

# 20 | CONCEPT 24 | NOTE

**Innovation in  
Epidemic Response**

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## Interdisciplinary Consortium for Epidemic Research (ICER)

### Executive Summary

The world is continually devastated by recurring epidemics and pandemics caused by emerging and re-emerging infectious diseases. These unpredictable and fast-moving public health threats pose substantial challenges to global, regional, and national health security, and to the patients themselves due to poor health outcomes and high case fatality. Unfortunately, limited clinical research infrastructure in low- and middle-income countries (LMICs), where epidemic-prone settings are concentrated, hinders the determination of the clinical presentations, pathophysiology, and outcomes of these infections. This, in turn, limits development of effective interventions and targeted countermeasures for prevention, control, and treatment of these pathogens, hence undesirable health outcomes during epidemics.

The high burden of infectious disease outbreaks in LMICs and the lack of effective medical countermeasures for some of these diseases, such as the most recent Ebola Sudan (SUDV) outbreak in Uganda, and the current outbreak of Marburg Virus Disease in Tanzania, underscore the urgent need for a systematic clinical research network and related resources to quickly initiate patient-oriented and translational research during an outbreak. Currently, scientists often work in silos driven by independent initiatives, which result in duplication and resource wastage.

To address this need for a coordinated response, the Interdisciplinary Consortium for Epidemics Research (ICER) proposes to bring together a network of scientists and clinicians with expertise in laboratory sciences, clinical management, product research & development, epidemiology and surveillance, and other key domains relevant to epidemic response. The aim of the consortium is to overcome the bottlenecks curtailing epidemic research and respond effectively and rapidly to current and future global health threats.

ICER proposes a frame work to be an institutionalized platform for evidence-based mitigation of outbreaks, epidemics, and pandemics. These activities will include coordination and mobilizing support and resources towards national epidemics priority research areas from local and international partners/collaborators, strengthening capacity for patient-centered epidemic research in emerging and re-emerging diseases in research entities [Institutions and Programs], developing pre-approved generic protocols to facilitate the conduct of real-time clinical trials to evaluate candidate medical counter measures [vaccines, diagnostics, therapeutics], and related priority high quality multi-site/country observational research during outbreaks and epidemics, promoting sustainable community engagement and dissemination of research findings, and contributing to the enhancement of national and international frameworks for collaborative and systematic acquisition, storage, access, sharing, use, and disposal of biodata, genomic sequencing data, and bio-specimens from outbreaks and epidemics.

In summary, the establishment of the Interdisciplinary Consortium for Epidemics Research (ICER) is critical in addressing the bottlenecks curtailing epidemic research and strengthening the global response to emerging and re-emerging infectious diseases.

### **Executive Summary: Breif Version**

The Interdisciplinary Consortium for Epidemics Research ICER is a proposed consortium aimed at addressing the lack of coordinated clinical research infrastructure in low- and middle-income countries, which hinders the development of effective interventions for epidemic-prone infections. To overcome the current limitations of independent initiatives, ICER aims to bring together a network of scientists and clinicians with expertise in various relevant domains. The consortium proposes to institutionalize a range of activities to support evidence-based mitigation of outbreaks, epidemics, and pandemics, including mobilizing support and resources, developing pre-approved protocols for clinical trials and disease epidemiology, promoting community engagement, and contributing to the enhancement of national and international frameworks for collaborative acquisition, storage, access, sharing, use, and disposal of biodata, genomic sequencing data, and bio-specimens. Overall, the establishment of ICER is critical in addressing the bottlenecks curtailing epidemic research and strengthening the global response to emerging and re-emerging infectious diseases.

