ADDIS ABABA UNIVERSITY, COLLEGE OF HEALTH SCIENCES, CENTER FOR INNOVATIVE DRUG DEVELOPMENT AND THERAPEUTICT TRIALS FOR AFRICA

ASSESSMENT OF CAPACITY FOR CONDUCTING DRUG TRIALS IN ETHIOPIA: A CROSS-SECTIONAL SITUATION ANALYSIS

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ADDIS ABABA, ETHIOPIA
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Declaration and Recommendation

Declaration

This thesis is my original work and has not been presented for a degree in any other University.

Signature:  ……Date: …….

Aliyi Amano

Recommendation

This thesis has been prepared and submitted with our approval as University Supervisors.

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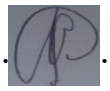
Signature:……  ……Date:……

Girmay Medhin (PhD)

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Abstract

Background: Several development organizations have argued that clinical trials (CTs) in LMICs are crucial for advancing public health and development. In order to ensure that clinical trials facilities (CTFs) can respond to this demand, it is vital that a country has sufficient capacity in various aspects including infrastructure to conduct CTs. Despite, different capacity challenges that affecting research systems in LMICs have been recognized; substantial amount of this evidence is inferred from experiences with specific institutions or programmes and does not build on systematic baseline data and conceptual frameworks. Furthermore, CTs funders are increasingly looking for evidence that investigators are linked to CTFs with sufficient expertise and infrastructure, so it is critical that the prevailing capacity of this resource is assessed and the need for any further capacity strengthening is identified.

Objective: To assess existing capacity of conducting clinical trials, perceived gaps and prioritiesfor capacity strengthening for CTFs in Ethiopia.

Methods: An institutional-based cross-sectional situational analysis was carried out using mixedmethods approaches: online semi-structured interviews with key informants, document review, and an email-based, self-administered checklist of key domains of CTs infrastructure and capacity. The data was collected from September-November 2020. Descriptive statistical methods were used to summarize quantitative data. Qualitative data were transcribed verbatim and analyzed using a framework approach. NVivo software version 12 (QSR International Pty Ltd.) was used to manage qualitative data Findings from quantitative and qualitative study components were triangulated.

Results: Of the 27 CTFs currently conducting drug trials in Ethiopia, 13 (48% response rate) responded to at least one assessment, 7 responded to both assessments, 3 responded only to the quantitative questionnaire and 3 responded only to qualitative interview. The results from the 10 CTFs who responded to the quantitative assessment indicated that they had 159 staff linked to the CTF, comprising 112 (70.4%) of the scientific staff and 47 (29.6%) support staff. Among the10 leading causes of death in Ethiopia, only two were included in the trial portfolio of the CTFs. A total of 35 CTs had been conducted in the 10 CTFs, with 46% of these being locally developed protocols and phase III trials. Two CTFs reported ownership of research laboratory and data management units with external certification. Onsite monitoring was used by most CTFs, but the indicators that were monitored varied across the CTFs. Synthesis of nine key informant interviews highlighted the current capacity challenges, identified priority areas to develop capacity and the factors affectingavailability of CTF funds and the sustainability of CTFs infrastructure.

Conclusions: This study has identified that Ethiopian CTFs have limited capacity to conduct CTs due to a lack of physical infrastructure, workforce, CTs experiences, and data management, as well as a lack of institutional structures to support CTs at various levels. Furthermore, a number of priority areas for capacity development have been identified, calling for a coordinated effort of different stakeholders and funders.

Key words: Capacity, Capacity Assessment, Clinical trials, Good Clinical Practice, Clinical trials facility.

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ACRONMYS/ABBREVIATIONS

AAU:	Addis Ababa University
AHRI:	Armauer Hansen Research Institute
CTFs:	Clinical Trials Facilities
CTs:	Clinical Trials
CDMS:	Clinical Data Management Systems
DM:	Data Management
ECRIN:	European Clinical Research Infrastructure Network
EBTi:	Ethiopian Biotechnology Institute
EFDA:	Ethiopian Food and Drug Administration
GCP:	Good Clinical Practice
GCLP:	Good Clinical Laboratory Practice
UOG:	University Of Gonder
JU:	Jimma University
ICTRP:	International Clinical Trials Registry Platform
IVTF:	International Vaccine Task Force
LMICs:	Low and middle income countries
MoH:	Ministry of Health
MiNT:	Ministry of Innovation and Technology
RCT:	Randomized Control Trials
WHO:	World health Organization

1. Introduction

1.1. Background

A clinical trial is any clinical research study in which human participants or teams of humans are randomly allocated to one or more health-related interventions and prospectively followed to assess the effect of the interventions on health outcomes (1). Clinical trials may also be described as interventional trials (2). Interventions can include medication, surgical procedures, cells and alternative biological products, radiological procedures, devices, process-of-care variations, behavioral treatments and preventive care (1,3).

Randomized clinical trials (RCTs) embarks on elements of randomization and masking of different parties (4). This allows investigators to have control over the intervention assignment to participants. This control helps to minimize a number of potential biases that are challenges of observational studies. Consequently, findings from RCTs have higher validity as compared to findings from other study designs. For this reason, a well-designed clinical trial is considered as the gold standard design for clinical study planned to evaluate the safety and effectiveness of an intervention (5). In other words, evidences generated from carefully conducted clinical trials are considered as the most reliable to improve and advance medical science and public health (3,6).

As part of medical research, clinical trials have been acknowledged to play a key role in progress towards the Sustainable Development Goals (7). Specifically, in part 9.5 of the SDGs the following targets are to be achieved by the end of 2030: encouraging innovation and substantially increasing the number of research and development workers per 1 million people and public and private research and development spending (8). To achieve these targets, it is necessary to have the required capacity in terms of relevant infrastructures that can support clinical trials. Unfortunately, this capacity may be limited in low- and middle-income countries (LMICs), where the health needs are greatest (9–11). In LMICs, the limited level of economic resource means that development of capacity to conduct clinical trials mostly depends on foreign aid. This situation means that LMICs currently have little control over the development of capacity to generate high quality trial evidence to address their priority health needs (11,12).

Funders and/or sponsors of clinical trials are increasingly looking for evidence that investigators in LMICs are linked to a clinical trials facility of sufficient expertise and other infrastructures

vital for or clinical trials and have also involved clinical trials facilities expertise in the development of research proposals and conduct partly as an indication of expert input and quality assurance.

The demand for proficiency within clinical trials facilities is, therefore, anticipated to increase substantially as there is an increased focus on clinical trials in low-income countries. In order to ensure that clinical trials facilities can meet these requirements, it is indispensable that the prevailing capacity of this resource is assessed and the need for any further development and strengthening is identified and quantified if possible (13). It is also useful to hear from Ethiopian experts about their perceived needs and priorities for capacity building. This information is essential to ensure that future capacity-building efforts are targeted where they will be most useful.

1.2. Statement of the problem

Different capacity challenges affecting research systems in LMICs have been recognized. However, substantial amount of this evidence is inferred from experiences with specific institutions or programmes and does not build on systematic baseline data and conceptual frameworks (14). In many LMICs higher education institutions lack incentives to provide research performance data for the central data administrator to report to the government and there is a data needs on the institutional research capacity levels. The lack of availability of baseline data in many research organisations makes it difficult to prioritise interventions in the context of multiple gaps and competing needs (14). Scarce resources in low-income countries are nearly all spent on program execution. Research can be considered an extravagance in low-income countries due to financial and other economic limitations (15). However, the lack of resources in low- and middle-income countries ironically intensifies the need for reliable evidence to prioritize the use of these scarce resources and mapping of the existing capacity.

Notwithstanding the advantages and clear benefits that clinical trials can offer, available data show that there is a paucity of clinical trials in Ethiopia (16–18). Indeed, all reports emphasize that clinical trials conducted in Ethiopia have been very much limited not only in quantity, but also in type and quality (16,18). Low resources, weak regulatory and administrative systems, few learning opportunities, little human and material capacity, and few incentives for doing research

are the common cited challenges of locally led clinical trials in Ethiopia and Cameroon (16,19,20). In Ethiopia, lack of awareness, low confidence, and limited motivation to undertake trials were also key individual barriers identified by one study (19). Another barrier is the scarcity of research and development scientists in some lower-income regions compared with richer regions (21,22). However, there is little evidence about how, and in what manner, capacity is weak (23) within specific low-income countries. On the other hands, there is increasing recognition that local investigator-initiated clinical trials have a potential to generate pertinent data for national governments of LMICs (19). However, too few clinical trials are led by LMIC investigators, and there is little information about how best to increase the number of locally initiated trials (19). There is also a growing need to advocate for better coordination to ensure that, relatively sophisticated and expensive equipment with capacities for shared use in different institutions in particular field of health research are appropriately utilized inter-institution for research (15)**.** On top of this, currently there is no well-accepted method or consensus reached on the method of rating to assess capacity for clinical trials research at different levels (e.g. research institutions or national health research systems) of LMICs. Nevertheless, a few tools that define competencies and/or benchmarks for specific sub-elements of research capacity, or report on capacity assessments are in use but they have narrow scope and acceptance (24,25).

In a review of the scientific literatures such as status of clinical trials, editorial, commentary, systematic review of clinical trials in Ethiopia ,there were no formal studies reporting on assessment of clinical trials facilities in Ethiopia to measure their existing capacity to conduct clinical trials for at least high priority areas (16,18–20,26–30) though centers/institutions hosting trials are expected to have developed critical core competencies including in administrative services. In order to increase the capacity and diversity of clinical trials and improve their quality, available evidence on gaps, key challenges, and potential enablers need to be critically appraised and systematically addressed (18)**.** In this work existing capacity of clinical trial, perceived gaps and priorities for capacity strengthening of selected drug trials facilities in Ethiopia were analyzed and assessed against various capacity domains.

1.3. Rationale of the study

The effectiveness of capacity building works best when it is based on an initial assessment of the existing strengths and weaknesses, as well as the priorities of potential beneficiaries (31,32) This

allows capacity building efforts to be designed to have inbuilt elements of sustainability for over the long-term.

A systematic needs assessment can be very worthwhile for funders and LMIC researchers of clinical trials. It will help identify what governance, management and administration structures are already in place and how they function in practice; staffing levels; and the skills mix of staff, including lists of the key stakeholders currently involved in research (23,28).
Any planned capacity assessment should take into consideration the capacity currently in place, any future planned capacity and the way that dynamics of continuous development programs will interact with any proposed initiatives in the health research sector (28).

Furthermore, any change or new intervention should build on, and work in synergy with, existing capacity, instead of repeating or bypassing it. An appropriate assessment of existing capacity at the start of an initiative provides an accurate baseline for monitoring and evaluation efforts to be successful. The engagement in clinical trial activity with suitable stakeholders can begin; only once the existing research system and all-encompassing context is understood, gaps and opportunities can be identified.

Recognizing the existing capabilities and capacities of clinical trials facilities within a country or within a geographic region in terms of administrative structure & business continuity, workforce, training and clinical experience, laboratory infrastructure, data management, and data quality management approach is essential to understand the challenges and opportunities that people are facing while doing clinical research in LMICs. Evidence obtained from capacity assessment; can be used to pinpoint needs and support to develop policies and interventions to reinforce clinical research capacities, with the ultimate aim of improving health. Such an assessment should assist to provide the required knowledge foundation and framework for building national clinical trial capacity, to the benefit of both clinical trial sites and sponsors of medication clinical trials.

2. Literature review

From a public health perspective, clinical trials in sub-Saharan Africa, where a high burden of disease exists, are of particular importance (33). Conversely, the bulk of global clinical trials are done in developed nations, predominantly in North America and Europe (34). This global disparity in clinical research capacity and service delivery may be revealed simply through the

number of clinical trials a country or a region has registered in clinical trial registry databases (35). In the years from 2004 to 2013, 82.5% of the registered clinical trials were contributed by high income countries (34). During these years, Africa accounted only for 2.3% of clinical trials carried out in the world (36), although the region represents around 15% of the world population. Recent evidence also shows that the contribution of Africa to clinical trials is not changing. According to the International Clinical trials Registry Platform, as of April 22, 2021 only 2.38% (about 22,304 from a total of 937,847) of clinical trials were registered from the African region (37).

Numerous development organizations have argued that clinical trials in LMICs are crucial for advancing public health and development (26,38). Nonetheless, in LMICs, clinical trial research capability remains insufficient (26). This propagates the '10/90 gap', where solely 10% of worldwide health-related study expenditure is allotted to diseases that predominantly have an influence on 90% of the world's population (21,27). This results in a scarcity of evidence to support effective interventions for some of the world's most substantial diseases (27). Evidence from Western nations may not be pertinent to LMICs, and its adoption into clinical practice can be sluggish and should be treated with caution as there are huge variations in medical environment, dietary (39),biologic/genetic factors, effect sizes (40)(41), cultures and views across the world, and what is right in one place might not be in another (27,38). At the same time that the priorities of developed countries drives the research agenda of pharmaceutical companies (27). During the last 30 years, when poor and low-income countries were most involved in multicenter clinical trials, only slightly more than 1% of pharmacological innovations were directed at diseases that primarily affected the populations in these countries (42). There is an alarming underrepresentation of research addressing urgent issues for LMICs (27). Increasing the number of clinical trials conducted in LMICs would help produce home-grown solutions, which may be more likely to have a faster influence on policy and practice (16,20).

As defined in the work of Sitthi-amorn *et al*., health research capacity is "the ability to identify problems, set objectives and priorities, build sustainable institutions and organizations, and find solutions to key national health problems (43,44)." In several LMICs, commonly there is lack of capacity in terms of broad-based research and scientific leadership to compete for research grants

and systems to manage research projects. This seriously handicaps scientists from these regions from being in the driving seat and able to lead their own research programs (36).

There are many research capacity strengthening initiatives, at national and international level, all based upon a premise that LMICs, particularly lower-income countries, currently have weak health research capacity (9).

