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ORIGINAL ARTICLE

CURRENT STATUS OF CLINICAL TRIALS IN ETHIOPIA: HOW MUCH IS DONE?

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ABSTRACT

Introduction*: Clinical trials are a cornerstone of modern evidence based medicine. They are an important step in discovering new treatments for certain diseases as well as new ways to detect, diagnose, and reduce the risk of disease. They also highly support the clinical practice by generating local evidence. The aim of this study is to evaluate the status and trends of clinical trials in Ethiopia from international trial registries.*

Methods: *We have searched the World Health Organization International Clinical Trial Registry Platform for all trials with at least one recruitment center in Ethiopia. The results were exported in XML format and a rational database was formed.*

Results: *Up to November 15, 2016, 145 clinical trials were found to be registered from Ethiopia. A majority (n = 87, 60%) of the trials were designed on infectious disease and the rest were done on non-communicable diseases. The five most common infectious diseases evaluated were malaria (n=15; 10%), tuberculosis (n=13; 9%), trachoma (n=12; 8%), HIV (n=11; 8%) and helminthiasis (n=6; 4%). The most common non-communicable disease was malnutrition (n = 19; 13%) and only one trial was on cancer, namely Wilms tumor (1%). The London School of Hygiene and Tropical Medicine was the sponsor with the highest number (n=11, 8%) of all registered trials, followed by Columbia, Jimma and Ghent University with 5 (3%) trials each.*

Conclusions*: The clinical trials done in Ethiopia are very much limited in number and variety. To improve the situation the government, industry, academic institutions, patient advocacy groups, professional societies and other organizations should work together.*

Key words*: Clinical trial, evidence registry, Ethiopia*

INTRODUCTION

Clinical trials are medical research studies conducted on human beings. They test potential preventive measures, diagnostic tests or treatments in healthy human volunteers and/or patients. If the results of a trial are found to be valuable, they may lead to further investigation or utilization in everyday practice. Today, clinical trials represent a cornerstone of modern evidence based medicine (1). In addition, they are an important step in discovering new treatments for a certain disease as well as new ways to detect, diagnose, and reduce the risk of disease (2).

Clinical trials are a key research tool for advancing medical knowledge and patient care. It is often obvious that the type and distribution of diseases varies among countries, even within different areas of the same country. This variation is due, but not limited, to differences in environmental and lifestyle risk factors, genetics, age and socio-cultural factors (3). Ethnic differences in exposure and response to interventions are well-documented and should be taken into consideration (4). Therefore, it is important for countries to design comprehensive research projects, including trials targeting their population's individual needs and conditions.

In addition to previously mentioned direct benefits,

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local investigator-initiated trials could generate highly relevant data for governments and are more likely to influence health policy and practice (5). Economists have found that medical research can have an enormous impact on human health and longevity, not only contributing to the individual's benefit of improved health, but also by resulting in an increase of productivity which in turn contributes greatly to the national economy (6, 7). The quantity of research in developing countries continues to seem inadequate, with clinical trials comprising a small fraction of the total research output. This perpetuates the '10/90 gap', where only 10% of global health research expenditure is allocated to diseases that primarily affect 90% of the world's population (7-9). The main challenges in the conduct of clinical trials in developing countries are poverty, weak regulatory and administrative systems, few learning opportunities, limited human and material capacity as well as fragmented healthcare systems. This results in inadequate locally-obtained evidence for clinical practice which in turn leads to adoption of the "developed world's"- clinical practice standards and guidelines which may not be relevant or even harmful (9,10).

The health care system of Ethiopia with its primary focus on prevention and primary care has shown a remarkable improvement in recent years (11). This improvement is clearly demonstrated by the significant decline in under-five mortality rates and maternal mortality rates (12). Such improvement in health service can be augmented, maintained and expanded in other health sectors, if they are supported by problem based, high impact and cost-effective health research. However, health research, especially in form of clinical studies is not done sufficiently. In 2014 the number of registered clinical trials conducted in Ethiopia made up only 1.5% of all clinical trials done in Africa (13). Among these, most focused on the area of infectious disease (13). Clinical research on the topic of cancer and other non-communicable disease (NCD) are too scarce, despite the fact that these diseases are increasing alarmingly and are becoming major public health threats (14).