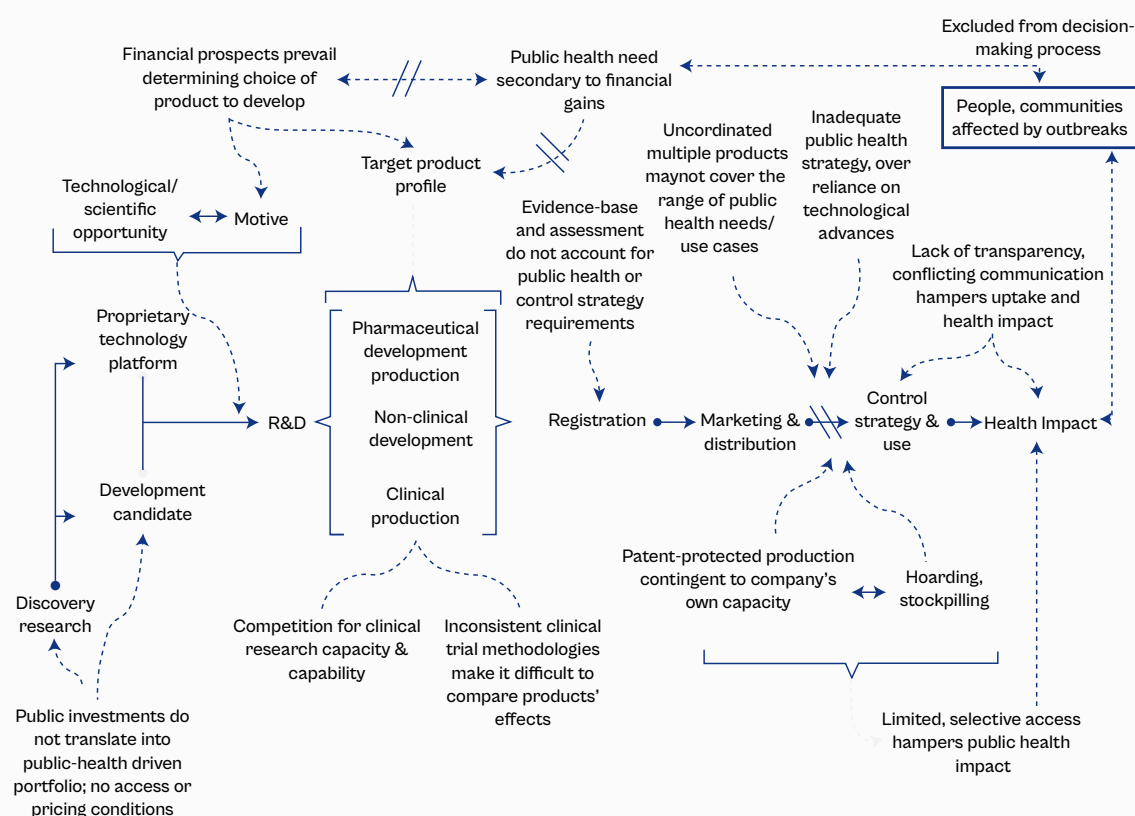




## Background: Epidemic and pandemic-prone emerging and re-emerging infectious diseases needs and challenges

Recurrent pandemics and epidemics of emerging and re-emerging infectious diseases represents an unpredictable and fast-moving public health threat that threatens global, regional and national health security. Due to limited clinical research infrastructure in low- and middle-income countries (LMICs), where epidemic-prone settings are concentrated, the determination of the clinical presentations, pathophysiology, and outcomes of emerging and re-emerging infections is poor. Furthermore, interventions and targeted countermeasures for prevention, control and treatment of these pathogens are limited.

The recurrent burden of high-consequence infectious disease outbreaks in LMICs and death of preventive and targeted treatments, has impacted significantly on containment capabilities. Uganda is currently experiencing an evolving Ebola Sudan (SUDV) outbreak for which there are no licensed therapeutics or vaccines, despite having been discovered almost 50 years ago. Although the reasons for this are many, the lack of systematic clinical research network and related resources to quickly initiate patient-oriented and translational research during an outbreak are among the most important bottlenecks. Such challenges are highlighted in [Figure 1] as practical limitations to access medical counter measures for epidemics response in absence of preparedness systems.



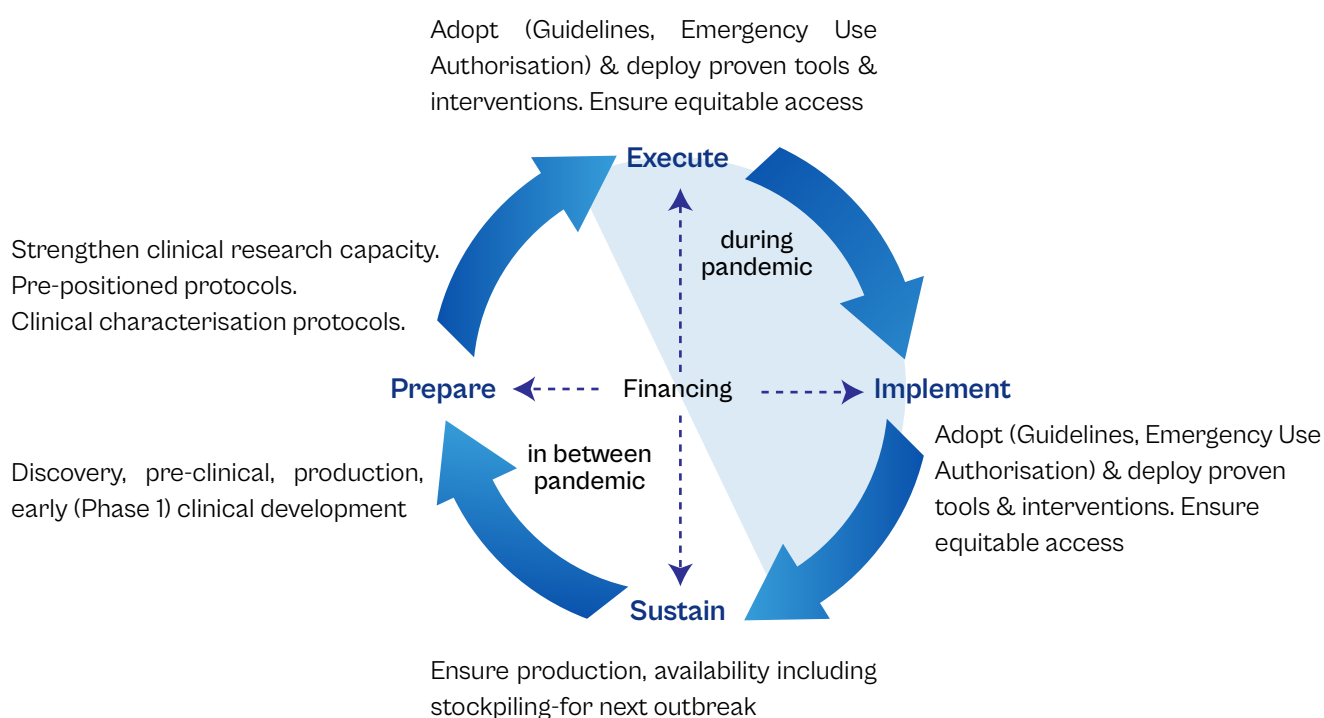
**Figure 1:**  
Critical disruptions at main steps in product development and use conspiring against mounting an effective epidemic response system.

Strengthening and implementing research capabilities, especially during outbreaks are critical for containing the outbreak, including, preparedness, response, and possibly revisions in treatment protocols to optimize patient care in real-time, inform clinical trial protocols, and identify at risk groups for early intervention<sup>1-2</sup>.

Scientists often work in silos driven by independent initiatives which do not augur for national priority-driven research activities, which are often compounded by limited funding. This often results in duplication and resource wastage.

In context, there is urgent need for scientists locally and internationally to synergize and avail solutions to challenges that perpetually impede epidemic response research. In light of recurrent epidemics of emerging and re-emerging infectious diseases, establishment of interdisciplinary clinical research networks to mobilize and coordinate related financing mechanisms [Figure 2] is essential to facilitate implementation of high quality observational and interventional studies before and during epidemics<sup>3</sup>.