In analyzing capacity it is worthwhile first to think about whose capacity (or the capacity of what) is important. A systems approach to understanding national health research recognizes that capacity resides at different levels, including individual, institutional, national and global levels (9,23). Whilst the importance of institutional capacity is starting to be understood, studies point out that some practitioners and analysts continue to see capacity mainly as a human resource question to do with skill development and training at the individual level; 'This 'capacity as training' view has a long-lasting history and is still a widely-held view both in International Development Agencies and in country governments'(45). Capacity within health research systems at the national level (and wider) receives much less attention (23). The next key issue to think about is what capacity is vital (23). Unfortunately, there is no widely adopted, standard system for assessing/measuring clinical trial capacity, especially at the institutional and country/national level (28,46). In the absence of common metrics and indices, stakeholders adopt proxy measures, which could lead to inaccurate indications of prevailing capacity status, and poor articulation of capacity gaps. This issue has been widely acknowledged, and recommendation 5 of the International Vaccine Task Force (IVTF) report calls for that by the end of 2018,WHO should consolidate a robust set of indicators, to the extent possible building on indicators already used by countries, develop a tool for assessment of country-level capacities for clinical research, and suggest a method to help countries rapidly conduct these assessments (28). Although concrete action to improve this has not so far, come into effect. The conceptual framework adopted from the literature and used in the capacity assessment of CTFs is depicted in Figure 1 below.

According to Chu and Langer et al., four pre-requisites are essential for effective research: individual research ability and skills, proper infrastructure, significance of the research topic to national policies, and the capacity to contribute to global research and policy requirements

(47,48). Furthermore, other studies have shown that financial resources have always been a critical factor in scientific studies(49) and with financial constraints accounting for up to, 22% of late phase clinical trial failures(50).

The existence of only small numbers of competent researchers, low amounts of funding, poor infrastructure such as laboratories and computers, and absence of expertise in preparing manuscripts for publication have been mentioned as some of the numerous reasons that African research capacity has not paralleled capacity in high income countries (51).

Even though there has been significant progress over the preceding two decades, it has been said that research capacity in the South remains one of the world's unmet challenges (11,52). This is especially true for the region of sub-Saharan Africa, where health budgets are financed with less than 1% of gross domestic product and the health research budget in most countries has an allocation of less than 0.5% of national health budgets (11). In Ethiopia, the number of clinical trials conducted is increasing over time. However, when compared to other African countries it is still much lower (16,29). As of April 22,2021, only 1.49% (333 of 22,304) of all clinical trials registered from Africa in the International Clinical Trials Registry Platform (ICTRP) had at least one of the recruitment sites in Ethiopia (37).Although the country representing around 8.5% of the population of the African continent (53,54).

Conceptual Framework

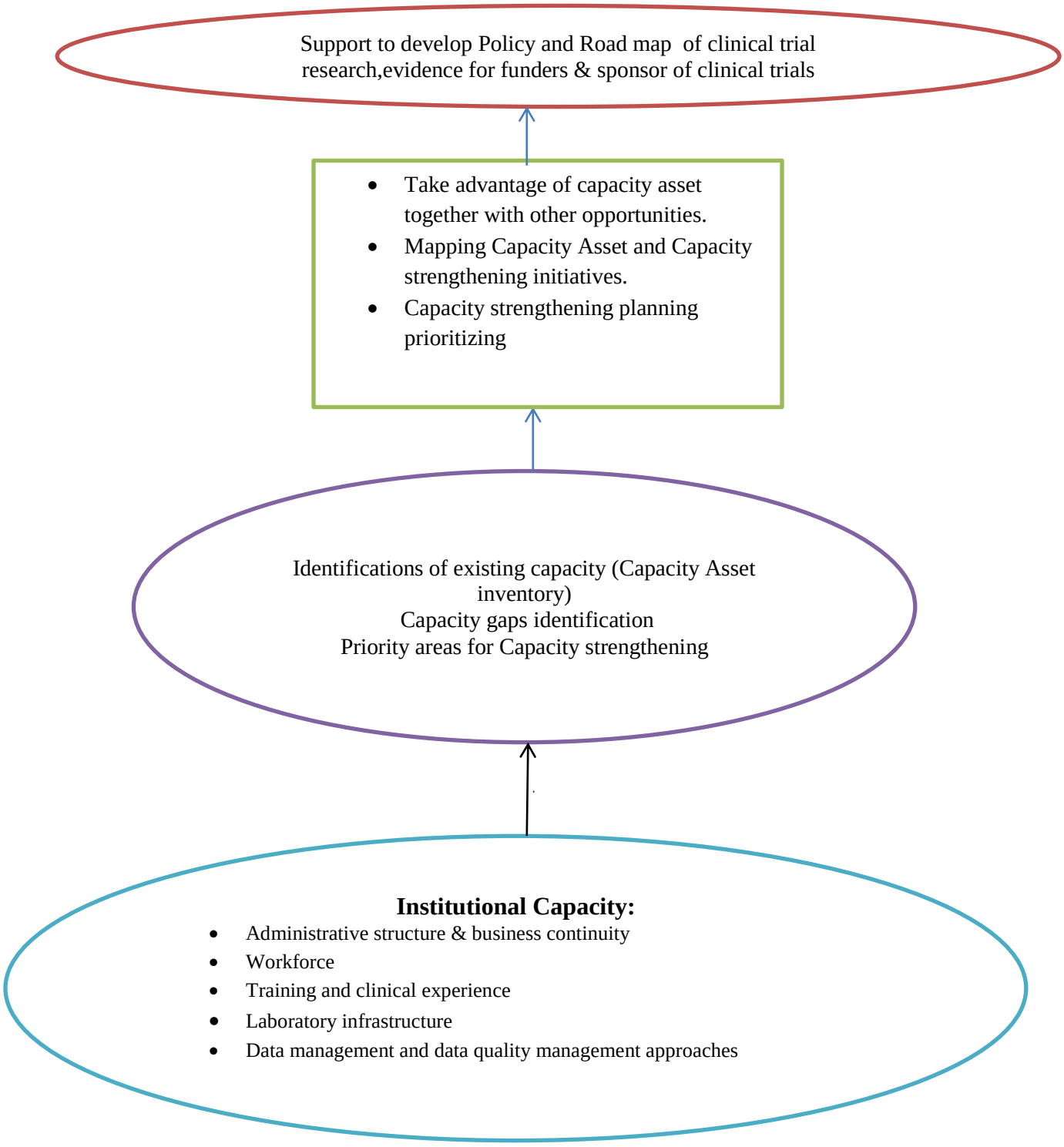

Figure 1 Conceptual Framework for clinical trial capacity assessment adapted from literature review

Research questions

RQ1: What is the existing clinical trial conducting capacity of clinical trial facilities in Ethiopia?

RQ2: What priorities are identified for capacity strengthening activities?

RQ3: What are data management (DM) systems, software tools being utilized, and data quality management procedures used within clinical trial facilities in Ethiopia?

3. Objectives

3.1. General objective

- To assess existing capacity of CTFs to conduct drug trials, gaps and priority for capacity strengthening of clinical trials in Ethiopia

3.2. Specific objectives

- To assess existing capacity of CTFs to conduct drug trials
- To explore gaps and priorities for capacity strengthening as perceived by CTFs in terms of workforce, laboratory and data management in its different components
- To explore data quality management and clinical data management systems employed in CTFs.

4. Materials and Methods:

4.1. Study area and period

The study was conducted in 13 clinical trial sites /units/centers, two ministries and one research institute in Ethiopia between September and March 2021. These sites /units/centers were affiliates of the following institutions: Addis Ababa University (AAU) clinical trial center (Black Lion Hospital), Armauer Hansen Research Institute (AHRI), , Ethiopian Public Health Institute collaborating Clinical trial Site, University of Gonder (UOG) clinical trial center, Jimma University (JU) clinical trial Unit, SaintPeter's Specialized Hospital, Arbaminch hospital leishmaniasis treatment and research center, Hawassa University clinical trial Site, Dilla University clinical trial site, and Saint Paul's Hospital Millennium Medical College clinical trial site. The two ministries and research institutes were: Ministry of Health (MoH), Ministry of Innovation and Technology (MinT) and Ethiopian Biotechnology Institute (EBTi) correspondingly. Though the numbers of sites/Units/ center/ included in this study are small, these are the only clinical trial centers or sites in Ethiopia that are actively involved in clinical trials that are not specific to a single project. Furthermore, these centers represent different levels

of activity in regions of Ethiopia, as well as in the capital city.

4.2. Selection of study Participant clinical trial sites

Participants were identified by searching the online ICTRP and the primary registries hosted by ICTRP database for clinical trials to identify those with at least one recruitment site in Ethiopia. Then the principal investigator (PI), co-principal investigators (Co-PI), study coordinators and trial manager were identified or contacts provided in the registry for any site-related enquiries were included if there was no other information on the selected trial site as described in participants selection flow diagram shown in Fig.2.

4.3. Study design

A descriptive cross sectional, institution-based mixed methods study utilising both quantitative and qualitative research methodology was carried out.

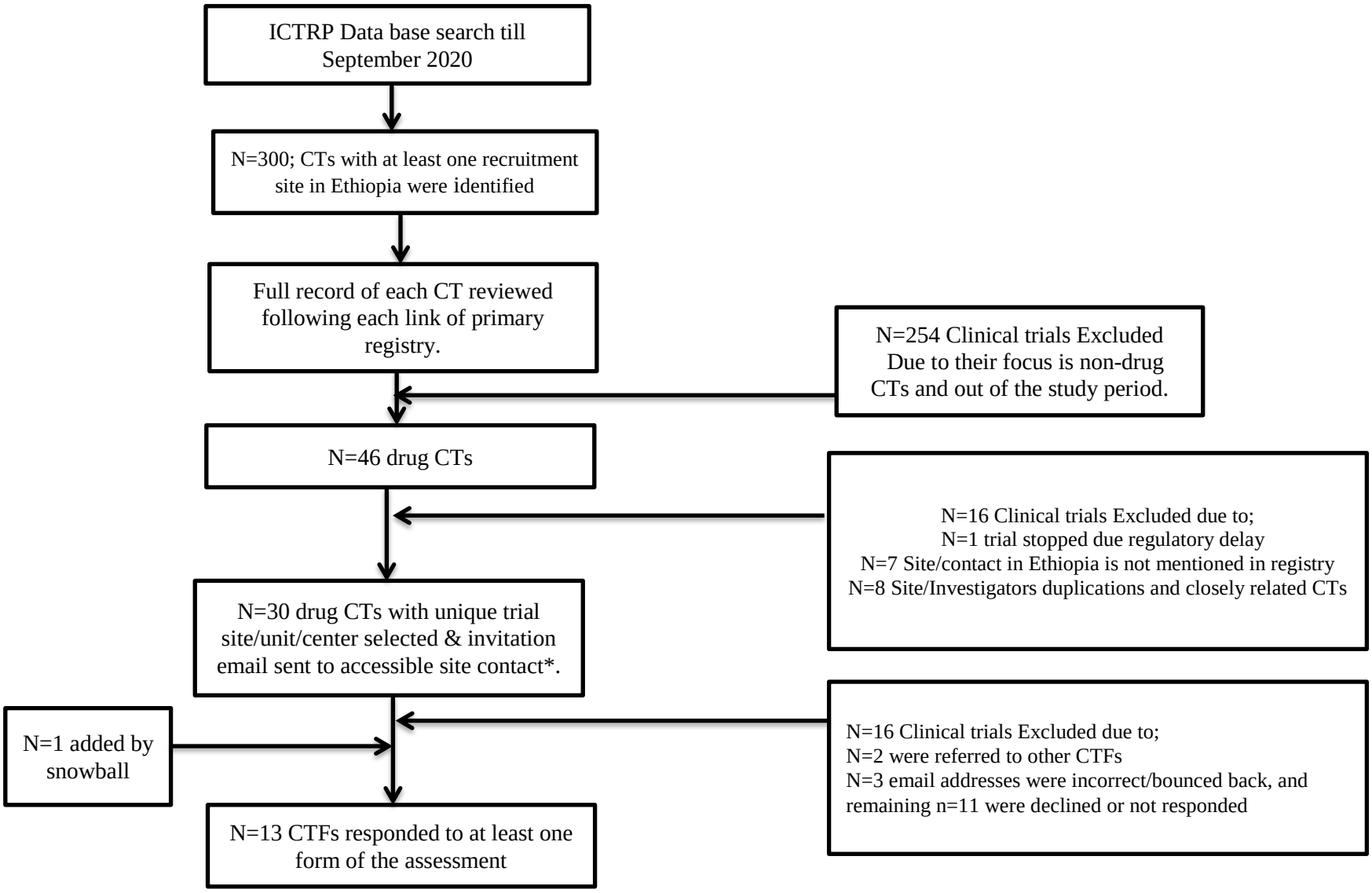

Figure 2 Eligible CTs Site/Unit/Center identification, selection, and survey invitation flow diagram.

* The invitation to solicit email was sent to PI, Co-PI, Trial managers or study coordinators depending on structure, information provided in the registry and contact accessibility.

4.4. Operational Definitions

Capacity: the ability to identify problems, set objectives and priorities, build sustainable institutions and organizations, and find solutions to key national health problems.

Core staff: staff specifically available in the center/unit regardless of the project.

Core funding; funding awarded specifically to support the center's/unit's core activities and infrastructure as a whole rather than a particular project or individual.

Clinical Trials: any clinical research study in which human participants or teams of humans are randomly allocated to one or more health-related interventions and prospectively followed to assess the effect of the interventions on health outcomes.

Clinical Trial site: the location where trial-related activities are actually conducted (this is most specific related to conducting the study in a particular hospital/clinic).

Clinical Trial Center: the location where trial-related activities are actually conducted or the structure that includes one or more clinical trials site, or plays role of doing actual clinical trials activities and /or coordination depending on the structure of the institute.

Clinical Trial Unit; the structure that includes one or more clinical trials site, or plays role of doing actual clinical trials activities and /or coordination depending on the structure of the institute.

Drug: any substance or mixture of substances including vaccines used for human health care (i.e. diagnosis, treatment, mitigation or prevention of diseases or symptoms).

Clinical Trial Facilities (CTFs): The common term to refer the Clinical Trials settings like site, Unit and Center.

4.5. Eligibility criteria

Inclusion criteria:

All clinical trials sites/ units/centers reported initiated/ongoing/completed drug trials on International Clinical Trials Registry Platform (ICTRP) from January, 2017 to September, 2020 and with at least one recruitment site in Ethiopia and consented to participate.