The main objective of this study is to evaluate registered clinical trials conducted in Ethiopia from international cancer registry databases, in terms of numbers, evaluated indications, type of investigated interventions and type of primary sponsor of a trial.

MATERIALS AND METHODS

Seventeen clinical trials registries conformed to the World Health Organization (WHO) standard (15). WHO clinical trial portal serves as an aggregator for all other registries, which basically means that all clinical trials registered within other systems are gathered and curated within the WHO system. Currently, 16 primaries and 3 partner registries contribute to the data pool. WHO portal can be searched for specific terms and data are exportable in XML format.

On October 15, 2016, we searched the International Clinical Trial Registry Platform (ICTRP) hosted and managed by WHO for all trials with at least one recruitment center in Ethiopia. In total, 150 trials were found. The retrieved results were exported in XML format.

A rational database was formed to facilitate further analysis. Every data point from XML files was represented with one column within database table. Two of the authors evaluated every trial entry separately, and categorized them manually. In first step, we have excluded 5 (3%) of the trials as Ethiopia was mentioned in other context rather than research localization. The remaining 145 trials were selected for further categorization and analysis. We categorized trials according to the type of evaluated disease and type of primary sponsor of a trial.

Diseases that were in focus of a trial were classified into two main categories: infectious disease and NCD. Furthermore, we classified NCD trials according to the medical specialty and infectious diseases according to etiological factors.

In addition, we classified primary sponsors into following categories: Academic Center-Ethiopian, Academic Center - Non-Ethiopian, Governmental, Industry, and Non-Government Organization (NGO) - Ethiopian, NGO - Non-Ethiopian.

RESULTS

The majority of trials evaluated infectious diseases (n = 87, 60%). Most commonly evaluated disease was malaria (n=15,10%), followed by tuberculosis (n=13, 9%), trachoma (n=12, 8%) and HIV infection (n=11, 8%). Those four diseases combined together comprise 60% of infectious disease portfolio and one quarter of complete research portfolio.

Most common NCD (n=19, 13%) was malnutrition and only one trial was on cancer, namely Wilms tumor (1%). The distribution of all evaluated health conditions is shown on Figure 1 and the distribution of infective diseases in Table 1.

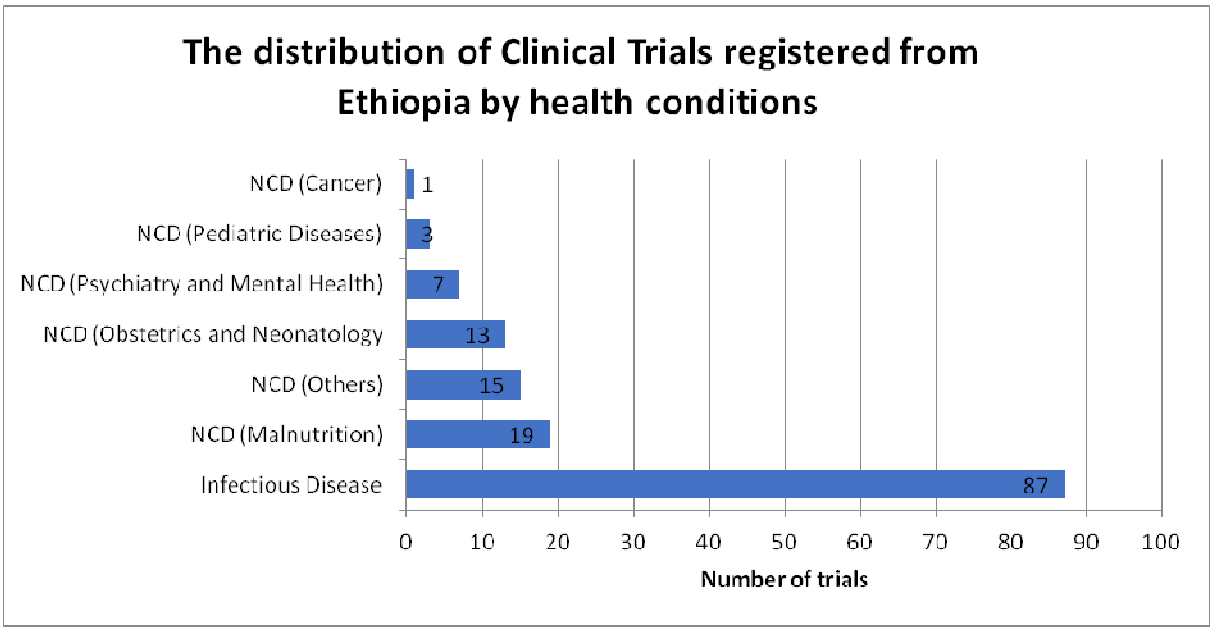

Figure 1: The distribution of clinical trials registered from Ethiopia by health conditions