**Figure 2: Building a global research and response architecture for infectious disease epidemic**



Directly addressing this critical need, the Interdisciplinary Consortium for Epidemics Research (ICER) is envisaged to bring together and coordinate a network of scientists and clinicians experienced in key domains relevant to epidemic response that include laboratory based sciences, clinical management, product development and research, intervention and surveillance, to overcome the bottlenecks (Figure 1) curtailing epidemic research in order to respond effectively and rapidly to current and future global health threats.

## Rationale

Despite the recurring and diverse nature of emerging and re-emerging infectious disease pandemics and epidemics, resources and research programs focused on epidemic research and development (R&D) of effective countermeasures, including vaccines, diagnostics, drugs, and therapeutics, are limited in sub-Saharan Africa, which remains a global hotspot for high impact infectious disease epidemics due to high consequence pathogens, such as summarized in [Fig 7]. The under developed health care system in the region is overwhelmed hence exacerbate poor health outcomes of these outbreaks and highlight the need for a sustainable preparedness and research framework to contribute to response strategies for rapid detection, containment, and control of ongoing and future epidemics due to pathogen x.

In 2005, the World Health Organization (WHO) and UN member states developed the International Health Regulations (IHR) to promote health security and enable public health authorities to detect and respond to emergencies rapidly. However, several African countries have not met these requirements, as assessed through the WHO-led joint external evaluations (JEE) developed to strengthen preparedness and response to pathogens of public health significance. During epidemics, current surveillance and response approaches become overwhelmed besides omit critical aspects of active surveillance, rapid assessment, and clinical management, including implementation of approved countermeasures to contain epidemics and prioritize patient outcomes.

Relatedly, the lack of robust molecular surveillance and monitoring of antigenic evolution of mutant pathogens in LMICs also challenges the assessment of the effectiveness of countermeasures such as vaccines and monoclonal antibodies. While cutting-edge and rapid genome sequencing platforms and related bioinformatics capacity are increasingly available in LMICs, most research has focused predominantly on the specific pathogen. Adding host genomics could provide critical information on pathogens with pandemic-prone properties within specific populations.

Additionally, there is a notable absence of adaptive clinical trial capacity to rapidly evaluate counter interventions, especially of un-licensed therapeutics, therapeutic antibodies, and vaccines, to inform the ongoing pandemic response. Despite several research entities [Institutions and Organizations] in Uganda locally and internationally involved in surveillance and response, the scope of work often excludes critical aspects for a comprehensive response. We propose to leverage Uganda's and of Makerere Lung Institute's (MLI), substantial capacity, and expertise developed through previous outbreaks including most recent due to COVID-19 and EVD outbreak research, to champion the development of an interdisciplinary multi-country integrated research platform incorporating critical disciplines and partners aimed at enhancing and providing real-time scientific evidence to enhance epidemic response thereby contributing to African health security strategies.

**Mission:**

To support research entities [institutions, agencies, and governments] to maintain, improve, and sustain the health of the people through development of evidence-based countermeasures for rapid prevention, detection, and response to emerging and re-emerging diseases of epidemic-pandemic potential.

**Vision:**

Research is an integral part of epidemic preparedness and response

**Aim:**

To rapidly and efficiently generate and disseminate research evidence before, during, and after emerging and re-emerging infectious diseases epidemics

**Goal:**

ICER's goal is to foster interdisciplinary research collaboration to enable rapid infectious diseases epidemic detection, containment, and optimized clinical care delivery that will inform policies to improve health outcomes.

**Five Years Objectives**

Contingent upon political/governments approvals and the requisite funding, the consortium proposes the following activities objectified towards institutionalizing ICER as a platform for evidence-based mitigation of outbreaks, epidemics and pandemics.

- Mobilize support and resources towards national epidemics priority research areas from local and international partners/collaborators, and coordinate funding proposal submissions on epidemics research from consortium members.
- Strengthen capacity for patient centered epidemic response-research in emerging and re-emerging diseases at institutional levels
- Support development of pre-approved generic protocols to facilitate the conduct of real-time clinical trials to evaluate candidate vaccines, diagnostics, therapeutics and related priority research during outbreaks and epidemics
- Promote sustainable community engagement and dissemination of research findings and tailored information products to various stakeholders for improved understanding, acceptance, and awareness of research during outbreaks and epidemics
- Contribute to and facilitate the enhancement of national and international frameworks for collaborative and systematic acquisition, storage, access, sharing, use, and disposal of biodata, genomic sequencing data, and bio-specimens from outbreaks and epidemics

## **ICER Capacities and Current Approaches for Epidemics Research in Context of Epidemics in Uganda**

ICER, as a semi-autonomous inter-government entity in formation, is coordinating partners across agencies and departments locally and internationally to conduct Ebola Virus Disease [EVD] epidemic research in Uganda. These partners bring diverse expertise, resources, and capacities to support ICER's efforts to strengthen preparedness and response to current EVD outbreaks including for future emerging and re-emerging infectious diseases.

The Ministry of Health Uganda in collaboration with local and international partners who include Uganda Virus Research Institute (UVRI), Baylor College of Medicine Children's Foundation-Uganda, Infectious Diseases Institute (IDI), CDC, Makerere University Walter Reed Project, Makerere University College of Health Sciences (MakCHS), Africa Centers for Disease Control and Prevention (AfCDC), the World Health Organization (WHO), the Centers for Research in Emerging Infectious Diseases - East and Central Africa (CREID), have together provided technical support, capacity building, funding, and international standards for the EVD epidemic research. Through such collective efforts of inter-government agencies, academic institutions, and research entities, Uganda and Africa at large has demonstrated abilities to strengthen epidemic research capabilities of potential to respond effectively to current and future emerging and re-emerging infectious diseases. These research entities have a wealth of experience in epidemic response, including clinical management, surveillance, and laboratory science, and will continue to play a critical role in capacity building for patient-centered epidemic response and research.