4.6. Data collection method

The following methodologies were used for the data collection:

Quantitative situation analysis checklist: An email based structured questionnaire and capacity gap assessment checklist adapted from different sources were used to collect quantitative data. These measures were adapted from the Global health network (49), the European Clinical Research Infrastructure Network (ECRIN) (50), the Health research board Ireland (13) and the International Vaccine Task Force (IVTF) (28) working draft Model of clinical trials capacity assessment framework. The domains that were assessed included general administrative structure and business continuity, workforce, clinical trial experience, laboratory infrastructure, data management infrastructure and data quality management approaches.

Qualitative section: Topic guide questions were adapted from prior related studies exploring health research capacity and refined by investigators. The domains assessed included general administrative structure and business continuity, workforce, clinical trial experience, laboratory infrastructure, data management infrastructure and data quality management approaches and priority area to develop capacity. The interviews were undertaken via Zoom meeting or phone call.

Documents review: The availability and content of relevant documents, including policies/ strategy plans/ road maps for clinical trials in the respective institutions were reviewed.

4.7. Data collection procedure

Quantitative and qualitative data were collected using English language capacity assessment structured questionnaires (capacity gap check list) and English /Amharic language semi-structured questionnaire for key informant interviews, respectively. Pretest was done with researchers who had some level of similar characteristics to the target participants but who were ineligible for the study due to the small sample size of target participants. Based on the findings of pretest, necessary modifications were made to the questions. For the quantitative component, the principal investigator or, if not reachable, the co-principal investigators, study coordinators, trial manager and other contacts given as sources for scientific enquiry were contacted by e-mail to solicit their participation. They were invited to click on a link to Paper Forms, where they viewed an informed consent disclosure and survey questionnaires. Similarly, for the qualitative

component, the same people were approached by e-mail to solicit their participation after viewing an informed consent disclosure. They were invited to respond to their willingness to be interviewed and to suggest a suitable schedule for the interview. Then a link to zoom meeting and schedule for interview was sent by the investigator. All key formant interviews were audio recorded if permission was obtained. If permission was not obtained, detailed notes of the interviews were taken. Additionally, every transcript was reviewed prior to the next interview and final data analysis. The interviews were conducted through either online platform Zoom meeting or phone call. Efforts were made to keep the interviews place as confidential as possible. The interviews took up to 30 minutes, on average, to complete. Email reminders were sent twice to non-respondents. All data collection was administered by principal investigator.

4.8. Data processing and analysis

After the completion of data collection, the raw data from the quantitative assessment were exported to an excel spread sheet for editing, cleaning, coding, and check completeness and consistency. Finally, data were exported to SPSS for windows version 21 for data management and descriptive statistics analysis.

For the qualitative component, nine key informant interviews were carried out; Eight by Zoom meetings; Video Communications, Inc. and one by telephone. Six interviews were audio recorded and for three interviews detailed notes were taken with participant consent. The key informant interviews were transcribed verbatim by the principal investigator and translated into English for those which were collected in Amharic.

Following transcription, thoroughly reading and re-reading of each transcript, and listening back to the audio-recorded interviews was carried out to become familiar with the whole dataset. Then transcript data were exported to NVivo software version 12 (QSR International Pty Ltd. and initial thematic framework (theme) were created. Finally, the process of indexing (coding), charting, and interpretation of the data was done. Triangulation of data sources from the questionnaires and key informant interviews was conducted to obtain a comprehensive assessment around the focus areas of the research question.

5. Ethical considerations

The study was approved by Addis Ababa University, Center for Innovative Drug development

and Therapeutic Trials for Africa Scientific and Ethics committee. Written consent via email confirmation from each of the study participants was obtained after clear explanation on the purpose of the study. To this end, the right of each respondent to refuse, answer for few or all questions was respected and participants' confidentiality of information was maintained throughout the study. There was no any formal monetary payment for the study participants.

6. Dissemination of findings

The findings of this study will be disseminated to Center for Innovative Drug development and Therapeutic Trials for Africa, Addis Ababa University, respective clinical trial facilities and MoH. Furthermore, efforts will be exerted to publish the findings on reputable local/ international journal.

7. Results

7.1. Quantitative Results

7.1.1. Clinical Trials Facilities profile (Institutional characteristics

As depicted in Table 1, the legal status of all CTFs is registered through the Ethiopian government, although the primary funders for most CTFs are non-Ethiopian academic institutions. Figures from the eight CTFs showed that, estimated average annual cost to run eight facilities was11.58 million Ethiopian birr, including sources from local supports and foreign collaborations. Estimation of the explicit proportion of funding (the research budget) from abroad and local (national) sources was not readily available.

Table 1 Profile of Clinical Trials Facilities

Site/Unit / Center	**Establishment**	**Legal status**	**Current primary funder**	**Funding (Annual App.ETB)**
CTF1	Academic Institution(AI)*	Government	AI*	3,000,000
CTF2	AI*, Research Institution(RI)*	Government	RI**	1,500,000
CTF3	RI*	Government	RI*	-

CTF4	AI*	Government	PC**,Funds from international agencies	Varies
CTF5	AI*	Government	Academic Institution*	150,000
CTF6	RI**	Government	Funds from international agencies	1,000,000
CTF7	AI*	Government	AI*	130,000
CTF8	AI*	Government	PC**, RI**, international organizations	2, 000,000
CTF9	RI*, RI**	Government	RI**, PC**	800,000
CTF10	AI**	Government	AI**	5,000,000
				=11,580,000

*Ethiopian Institutions

**Non-Ethiopian Institution

AI: Academic Institution**;** **RI**: Research Institution; PC: Pharmaceutical Company

7.1.2. Clinical Trials Physical Infrastructure

As shown in Table 2, in approximately half of CTFs where physical infrastructure was assessed, administrative offices, monitor room, consenting/counseling room(s), inpatient beds and outpatient beds were not available (see also additional file Table 10).

Table 2 CTs Physical Infrastructures available in assessed facilities (all numbers in brackets are in percentage)

	Domain of **Clinical Trials Physical Infrastructures Assessed**					
	Administrative offices	Monitor room	Consenting/counseling room(s)	Examination room(s)for subjects	Inpatients beds	Outpatient beds
Dedicated N (%)	6(60)	5(50)	5(50)	7(70)	5(50)	4(40)
Not dedicated N (%)	2(20)	4(40)	4(40)	3(30)	4(40)	4(40)
Not applicable N (%)	2(20)	1(10)	1(10)	0	1(10)	2(20)

7.1.3. Clinical Trials workforce

As depicted in Fig. 3, the total workforce in CTFs was 159 staff members, comprising 112 (70.4%) scientific staff, and 47(29.6%) support staff. More than half (about 55%) of the workforce were clinical nurses or laboratory technologists by profession (see also additional file Table 11).

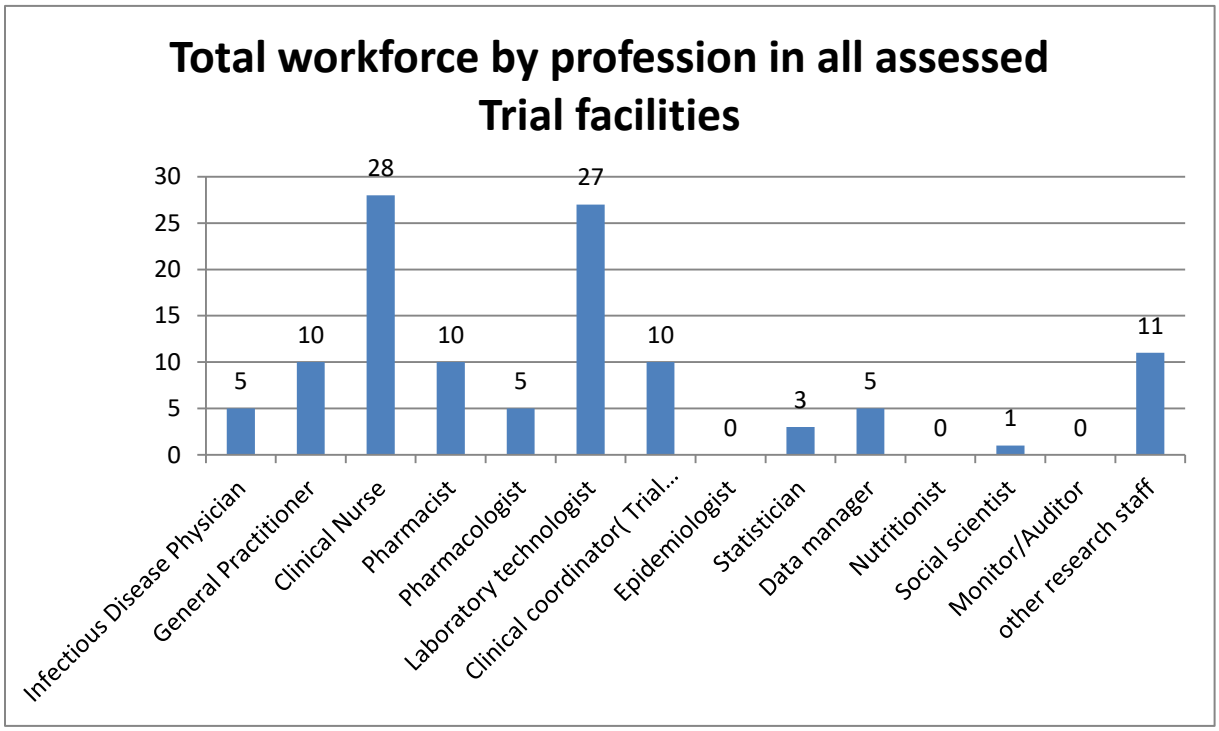

Figure 3: Descriptive Statistical Analysis of work force Capacity in 10 assessed facilities

* Other research staff reported includes (internal medicine, Psychiatrist, Immuno-pathologist, Microbiologist, Pharmaceutical Sciences, Ethnobotanist, and Anesthetist.

7.1.4. Clinical trials Experience (center/unit/site)

Clinical Trials Scope and Diversity

As depicted in Table Fig.4, Out of the top ten leading causes of death in Ethiopia, only tuberculosis and HIV/AIDS were included in the clinical trials lists of the CTFs. None of the CTFs reported having capacity to conduct CTs in the therapeutic areas of asthma, diabetes mellitus and congestive health failure, while relatively higher numbers of CTFs reported the capacity to conduct trials on malaria and tuberculosis. Similarly higher numbers of CTFs reported having the capacity to conduct phase III and IV CTs (Fig. 4). (See also additional file

Table 12).

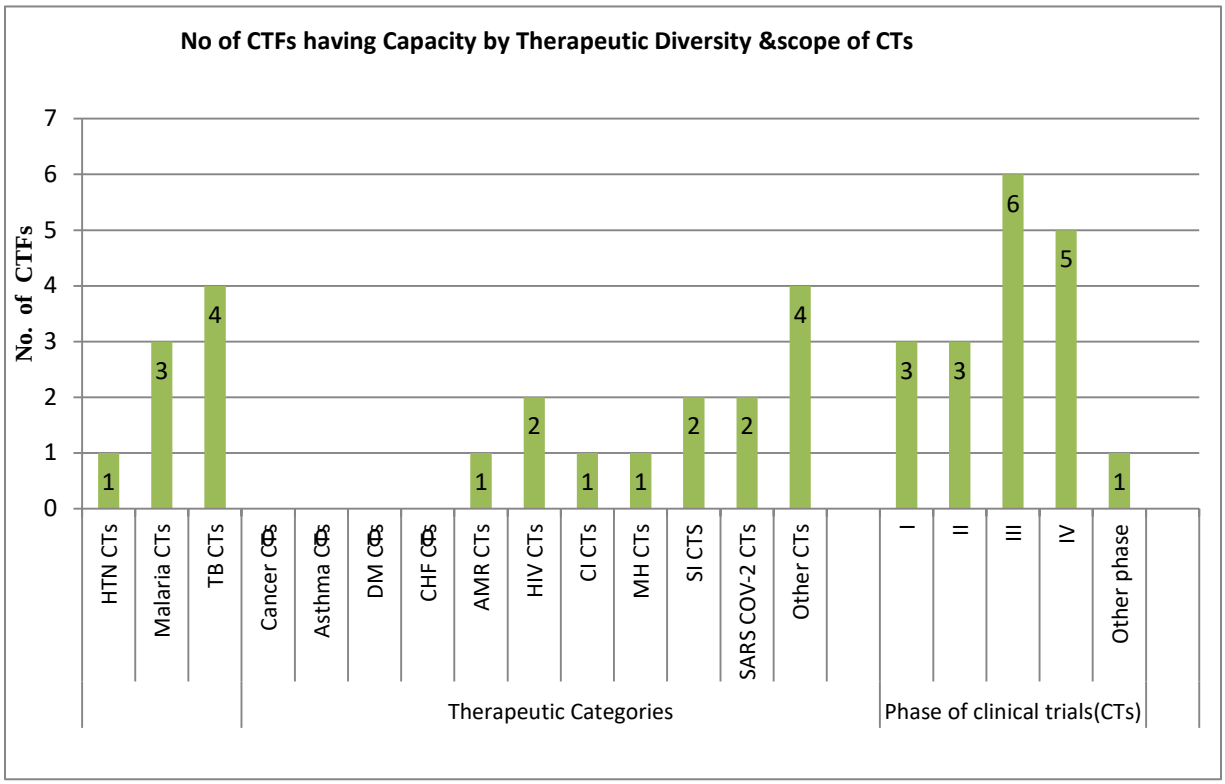

Figure 4: number of CTFs having the capacity by the therapeutic diversity and scope of CTs in10 assessed facilities.

*other CTSs mentioned includes; Anesthesia, Pain management, Bioequivalence clinical studies, Dermatological, Mental health Clinical trials, Complex Intervention trials, Service intervention and Leishmaniasis.

HTN; Hypertension, TB CTs; Tuberculosis Clinical Trials, DM; Diabetes, AMR; Antimicrobial resistance, CHF; Congestive Heart Failure, MH CTs ;Mental Health Clinical Trials, CI CTs; Complex Intervention Trials ,SI CTs ;Service Intervention Trials

Characteristics of CTs conducted in the CTFs

As shown in Fig.5, of 35 CTs were conducted in 10 CTFs, close to half were phase III and a smaller number were phase I, II and IV. Half of CTFs were not conducting phase I CTs due to insufficient infrastructure (Table 3). For the clinical trials conducted by the 10 CTFs, only about half the protocols had been locally generated. On the other hand, the typical size of clinical trial that could be conducted by most CTFs (i.e. number of participants most commonly enrolled) was in the range of 101-200 participants (Table 3 and See also additional file Table 13).

