regionally led network needs to be equipped with the knowledge, methods, skills and capabilities to support a high quality, rapid and coherent research response to the Zika outbreak in the short term. In addition, this network sets out to establish lasting capacity to conduct research in the event of other vector-borne and emerging infectious disease outbreaks in Latin America and the Caribbean in the long-term.

Reference Link: https://rede.tghn.org/about/

4. ZikaPLAN (Zika Preparedness Latin American Network)

It brings together 25 leading research and public health organizations in Latin America, North America, Africa, Asia, and Europe, taking a comprehensive approach to tackle the Zika threat. Its aim is to address ZIKA by tackling knowledge gaps and needs in key areas of interest to the current Zika outbreak and to prepare for beyond Zika by building a sustainable Latin-American Emerging Infectious Diseases. The project work plan was designed to address these dual, complementary objectives and includes comprehensive, encompassing epidemiological surveillance, clinical studies, the development of innovative diagnostic tools and control strategies, in addition to education and knowledge sharing.

Reference Link: https://zikaplan.tghn.org/about-zikaplan/

3.2.6 North America

1. North American Clinical Trials Network (NACTN) for the Treatment of Spinal Cord Injury

The NACTN was established with the goal of bringing recent molecular and cell-based discoveries in neuroprotection and regeneration from the laboratory into clinical trials that optimize meaningful data outcomes and maximum safety to patients. It is a consortium of 10 neurosurgery departments, a data management center, and a pharmacological center.

Reference Link: https://pubmed.ncbi.nlm.nih.gov/22985365/

2. NCI's(National Cancer Institute) National Clinical Trials Network (NCTN)

The NCTN is a collection of organizations and clinicians that coordinates and supports cancer clinical trials at more than 2,200 sites across the United States, Canada, and internationally. NCTN provides the infrastructure for NCI-funded treatment and primary advanced imaging trials to improve the lives of people with cancer.

Reference Link: https://www.cancer.gov/research/infrastructure/clinical-trials/nctn

3. Blood and Marrow Transplant Clinical Trial Network (BMT CTN)

A network established to conduct large multi-institutional clinical trials. The trials hope to address important issues in hematopoietic stem cell transplantation (HSCT), thereby furthering understanding of the best possible treatment approaches. Participating BMT CTN investigators collaborate through an organization designed to maintain continuity of operations, facilitate effective communication and cooperation among participating transplant centres and with collaborators at the National Institutes of Health, and offer trial participation to patients in all regions of the U.S.
Reference Link: https://web.emmes.com/study/bmt2/

4. Strategies to Innovate Emergency Care Clinical Trials Network (SIREN)

SIREN seeks to improve the outcomes of patients with neurologic, cardiac, respiratory, hematologic and trauma emergencies by identifying effective treatments administered in the earliest stages of critical care. It is funded by the National Institute for Neurological Disorders and Stroke (NINDS), the National Heart Lung and Blood Institute (NHLBI) and the National Center for Advancing Translational Science (NCATS).
Reference Link: https://siren.network/about-siren

5. Microbicide Trials Network (MTN)

This is an HIV/AIDS clinical trials network established in 2006 by the National Institute of Allergy and Infectious Diseases, with co-funding from the Eunice Kennedy Shriver National Institute of Child Health and Human Development and the National Institute of Mental Health, all components of the U.S. National Institutes of Health. The MTN brings together international investigators and community and industry partners whose work is focused on the rigorous evaluation of promising microbicides – products applied inside the vagina or rectum to prevent the sexual transmission of HIV – and of dual-purpose products for preventing both HIV and unintended pregnancy.

Reference Link: https://www.niaid.nih.gov/research/microbicide-trials-network

5. Society of Nuclear Medicine & Molecular Imaging Clinical Trial Network (SNMMI-CTN)

The network is a collaborative effort assigned to address the widely recognized need for validated imaging biomarkers that can be used in streamlining the development and registration of investigational therapeutics. Standardization in molecular imaging is critical for a trial to be successful, and the elements of the CTN have been carefully developed to make it possible. CTN also works collaboratively with other imaging associations such as RSNA, government agencies such as the FDA and industry leaders to move the entire field forward.

Reference Link: https://www.snmmi.org/Research/Content.aspx?ItemNumber=9937&navItemNumber=6832

6. SWOG Cancer Research Network

SWOG Cancer Research Network is a pioneer in cancer clinical trials, one of the first cooperative groups created by the National Cancer Institute. Along with being publicly funded, SWOG trials seek to improve medical care across the cancer continuum - prevention, treatment, care delivery, symptom control and quality of life, survivorship, and palliative and end-of-life care.