In consideration of success through this pilot initiatives, additional inter-governmental/ MOH implementing partners that include Makerere Joint Aids Program (MJAP), Makerere University Johns Hopkins University (MU-JHU) research collaboration, and Uganda-Case Western Reserve University Research Collaboration, Ministry of Science, Technology and Innovation Uganda, Ministry of Agriculture, Animal, and Fisheries (MAAIF), Uganda National Drug Authority (NDA), Uganda Chemotherapeutic Institute, Uganda National Council of Science and Technology (UNCST), Uganda National Health Research Organization (UNHRO), and Joint Clinical Research Centre (JCRC), World Bank, AFINET, are all other, with unique capacities to epidemic response that contribute to the one-health global agenda, are potential partners into this consortium. They will support ICER's efforts to formally institutionalize the Uganda platform site for evidence-based mitigation of outbreaks, epidemics, and pandemics by mobilizing support and resources towards national epidemic priority research.

### **Pre-Outbreak and Inter-Epidemic Activities**

- Develop a framework for strategic partnerships with Government institutions, academia, and private sector entities in Uganda.
- Engage with social scientists to complement the proposed clinical research before and during outbreaks. This will provide an entry for community participation especially for trials for

therapeutic interventions.

- Initiate a rapid assessment of institutional capacities for pathogen detection and characterization.
- Assess active disease surveillance capabilities within national institutions.
- Determine national-level capacities for genomic surveillance to establish disease trajectories with respect to sources and sinks, and the emergence of variants.
- Review available countermeasures and prioritize interventions for clinical assessment for safety and efficacy.
- Conduct timely epidemiological and clinical research while ensuring timely lab/field-to-bedside implementation of the recommendations for (re-)emerging and epidemic-prone infectious diseases. Explore institutional collaboration with entities in the public and private sectors in the East African sub-region. This may be achieved through linkages with the Africa CDC Regional Collaborating Centers (RCCs) and its network of quality assured laboratories within the Regional Integrated Surveillance and Laboratory Networks (RISLNET).
- Develop platforms for dissemination of scientific findings on epidemics to policymakers and the general public during emergency disease outbreaks that utilize professional networks, social networks, and public access mechanisms.
- Establish a comprehensive training program and framework focused on strengthening the conduct of adaptive clinical trials for evidence-based health innovation, intervention, and policy for epidemic and pandemic response.
- Develop a framework for fast-tracking development, approval, and implementation of research protocols on epidemics.
- Mobilize support and resources towards national epidemics priority research areas from local and international partners/collaborators, and coordinate funding proposal submissions on epidemics research from consortium members.
- Develop and implement a framework for the collection of critical data along with security protocols, and institute a centralized database with stratified access by collaborating institutions.

### **Intra-Epidemic and Outbreak Activities**

- Develop information packages to inform communities about the necessity for research to provide evidence for outbreak mitigation.
- Implement appropriate social sciences research to inform appropriate sociocultural sensitive



engagements with communities.

- Strengthen supply chains and logistics to optimize research activities.
- Engage health care workers to assist with research activities.
- Sensitize ethics review committees and regulators to the importance of expedited protocol review. This may be achieved by extending an invitation to serve as members of ICER to the concerned.
- Seek and implement community engagement and response before and during the initiation of research activities.
- Collect samples to support future target identification for new therapeutics, vaccines, and diagnostics. Implement ongoing bio-specimen repositories with well curated information to promote and enable future use of data.

### **Intra-Epidemic and Outbreak Activities**

Priority ICER membership is open to Ministries of Health and its implementing partners operating in the epidemic prone African countries. As such, the focus is funding agencies, research regulators, and research entities [Research Institutions and MoH IPs] with track record in epidemics research. ICER will initially be registered in Uganda as a not-for-profit consortium promoted by membership organizations operating in Uganda. Subsequently it may be registered in other countries if need arises for its operations in those countries.

ICER's strategic leadership and coordination will be overseen by an Independent Advisory Board of Directors supervised by Ministers of Health in respective countries. Day-to-day management will be undertaken by its Secretariat. The Board will have a Chair and Co-Chair. To ensure stable coordinated planning, implementation and sustainable funding, ICER executive secretariat will be headed by a Director, a Deputy Director; core structures will include a Grants and Finance Administrator, a Research and Regulation Expert, an Implementation Science Field Epidemiologist, a Clinical Care Physician, and Advocacy Risk-Communications Community Engagement Coordinator. At the national level, in the region and internationally, the secretariat will:

- I) Mobilize resources to facilitate and strengthen partner local and international collaborations to realize contingency research and preparedness financing for collective actions, and mutual coordinated epidemic response
- II) Advocate for collective epidemics research to strengthen strategic operational coordinated leadership and partnerships
- III) Promote collective epidemics research platform for real-time collaborative engagement to

co-generate policy-relevant evidence to inform decision making to support response

- IV) Jointly promote individual, collective and community equity-informed responses and enhance contextualized specific, acceptable and appropriate governments' research priorities for clinical case management capacities during rapid response
- V) Promote integration of collective epidemics research into on-going activities to effectively respond to epidemics

Based in Uganda, the Secretariat's Director will also be the secretary to the ICER's Independent Advisory Board of Directors. The Board will provide leadership, strategic direction, and guidance on priority research questions that ICER will address, as well as recommend individual experts from academia, industry, government, and non-government organizations to the different ICER implementation fora. The Board will rotate its leadership and membership from among participating Government Ministries of Health within the region and its partners.