Table 1. Trials evaluating infectious diseases

Evaluated Condition	Number	Percentage
Malaria	15	10
Tuberculosis	13	9
Trachoma	12	8
HIV infection	11	8
Helminthiasis	6	4
HIV and Tuberculosis	5	3
Infective Diarrhea	4	3
Leprosy	4	3
HIV and Leishmaniasis	3	2
Leishmaniasis	3	2
Cholera	2	1
Hepatitis B	1	1
Hepatitis C	1	1
Intestinal Parasitic Infections	1	1
Meningococcus	1	1
Pneumonia	1	1
Schistosomiasis	1	1
Sepsis	1	1
Tuberculosis and Helminthiasis	1	1
Unclassified fever in children	1	1

During 2014 and 2015, there were 17 trials registered each year, which was the highest in number compared to previous period. In 2003 and 2007 there was only one clinical trial registered each, which was the lowest number. However, there was an overall increase in the number of clinical trials from 2001 through 2016 (Figure 2)

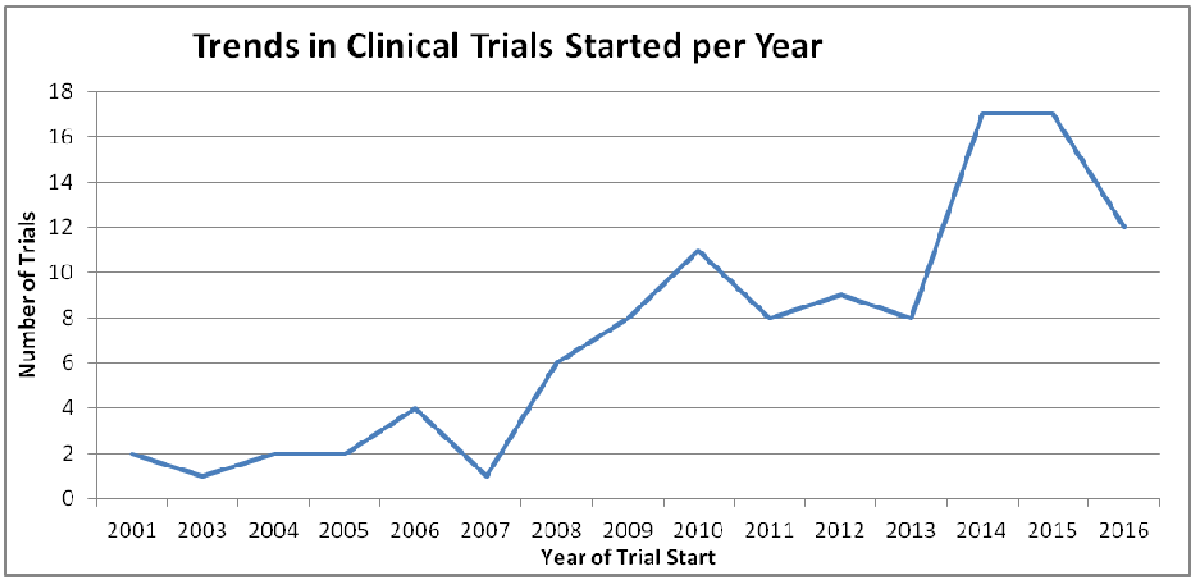

Figure 2: Trends in clinical trials number started per year

Primary sponsors were not reported for three trials (3%). A total of 142 (100%) of all trials with reported sponsor) trials were driven by 95 sponsors. London School of Hygiene and Tropical Medicine was the sponsor with the highest number (n=11, 8%) of all registered trials, followed by Columbia University (USA), Ghent University (Belgium) and Jimma University (Ethiopia) with 5 (3%) trials each. Thirteen primary sponsors conducted two trials each and 74 sponsors were in charge for one trial only.