Reference Link: https://www.swog.org/clinical-trials

7. AIDS Clinical Trials Group (ACTG)

ACTG is an entity that centrally coordinates a number of Clinical Research Sites (CRS). Clinical Trial Units (CTUs) have established robust systems that ensure high-quality conduct and delivery of clinical trials at the CRSs that are affiliated with them

Reference Link: https://actgnetwork.org/

8. HIV Vaccine Trials Network (HVTN)

The mission is to fully characterize the safety, immunogenicity, and efficacy of HIV vaccine candidates with the goal of developing a safe, effective vaccine as rapidly as possible for the prevention of HIV globally. To date, the network has conducted the majority of the published, presented, or ongoing clinical trials of preventive HIV vaccines worldwide.

Reference Link: https://www.hvtn.org/en/about/hvtn-mission.html

9. Alliance for Clinical Trials in Oncology

The Alliance for Clinical Trials in Oncology seeks to reduce the impact of cancer by uniting a broad community of scientists and clinicians who are committed to the prevention and treatment of cancer. The Alliance for Clinical Trials in Oncology develops and conducts clinical trials with promising new cancer therapies, and utilizes the best science to develop optimal treatment and prevention strategies for cancer, as well as research methods to alleviate side effects of cancer and cancer treatments.

Reference Link: https://www.allianceforclinicaltrialsinoncology.org/main/#!

10. ASH RE Sickle Cell Disease Clinical Trials Network

The network was launched with a mission of improving outcomes for individuals with Sickle Cell Disease (SCD) by expediting the development of treatments and facilitating innovation in clinical trial research. The Network is an unprecedented national effort to streamline operations and facilitate data sharing to expedite the development of new treatments for this rare disease.

Reference Link: https://www.ashresearchcollaborative.org/s/clinical-trials-network

11. National Drug Abuse Treatment Trial Network

The National Drug Abuse Treatment Clinical Trials Network (CTN) is a means by which medical and specialty treatment providers, treatment researchers, participating patients, and the National Institute on Drug Abuse cooperatively develop, validate, refine, and deliver new treatment options to patients

Reference Link: https://www.drugabuse.gov/about-nida/organization/cctn/ctn/about-ctn

12. The Cancer Immunotherapy Trials Network (CITN)

The CITN and affiliated Immune Oncology Network (ION) strive to make promising experimental immunotherapies broadly available to people with cancer. CITN and ION benefit from the collective expertise of top academic immunologists to conduct multicenter research on immunotherapy agents capable of unleashing patient immunity to fight cancer. They conduct studies of experimental cancer immunotherapies and focus on testing novel agents in innovative, early-phase clinical trials.

Reference Link: https://www.fredhutch.org/en/research/institutes-networks-ircs/cancer-immunotherapy-trials-network.html

13. Pediatric Early Phase-Clinical Trial Network (PEP-CTN)

The PEP-CTN was set up to identify and develop effective new agents for children and adolescents with cancer through rational and efficient clinical and laboratory research. PEP-CTN clinical trials incorporate correlative genomic, biology, pharmacology, and imaging studies to further the understanding of the disposition and action of new agents introduced into the treatment of children with cancer. The network is composed of 21 premier Children Oncology Group (COG) pediatric core member sites in the U.S. and 21 non-core member sites in the U.S., Canada and Australia that were selected through a peer-review process.

Reference Link: https://childrensoncologygroup.org/index.php/pep-ctn-about-us

14. National Exercise Clinical Trials Network (NExTNet)

NExTNet was established to facilitate multi-site exercise clinical trials to address these knowledge gaps in a disease-specific or population-specific manner. Currently, 77 institutions from coast to coast are members of the growing network. One of NExTNet's primary functions is to foster standardization of procedures for rigorous multi-site trials.

Reference Link: https://www.uab.edu/medicine/nextnet/

15. Pediatric Trials Network (PTN)

The Network studies the formulation, dosing, efficacy, and safety of drugs, as well as the development of medical devices, used in pediatric patients. They conduct trials primarily with off-patent drugs that are lacking data in pediatric populations. Data collected from PTN trials help regulators to revise drug labels for safer and more effective use in infants and children.