**Figure 3: ICER's governance and collaboration framework adopted from the WHO HEPR ecosystem<sup>4</sup>**



## ICER's Strategic Approaches

### (1) ICER's Component on Political and Policy Support Partnerships

**(1.i ) Collaborations:** In consideration of the ICER framework [Figure 3] adopted from the Health Emergency Preparedness and Response [HEPR]-World Health Organization, collaborations with Government partners involved in health care, research, surveillance and those involved in research development of medical counter measures, and respective funding, regulators, and ministries of health leadership, in respective countries in preparing and responding to outbreak and epidemics by offering a one-health wide range of services including scientific and technical support, project

management, initiation, and design; networking, are planned in order for ICER to enhance coordination for epidemics Research Development [R&D] and Implementation Science, primarily to expedite access to epidemic medical counter measures for epidemics response, not limited to;

- I) New therapeutics, vaccines, medicines and diagnostics for use in epidemics
- II) Point of care diagnostics for timely and accurate diagnosis to avert community transmission
- III) Surge health workforce capacities to participate in integrated clinical care and research, and [iv] A collaborative one-health research platform

**To do this, ICER will:**

**(a) Map institutional resource strengths for broad connections, coordination and engagements:**

Through a consultative process, develop an inventory of scientists in global regional initiatives, product development, specialized projects, and specialized institutions actively engaged in epidemic control (national, sub-regional, and global) including those involved in routine clinical care, disease surveillance and preparedness, for shared roles and functions to implement relevant countermeasures. Stakeholder mapping, engagement, re-distributing/sharing of core outbreak response-research roles and functions will be essential for ICER's planning, and execution will progressively be integrated on an on-going basis. This will assist in developing a compendium of sustainable capabilities in partner Government health partners and institutions. Relatedly, identified gaps will inform current and future priority funding areas and also help understand potential funding sources, while observing a stepwise adoption of implementation into government planning and financing systems as external funding gradually reduces.

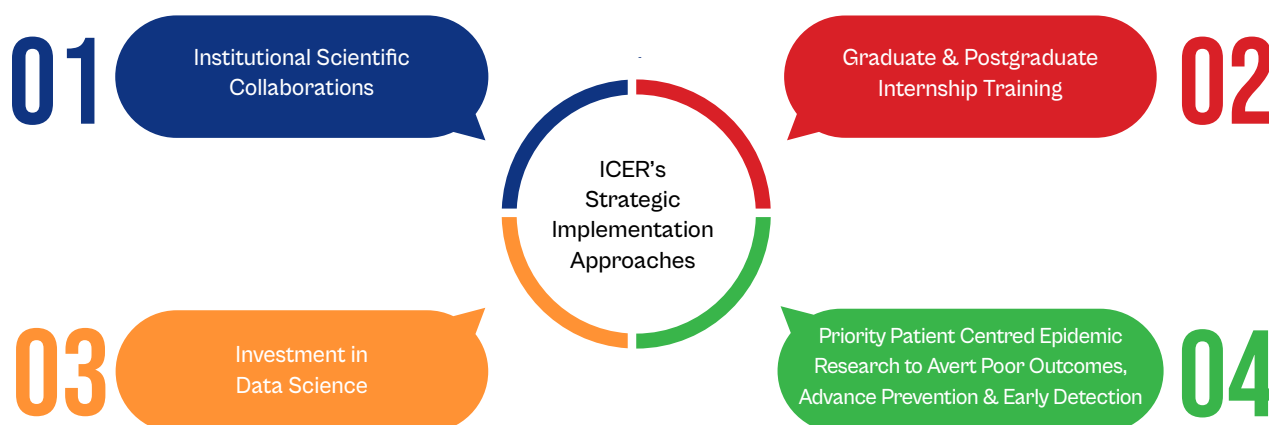
**(b) Collaborations and community engagement:** Build on existing strategic partnerships to reach out to other potential collaborators. In Uganda for example, the role of the Military in disease surveillance and response is key as was seen in COVID-19 and now Ebola. Having collaborated with them on COVID-19 health projects, we shall further strengthen this collaboration while using the same link to bring on board other security organs.

**(c) Collaborations with health care practicing professionals:** Through on-going research on priority endemic outbreak prone diseases, support and promote clinicians involved in routine patient care through mentorships to establish surge capacity in clinical and supportive care of patients for future outbreak-epidemics.

**(d) Resource mobilization, financing and accountability:** Contingency/surge and on-going human and financial resources will be needed to sustainably execute ICER's project objectives. A working group will be convened to source for potential funding, develop fundable outbreak response-research proposals with special focus on those that promote clinical care and enhance disease burden countermeasures. These will include Requests for Proposals as well as galvanizing support from stakeholders and partners to allocate or increase finances for ICER in their health budgets.

**(e) Policy, and regulation on Fast-tracking outbreak-epidemics research protocol approvals:** In collaboration with the Uganda National Council for Science and Technology, NDA, WHO, ICER will develop a public-private platform for fast-tracking ethics regulatory approvals, and implementation of mechanisms for adapting operating procedures for research on outbreaks-epidemics and re-emerging diseases with special focus on clinical trials for potential new and especially unlicensed therapeutics, medicines and vaccines. In addition, obtain approval for ICER to function as an interdependent platform to inform relevant regulatory, ethics, and policy frameworks.

**(f) Leadership:** Serve as a secretariat to coordinate day-to-day operations, including meetings, workshops, and events in support of strengthened strategic partnerships and alliances at sub-national, national, regional and international levels in outbreaks-epidemics diseases research, prevention, mitigation, health promotion and education.