Majority of trials entries contain data on trial registration date (n=140, 97%) and trial start date (n=111, 77%). Obviously higher number of started trials is seen in period from 2009 to 2016 compared with period between 2001 and 2008, with median number of trials per year 14.5 (range 11-22) versus median two trials per year (range 1-6), respectively. This trend is depicted in Figure 2 above.

A majority of trials with recruiting center in Ethiopia (n=109,75,2%)was registered within www.clinicaltrials.gov registry, followed by Pan African Trial Registry and National Registry for Health Research (United Kingdom) with 13 (9%) trials each. The volume of active trials, where reported recruitment was ongoing, by invitation or active were low (n=45,31%). Most of the trials were initiated by academic centers outside Ethiopia (n=93, 64%), followed by non-government organizations (n=20, 14%). Other non-design characteristics of a trials are showed in Table 2.

Clinical trials design elements are summarized in table 3. In short, majority of trials were of interventional type (n=119, 82%), with median sample size of 524 patients. Fifty percent of the reported trials has reported sample size of 500 patients or bigger. The reporting of trial phase was poor. Only 47 (39%) of interventional trials reported the trial phase. Of those, Phase 0 was reported in 1 (1%), Phase 1 in 3 (3%), Phase 2 in 11 (9%), Phase 2/Phase 3 in 2 (2%), Phase 3 in 11 (9%) and Phase 4 in 19 (16%) of the trials.

Registrants are obliged to categorized reported interventions in one of nine categories. Within 119 trials, a total of 229 reported interventions was evaluated. Predominantly, the interventions were categorized as “Drugs”(96) followed by “Other” (41), Behavioral” (22), “Dietary Supplement” (14), Procedure” (7), “Biological” (5) and “Genetic” (1). Device” and “Radiation”, although other possible category might not reported.

Table 2. Basic data in clinical trials conducted in Ethiopia

Primary Source Register	Number	Percentage
ANZCTR	4	3
ClinicalTrials.gov	109	75
CTRI	3	2
EU Clinical Trials Register	2	1
ISRCTN	13	9
PACTR	13	9
REBEC	1	1
Trial Status		
Completed	76	52
Active, not recruiting	13	9
Recruiting	27	19
Enrolling by invitation	5	3
Not yet recruiting	17	12
Terminated	1	1
Withdrawn	1	1
Not registered	4	3
Primary Sponsor of a Trial		
Non-Government Organization (international)	20	14
Academic Center (Non-Ethiopian)	93	64
Academic Center (Ethiopian)	16	11
Industry	10	7
Non-Government Organization (Ethiopian)	2	1
Government organization	1	1

Legend and links:
ANZCTR (Australian New Zealand Clinical Trials Registry) - http://www.anzctr.org.au/
ClinicalTrials.gov (United States Registry) - https://clinicaltrials.gov/
CTRI (Clinical Trials Registry- India) - http://ctri.nic.in/Clinicaltrials/login.php
EU Clinical Trials Register (European Union) - https://www.clinicaltrialsregister.eu/
ISRCTN (National Institute for Health Research) - https://www.isrctn.com/
PACTR (Pan African Clinical Trials Registry) - http://www.pactr.org/
REBEC (Brazilian Clinical Trials Registry) - http://www.ensaiosclinicos.gov.br/

Table 3. Design data in clinical trials conducted in Ethiopia

Clinical Trial Design Elements	Number	Percentage
Trial Type		
Observational	25	17
Interventional	119	82
Observational [Patient Registry]	1	1
Sample Size		
0-100	15	10
101-200	16	11
201-500	36	25
501-1000	23	16
Higher or equal to 1001	49	34
Not Registered	6	4
Intervention Model		
Factorial Assignment	7	5
Parallel Assignment	64	44
Single Group Assignment	13	9
Not Registered	24	17
Endpoint Classification		
Bio-availability Study	2	1
Efficacy Study	36	25
NR	39	27
Safety Study	5	3
Safety/Efficacy Study	27	19

DISCUSSION

Majority of the worlds' clinical trials are done in developed nations, mainly in North America and Europe. In period from 2004 to 2013 82.5% of the registered clinical trials were accounted for by high income countries (16). During these years Africa contributed only to 2.3 percent of clinical trials of the world. In Ethiopia, the number of clinical trials done keeps rising throughout the years. However, compared to other countries it is still much lower. Ethiopia shares only 2.2% of clinical trials generated out of Africa (13, 17).