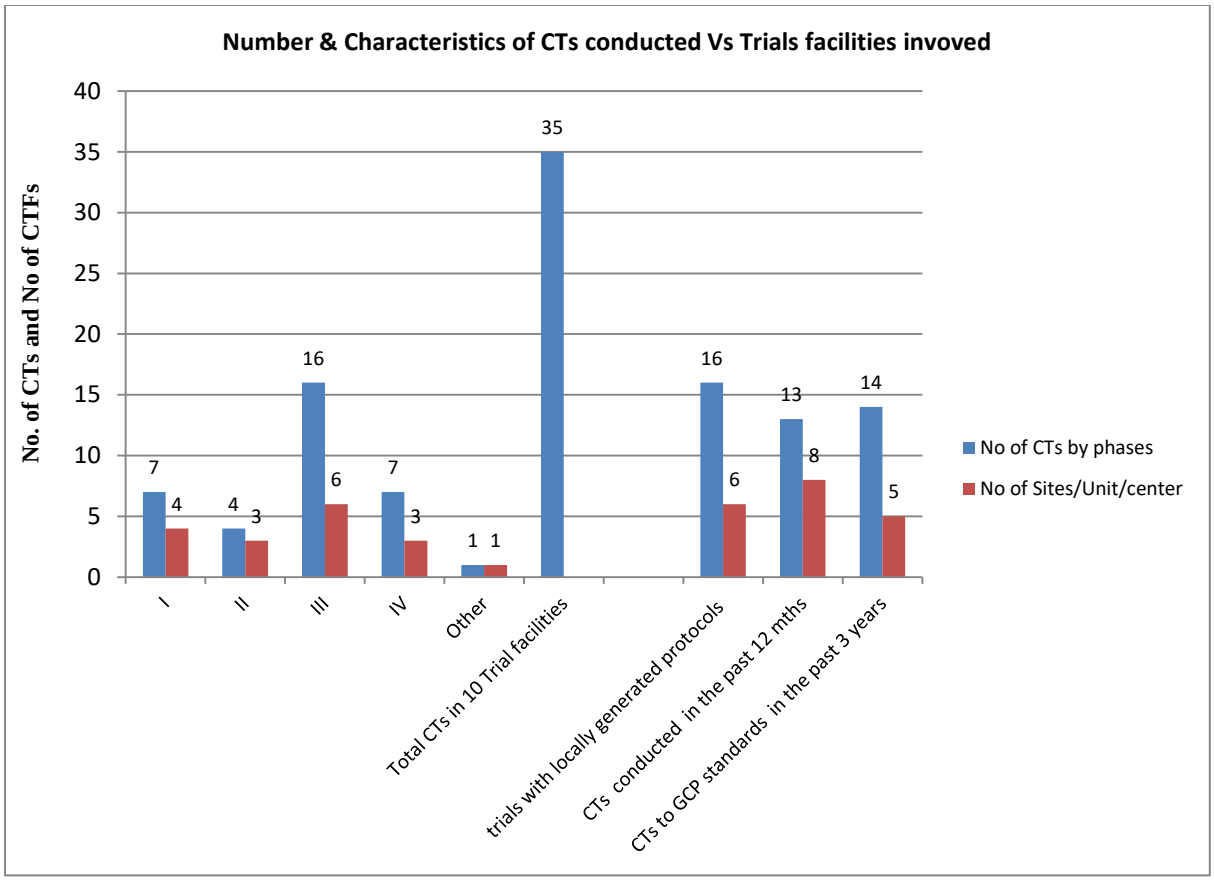

Figure 5 Number and characteristics of CTs conducted against CTFs involved in 10 assessed facilities

Typical size of clinical trial that could be conducted in CTFs is less than 200 participants. On the other hand most CTFs were not conducting CTs due to insufficient infrastructures mentioned in Table 3.

Table 3 Typical size of CTs that could be conducted in the CTFs and reason for not conducting phase I CTs

	Typical size of clinical trial that could be conducted in unit/center?(i.e. number of participants most commonly enrolled)					Reason for not conducting phase I Insufficient		
	<50	50-100	101-200	300-400	1400	Emergency equipment & infrastructure	emergency equipment, infrastructure, trained & experience staff, Fund	Current projects do not have pharmaceutical interventions
Number of CTFs	**1**	**2**	**3**	**1**	**1**	**2**	**3**	**1**

7.1.5. Laboratory facilities

As shown in Table 2, most CTFs reported the availability of laboratory facilities, although not all had external certifications or quality assurance systems, for example, laboratory (ies) local reference ranges and a disaster plan. (See also additional file Table 14).

Table 4 CTs laboratory facilities available in assessed facilities (all numbers in brackets are in percentage)

laboratory facilities assessed	N(%)a Yes	N(%)b No
research laboratory	7(70)	3(30)
laboratory (ies) Quality Assurance System(QAS)	7(70)	3(30)
laboratory(ies) external certifications	3(30)	7(70)
laboratory(ies) local reference ranges	5(50)	5(50)
SOP for recording data and acceptance and release of results	10(100)	0
Disaster plan for the laboratory(ies)	5(50)	5(50)
Provide GCLP training before launching clinical trials	9(90)	1(10)
Refresher courses for laboratory personnel	6(60)	4(40)
Staff training records maintained	7(70)	3(30)

7.1.6. Data Management

About two thirds of the CTFs had data management and storage facilities at different levels. However, only two CTFs had data management units with external certification (Table 5). On the other hand, OpenClinica, Redcap, REDfox and Marvine are types of Clinical Data Management Systems (CDMS) softwares in use by the CTFs. (see also additional file Table 15 and Table 18).

Table 5 CTs data management facilities available in assessed facilities (all numbers in brackets are in percentage

Data Management facilities	**N(%)[a]**	**N(%)[b]**
Data management facility on site	7(70)	3(30)
Central data management facility	8(80)	2(20)
designated study document archiving room on site	8(80)	2(20)
Long term document archiving facilities on site	6(60)	4(40)
long term document archiving facilities off-site	4(40)	6(60)
Data management unit quality assurance system	8(80)	2(20)
Data management unit external certifications	2(20)	8(80)
Clinical data management plan in place	6(60)	4(40)
Direct entry of observations into a computerized system	6(60)	4(40)

[a] No of site with specified capacity ;[b] No of site without specified capacity

As shown in Table 7, the onsite source data verification (SDV) monitoring approach was used in two thirds of the CTFs. Half of CTFs use remote monitoring and centralized monitoring and one third of CTFs use risk-based targeted monitoring and logic, range, and consistency checks whereas none of the CTFs use error acceptance level and risk-based triggered monitoring as approaches. All (100%) data points by four CTFs, critical data points by three CTFs, critical and noncritical data points by one CTF were used as variables included in data monitoring while the other four CTFs reported variables to be included in monitoring to vary between projects and study design**.(see also additional file Table 16 and Table 17).**

Table 6 Types CDMS in use, electronic data storing and SOPs for data quality management and CDMS

	Types of CDMS in use				**Electronic data storing**				**SOPs for data quality management and CDMS.**				
	OpenClinica	Redcap	REDfox	Marvine	Secure server	Individual computers	CDs	Zip drives	Data Collection & Handling	System Maintenance	Data Back-up	Data Recovery	Contingency Plans
No of CTFs using	**4**	**2**	**1**	**1**	**6**	**5**	**1**	**1**	**8**	**6**	**6**	**5**	**3**

Table 7 Data monitoring and variables included in the data monitoring of assessed CTFs

	Procedures in place to ensure high-Quality data are produced							variables included in data monitoring					
	Risk-based targeted monitoring	Statistical techniques	Onsite – SDV†	Remote monitoring	Error acceptance level	What percentages of the data monitored	Risk-based triggered monitoring	Logic, range, and consistency checks	Centralized monitoring	All(100%) data points	Critical& noncritical data points	Critical data points	Varies b/n projects & study design
No of CTFs utilizing Approaches	3	2	7	5	0	2	0	3	5	4	1	3	4

†**Source data verification (SDV)**

7.2. Qualitative Results

In total, nine (9) semi-structured interviews of key informants were undertaken, lasting on average 30 minutes. Most of the participants were male by gender and held different research positions in nine (9) clinical trials facilities from all geographic locations of Ethiopia (Table 8). Analysis of the interview data generated three global themes and thirteen sub-themes (including categories of factors) in the context of research objective (Table 9).

Table 8 Summary of key informant interview participants' Characteristics

Characteristics of the Participants (n=9)

Characteristics		Count (%)
Level of education	MSc	2(22)
	MD, specialty	5(56)
	PhD	2(22)
Years of experience in CTs	0-5 years	3(33)
	6-10 years	4(44)
	11-15 years	2(22)

Table 9 Themes and Subthemes emerged

Themes	Subthemes
Current Capacity challenges	CTs infrastructures related capacity challenges
	Bureaucracy within institutions
	Regulatory and ethical approval process challenges
	Stakeholders perceptions' towards clinical trials
	factors related to structural capacity limitations
	Inadequacy of trained CTs workforce related factors
	Availability of clinical trials funds

Priority area to develop capacity	Establishing and strengthening data management capacity of clinical trials
	Establishing and upgrading clinical research laboratory capacity (strengthening laboratory capacity)
	Human resource related capacity developments
	Quest for funding
	Increasing awareness level of insurance companies on clinical trial insurances.
	Structural revision (upgrading the site/unit to research center)
Sustainability of CTs infrastructure capacity and the settings	

The following section summarizes the global themes and sub-themes that emerged from the key informant interviews with corresponding quotes.

Global theme 1: Current Capacity challenges

This theme addressed many of the key capacity challenges that key informant participants raised as factors that hamper clinical trials from their setting through national level. The following six sub-themes emerged from this global theme:

Sub-theme 1: Clinical Trials infrastructure; factors related to physical premises, laboratory, pharmacy and information technology infrastructure

The availability and quality of the clinical trials infrastructure, including laboratory, pharmacy services, data management that are required to improve the quality and increase the credibility of clinical trials data. Most of the participants identified multi-level capacity challenges with the following clinical trials infrastructures in their settings.

Laboratory and Pharmacy services: Four of the CTFs mentioned the availability of dedicated research laboratory in their settings with limited capacity, while others reported as lacking. All

CTFs raised the unavailability of a Good Clinical Laboratory Practice (GCLP)-compliant laboratory in collaborating facilities as one of the major capacity challenges they are facing. Two CTFs described lack of availability of appropriate premises for storing, handling and proper dispensing of investigational medicinal products (IMPs) in collaborating facility. One CTF also noted an inadequacy of available space as the dimension of service given by the CTF is increasing.

"*We are working on the previous structure and system; the system is fortunately comfortable for such activities, except for the level of the laboratory. What we lack is a laboratory and we are upgrading the laboratories to biosafety level 3… to establish a culture laboratory" (*P02).

…. "National reference laboratory is expected to used as a backup and do most of the tests that are not done in other parts of the country including different hematological parameters, chemistry parameters, PCR tests, culture, different drug susceptibility test, parasitological test and the like. However, there are higher level tests related to some clinical trial studies like pharmacokinetic and the like of which are lacking" (P06).

Data management system: Capacity, organization and information technology backed data management system is central to clinical trials. All of the participants described capacity of data management facilities in their settings as inadequate. Four participants noted that they had a separate facility for data management (e.g. separate room for data documentation and storage with limited /no staff). Two indicated their site had a shared data management facility with other services. While another two CTFs mentioned that they were using a paid data management center. Three CTFs mentioned internet connectivity as relatively better than previously except when there was instability in country and the other five participants reported interruptions and limited capacity. One CTF mentioned that the data center had no difficulty with data security, or with capacity of the server as it was hosted by an external sponsor for electronic data collection and storage.

…"*So far, as I said there is a data room. But we haven't appointed staff because our trials are very limited. We have not yet developed this data management team unit. …but in the future that is one of our plans... We identified the data management room and also controlling data based on GCP"… (P04).*

…"The major problem is an internet connection. As always, we send the daily patient evaluation

as the severe adverse event, whatever the event is…but if there is a poor connection that is a problem"… (P02).

Sub-theme 2: *Bureaucracy within the institutions*

Institutional bureaucracy is necessary in providing rules and guidance for the conduct of clinical trials and to regulate research staff as well. However, there are occasions when the system becomes unreasonably multilayered and time consuming. Three participants had described that, some of the bureaucracies within the institutions, like procurement procedures of trial input supplies e.g. equipment, laboratory reagents, as challenges in their settings.

… "Some other problem is bureaucracy especially in the universities and these are common problems that we usually face…Purchasing problem is also another issue, especially when you want to purchase there are several bureaucracy that could prolong. I mean, the time …this actually affect the proper conduct of research. So, the problem is in the delay,… I don't know it is a sort of bureaucracy" (P01).

…"The institutional bureaucracy for procurements is another major headache as inputs and supplies like laboratory reagents, equipment, for clinical trials needs higher standard with certifications"… (P06).

Sub-theme 3: Regulatory and ethical approval process challenges

Regulatory and ethical approval process challenges have been described by almost all participants. The current regulatory processes for the conduct of clinical trials were not smooth, time consuming and the delay was reported to be unreasonable. The regulatory administrative demands associated with protocol approval, approval fees, pre-import permits, and shipment regulations were not conducive to the conduct of trials and partly responsible for the rising costs of clinical trials.

…"*Making a conducive environment and a hastening clearance is essential as this is not smooth, especially the timing for ethical clearance and Ethiopian* Food and Drug Administration *(EFDA) approval is not as expected, there are some improvements that I have seen from what have been 10 years back, but it's still lagging behind and compared to even other African countries and that should also be improved" (P04).*

"I think at the government level, especially the regulatory bodies and the ethics committees, they have to protect the public, but at the same time, they have to make decisions as soon as they can,

the delay is most often inappropriate it might take months, actually several months and the other problem as I said like policy of especially in importing goods and other materials" (P01).

Sub-theme 4: Key stakeholders perceptions towards clinical trials

Key stakeholders' recognition of the need and significance of clinical trials for the improvement of healthcare services and health outcomes of the community is critical for the success of clinical trials projects. Some of the participants pointed out the following categories of stakeholder perceptions as capacity challenges in their respective settings.

Clinical trial consideration as other research by institutions; Recognition of clinical trials importance and its unique feature by institutional hierarchal leadership is critical.