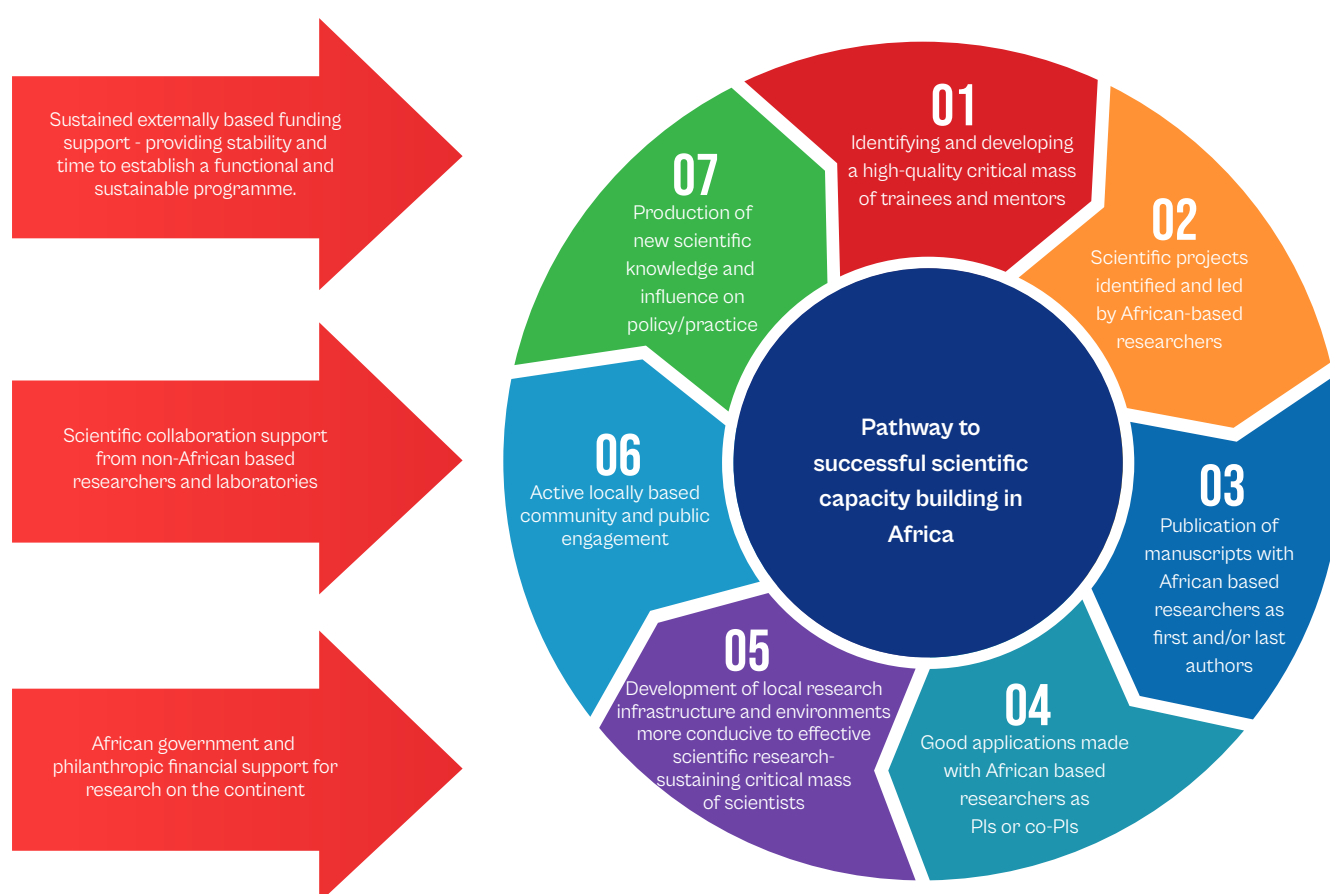
**Figure 4:** ICER's strategic implementation approaches adopted from the NIH-Wide Strategic Plan for COVID-19 priority research

**(1 ii) Sustainable health professionals' training program for enhanced workforce for outbreak surge capacity :** Leveraged from the sustainability model (Figure 5), through training fellowships targeted for health care graduate and postgraduate internship mentees, ICER shall develop outbreak research curriculum and provide a Regional Clinician-Scientists Hospital-Based Facilitated [CHFPM] Peer Mentored program built on-going research during inter-outbreak-epidemic phase. The peer mentoring will be a research specialist led program in university teaching hospitals, focused on research-in-progress.

Real-time patient-centered epidemic research curriculum domains will include (a) non-pharmacologic supportive patient care, (b) patient values/preferences and evidence-based care, (c) access and equity to bedside interventions, (d) Relevance of epidemic research to patients and factors Influencing Patient-Centered Care in the Primary Health Care during epidemics. Such will be delivered through webinars, seminars, hybrid didactic lectures, and in-person peer exchange engagements.

Besides the support to fellowship mentees' research academic requirements through supervised on-job mentorship by research experts, and importantly offering opportunities for academic thesis proposal development and execution, such will provide technical support and suitable environment for networking and skills development.

Importantly, this will create a pool of expert clinicians [medical doctors and nurses] from academic. This will create a pool of independent expert clinicians [medical doctors and nurses] from academic training institutions eligible for entry into public and private in-service at different levels of the Ugandan health care system. The pool of a young generation of expert clinician-scientists from the clinical arm will also have the skills to undertake design and implement research to inform response when outbreaks strike. The training of young scientists to become independent scientists to undertake integrated outbreak response research, will require formal engagement with Ministry of Education, MOH, and Universities.



**Figure 5:** ICER sustainable health professionals training strategy for enhanced outbreak surge capacity

**(1 iii) Data science, knowledge management and sharing to inform public health policy:** Open and timely sharing of essential minimum outbreak response research pathogen, genomic and burden related data needs to be publicly available to National, Regional and Global platforms to inform current status, gaps and desired actions. Establish data linkage frameworks and agreements to

enable safe access to facilitate pooled analysis for improved monitoring of disease burden and the success of interventions rapidly and precisely.

## 2 (I) Icers's Component On Technical Strategies To Generate Research Evidence Through Priority Patient Centered Integrated Epidemic Research (Fig 4-(IV))

Coordinate the implementation of research to generate and disseminate clinical evidence whenever and wherever outbreak prone infectious diseases occur. During an on-going disease transmission, integrate patient centered outbreak-epidemic research and development [R&D] into response, primarily to mitigate mortality and morbidity through [a] development and implementation of participatory improvement of quality clinical practices across the continuum of standard of care and continuum of infection cycle [b] contribute to improvement of evidence-based guidelines, [c] provision of on-job mentorship and experiential learning from clinicians, and [d] publications.