Reference Link: https://pediatrictrials.org/our-research/

16. Facioscapulohumeral Muscular Dystrophy Clinical Trial Research Network (FSHD CTRN)

FSHD CTRN is a consortium of academic research centres with expertise in FSHD clinical research or in conducting neuromuscular clinical trials. They offer researchers the ability to leverage existing clinical trials infrastructure and common standard operating procedures (SOPs) for handling projects, regulatory approval, data collection and analysis – hastening the ability to reach our common goal of making new FSHD therapies available.

Reference Link: https://www.kumc.edu/fshd-clinical-trial-research-network.html

17. International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) Network

The mission of IMPAACT is to significantly decrease incident HIV and HIV-associated infections and to decrease mortality and morbidity due to HIV and HIV-associated infections and co-morbidities among infants, children, adolescents, and pregnant/postpartum women.

Reference Link: https://www.impaactnetwork.org/about/mission

3.2.7 Other Global Clinical Trials Infrastructure

1. *International Severe Acute Respiratory and emerging Infection Consortium (ISARIC)*

Its purpose is to prevent illness and deaths from infectious diseases outbreaks. We are a global federation of clinical research networks, providing a proficient, coordinated, and agile research response to outbreak-prone infectious diseases. It represents 52 ratified networks and has created tools for investigators to collect and store data in a standardized way and has supported clinical trials of treatments.

Reference Link: https://isaric.org/

2. *Research And Action Targeting Emerging Infectious Disease (REACTING)*

This is a network of French research organizations, coordinated by Inserm, the French National Institute for Health and Medical Research. Its activity covers the geographical range of France, Africa, the Caribbean and the Indian Ocean. It has coordinated several studies in recent years, from Chikungunya in the Caribbean to multiple aspects of study on Zika virus, Ebola virus disease and Lassa fever in West Africa, plague in Madagascar and others. In collaboration with other partners, the network is currently implementing an Ebola vaccine study in West Africa. Its overall goal is to prepare and coordinate research to control unforeseeable emerging infectious threats more effectively. This is to be achieved through multi-disciplinary collaboration and keeping a broad scope, from basic research to the human and social sciences, including environmental sciences, epidemiology, and public health.

Reference Link: https://www.glopid-r.org/clinical-trial-network/reacting-research-and-action-targeting-emerging-infectious-disease/

3. *The Worldwide Antimalarial Resistance Network (WWARN)*

It works with partners across the world to optimize the efficacy of antimalarial medicines and treatment regimens - especially for vulnerable groups such as pregnant women, infants and malnourished children. WWARN also engages and works with other disease research communities to replicate this model for other devastating tropical and neglected diseases. The network supports regional efforts to build capacity, provide training and advise to local researchers and healthcare workers. These regional centres are in Asia, East Africa, West Africa, and Latin America.

Reference Link: https://wwarn.tghn.org/about/

4. *The Childhood Acute Illness and Nutrition Network (CHAIN)*

This is a global research network of clinical experts, scientists and advisors seeking to optimize management and care of highly vulnerable in resource-limited settings to improve survival, growth and development. The network aims to identify the biological mechanisms and the socio-economic factors that determine a child's risk of mortality in the six months following presentation to medical care with an acute illness. Investigators from the CHAIN Network are also involved in a number of on-going clinical trials that will contribute to the Network's overarching goals. The results obtained from these trials will be used

to prioritize future clinical trials. Two particularly relevant ongoing clinical trials are: The FLACSAM trial, which is testing the efficacy of novel antibiotic regimens in children admitted to hospital with severe acute malnutrition, and The Toto Bora trial, which is assessing the benefits of a short course of azithromycin to reduce mortality among children after they are discharged from hospital.

Reference Links: https://chainnetwork.org/about/, https://chain.tghn.org/

5. *Global Pediatric Clinical Trials Network (G-PCTN)*

A network sponsored by the FDA which aims to support efficient pediatric clinical trials by developing scientific and operational infrastructure; fostering collaborative networks; sharing knowledge and engaging stakeholders. The principal investigators for this program will be Daniel Benjamin, Jr., MD, MPH, PhD, and Michael Cohen-Wolkowiez, MD, PhD.

Reference Links: https://dcri.org/global-pediatric-clinical-trials-network/ & https://dcri.org/wp-content/uploads/2019/11/GPTN-whitepaper_07nov2019.pdf

6. *HIV Prevention Trials Network*

The HIV Prevention Trials Network is a worldwide collaborative clinical trials network that develops and tests the safety and efficacy of interventions designed to prevent the transmission of HIV. As of November 2021, HPTN had more than 50 ongoing or completed clinical trials in 14 countries at more than 60 research sites.