There is need of many infrastructures requirement and there are challenges and limitations as well. Institutional level clinical trials are considered as other research projects but clinical trials are demanding by quality and infrastructure (many quality and infrastructure requirements). Unlike doing other research projects, everything in clinical trials has to be documented, done by higher quality….It is difficult to me to say capacity; it is a sort of negligence, not understanding demanding nature of clinical trials… Even at a country level there is a problem on the understanding of clinical trials' needs. There is such a problem in administrative level (P09).

Bad perceptions of the community to wards clinical trials; As a community is a source of participants of clinical trials, community awareness of the importance of clinical trials is required for successfulness of intended CTs.

…"But when it comes to our country, when we talk about clinical trials, people say that Oh, they are going to try medicine for our woman's or our man's whatever …Oh, there is a bad perception, bad perception from the top to the lower level" (P07).

Awareness of insurance company about clinical trials: Obtaining health insurance coverage for clinical trials is a great challenge especially if the insurance companies do not have fine-tuned understanding and experience with insuring clinical trials. Two participants indicated that insurance companies had no experience with clinical trials. There was low interest to provide insurance or ask for large amount of money not matching to project budget.

"The other most important issue which I believe, we have come up with a solution, is a clinical trial insurance. There was no insurance company for clinical trials in Ethiopia, actually, which

would give us a reasonable cost. The cost we were requested for the insurances is like probably how I can tell you. It is like one tenth of the total budget of the project" (P06).

Sub-theme 5: factors related to *structural capacity limitations*

Presence of enabling and active institutional structures with strategic plan specific to clinical trials is required to attract researchers and funders of clinical trials. Two participants identified that there was limited upper institutional structure for clinical trials. All participants mentioned that the availability of strategic management plans for research in general in their organization but strategic management plan for clinical trials with specific targets were lacking. Two noted availability of strategic management plan for the clinical trials without specific targets in their institutions.

"The clinical trial was started with intention and the interest of some interested guys without having the structure. So, we need to revise the structure and related issues to conduct such big trials" (P02).

"There is no a strategic management plan for conduct of clinical trials at the university level…basically they focus on cross sectional study and like that" (P05)

Sub-theme 6: **Inadequacy of trained Clinical trials workforce related factors**

Trained human resources are required not only to design, conduct, manage, analyze, and publish the studies but also to build and maintain infrastructure necessary for the clinical trials research. Availability of qualified workforce by education, training, and experience both at coordinating unit and collaborating facility is crucial for clinical trial industry to bloom.

"One of the biggest challenges of all time is that, most of the professionals associate the research with incentives. We do have some of the professionals like microbiologist, public health specialists, and epidemiologist but there is shortage of immunologist, statistician or any PhD holder inclined to do such research" (P02).

The human resource capacity, of course, that is a little bit a challenge, obtaining human resource like physician, nurses, pharmacists, laboratories, among 11 best hospitals who are trained with GCP and GCLP was a challenge actually. So we have given trainings and we have certified now almost 80 persons as better solution… (P07).

Sub- theme 7: ***Availability of Clinical trials funds***

Participants indicated that availability of clinical trials funds could be impacted by a number of

interlinking factors. The capacity of clinical trials infrastructure, capacity of the researchers, competition, availability of organizations funding clinical trials, number of clinical trials conducted in the set up and enabling environments like ethical clearance, the shipment regulations and the EFDA regulations increases the availability of the clinical trials funds. Even though, there is no existing adequate and sustainable funding for running clinical trials that approaches the site, availability of funds for establishing the early preparatory phase of the infrastructures stated as not being a problematic by some participants.

…" So in order to get funded, you need to have more clinical trials in your setup or in your country…also the conducive environments should be there, like ethical clearance, the shipment regulations, EFDA the regulations all this should be conducive. A trained number of staffs should also increase…then… through time with this funding opportunity may increase, because we have seen some African organizations are now promoting for clinical trials in Africa" (P04).

… "I don't think there is problem with adequacy and sustainability of funds for preparatory stage of the facility. We have already secured the grants from our funder and other networks working on clinical trials .But there is limitation on sustainability of fund beyond establishing preparatory phase. There is no existing fund for running forthcoming clinical trials and should come with their own funds" (P09).

Global theme 2: Sustainability of clinical trials infrastructures capacity and the settings

Institutional capacity is not a fixed entity that can be counted on to remain in perpetuity. Institutional sustainability is about continued effectiveness, about creating and maintaining an acceptable level of capacity, and then about converting that capacity into actual performance. Institutional viability is critical to transforming clinical trials infrastructure capacity investments into future actual service delivery. Therefore, setting-up resilient clinical trials infrastructures is essential to conduct clinical research within stringent quality guidelines and international regulations. As elucidated by some of the participants, sustainability of capacity of clinical trials infrastructures is also influenced by a number of interconnected elements including institutional priority, availability of research, permanent staff, availability of funds, and integration with existing structure with greater level autonomy and flexibility.

"This trial is for a short period, it will be completed maybe in a year or two. But after that the site will be maintained. I think it will be part of the university... I mean, in the future, one of the

priorities research… nowadays, people are engaged in research, I mean, when we compare it from the previous times it is really increasing. People are getting trainings in different fields and such engagement will make the site more and more functional in the future. … I think it will be sustainable. .. As long as it is one of the priority areas" (P01).

Global theme 3: Priority area to develop capacity

Participants identified a number of priority areas to develop capacity that should seek strategy or broader policy attention from their setting to nationwide. The followings are insights on mechanisms and strategies mentioned by participants to be implemented.

Sub-theme 1: Establishing and strengthening data management capacity of clinical trials

Two participants identified establishment of data management facility and one participant strengthening data management capacity by assigning more staff and high level expertise as priority area to develop capacity.

… "In the future that's one of our plan, putting a data management unit appointing staff but we have you know, identify the data management room and also controlling data that one based on GCP"… (P04).

Sub-theme 2: Establishing and upgrading research laboratory capacity (strengthening laboratory capacity)

Three participants identified establishment and strengthening of laboratory capacities as priority areas.

"The university has also been building several laboratories, which could be research laboratory…. where there could be a preclinical, I mean, research laboratory. Probably this will be… I mean, incorporating clinical and preclinical laboratories will be one of the priorities of the university I hope in the future" (P01).

Sub-theme 3: Quest for funding

Some participants noted the search for funding from local source as the priority for capacity strengthening even though they believe that the priority is of making the wider CTs environment more enabling should precede this effort. Participants also highlighted that, more efforts were needed from the researchers of clinical trials themselves. Further, the participants have also indicated that the government (e.g.MoH) has to find way of funding clinical trials.

…"One of which should be also included in the strategic plan, should be like facilitating the fund… all most, all of the clinical trials has been funded by foreign funders. So what I am thinking is, there has to be some way to Ethiopian researchers to conduct clinical trials to be funded by the government on competitive based for Ethiopia" (P07).

Sub-theme 4: Human resource Related capacity developments

Besides increasing the number and professional diversity of clinical trials workforce, ensuring appropriate capacity development of individual is critical to conduct quality trials. Similarly, the need of institutional strategic recruiting and retaining of qualified staffs is also identified as one of the priority areas.

"The first point may be the human resource. So, I mean, both clinical and preclinical research should be strengthened and faculty should be trained and should be involved with in research, so they will get more experience"(P01).

Sub-theme 5: Increasing awareness level of insurance companies on Clinical trial insurances

Although there is no legal/regulatory evidence to support the necessity of other types of clinical trials insurance packages in Ethiopia, medical insurance coverage for trial participants became regulatory mandatory for every CTs to be conducted in Ethiopia. Therefore, availability of insurance companies having understanding the nature of clinical trials research is vital.

"We have also a plan to conduct some workshop or some awareness for all Ethiopian insurance companies, to provide clinical trials, insurance we have a plan probably in the coming one year or two years" (P07).

Sub-theme 6: Structural Revision (Upgrading the site/unit to research center)

Institutional structure is required to attract and retain competent trialists, more trials proposals, and funders. It is also vital to the stability of the clinical trials infrastructure and excellence of work, which the institutions is undertaking. Two participants indicated that up grading of the clinical trials unit and clinical trials center was their priority capacity development for the set up sustainability.

…"We have small units and we are struggling so far to maintain the unit and staff and changing it to suit the center" (04).

"So there is a need to revise the structure and related issues to conduct large trials, perhaps left or right we have started it …As I said earlier, we are planning to have five year strategic plan.

This five year strategic plan includes the whole structure and the budget of the research wing, if this structure is approved by the higher officials problem will be solved easily" (P02).

7.3. Documents Review

Documents review in 11host institution of CTFs, one research institute and two ministries was done. Accordingly, there is research Strategic plan for health in general in all institutions. In two institutions, clinical trials were stated as one of research direction but lacked some specific targets and non-publicized roadmap for clinical trials is available in ministry of health.

8. Discussion

This study presents a snapshot of the existing capacity to conduct clinical trials, gaps, and priority for capacity strengthening of clinical trials in 13 clinical trials facilities and document review of three organizations in Ethiopia. The focus of the assessment was predominantly on capacity domains of general administrative structure and business continuity, workforce, clinical trial experiences, laboratory infrastructure, data management infrastructures and data quality management approaches and review of availabilities and the direction of documents like policy/ strategy plan/ roadmap for clinical trials in respective institutions.

8.1. Physical infrastructures for Clinical trials

The size and organization of physical infrastructures required to conduct clinical trials is guided by the type of study, trial design and study protocol (55,56), while organizational capacity assessment and physical infrastructures are often overlooked (55). For most clinical trials projects, required physical infrastructures can be acquired from health facilities (57) with some improvisations that can accommodate CTs work flow needs. However, this and other study findings revealed that, there are few physical infrastructure and dedicated physical space (58) for services like research administrative offices, monitor room, consenting/counseling rooms, examination rooms for participant evaluation/treatment, inpatients beds, outpatient beds, data management, research laboratory (59), pharmacy services equipped to handle investigational products (60) both at collaborating health facilities and coordinating CTFs found in most of the African countries to fully deal with their responsibilities. For this reason, to conduct clinical trials in compliance with international standards in resource-poor settings, it is widely recognized that there is a need to build healthcare and research infrastructures (59,61,62) too. However, creating new physical premises may be associated with high start-up costs for clinical

trials (58,63,64).

8.2. Clinical Trials Laboratory

The Clinical trials facility should have appropriately designed areas of sufficient size for the type of work being performed and provide an adequate degree of separation and security to assure the integrity of trial samples at all times (65). At the same time, the laboratory/tests competence should be certified or accredited or bear external quality assessment to support the reliability of results (66). Significant numbers of CTFs have reported ownership of dedicated research laboratory premises with some claimed QAS, biological safety levels lower than 3 and limited scope of tests that are required for most studies. Non-availability of the external quality assessment/certifications /accreditations for most tests, both at the main CTFs and collaborating health facilities is the other capacity limitation identified in relation to laboratories. As a result, this may have a negative impact on the credibility of the research findings from these laboratories (67).While some of these laboratories have some past experience in participating in clinical trials and some capacity building activities have been carried out, establishment of GCLP-compliant laboratories at least centrally coordinating CTFs appears not to be in effect so far.

8.3. Clinical Trials Workforce; Size, composition and distribution of human resource for CTs in CTFs

As analysis of the workforce in CTFs has shown that the size of current Clinical trials workforce is much lower than the anticipated clinical trials workforce, (68). The size of workforce involved in running clinical trials is not only small in terms of number but also by professional diversity despite the country having rapidly increasing number of health practitioners and huge population size in the African continent. Although we did not found studies specific to workforce in clinical trials , the current finding accords with other workforce studies conducted in general health research (69,70) . One of the underlying causes for the small clinical trials workforce may be attributed to the lack of institutional strategies for attracting and retaining qualified researchers, and the lack of a wider enabling researcher environment. Meanwhile, involvement of large number of clinical nurse and laboratory technologist by profession may not be unusual as most of clinical trial activities in the assessed facilities are predominantly drug related trials. Additionally, the small number or lack of some critical areas of expertise, such as Epidemiologist, Monitor/Auditor, Statistician, Data manager, Infectious Disease Physician have

been observed in this study and in previous studies (71). Non-participation of these professions should be taken seriously. As significant number of these professionals could be investigators and methodologists of clinical trials (68), non-involvement of these professionals may have ramifications on some quality aspects of the trials. There is also deleterious effect on creation of the future generation skill mix workforce critical mass for the CTFs and nationwide. Unavailability of workforces having training and experience pertinent to clinical trials may also have a detrimental effect on sustainability of CTFs.

8.4. Therapeutics diversity and Scope of CTs

An analysis of research portfolio of CTFs in terms therapeutic/service area shows that some new therapeutic/service area different from what have been previously reported emerged in the landscape of Ethiopian CTs (72). However, less participation in terms of disease/service category and disease categories listed as top 10 leading cause of death for the country. Only tuberculosis and HIV/AIDS trial are covered by the CTFs among the disease categories listed as top 10 leading cause of death in Ethiopia. Unfortunately, the disparities do also exist in terms of phase of clinical trials and number of CTFs participating in the trials. The majority (n=16; 46%) of the conducted clinical trials were phase III and less number of phase I,II and IV (73,74) trials have been conducted by the CTFs. This is expected, as most CTFs reported limited capacity to participate in phase I and II trials. A linear increase in capacity to participate in clinical trials by trial category (phase I through phase IV) was not observed in this study as indicated in previous studies (73,74). In particular, less participation in phase I CTs is witnessed as a result of capacity limitations such as; insufficient emergency equipment, trained and experience staff, funds and other infrastructures (75). The reason for low participation for other phase like phase II and IV should be assessed in future studies.

8.5. Data Management and data quality monitoring

As the results of both the qualitative and quantitative studies indicated, most CTFs owned data management and archiving physical facilities both onsite and off-site, with only one CTFs having external certification of the data management system. This condition ascertains the need of capacity strengthening to conduct clinical trials to international standard. Similarly, only about half CTFs are employing CDMS. In line with this, two softwares, namely; Openclinica and Redcap are the most utilized. This may be due to free availability of these softwares or some

capacity building was done as a result of past external collaboration. Utilization of quality management systems for data management such as, SOPs for data management (e.g. data collection and handling, system maintenance, data back-up, data recovery) are in place in most CTFs. However, evidence of system validation as per GCP requirements is missing. Regarding data monitoring, majority of CTFs are using traditional approaches like onsite source data verification (SDV) while, a move to use recent monitoring approaches such as, remote monitoring and centralized monitoring is lagging and have been reported by limited number of CTFs and none of the CTFs reported use of risk-based targeted monitoring, statistical techniques error acceptance level, or risk-based triggered monitoring. Although one reason for sticking to traditional monitoring approaches by the CTFs could be attributed to information technology related infrastructure such as poor internet connections further study is required to explore the reasons behind.