## 2 [Ii] ICER's Framework for Pilot Priority Research Agenda

Worldwide, the diversity of [re]emerging priority pathogens either associated with on-going outbreaks-epidemic, or endemic disease, or caused previous outbreak-epidemics, is driving increased potential to cause future health threats. To ensure that ICER's efforts are targeted and productively relevant, the initial focus will be on public health concerns in Uganda and the East African sub-region to ensure public health impact and buy-in. For differentiated pathogen specific outbreak-epidemic, ICER Priority pathogens associated with emerging infectious diseases adopted from Centers for Research on Emerging Infectious Diseases [CREID], examples of these to include: Ebola virus disease, COVID-19, Monkey poxvirus disease, Crimean-Congo hemorrhagic fever, Marburg virus disease, Lassa fever, Nipah and henipaviral diseases, Rift Valley Fever Virus, Zika Middle East respiratory syndrome coronavirus (MERS-CoV) and severe acute respiratory syndrome (SARS). In this regard, ICER will advance epidemics landscape encompassing development of pre-approved master protocols on themes indicated in table 1 to serve both inter and intra epidemic research.

|    | Studies                                                                                                              | Syndromes                               |
|----|----------------------------------------------------------------------------------------------------------------------|-----------------------------------------|
| 1. | Clinical-immunologic characterization of disease progression, outcomes and recovery                                  | ARI/SARI                                |
| 2. | Ecological studies to determine source of infection                                                                  | EVD                                     |
| 3. | Determine mechanisms of pathogen human to human transmission                                                         | Neurologic                              |
| 4. | Socio-cultural studies to assess community impact and public health messaging                                        | Un-differentiated Acute Febrile Illness |
| 5. | Clinical chemistry, hematology and other laboratory profiles in predicting outcome and managing infected individuals | All                                     |

**Table 1:** : Suggested thematic protocols non-pathogen specific



Relatedly, pre-approved protocols designed as perpetual observational studies will provide a firm foundation for the conduct of quality research on disease burden associated with diseases due to prevalent priority pathogens of known pandemic and or epidemic threat to inform policy, and would as well in real-time offer established broad-based capacities and platforms to rapidly implement outbreak response research [clinical trials, predictors of severe disease outcomes, therapeutic effectiveness, and diagnostic performance, incidence estimates etc.] when an outbreak strikes.

## **2 (iii) ICER's Implementation Plans will Include:**

- I) To valuate new or repurpose existing therapies/vaccines and define implementation strategies
- II) To characterize clinical-immunology of disease progression, outcomes and recovery
- III) To advance pathogen genomics for enhanced early and accurate diagnosis and variant tracking
- IV) To accelerate research and develop implementation models to prevent transmission
- V) Prevent and redress undesirable outcomes in health disparity and vulnerable populations

## **Research Questions Related to Transmission**

- 1) Is there transmission that is sub-clinical (asymptomatic transmission)?
- 2) What happens in the first day or two of being symptomatic?
- 3) What is the viral load during different phases of EVD?
- 4) Detailed studies of potential household transmission
- 5) Environment and behavior
- 6) Detailed case study of domestic cases
- 7) What can be learned from epidemiological data from West African EBV outbreak (2014-16), natural history studies of viral shedding?
- 8) What are surrogates of transmission that can be traced through bodily fluids to detect infection prior to presenting symptoms?
- 9) Modes of transmission: Is EVD an aerosol-spread disease?
- 10) What is the potential for the virus to be aerosolized?
- 11) Does the potential for aerosol transmission vary depending on the viral load and how the viral load may have changed in comparison to previous outbreaks?
- 12) What potential does genetic modification of the virus have on the potential for aerosolized transmission?
- 13) What is the difference in risk to a patient if exposed to airborne particles versus aerosol droplets versus fomites?

- 14) What is appropriate handling of deceased bodies?
- 15) Maintenance of virus in bodily fluids
- 16) What are the surrogates for transmission through bodily fluids?
- 17) Introduction into intermediate hosts or vectors for transmission
- 18) Can agricultural animals (e.g., pigs and their bedding) act as an intermediate host and vector of transmission?
- 19) Companion animals: What are the data on different identified hosts?
- 20) Can dogs and cats act as intermediate hosts, harboring virus on or within their fur, that might be transmitted to other individuals who come in contact with those animals?
- 21) How long would the virus survive on the external surface of a dog or cat?
- 22) What are co-factors that could impact transmissibility or susceptibility of populations?
- 23) Are all contacts equally likely to lead to transmission?
- 24) Could immune function affect shedding/susceptibility (HIV& co-infections & morbidities)?
- 25) Can sub-populations (e.g., mentally ill, homeless) & their behaviors impact transmission rates?
- 26) Are the dynamics of transmission different in pregnant women and children?
- 27) What is the role of the placenta, in utero infection?
- 28) Can genetic sequencing of samples enable the tracking of variants, and can this strategy be decentralized?

### **Research Questions Related to Survival and Infectivity of the Ebola Virus**

- 1) Define the relationship between symptoms, viral load, and infectivity (spectrum of illness)
- 2) What is the level of virus in different body fluids/tissues over time?
- 3) Does the virus contaminate the environment and/or spread by fomites? Laboratory equipment, PPE, Household surfaces, Wastewater, Hospital and other clinical points of entry
- 4) What is the efficiency/limitation of current sampling methods?
- 5) Sensitivity and specificity
- 6) What is the definitive incubation period?
- 7) Does the incubation period vary with infectious dose and/or route and/or tissue source of exposure?
- 8) How can the Ebola virus be rendered noninfectious?