Reference Link: https://www.hptn.org/

7. *WHO COVID-19 Solidarity Therapeutics Trial*

This large, global randomized control trial is designed to provide robust results on whether a drug can save lives in those hospitalized with severe or critical COVID-19. It empowers local researchers and provides them with opportunities to contribute their expertise and resources to the global research needs. It helps us prepare for future pandemics. Not only is this an important trial, in terms of potential new treatments for COVID-19, but it could open a new global approach to the robust evaluation of several therapeutics as we respond to this pandemic and prepare for future ones. *Reference Link: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments*

8. *A Randomized, Embedded, Multi-factorial, Adaptive Platform Trial for Community-Acquired Pneumonia (REMAP-CAP)*

REMAP-CAP is a global network of leading experts, institutions, and research networks. With over 250 participating world-wide, REMAP-CAP is a truly global trial. Community-acquired pneumonia (or CAP) is a significant cause of hospitalization and illness world-wide. Respiratory tract infections are the leading cause of deaths from infectious disease globally and are the leading cause of deaths in developing nations. REMAP-CAP uses a novel and innovative adaptive trial design to evaluate a number of treatment options simultaneously and efficiently. This design can adapt in the event of pandemics and increases the likelihood that patients will receive the treatment that is most likely to be effective for them.

Reference Link: https://www.remapcap.org/

9. *Randomised Evaluation of COVID-19 Therapy (RECOVERY Trial)*

RECOVERY Trial is a large-enrollment clinical trial of possible treatments for people in the United Kingdom (UK) admitted to hospital with severe COVID-19 infection. The trial was later expanded to Indonesia, Nepal and Vietnam where it initially focused on the treatments aspirin and colchicine. The trial has tested about 15 different interventions on adults and a few on kids. It was founded by the UK Research and Innovation (UKRI)'s Medical Research Council and the National Institute of Health Research (NIHR). The trial is sponsored by the University of Oxford and collaborated by other institutes, councils, and foundations.

Reference site: https://www.ukri.org/our-work/tackling-the-impact-of-covid-19/vaccines-and-teatments/recovery-trial-identifies-covid-19-treatments/ , https://clinicaltrials.gov/ct2/show/NCT04381936 , https://www.recoverytrial.net/

10. *Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV)*

ACTIV was introduced in 2020 by the National Institutes of Health (NIH) as a public-private partnership to develop a coordinated research strategy for prioritizing and speeding the development of the most promising treatments and vaccines. It is coordinated by the Foundation for the National Institutes of Health (FNIH). Activ pursuing four fast-track focus areas most ripe for opportunity. Each is led by a working group of senior scientists representing government, industry, non-profit, philanthropic, and academic organizations. The fast track areas are: Develop a collaborative, streamlined forum to identify preclinical treatments; accelerate clinical testing of the most promising vaccines and treatment; improve clinical trial capacity and effectiveness; accelerate the evaluation of vaccine candidates to enable rapid authorization or approval. Working in an unprecedented timeframe, the ACTIV public-private partnership has evaluated hundreds of available therapeutic agents with potential application for COVID-19.

Reference Site: https://www.nih.gov/research-training/medical-research-initiatives/activ , https://www.nih.gov/research-training/medical-research-initiatives/activ/covid-19-therapeutics-prioritized-testing-clinical-trials

11. *European Research and Preparedness Network for Pandemics and Emerging Infectious Diseases (EU-RESPONSE)*

The project focuses on the expansion of the DisCoVeRy trial in Europe, to test potential treatments for COVID-19. It aims to design and run a new adaptive European platform trial for emerging infectious diseases, called EU-SolidAct, thus improving Europe's responsiveness to pandemic crises. The EU-SolidAct provides a modular trial network enabling European hospitals to participate at the level of commitment that aligns with their capacity. Data collection ranges from clinical assessment parameters to PROMs and advanced biobanking. The project also includes a coordination module with the EU-funded RECOVER project, led by ECRIN, ensuring complementarity and cooperation across all large European COVID-19 Adaptive Platform trials, and their capacity to answer the needs of society through dialogue with the EMA, national competent authorities, HTAs and industry partners.

Although in the short term this project will focus on COVID-19, the mid- and long-term objectives are to build a platform trial network on emerging infectious diseases in general.

Reference Site: https://eu-response.eu/the-project/

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