8.6. Regulatory and Ethical Approval process of Clinical Trials

Presence of independent functional and effective regulatory and ethical infrastructure is critical to ensure the rights, safety and wellbeing of the trial participants and the scientific integrity of clinical trial data (76,77).Whereas, disproportionate regulation (78) and differing interpretations of the guidelines can create extra bureaucracy and makes it increasingly difficult for investigators to carry out clinical trials, without increasing safety of the study participants (79). Findings from key informant interviews indicated that regulatory and ethical approval process environment in Ethiopia are not conducive and suffer from a varied range of capacity challenges require attention. The Ethiopian Food and Drug Authority (EFDA) is the national regulatory body for Clinical Trial Authorization and oversight in Ethiopia. The current regulatory processes associated with protocol approval, lack expertise capacity of expertise, experience (80), pre-import permit, and shipment regulations are not smooth, time consuming and the delay is often unreasonable.

8.7. Bureaucracy within the institutions and considering CTs like other research projects by hierarchal leadership of the institutions

Institutional bureaucracy is necessary in providing rules and guidance for the conduct of clinical trials and to regulate research staff as well. However, an inefficient bureaucracy in public institutions can be impediments to the clinical research projects and motivation to develop new research protocols (20,81–83). Findings from key informant interview revealed that there are

varied ranges of capacity challenges encountered due to institutional bureaucratic in procurement procedures and lack of hierarchal institutional leadership that respond to the clinical trials demand (84). A current working environment is reported as not only discouraging and impeding but also frustrates the investigators even to think of clinical trials (85). Procurement system of trials inputs like purchasing of equipment,chemicals, reagents and different supplies is difficult as institutional procurement system and bureaucracy is time consuming, unanticipated, multipart and sometimes the project opportunity may be missed due to the delays.

unanticipated, multipart and sometimes the project opportunity may be missed due to the delays.

8.8. Perception of some stakeholders towards clinical trials needs a change

Recognition of the importance and distinctive features of clinical trials with respect to other research by key stakeholders is required, as each stakeholder offers a diverse set of tools to support the essential components of a clinical trial (86). A key finding from the interviews identified passive engagement of stakeholders like local community, hierarchal institutional leaders and insurance companies are the capacity challenges that CTFs are facing as a result of unbalanced perceptions towards CTs. More particularly, negative perception of community towards clinical trials (87) such as fear of being a “guinea pig” could create potential barrier (86,88). Similarly, lack of optimal (sensible) commitments and support from hierarchal leadership in and outside institution that a clinical trials demand was also identified as challenges. Finally, though there is a signal that one or two companies are showing some level of interest to cover clinical trials insurance due to constant requests from different trial facilities and sponsors, the high cost requested and low interest of insurance companies to cover trial participants is yet one-of the areas that need capacity development.

8.9. Structural capacity limitations for Clinical Trials

The existence of a scattered clinical trials infrastructure, laboratory, data management facilities, human resource due to a long history of capacity development efforts supported by developed countries, does not necessarily guarantee access to the capacity to conduct clinical trials. The existence of functional institutional structures and systems to guide and support the researchers, and strong national research policies and funding specific to clinical trials is essential (85,89). According to the interviewees, in all host institutions and collaborating health facilities there is a basic institutional structural capacity limitation for clinical trials. In many of the institutions,

there is no formal institutional structure and strategic management plans for attracting clinical trial funders, recruiting and retaining competent trialist, absorbing and creating future generation trialist, and enthusing researchers to engage in clinical trials. As explained in works of Jaiswal this could have been happened due research capacity developments that have focused primarily on developing individual skills without the necessary institutional and national structures and systems to support the trained individuals. Available clinical trials are initiated by interested individual researchers (90) or donor driven not by the structure or strategic management plan of the institutions. Furthermore document review at the EBTi, MiNT and MoH revealed that only road map for clinical trials is found at Ministry of health. However, it seems that road map is not well publicized and implementation is not yet came to in effect.

8.10. Institutional Sustainability of Clinical Trials Facility

Sustainable capacity is the ability of an organization to retain structured practices and its benefits over time (91,92). Institutional sustainability is critical for transforming clinical trials infrastructures capacity investments into future actual service delivery (93). Nevertheless, there is no widely accepted sustainability assessment tool for clinical trials facilities, various indirect indicators are reported in literatures. One approach is expression through systems approaches capacity development at different levels: individual, organisational, and environment (94,95), the existence of efficient structures and processes that allow a program to leverage resources to effectively implement and maintain evidence-based policies (56,96) . Dearth of these structures in most of Ethiopian institutions is confirmed through document review and in-depth interview. The other indirect approach is availability of sustainability capacity domain and the contributors to sustainability are like developed a full trial portfolio that goes beyond a single disease aspect and single disease research programme, a mid- to long-term strategic management planning portfolio (61), funding stability, core staff and core funding. As these sustainability capacity domain and the contributors to sustainability are lacking in Ethiopia sustainability of the CTFs seems questionable. However, most participants of the current study believed that their facility would be sustainable with all challenges they had been facing as far as the research was priority of their institution and the number of researcher interested to participate in clinical trials are increased.

8.11. Availability of Funding for Clinical Trials

Clinical trials are known to be expensive to carry out (97,98) and thus lack of funding for clinical trials is a frequently stated capacity challenge in the Ethiopian clinical trials landscape (27). Although findings from this study also confirm inadequate funding as a challenge, it might not be the most prominent capacity challenge (99) for CTFs have already built some level of infrastructure and secured grants for some years from different organizations supporting CTs . In addition, availability of funding for Clinical trials in itself is not a capacity to conduct clinical trials, rather often a support to the capacity development. Participants have indicated that availability of funding is determined by factors like the available capacity of clinical trials infrastructure, capacity of the researchers, competition, availability of organizations funding clinical trials, number of clinical trials conducted in the set up and enabling environments like timely ethical clearance, the shipment regulations, and the regulations of EFDA. Therefore, the requirement of doing relevant background works with available institutional resource to strengthen the capacity on these areas and maximize the competitiveness for funding is the assignment of researchers interested in clinical trials. There is a green light in Ethiopia for availability of funding for clinical trials as some African and international organizations are now promoting clinical trials. Some Ethiopian academic and research institutions are also partly funding clinical trials. However, analysis of funding source of clinical trials in Ethiopia revealed that clinical trials funding is sourced largely by non-commercial international organization and only few clinical trials are funded from local source. Consequently, the quest for funding from local source and establishment of strategy and mechanisms that supports availability of funding from local source for Ethiopian scientists on competitive based should be emphasized seriously. Funding from local source may play central role to integrate clinical trials into institutional healthcare and research system, develop clinical trials infrastructures more relevant to local research questions in a sustainable ways.

8.12. Priority areas to develop capacity for Clinical Trials

Although, different stakeholders hold different perspectives on capacity development priority settings, allocation of public resources to capacity development priorities is related to a political matter (100–102). Hence, effective priority-setting may requires more than high quality economic research. Findings from the interview of the CTF participants indicated that wide-ranging capacity development was a priority across the facilities. Even though strong agreement

was not observed across the capacity development priorities identified by the participants, most of the identified capacity development priorities are closely related and capacity developments planning's may be overlapping as result of capacity development priorities areas identified necessitates integrated and structural approaches. Establishing or upgrading existing data management, research laboratory capacity of clinical trials, human resource related capacity strengthening, revision (upgrading the site/unit to research center), Creating enabling environment; related to regulatory approval, ethical clearance and institutional bureaucracy and increasing awareness level of insurance companies are the core areas identified as a priority for capacity development from the interview. The results from capacity assessment check list is also in agreement with some of these points. One interesting point about identified priority for capacity developments is, the issue being not only about establishing the infrastructure or capacity strengthening with available but also stressed on the issues of sustainability of infrastructure which is indeed an important aspects of capacity and capacity strengthening. These capacity development priorities may guide and initiate various institutions, policy maker and stakeholders who have roles and responsibilities in health research capacity strengthening. To this end, the CTFs are conducting trial research at varying levels, with unsupportive research administration structures and environments. This could be one of the reasons why, Ethiopian clinical trials industry is lagging far behind the Sub-Saharan African countries like Kenya and Uganda (37) . Nevertheless, still there is a room to be productive and internationally competitive, given that the most critical issues stated as priority area for capacity development by the participants are addressed by respective stakeholders.

9. Strengths and Limitation

One of the strengths of this study emanates from its utilization of a mixed methods design, which helped examine more comprehensive capacity dimensions of each CTF and divergent views between them. The other strength is that, to my understanding it is one of the first extensive cross sectional studies to assess capacity of CTFs located at different geographic settings of the country and managed by different institutions. On the other hand this study has also several limitations. First, the clinical trial facilities included in the study are those only conducting clinical trials of drugs; the findings may not be generalizable for other types of clinical trials such as service intervention. An additional restriction is that the survey respondents were almost all associated with clinical trials listed on the ICTRP and indexed primary registries database. Even

though recently prospective registration of clinical trials became mandatory for clinical trials and there are only few clinical trials which have not been registered, nonregistered CTs could have been excluded from this study. The study results could also be subject to potential bias in a positive direction as the CTFs who completed the survey may have more capacity organized better experience than those who chose not to participate. Due to unavailability of standardized capacity scoring method for clinical trial capacity assessment unlike other institutional capacity assessments, we did not do capacity scoring of each CTF. The lack of a standardized measure could also have introduced information bias and limits comparisons across studies.

10. Conclusions

In conclusion, this study has identified that Ethiopian CTFs have limited capacity to conduct CTs due to a lack of physical infrastructure, workforce, CTs experiences, and data management, as well as a lack of institutional structures to support CTs at various levels. Furthermore, establishing or upgrading existing data management, research laboratory capacity of clinical trials, human resource related capacity strengthening, structural revision of CTFs, creating enabling environment; related to regulatory approval, ethical clearance and institutional bureaucracy have been highlighted as a priority for capacity development.

12. Recommendations

There is a need for effective coordinated efforts among different stakeholders including but not limited to MoH, EFDA, Ministry of Science and Higher Education (MoSHE), Ministry of Finance (MoF), MiNT, academic institutions, research institutions, local pharmaceutical companies, insurance companies, investigators and international organization supporting CTs to create enabling environments for the CTs. MoH should take the leading role, together with or via its technical wing institutions to convene stakeholders, to formulate national programmes that could make CTs capacity strengthening one the flagship programmes(initiatives) and pave the way to the implementation of the CTs road map. The platform should give emphasis towards addressing at least the following issues;

- Strengthening the existing CTFs; considering establishment of institutional structures that can support CTs in the institutions and devising funding mechanisms directed towards to clinical trials is essential to safeguard sustainability of CTFs.
- CTs workforces; designing of strategies directed towards attracting and retaining

competent workforces.

- Laboratory accreditation; most CTFs are suffering from lack of GCLP compliant laboratories. Formulation of national programme that could support in accrediting the laboratories doing clinical trials samples should be considered.
- Improve regulatory processes; there is a need to streamline and improve the regulatory and ethical approval processes without compromising public safety to support the CTs industry.

Lastly, future research should consider validating the measurement tools (metrics) used in this study for larger sample sizes, such as the Sub-Saharan Africa, as well as their applicability to other non-drug clinical trials.

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Annex 1 Consent forms

A. Consent form for investigator administered questionnaires and checklist

Dear_____

Greetings,

I am Aliyi Amano and a student at the Center for Innovative Drug Development and Therapeutic Trials for Africa (CDT-Africa). We are doing Clinical trial capacity assessment to assess the capacity of clinical trial center/sites in Ethiopia to undertake clinical trial research. The capacity assessment will involve an overview of your site/Unit/center/ profile, physical infrastructure, Workforce, Training, clinical trial experience, and Data Management. The results of the capacity assessment will inform the preparation of a capacity development plan which will be implemented by the governments, sponsors and Funders of clinical trial sector.

For this particular part of the study, you have been identified as a critical and valued member whose opinions would assist in this assessment. Your Center/site/Unit trials could be at any stage (planning, ongoing, suspended or completed). We are therefore requesting you to complete self-administered questionnaires. The questionnaire should take about 40 minutes to complete. There are no risks in your participation in this study. Please be assured that your name will be kept anonymous. You are free to refuse to participate. If you do agree to participate, we kindly request that you answer all the questions but you are free to skip any question that you prefer not to answer. Please go to https://iwtizakg.paperform.co/to proceed. You are free to ask any questions about the study. Should you wish to contact us, you can do so at aliyiamanog@gmail.com.

Aliyi Amano ……Phone number [0947407134]

Email: [aliyiamanog@gmail.com]

B. Consent form for key informants for clinical trial centers/Sites capacity assessment

Dear_____

Greetings,

I am Aliyi Amano and a student at the Center for Innovative Drug Development and Therapeutic Trials for Africa (CDT-Africa). We are doing Clinical trial capacity assessment to assess the capacity of clinical trial sites/Unit/center/ in Ethiopia to undertake clinical trial research. The capacity assessment will involve key informant interviews about **Structure of Clinical Trials Center, Workforce, Training, Clinical Trial Experience, and Data Management**. The results of the capacity assessment will inform the preparation of a capacity development plan which will be implemented by the governments, sponsors and Funders of clinical trial sector.

For this particular part of the study, you have been identified as a critical and valued member whose opinions would assist in this assessment to serve as a key informant for the capacity assessment. Your /site/Unit/Center trials could be at any stage (planning, ongoing, suspended or completed). If you decide to participate, your responses will be audio recorded or only notes of interview will be taken if you don't want audio recording. The interview should take about 45 minutes to complete. There are no risks in your participation in this study. Please be assured that your name will be kept anonymous. You are free to refuse to participate. If you do agree to participate, we kindly request that you answer all the questions but you are free to skip any question that you prefer not to answer. You are free to ask me any questions about the study. Should you wish to contact us, you can do so at the address below.

The interview will be online via the Zoom meeting due to the current pandemic.

Please inform me your convenient time through this email if you are willing to participate so that I will forward the zoom address link for the meeting.