Several important barriers which limited the capacity to undergo clinical trials in Ethiopia are recognized. In the late work from Franzen et al they are categorized into three major groups, namely macro and institutional, individual, and operational level (18). The authors evaluated obstacles and enablers for clinical research within Cameroon, Sri Lanka and Ethiopia. Obstacles for conducting research in healthcare environments were similar in all mentioned countries. Stewardship and governance capacity, and the availability of human resources capable of conducting clinical trials, were noted as most important. This resulted further in limited funding allocation, weak regulatory and administrative systems, few learning opportunities, limited human and material capacity and poor incentive for conducting research. Other obstacles consist of individual barriers such as lack of awareness, confidence and motivation to undertake trials, which is also recognized as major limiting factor by other researchers (5). The trial portfolio was similar with exception of Sri Lanka in terms of number of locally initiated academic trials due to higher availability of systemic support by the government.

Those findings in terms of trial number are in good concordance with our data, which show, that trials conducted in Ethiopia are mostly large, part of multinational effort, driven by non-Ethiopian academic centers or industry. However, it seems that the portfolio of clinical trials in Ethiopia is slowly changing. As noticed in work from Fekadu et al. in 2014, the trials conducted within Ethiopia were almost exclusively on infectious diseases (13). In our analysis we have noticed that in period 2014-2016 more trials on NCD diseases were started than those on infective diseases. Unfortunately, due to low number of trials and high variability and lack of some data we did not get to show significance. On follow up report, Fekadu and collaborators reports on short term success made by institutionalization of a clinical trial day (19). The first clinical day celebration was in the 2014. It is possible that this incentive has raise awareness about importance of clinical trials, which have led towards this shift.

Those shift gain on importance if we consider changing lifestyle of the Ethiopian people, and the fact that the rates of NCDs such as ischemic heart disease, cancer and cerebrovascular disease are rising (14). Additionally, psychiatric disorders remain the main cause of disability in the country. Therefore, carefully designed, problem based and innovative clinical trials should be launched in all areas of clinical specialties to generate local evidence. These efforts should be shared by the government, industry, academic institutions, patient advocacy groups, professional societies, and other organizations.

Still, non-communicable diseases share 20% of disease burden and make up 12% of mortality (20), while communicable disease are responsible for about 74% of disease burden they are responsible for 82 % of total mortality. With information and newer solutions generated from those clinical trials and other health research, Ethiopia could gain marked improvement in prevention and reduce mortality due to communicable disease such as HIV/AIDS, malaria and tuberculosis (20, 21). Compared to 2005, the mortality due to HIV/AIDS, malaria and tuberculosis is significantly decreasing. The life expectancy of the people has risen in past two decades from 43 years to 63 years (22).

Further exploration of barriers exceeds scope of this work and they are very well elaborated in the recent work by Franzen et al and Fekadu et al. (5, 10, 13, 18, 19). But we will suggest some corrective measures that may be considered by the trialists in Ethiopia.

To combat any kind of barrier, strong collaboration with local and international organizations is important. Collaboration helps to improve the number, quality and acceptance of clinical trials from developing countries (23,24). It also provides funding opportunity, provision of training and knowledge sharing, experience exchange and technical support (25). More than 70% of clinical trials done in Ethiopia are supported and/or done by non-Ethiopian organizations, mainly academic institutions. However, it is important to keep in mind that local investigator initiated clinical trials still generate highly useful and applicable data (5). Local investigator initiated clinical trials are likely to bring long lasting impact, influence policy making and the allocation of scarce health-care resources (5,24,26). Therefore, collaborative partnership should involve local investigators

and be carefully assessed in respect to the importance of the health issues and the value of the research to the community. It should be based on mutual respect and consideration for the communities' distinctive values, culture, and social practices (26).