## Research Questions Related to Personal Protective Equipment and Behaviors

- 1) Approach to evaluating system in which personal protective equipment and behaviors are embedded (e.g., training, competency assessment, hazard analysis, debriefing, medical)
- 2) Identify innovative approaches to the hierarchy of controls
- 3) What is the best way to optimize the PPE supply chain in real time?
- 4) How can predictive modeling assist in resource allocation?
- 5) How can methods of evaluating PPE be improved based on risk stratification?
- 6) Studies of work processes and practice
- 7) What design changes can be made to identify or develop PPE that is usable and effective in a range of temperatures or that is specifically designed to meet the needs of one temperature extreme, such as high temperature climates?
- 8) Determine and explore the data on health care worker fatigue (physical, mental, and social)
- 9) What are the testing methods for products originally designed and approved to be used separately but that in practice are used in combination as an ensemble?
- 10) What is the transparency level of the evidence base for PPE effectiveness?
- 11) Assess the functional utility of PPE and behavior effectiveness and tolerability
- 12) Assess PPE design: What are the appropriate standards for apparel and equipment considering safety, performance, and usability?
- 13) Can participatory research involving end-users and designers/manufacturers be used in assessment?
- 14) What is the sustainability and ease of use over time?
- 15) What is the user compliance level?
- 16) Targeted and risk-based training
- 17) Identify and evaluate the training needs of health care workers and others
- 18) How much training/education? What training, for what staff, with what risk, and how often?
- 19) Identify effective educational methods

## Research Questions Related to Waste Handling and Management

- 1) Safe decontamination practices
- 2) Is there a methodology that can be applied for performance of consistent sampling & analysis?
- 3) How clean is clean; how can safety be assured?
- 4) What alternative disinfectants are available for use, and what decontamination solution type (liquid, foam, or gas) is best?
- 5) Studies of work processes and practice
- 6) What is the optimized amount of contact time?
- 7) What is the occupational health exposure for those performing the decontamination process, and is it safe?
- 8) Validation of virus inactivation
- 9) What is a surrogate that can be used to study effectiveness of decontamination?
- 10) What are the effects of decontamination on other products in a facility, especially PPE?
- 11) Fatality and cadaver management
- 12) How infectious are dead bodies, and how is viral persistence determined?
- 13) How can impermeable body bags be developed at a low cost?
- 14) Training to an operational level of competence
- 15) How can we evaluate effectiveness of existing training, content, and modalities for different occupational settings?
- 16) To manage an Ebola patient in a community, what role does a process tool play in improving response?
- 17) Could a standard tool help guide communities so responses both inside and outside the hospital are fair and equitable to all affected?

## Research Questions Related to Survival and Infectivity of the Ebola Virus

- 1) What is the safety and efficacy of candidate drugs and vaccines (including herbal compounds) for treatment of EVD?
- 2) Can combination or regimen approach improve outcomes?
- 3) What are the bottlenecks in the drug discovery for epidemic diseases?

## (2iv) Ebola Virus Disease, Priority Filovirus Research Questions and Planned Studies

After formally constituting ICER, members of the team will develop national priority areas of research with regards to EBV prevention, treatment, and rehabilitation of EVD survivors as guided by the Ministry of Science, Technology and Innovation, and the Scientific Advisory Committee of the Ministry of Health. Examples of critical areas of research regarding EBV include transmission, survival and infectivity, personal protective equipment and behaviors, and waste handling and management.

Hence and in consideration of the current EVD SUD outbreak in Uganda, there are no licensed vaccines or therapeutics for the prevention and treatment of associated disease, however patients only receive supportive care and treatment of specific symptoms with variable outcomes. Through collaboration with CREID-ECA, MOH partners [JMEDDIC, IDI, Baylor, and others], Africa CDC, ICER will investigate the following specific objectives under study theme summary in Table 2;

**Objective 1:** To characterize host immune responses to Ebola infection, therapy, and vaccination to define responses associated with protection, reduced disease, clearance of virus, and long-term post-EVD sequelae.

**Objective 2:** To investigate the cellular and molecular determinants of Ebola disease severity and outcome using advanced genomic studies (nascent transcriptomics).

**Objective 3:** To conduct seroprevalence studies to determine the burden of Ebola infection among asymptomatic contacts of EVD patients in the affected areas.

**Objective 4:** Model periodic occurrence and transmissibility of Ebola virus within the community.

**Objective 5:** Characterize clinical chemistry, hematology and other laboratory profiles in predicting outcome and managing infected individuals.

| Study Themes |                                                                                                                                        |
|--------------|----------------------------------------------------------------------------------------------------------------------------------------|
| 1.           | Point-of-care diagnostics to improve turn-around time - pilot combination algorithms as used in HIV to enhance sensitivity/specificity |
| 2.           | Immune response and other factors that determine severe disease and clinical outcome                                                   |
| 3.           | Post-mortem and survivor follow-up study to investigate persistence and relapse                                                        |
| 4.           | Ecological study to identify reservoir                                                                                                 |
| 5.           | Transmission of EBOV from asymptomatic infections                                                                                      |
| 5.           | Intervention studies - vaccine & therapeutic development and trials                                                                    |

|    | Study Themes                                                                                                                                   |
|----|------------------------------------------------------------------------------------------------------------------------------------------------|
| 7. | Real-time genotype and phenotypic to monitor community disease burden and assess effectiveness of interventions-vaccines and Monoclonal (Mabs) |
| 8. | Social cultural studies to assess community impact and public health messaging                                                                 |

*Table 2: Suggested thematic protocols based on EVD research priorities*

<sup>1</sup>Heyman DL et al 2016. Partnerships not parachutists for Zika research. New England Journal of Medicine 374(16):1504-1505

<sup>2</sup>Lurie NT et al 2013. Research as part of public health emergency response. New England Journal of Medicine 368(13):1251-1255

<sup>3</sup>N. Hassoun-Kheir et al. / Clinical Microbiology and Infection 28 (2022) 1528e1532

<sup>4</sup>Strengthening the Global Architecture for Health Emergency Preparedness, Response and Resilience; World Health Organization March 24th 2022

<sup>5</sup>NIH-Wide Strategic Plan for COVID-19 Research