Aliyi Amano ……Phone number [0947407134]

Email: [aliyiamanog@gmail.com]

Annex 2: Tools for Data Collection

Assessment of Ethiopian clinical trial sites Capacity to conduct clinical trials to international standards

Part 1: Capacity check list adapted from Global health network, ECRIN and Health research board Ireland (online version).

Agreed to participate in the Ethiopian Clinical trial Site Capacity Assessment Study (ETCAS)? (Required)

Yes

No

I. Responsibility in center/site(Indicate in space below)_____

II. Gender (choose from dropdown box)

Male

Female

Other

III. Age (choose from dropdown box)

25-35

36-45

46-55

56-65

>65

IV. Maximum Degree hold and qualification(Indicate in space below)_____

V. Your center/Site/Unit/ name(Choose from dropdown box/specify if not available or leave it you do not want to mention)_____

1. When trial center/unit established (Indicate in space below) _____

2. Who established the trial center/Site/unit? (Tick all applies)

Research Institution (Ethiopian)

Academic Institution (Ethiopian)

Pharmaceutical Company (Non-Ethiopian)

Pharmaceutical Company (Ethiopian)

Research Institution (Non-Ethiopia)

Academic Institution (Non-Ethiopian)

Other

3. What is the current legal status of the center/site? (Select from dropdown box)

Public (Government)

Mixed (public-private Partnership)

NGO

Private

Other

4. Who is/are the current primary funder of your trial center/unit? (Tick all applies)

Research Institution (Ethiopia)

Academic Institution (Ethiopian)

Pharmaceutical Company (Non-Ethiopian)

Pharmaceutical Company (Ethiopian)

Research Institution (Non-Ethiopia)

Academic Institution (Non-Ethiopian)

Other

5. What is the center's annual level of funding (approximate)? (Indicate in space below)_____

6. Provide a list of organizations funding research at this center/unit? (Indicate in space below)_____

7. Which institute(s) uses this center for conducting clinical trials? (Indicate in space below)_____

8. How do you explain the stability of your center/site? (Select from dropdown box)

The center/site/Units established with intention of attracting other projects as it has some core funding and core staff. The center/Site/Unit along with its infrastructure is established for specific project.

The center/site/Unit has no core staff and core fund but the infrastructure is built with intention of attracting other projects coming with resources.

The center/site/Units established with intention of attracting other projects as it has infrastructure and core staff but no core funding.

9. Which of the Following facilities for clinical trials available in in your Site/Unit/Center?

I. Administrative offices (Select from dropdown box)

Dedicated

Not Available

Not dedicated

Not Applicable

II. Monitor room (Select from dropdown box)

Dedicated

Not Available

Not dedicated

Not Applicable

III. Examination room(s) for subject evaluation and treatment (Select from dropdown box)

Dedicated

Not Available

Not dedicated

Not Applicable

IV. Consenting or counseling room(s) (Select from dropdown box)

Dedicated

Not Available

Not dedicated

Not Applicable

10. Do your center/unit provide phase I trial service?

Yes

No

11. If no please select the reason/s that apply/ies from below or specify the reason (Tick all applies) Insufficient emergency equipment and infrastructure

Insufficient trained and experience staff

Insufficient Fund

Other

12. Is there dedicated inpatients beds available for clinical trials in your center?

Yes

No

13. What is the current number of inpatients beds available for the clinical trials in your center? (Indicate in space below)_____

14. Approximately what percentage of these inpatient beds are used on a daily basis if the trials are active? (Indicate in space below)_____

15. Is there a dedicated outpatient beds available for clinical trials in your center? (Indicate in space below)_____

16. What is the current number of outpatient bed available for clinical trial in your center? (Indicate in space below)_____

17. Approximately what percentage of these outpatient beds are used on a daily basis if the trials are active? (Indicate in space below)_____

18. What is the total approximate number of staff at the Unit/center? (Including supporting staff) (Indicate in space below)_____

a. Total number of study (trial) staff Scientists (Indicate in space below)_____

b. Total number of Support staff (if there is a support staff in your research team? (Indicate in space below)_____)

19. Who comprises your research team? (Tick all applies)

Infectious Disease Physician

General practitioners

Clinical Nurse

Pharmacist

Pharmacologist

Laboratory technologist

Clinical coordinators (project managers)

Epidemiologist

Statistician

Data manager

Nutritionist

Social scientist

a. Number of Infectious Disease Physician(Indicate in space below)

Please indicate the amount of time dedicated to clinical trial research by Infectious Disease Physician (Select from dropdown box)

b. Number of general practitioners (Indicate in space below)

Please indicate the amount of time dedicated to clinical trial research by general practitioners (Select from dropdown box)

c. Number of clinical Nurse (Indicate in space below)

Please indicate the amount of time dedicated to clinical trial research by clinical Nurse (Select from dropdown box)

d. Number of Pharmacist (Indicate in space below)

Please indicate the amount of time dedicated to clinical trial research by Pharmacist

e. Number of Pharmacologist (Indicate in space below)

Please indicate the amount of time dedicated to clinical trial research by Pharmacologist (Select from dropdown box)

f. Number of Laboratory technologist (Indicate in space below)

Please indicate the amount of time dedicated to clinical trial research by Laboratory technologist (Select from dropdown box)

g. Number of Clinical coordinators (project managers) (Indicate in space below)

Please indicate the amount of time dedicated to clinical trial research by clinical coordinators (project managers)

h. Number of Epidemiologist (Indicate in space below)

Please indicate the amount of time dedicated to clinical trial research by Epidemiologist (Select from dropdown box)

i. Number of Statistician (Indicate in space below)

Please indicate the amount of time dedicated to clinical trial research by the statistician (Select from dropdown box)

j. Number of Data manager (Indicate in space below)

Please indicate the amount of time dedicated to clinical trial research by the Data manager (Select from dropdown box)

k. Number of Nutritionist

Please indicate the amount of time dedicated to clinical trial research by Nutritionist (Select from dropdown box)

l. Number of Social scientist (Indicate in space below)

Please indicate the amount of time dedicated to clinical trial research by Social scientist (Select from dropdown box)

20. What % of the senior staff (scientific and technical) are nationals (Ethiopian)?

21. Please list specific staff training opportunities available to the members of the research team?

22. Which clinical trials phase is covered by your center? (Tick all applies)

Phase I

Phase II

Phase III

Phase IV

Other

22. a. Number of phase I clinical trials conducted in your center_____

22. b. Number of phase II clinical trials conducted in your center_____

22. c. Number of phase III clinical trials conducted in your center_____

22. d. Number of phase IV clinical trials conducted in your center _____

22. e. Number of other phases (other types of clinical trials) conducted in your center_____

23. How big is the clinical trial that could be conducted in your unit/center?(i.e. number of participants most commonly enrolled into your unit/center's trials_____

24. How many clinical trials does your center/unit conduct at any one time?_____

25. How many trials with locally generated protocols have been conducted in your center/unit so far? _____

26. How many clinical trials have been conducted by your center in the past 12 months? _____

27. Has your center undergone a GCP audit?

Yes

No

28. Who has conducted your center GCP audit?

Yes

No

29. How many years has this center/site been conducting clinical research to GCP standards?

____

30. How many clinical trials to GCP standards have your center/unit conducted in the past 3 years? ____

31. Do you provide GCP training for your clinical research staff before launching a clinical trial?

Yes

No

32. Do you provide refresher GCP training for your research staffs who are already involved in clinical trials?

Yes

No

33. If yes how often?

34. Do you maintain all training records?

Yes

No

35. If yes how do you maintain the training records?_____

36. On which therapeutic category/disease condition your center/Unit conducting trial? (Tick all applies)

TB Clinical Trials

Malaria Clinical

Hypertension Clinical Trials

Cancer Clinical Trials

Asthma Clinical Trials

Congestive Heart Failure Clinical Trials

Diabetes Clinical Trials

Antimicrobial resistance Clinical Trials

HIV Clinical Trials

SARS COV-2 Clinical Trials

Mental Health Clinical Trials

Service Intervention Clinical Trials

Complex Intervention Clinical Trials

Other

37. Is there a dedicated Laboratory to clinical trial (research laboratory) services on site?

Yes

No

38. Does the laboratory (ies) have a quality assurance system?

Yes

No

39. Does the laboratory (ies) hold any external certifications the methods) e.g. GCLP, ISO ...?

Yes

No

40. If yes please list below:

41. Does the laboratory (ies) have local reference ranges?

Yes

No

42. Is SOP for Recording of data and acceptance and release of results available?

Yes

No

43. Is there a disaster plan for the laboratory (ies)?

Yes

No

44. Do you provide GCLP training for your laboratory research team before launching clinical trials?

Yes

No

45. Indicate the number of laboratory personnel that have received GCLP training_____

46. Do the laboratory personnel receive refresher courses? Please note the frequency at which your institution conducts training refreshers

Yes

No

47. Are staff training records maintained?

Yes

No

48. Does your site utilise any of the following ethics review boards? (Tick all applies)

Local ethics review committee

Independent ethics review committee other than your institutions

A central investigational review board/national ethics review committee

Other

49. Is there a data management facility on site?

Yes

No

50. Is data sent to a central data management facility?

Yes

No

51. Is a designated study document storage area available on site (e.g. archiving room)?

Yes

No

52. Is there a long term document archiving facilities on site?

Yes

No

53. If yes, what % of storage space is used up?_____

54. Is there a long term document archiving facilities off-site?

Yes

No

55. If yes state below who owns the facility? _____

56. Does the center's data management unit have a quality assurance system?

Yes

No

57. Does the center's data management unit hold any external certifications?

Yes

No

58. If yes please list below (e.g. certified compliance to ISO19977, FDA 21 CFR 11 or WHO)_____

59. Where will the electronic data be stored? (Tick all applies)

Secure server

Individual computers

CDs

Zip drives

Memory sticks

Other

60. Does your institute currently have a clinical data management plan in place?

Yes

No

61. Does your institute have any of the following procedures in place to ensure high-Quality data is produced? (Tick all applies)

Risk-based targeted monitoring

Onsite source data verification (SDV)

Statistical techniques

Remote monitoring

Error acceptance level

What percentages of your data monitored

Other

62. Following on from the Question above, if the error rate is found to be higher than the approved acceptance level, does your institute implement further follow-up monitoring

Yes

No

63. What variables are included in data monitoring? (Tick all applies)

All (100%) data points

Critical and noncritical data points

Critical data points

Varies between projects and study design

Other

64. Please specify the type of staff training/development you conduct that is devoted to data quality for clinical trials? (Tick all applies)

Education prior to research

SOP training

ICH-GCP training

Education throughout clinical trial (as needed)

One-on-one education and training other

Skills training and development

Group education and training

Not applicable

Other

65. Who reviews the reports of data quality and consistency?_____

66. Different types of Clinical data management systems (CDMS) in use in your centers/units? (Tick all applies)

Proprietary

Open source

Commercial system

Other

67. Please provide the name Commercial Source CDMS products employed in your centers/units_____

68. Please provide the name Open Source CDMS products employed in your centers/units _____

69. Do you record original observations directly into a computerized system?

Yes

No

70. Are standard operating procedures in place for the following? (Tick all applies)

System Setup/Installation

Data Recovery

Data Back-up

System Maintenance

Data Collection and Handling

What contingency plans are in place in the event of failure of the computerized system?

Contingency Plans

Other

PART TWO: KEY INFORMANT INTERVIEW

I. Background information

1. Participant code: _____

2. Participant age: _____

3. Participant Sex: _____

4. Level of education and area of Specialization: _____

4. Experience as clinical trials specialist: _____

1. ***GENERAL ADMINISTRATIVE CAPACITY, STRUCTURE OF CLINICAL TRIALS AND BUSINESS CONTINUITY:***

How does the governance structure of this centre look like?

Is there a current strategic plan of clinical trials? (Publicised) How and when was this strategic plan prepared and explain about it?

What are the strategic priority research areas of this centre/Unit? How were they decided? How are researchers and externally funded projects encouraged to focus on these areas? What happens if an external funder approaches you with a proposal for a study in a non-priority area?

What do you think about the adequacy of possible funding opportunities for clinical trial research at this moment? How do you describe the availability of future funding the trial center to be continuing?

How do you explain about sustainability of clinical /durability of clinical trial infrastructure at your center?

What do you think are the main capacity challenges that your center/unit is facing at the moment?

What types of policy reforms or new programs is the center/government considering adopting in

order to address these challenges? Can you think of any needed capacity development for clinical trial capacity? What do you think are some of the priority areas to develop the capacity of clinical trial? What would be the best process to strengthen capacity?

2. WORKFORCE, TRAINING AND CLINICAL EXPERIENCE

What do you think as the major capacity available in your center?

How do you describe the adequacy of staff dedicated to clinical trial in this center? Is there available Staff future capacity development?

What do you think about availability of a competent trialist in your centre? Does the structure have the capacity to absorb and run new projects?

Specify if there are different strategies for recruitment of junior and senior staff. How easy is it to recruit qualified staff? How easy is it to retain qualified staff? What strategies have you tried/found useful for retaining staff?

Does the centre have core staffs? Would you tell me the number of core staff and their qualifications? Is there any formal core funding? (i.e. funding awarded specifically to support the center/unit's core activities and infrastructure as a whole rather than a particular project or individual) Is there non-formal core funding? (i.e. funding not awarded specifically to support the center/unit's core activities and infrastructure as a whole, but which may be used to support individuals carrying out core activities (e.g. individual fellowships or tenures; retained funds/overheads).Is other source available for funding core staff?

What do you think about the continuation of staff who was able to undertake quality research and attract research funding in this center/unit? How can this be achieved?

What about the gap available?

Can you think of any needed capacity development for clinical trial capacity? What do you think are some of the priority areas to develop the capacity of clinical trial?

Is there any movement towards broadening infrastructure or plan to develop capacity and to work on the following area of clinical trials?

-Non-communicable diseases

-Non-drug RCTs e.g. of complex interventions, service interventions, system strengthening innovations etc.

How do you explain about Sustainability of clinical /durability of clinical trial infrastructure at your center?

3. LABORATORY

.

What type of research studies can be supported by the laboratories (e.g. HPLC for pharmacokinetics; genomics/sequencing; etc.)?

Is there Organizational charts that identify the key personnel in each area, the independence of the quality assurance unit, the job description, qualifications and training of the individuals involved at any stage of the clinical trial process?