Most (over 90%) of the sponsorship for clinical trials conducted in Ethiopia came from academic institutions. This is in contrast to western countries where significant proportion of clinical trials are, directly or indirectly, sponsored by industry (17, 27-29). With changing economic profile and increased demand of chronic care drugs, due to marked shift in burden of disease to non-communicable diseases and continuing impact of HIV/AIDS, sub-Saharan Africa is emerging as an important destination for many pharmaceutical companies to carry out clinical trials and research. Additionally, Africa is the second most favored destination in terms of pharmaceutical spending, with a 10.6% compound annual growth rate (30). On top of the above rationale, multinational pharmaceutical industries are opting for new emerging countries primarily in Asia, South America, Eastern Europe and Africa to bypass various challenges in drug discovery and development (16, 31). For example, the average costs of conducting phase I, II, III drug trials in the US is around $20, $50, $100 million, respectively, whereas in India, it is 50-60% of the cost, in addition to being conducted 75% faster (32). However, one may not forget that profit driven research, directly or indirectly sponsored by the pharmaceutical or medical device industry has source of bias. This bias lead toward better outcome in industry sponsored trials that cannot be explained by "standard risk of bias" (33, 34). Therefore, it is important that Ethiopia and other sub-Saharan nations create a good relationship with major pharma or biotech companies, and carefully design clinical trials for mutual benefit.

Conclusion: From 2001–2016 the number of clinical trials in Ethiopia is increasing. Some shift in trial number towards non-communicable disease is noticed. Nevertheless, they are still very much limited in terms of number and variety. To minimize resource limitations and to encourage investigators in designing clinical trials the government, industry, academic institutions, patient advocacy groups, professional societies and other organizations should work together.

REFERENCES

1. Guyatt G, Cairns J, Churchill D, et al. Evidence-based medicine: A new approach to teaching the practice of medicine. JAMA. 1992;268(17):2420-5.
2. Rare Diseases and Orphan Products: Accelerating Research and Development. In: Field MJ, Boat TF, editors. Rare Diseases and Orphan Products: Accelerating Research and Development. The National Academies Collection: Reports funded by National Institutes of Health. Washington (DC)2010.
3. Aalen OO, Valberg M, Grotmol T, Tretli S. Understanding variation in disease risk: the elusive concept of frailty. Int J Epidemiol. 2015;44(4):1408-21.
4. Yasuda SU, Zhang L, Huang SM. The role of ethnicity in variability in response to drugs: focus on clinical pharmacology studies. Clin Pharmacol Ther. 2008;84(3):417-23.
5. Franzen SR, Chandler C, Enquselassie F, Siribaddana S, Atashili J, Angus B, et al. Understanding the investigators: a qualitative study investigating the barriers and enablers to the implementation of local investigator-initiated clinical trials in Ethiopia. BMJ Open. 2013;3(11):e003616.
6. Murphy KM, Topel RH. Measuring the gains from medical research: an economic approach: University of Chicago Press; 2010.
7. Buxton M, Hanney S, Jones T. Estimating the economic value to societies of the impact of health research: a critical review. Bull World Health Organ. 2004;82(10):733-9.
8. First F. Exceptional returns: the economic value of America's investment in medical research. New York. 2000.
9. Devasenapathy N, Singh K, Prabhakaran D. Conduct of clinical trials in developing countries: a perspective. Curr Opin Cardiol. 2009;24(4):295-300.
10. Franzen SRP, Chandler C, Atashili J, Angus B, Lang T. Barriers and enablers of locally led clinical trials in Ethiopia and Cameroon: a prospective, qualitative study. The Lancet. 2013;382(Supplement 1):14.
11. Organization WH. WHO Country cooperation strategy 2008–2011, Ethiopia. Canada; 2009.
12. Accorsi S, Bilal NK, Farese P, Racalbuto V. Countdown to 2015: comparing progress towards the achievement of the health Millennium Development Goals in Ethiopia and other sub-Saharan African countries. Trans R Soc Trop Med Hyg 2010;104(5):336-42.