Can you think of any needed capacity development for clinical trial capacity? What do you think are some of the priority areas to develop the capacity of clinical trial?

How do you explain about Sustainability of clinical /durability of clinical trial infrastructure at your center?

Do you have additional comments or thoughts?

4. DATA MANAGEMENT

What are the major resource are available at your center? What do think are the major capacity gaps available in your data center?

Does your center have any challenge with following services?

- Electric power
- Internet connection
- Space of data storage
- Capacity of serve if used for storage
- Security

How do you try to address these problems?

Any major policies data center have concerning data management, archiving?

How do you explain about Sustainability /durability of data center infrastructure at your center?

Can you think of any needed capacity development for data center capacity? What do you think are some of the priority areas to develop the capacity of data center? In your view, what is the best way for capacity to be strengthened?

Probe: how do you see the role of external partners? Or other clinical trial centers in Ethiopia?

Any additional comments or thoughts?

Thank you for taking the time to participate in this study.

Part 3.Document review

This part wills deals review of the documents related to; policy, strategic plan/road map for clinical trials at Ethiopian Biotechnology Institute (EBTi), Ministry of Health and Ministry of Innovation and Technology (MiT).Availability of these documents and their direction and specific targets relevant to clinical trials assessed.

Annex 3 Additional files (deidentified)

Table 10 Available CTs Physical Infrastructures by facilities (all numbers in brackets are in percentage)

Site/Unit/Center	Domain Physical infrastructures Assessed					
	Administrative offices	Monitor room	Consenting/counseling room(s)	Examination room(s)for subject evaluation/treatment	Inpatients beds	Outpatient beds
TF1	Dedicated	Dedicated	Not dedicated	Not available	Not Applicable	Not Applicable
TF2	Dedicated	Dedicated	Dedicated	Dedicated	No	Yes
TF3	Not dedicated	Not dedicated	Dedicated	Dedicated	Yes	Yes
TF4	Dedicated	Not dedicated	Not dedicated	Dedicated	Yes	Yes
TF5	Not Available	Not dedicated	Not dedicated	Not dedicated	No	No
TF6	Not dedicated	Not dedicated	Dedicated	Dedicated	No	No
TF7	Not available	Not available	Not available	Not dedicated	No	No
TF8	Dedicated	Dedicated	Dedicated	Dedicated	Yes	No
TF9	Dedicated	Dedicated	Dedicated	Dedicated	Yes	Yes
TF10	Dedicated	Not dedicated	Not dedicated	Dedicated	Yes	Not Applicable
N(%)[a]	6(60)	5(50)	5(50)	7(70)	5(50)	4(40)
N(%)[b]	2(20)	4(40)	4(40)	2(20)	4(40)	4(40)
NA	2(20)	1(10)	1(10)	1(10)	1(10)	2(20)

[a] No of site with specified capacity; [b] No of site without specified capacity; NA= not Applicable

Table 11 Descriptive Statistical Analysis of workforce Capacity in 10 assessed facilities

Site/Unit/Center	Number of professionals										Total work force by profession in all assessed Trial facilities
professional Categories	TF1	TF2	TF3	TF4	TF5	TF6	TF7	TF8	TF9	TF10	
Infectious Disease Physician	-	-	1	-	-	-	-	2	2	-	5(3.2%)
General Practitioner	-	1	3	-	1	-	1	1	1	2	10(6.3%)
Clinical Nurse	-	3	4	3	2	2	-	4	6	4	28(17.6%)
Pharmacist	-	1	2	-	-	2	-	2	2	1	10(6.3%)
Pharmacologist	-	-	2	3	-	-	-	-	-	-	5(3.2%)
Laboratory	10	3	-	2		2	-	3	2	5	27(17.0%)

technologist											
Clinical coordinator(Trial manager)	-	-	2	4	-	1	-	1	1	1	10(6.3%)
Epidemiologist	-	-	-	-	-	-	-	-	-	-	0
Statistician	-	-	-	1	1	-	1	-	1	-	4(2.5%)
Data manager	-	1	1	1	-	-	-	-	2	-	5(3.2%)
Nutritionist	-	-	-	-	-	-	-	-	-	-	0
Social scientist	-	-	1	-	-	-	-	-	-	-	1(0.6%)
Monitor/Auditor	-	-	-	-	-	-	-	-	-	-	0
other research staff*	-	1	2	3	1	-	1	2	-	-	11(6.9%)
Scientific Staff	7	10	18	17	5	7	3	15	17	13	112
Support staff	3	4	4	5	0	2	0	5	10	14	47
% of the senior staff	100	100	100	98	100	60	100	100	100	100	96
Total work force	10	14	22	22	6	9	4	20	25	27	159

* **Other research staff reported includes (internal medicine, Psychiatrist, Immuno-pathologist, Microbiologist, Pharmaceutical Sciences, Ethnobotanist, Anesthetist)**

Table 12 Summary of Clinical Trials Scope and therapeutics diversity for CTs interest in the assessed 10 sites

Sites/Unit/center	HTN CTs	Malaria CTs	TB CTs	Cancer CTs	Asthma CTs	DM CTs	CHF CTs	AMR CTs	HIV CTs	CI CTs	MH CTs	SI CTS	SARS COV-2 CTs	Other CTs*	Phase of clinical trials(CTs)				
															I	II	III	IV	Other
CTF1	-	-	X	-	-	-	-	-	-	-	-	-	-	-	-	-	-		x
CTF2	-	x		-	-	-	-	-	-	-	-	-	-	x	-	X	x		-
CTF3	X	x	X	-	-	-	-	-	-	-	-	x	x	x	x	x	x	x	-
CTF4	-	-	X	-	-	-	-	-	-	x	x	x	x	-	x		x		-
CTF5	-	-	-	-	-	-	-	-	-	-	-	-	-	x		-	-	X	-
CTF6	-	-	-	-	-	-	-	-	X	-	-	-	-	-		-	-	X	-
CTF7	-	-	-	-	-	-	-	-	-	-	-	-	-	x		-	-	x	-
CTF8	-	X	-	-	-	-	-	X	X	-	-	-	-	-	x	x	x	-	-
CTF9	-	-	X	-	-	-	-	-	-	-	-	-	-	-	-	-	x	-	-
CTF10	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	x	x	-
No of Sites / Units /center	1	3	4	0	0	0	0	1	2	1	1	2	2	4	3	3	6	5	1

*other CTSs mentioned includes; Anesthesia, Pain management, Bioequivalence clinical studies, Dermatological, Mental health Clinical trials, Complex Intervention trials, Service intervention and Leishmaniasis.

HTN; Hypertension, TB CTs; Tuberculosis Clinical Trials, DM; Diabetes, AMR; Antimicrobial resistance, CHF; Congestive Heart Failure, MH CTs ;Mental Health Clinical Trials, CI CTs; Complex Intervention Trials ,SI CTs ;Service Intervention Trials.

Table 13 Clinical trials experience and associated capacities in surveyed facilities

Domain assessed	CTF1	CTF2	CTF3	CTF4	CTF5	CTF6	CTF7	CTF8	CTF9	CTF10
Typical size of clinical trial that could be conducted in unit/center?(i.e. number of participants most commonly enrolled)	-	300-400	-	200	60	90	12	1400	140	135
Number clinical trials center/unit could accommodate at a time?(parallel trials)	-	2	-	1	2	2	2	2	1	1
Number of trials with locally generated protocols has been conducted in the center/unit so far?	-	0	2	5	3	0	3	0	1	2
Number of clinical trials has been conducted by the center in the past 12 months?	-	1	4	1	2	0	1	2	1	1
Number of clinical trials to GCP standards have center/unit conducted in the past 3 years?	-	3	5	1	0	0	-	4	1	-
Has site/unit/ center undergone a GCP audit?	no	yes	yes	yes	no	no	no	yes	yes	yes
Who has conducted your center GCP audit?	-	Spo	EFDa ,WHO	Local IRB	no	-	-	CRO,Sp,EFDA	Sp,EFDA	Spon
How many years has this center/site been conducting clinical research to GCP standards?	0	15	15	8	0	0	0	7	8	15
Provide GCP training for clinical research staff before launching a clinical trial?	-	yes	yes	yes	-	yes	no	yes	yes	yes
Provide refresher GCP training for research staffs who are already involved in a clinical trial	-	yes	yes	yes	no	no	no	yes	yes	yes
If yes how often?	-	Fnt	ADN	ADn	-	-	-	alw	yrl	yrl
Maintain all training records?	yes	yes	yes	yes	-	-	no	yes	yes	yes

Table 14 Laboratory and associated capacities in surveyed facilities

Laboratory facilities	CTF1	CTF2	CTF3	CTF4	CTF5	CTF6	CTF7	CTF8	CTF9	CTF10	N(%)[a]	N(%)[b]
Research laboratory	yes	yes	yes	yes	no	no	no	yes	yes	Yes	7(70)	3(30)
laboratory (ies) QAS	yes	yes	yes	yes	no	no	no	yes	yes	Yes	8(80)	2(20)

laboratory(ies) external certifications	yes	no	no	no	no	no	no	no	yes	Yes	3(30)	7(70)
laboratory(ies) local reference ranges	yes	yes	no	no	no	no	no	yes	yes	Yes	5(50)	5(50)
SOP for Recording of data and acceptance and release of results	yes	yes	yes	yes	yes	Yes	yes	yes	yes	Yes	10(100)	0
disaster plan for the laboratory(ies)	yes	yes	yes	no	no	no	no	yes	yes	No	5(50)	5(50)
provide GCLP training before launching a clinical trials	yes	yes	yes	yes	no	Yes	yes	yes	yes	Yes	9(90)	1(1)
refresher courses for laboratory personnel	yes	yes	no	yes	no	no	yes	yes	yes	No	6(60)	4(40)
Are staff training records maintained?	yes	yes	yes	yes	no	no	no	yes	yes	Yes	7(70)	3(30)

[a] No of site with specified capacity; [b] No of site without specified capacity

Table 15 Distribution of current data management facilities available in surveyed settings

Data Management facilities	CTF1	CTF2	CTF3	CTF4	CTF5	CTF6	CTF7	CTF8	CTF9	CTF10	N(%)[a]	N(%)[b]
Data management facility on site?	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	7(70)	3(30)
Central data management facility?	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	8(80)	2(20)
designated study document archiving room on site	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	8(80)	2(20)
Long term document archiving facilities on site?	No	Yes	Yes	No	No	Yes	No	Yes	Yes	Yes	6(60)	4(40)
long term document archiving facilities off-site	No	No	No	Yes	No	Yes	No	Yes	Yes	No	4(40)	6(60)
data management unit quality assurance system	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	8(80)	2(20)
data management unit external certifications	No	No	No	No	No	No	-	No	Yes	No	2(20)	8(80)
Clinical data management plan in place	No	Yes	Yes	Yes	No	Yes	No	Yes	Yes	No	6(60)	4(40)
direct entry of observations into a computerized system	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	No	6(60)	4(40)

[a] No of site with specified capacity; [b] No of site without specified capacity

Table 16 Monitoring approaches in use by surveyed facilities

	Procedures in place to ensure high-Quality data is produced								
	Risk-based targeted monitoring	Statistical techniques	Onsite source data verification (SDV)	Remote monitoring	Error acceptance level	What percentages of your data	Risk-based triggered	Logic, range, and consistency	Centralized monitoring

						monitored	monitoring	checks	
CTF1	-	-	x	x	-	-	-	X	-
CTF2	x		x	-	-	-	-	-	x
CTF3	x	x	x	x	-	-	-	-	-
CTF4	-		x	-		x	-	X	x
CTF5	-	-	-	-	-	-	-	-	-
CTF6	x	x	x	x	-	-	-	X	x
CTF7	-	-	-	-	-	-	-	-	-
CTF8	-	-	-	-	-	-	-	-	x
CTF9	-	-	x	x	-	-	-	-	x
CTF10	-	-	x	x	-	x	-	-	-
No of CTFs	3	2	7	5	0	2	0	3	5

Table 17 Variables included in the monitoring and Staff training/development devoted to data quality for clinical trials in the surveyed facilities

	Variables included in data monitoring				Staff training/development devoted to data quality for clinical trials						
	All (100%) data points	Critical and noncritical data points	Critical data points	Varies between projects and study design	Education throughout clinical trial (as needed	ICH-GCP training	Group education and training	SOP training	Education prior to research	Skills training and development	One-on-one education and training

CTF1	x	-	-	x	-	x	x	x	x	-	-
CTF2	x	x	x	-	-	x	-	x	-	-	-
CTF3	-	-	-	x	-	x	-	x	-	-	-
CTF4	-	-	x	x	-	x	-	x	x	-	-
CTF5	-	-		-	-	-	-	-	x	-	-
CTF6	-	-	x	-	-	x	x	x	-	-	x
CTF7	-	-	-	-	-	x	x	x	x	X	x
CTF8	x	-		-	-	x	x	x	x	X	-
CTF9	x	-	-	-	-	x	-		-	X	-
CTF10	-	-	-	x	-	x		x	-	X	--
No of CTFs	4	1	3	4	4	9	4	8	5	4	2

Table 18 Types CDMS in use, electronic data storing and SOPs for data quality management and CDMS.

	Types CDMS in use				electronic data storing					SOPs for data quality management and CDMS				
	OpenClinica	Redcap	RED fox	Marvine	Secure server	Individual computers	CDs	Zip drives	External hard disc	Data Collection & Handling	System Maintenance	Data Back-up	Data Recovery	Contingency Plans
CTF1	x	-	-	-	x	-	-	-	-	x	X	x	x	x
CTF2	-	-	-	-	-	x	-	-	-	x	X	x	x	-
CTF3	x	x			x	x	x	x	x	x	X	x	x	-
CTF4	x	x	-	-	x	-	-	-	x	x	-	x	-	-
CTF5	-	-	-	-	-	x	-	-	-	--	-	-	-	-
CTF6	-	-	-	-	x	-	-		-	x	-	-	-	-

CTF7	-	-	-	-		x	-	-	-	x	X	x	x	
CTF8	-		-	x	x	-	-	-	-	x	X	-	-	-
CTF9	-	-	x	-	x	x	-	-	-	x	X	x	x	x
CTF10	x	-	-	-	x	-	-	-	-	-	-	-	-	x
No of CTFs using	4	2	1	1	7	5	1	1	2	8	6	6	5	3