13. Fekadu A, Teferra S, Hailu A, Gebre-Mariam T, Addissie A, Deressa W, et al. International Clinical Trial Day and clinical trials in Ethiopia and Africa. Trials. 2014;15:493.
14. Woldeamanuel YW, Girma B, Teklu AM. Cancer in Ethiopia. Lancet Oncol. 2013;14(4):289-90.
15. Organization WH. WHO International Clinical Trials Registry Platform (ICTRP) Internet: World Health Organization; 2017 [cited 2017 15.09.2017]. The mission of the WHO International Clinical Trials Registry Platform is to ensure that a complete view of research is accessible to all those involved in health care decision making. This will improve research transparency and will ultimately strengthen the validity and value of the scientific evidence base.]. Available from: http://www.who.int/ictrp/en/.
16. Viergever RF, Li K. Trends in global clinical trial registration: an analysis of numbers of registered clinical trials in different parts of the world from 2004 to 2013. BMJ Open. 2015;5(9):e008932.
17. Califf RM, Zarin DA, Kramer JM, Sherman RE, Aberle LH, Tasneem A. Characteristics of clinical trials registered in ClinicalTrials.gov, 2007-2010. JAMA. 2012;307(17):1838-47.
18. Franzen SRP, Chandler C, Siribaddana S, Atashili J, Angus B, Lang T. Strategies for developing sustainable health research capacity in low and middle-income countries: a prospective, qualitative study investigating the barriers and enablers to locally led clinical trial conduct in Ethiopia, Cameroon and Sri Lanka. BMJ Open. 2017;7(10):e017246.
19. Fekadu A, Hailu A, Makonnen E, Belete A, Yimer G. Short-term impact of celebrating the international clinical trial day: experience from Ethiopia. Trials. 2017;18(1):332.
20. Organisation WH. Ethiopia: Analytical summary - Health Status and Trends [Internet]. Internet: World Health Organisation; 2017 [cited 2017 20.08.2017]. Available from: http://www.aho.afro.who.int/profiles_information/index.php/Ethiopia:Analytical_summary_-_Health_Status_and_Trends.
21. (IHME) TIfHMaE. The Institute for Health Metrics and Evaluation (IHME) - Ethiopia. Internet: The Institute for Health Metrics and Evaluation (IHME), University of Washington., 2017.
22. Centers for Disease Control and Prevention US. Centers for Disease Control and Prevention - Global Health - Ethiopia [Internet]. Internet: Centers for Disease Control and Prevention, United States; 2017 [cited 2017 20.09.2017]. The CDC office in Ethiopia was established in 2001 and works closely with the Ministry of Health and other partners to maintain strong programs in training, treatment, counseling and testing, and laboratory capacity building.]. Available from: https://www.cdc.gov/globalhealth/countries/ethiopia/.
23. Participants in the Conference on Ethical Aspects of Research in Developing C. Ethics. Fair benefits for research in developing countries. Science. 2002;298(5601):2133-4.
24. Emanuel EJ, Wendler D, Killen J, Grady C. What makes clinical research in developing countries ethical? The benchmarks of ethical research. J Infect Dis. 2004;189(5):930-7.
25. Gaym A. Health research in Ethiopia--past, present and suggestions on the way forward. Ethiop Med J. 2008;46(3):287-308.
26. Weijer C, Emanuel EJ. Ethics. Protecting communities in biomedical research. Science. 2000;289(5482):1142-4.
27. Lexchin J. Sponsorship bias in clinical research. Int J Risk Saf Med. 2012;24(4):233-42.
28. Cihoric N, Tsikkinis A, Minniti G, Lagerwaard FJ, Herrlinger U, Mathier E, et al. Current status and perspectives of interventional clinical trials for glioblastoma - analysis of ClinicalTrials.gov. Radiat Oncol. 2017;12(1):1.
29. Tsikkinis A, Cihoric N, Giannarini G, Hinz S, Briganti A, Wust P, et al. Clinical perspectives from randomized phase 3 trials on prostate cancer: an analysis of the ClinicalTrials. gov database. European Urology Focus. 2015;1(2):173-84.
30. Puppalwar G, Mourya M, Kadhe G, Mane A. Conducting clinical trials in emerging markets of sub-Saharan Africa: review of guidelines and resources for foreign sponsors. Open Access J Clin Trials. 2015;7:23-34.
31. Alvarenga LS, Martins EN. Biopharmaceutical industry-sponsored global clinical trials in emerging countries. Rev Assoc Med Bras (1992). 2010;56(4):428-33.
32. Selvarajan S, George M, Kumar SS, Dkhar SA. Clinical trials in India: Where do we stand globally? Perspect Clin Res. 2013;4(3):160-4.
33. Lundh A, Lexchin J, Mintzes B, Schroll JB, Bero L. Industry sponsorship and research outcome. Cochrane Database Syst Rev. 2017;2:MR000033.
34. Reis LL. [Pharmaceutical companies as sponsors of clinical trials--advantages and limitations]. Rev Port Cardiol 1992;11(4):333-8.