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**An Investigation on the Responsiveness of
International Clinical Trials on the Gravest Needs of
the Population**

**A look at three LMICs with high number of international
clinical trials**

**An Investigation on the Responsiveness of International Clinical Trials
on the Gravest Needs of the Population: A look at three LMICs with high number of
international clinical trials**

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The paper is a qualitative research paper done to assess whether the clinical trials carried out in low and middle-income nations like India, Brazil and Philippines were to address the gravest needs of those nations. To do so the indicators like the Years of life lost (YLL), Years of life lived with Disability (YLD) and the number of clinical trials (CT) were observed and compared with that of USA. All the informations were gathered from two online sites which being healthdata.org and clinicaltrials.gov. The data thus collected were entered and assembeled in SPSS for futher analysis after which the trend of health problems that contributed to YLL and YLD of the host nations and that of USA was studied which was one of the results and finding of this paper. The paper is mostly descriptive analysis and when the health problems exclusive to host nations were compared to the clinical trials done in those nations were compared the result showed that not many clinical trials addressed them. Whereas, when the exclusive health problems of USA was compared to the clinical trials that were done regarding the same in host nations then we saw that there were significant number of clinical trials being done in host nations for those health problems. This showed that the clinical trials were not responsive to the gravest needs of the host nations; India, Brazil and Philippines in accordance with YLL and YLD

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List of Abbreviations and Acronyms

EU	-	European Union
ROW	-	Rest of the World
EMA	-	European Medicines Agency
GCP	-	Global Clinical Practice
YLL	-	Years of life lost
YLD	-	Years of life lived with Disability
ICH	-	International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
DALY-		Disability Adjusted Life Year
CTRI	-	Clinical Trials Registry India
SSA	-	Sub-Saharan Africa
RCT	-	Randomized Clinical Trials

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Introduction

In this modern era of new things and globalization, rise of new health problems and disease is also an added thing which brings about advancement in clinical aspect of the whole thing. The concept of globalization has been the strategy also for the pharmaceutical companies to blossom (Gickman, et al., 2009). They have specially focused on the clinical trials as their global marketing strategy. The clinical trials are indispensable means to test the drugs they intend to sell around the world. With increase in new medical issues, researches and inventions for those medical issues are also done. In doing so many invented medicines are tested and tried on certain group of human population before it is applied to the targeted population.

In the EU, from 2011 onwards, the number of patients in pivotal trials from the “Rest of the world” (ROW) submitted in marketing authorization applications to the European Medicines Agency (EMA) has outnumbered the number of patients from the European Union and North America, respectively (Agency, 2013). In terms of global/offshored clinical trials submitted to the EMA for marketing authorization applications, Central/South America and Asia have the greatest number of patients in pivotal trials submitted to the EMA (Agency, 2013). These countries having so many clinical trials also adds up to one thing which is middle income nations are the leading countries regarding clinical trials in the world and the ones that are done in these countries are those which take longer time to be complete (Merriel, Harb, Williams, Lilford, & Coomarasamy, 2014).

The globalization of clinical trials may be explained by several factors, the most prominent of which are cost savings; shorter recruitment timelines; and less stringent regulatory constraints (Gickman, et al., 2009). That clinical trials are conducted for these reasons is not necessarily ethically problematic if, aside from the usual ethics requirements of informed consent and ethics committee review, these trials contribute to increased access to essential and innovative medicines in the region. Specifically, this means that trials are **responsive** to the health needs of the host country and that post-trial access is in place. This master’s thesis will concern itself with the former. By **responsiveness** we mean that the research aims to “provide new knowledge about the best means of addressing a health condition present in the community or region” where the trial is taking place, (CIOMS, 2016) and since health conditions differ in terms of incidence in a

population, we can also say that a clinical trial may be responsive to or not to the gravest needs of a population.

The state of affairs in global health are not encouraging: new therapeutic products address only 3.8% of neglected diseases, even though these diseases account for 10.5% of the global burden of disease (Borders, 2012). This alludes to problems regarding responsiveness, but at the same time, the literature is silent in terms of the exact picture. To date, we know nothing as to how responsive (or not) clinical trials are to the gravest needs of a population. To respond to this need, this master's thesis will investigate if clinical trials respond to the gravest needs of populations from Philippines, India and Brazil.

The report made by European Medicines Agency on Clinical trials submitted in marketing - authorization applications to the European Medicines Agency gives an overview on the state of international clinical trials being conducted all over the world. It has data regarding the number of clinical trials being conducted, the number of people being involved for the clinical trials, supervision regarding the clinical trials being and much more. Being based on that specific paper, the three different country for study has been chosen. Since we are trying to see the responsiveness of the clinical trials on middle and low-income nations, we have tried to include those nations which are in middle or low-income nations and have had many clinical trials conducted. Clinical trial is a research study that contains one or more human subjects who are assigned to one or more interventions to evaluate whether the interventions effect on the health-related biomedical or behavioral outcomes (health, 2018). It is a process of exploring whether the designed intervention does what it is supposed to do.

The major contributors for number of patients in pivotal clinical trials are brazil from Central/south America whereas India and Philippines were the major contributors from Middle East/Asia/Pacific (Agency, 2013, p. 12). Brazil with 153 clinical trials, India with 148 and Philippines with 57 pivotal clinical trials were some contributors from 2005 to 2011 (Agency, 2013, p. 19). Philippines among the three nations had the highest patient to investigation ratio and then it was brazil followed by India, even for this particular category of study these three-country stood out among all the other nations (Agency, 2013, p. 23). Brazil, India and Philippines even had highest number of requested investigations from GCP (Global Clinical Practice), India coming only second to USA

(Agency, 2013, p. 30). All these factors lead to this paper focusing on these three countries which would also help us give more elaborative description if the large-scale clinical trials being done in India, Philippines and Brazil are responsive towards their needs.

Now exploring the context of clinical trials with respect to the nations that are being focused by this study, first let's have a brief look at the scenario of clinical trials in India. India was the world's most preferred destination for clinical trials after grabbing clinical trials business (Chatterjee, 2008). India has been a major focus for clinical trials because more of the pharmaceutical companies are moving towards Asian countries to overcome obstacles and barriers which might be faced in discovering and growth of drug. There is more focus also because if the clinical trials are carried out in US rather than Asian countries like India then the cost for conducting the same would be 50% more. Moreover, the same trial would be done and dusted 75% quicker than if it's done in US (Selvarajan, George1, S, & Dkhar, 2013). The trend of clinical trials in India has been a very slow and gradual one with ever so slow growth in the number. India is only lagging nations like China and Japan with regards to the clinical trials that's being carried out (Selvarajan, George1, S, & Dkhar, 2013). The reason why India has been a choice for clinical trials is the fact that the cost of operation is very low, the regulatory reforms recently made in India also facilitates clinical trials and the logistic advantages (Gupta & Padhy, 2011). All these reasons have made India a very lucrative destination for clinical trials.

The number of clinical trials in Brazil from 1995-2000 has grown exponentially. Over the same period there has been 1000% increase in the number of clinical trials carried out in Brazil (Virk, 2010). The things that make Brazil an attractive area for clinical trials is the fact that there is a large, increasing, treatment oriented and scattered patient population. The cost for conducting any clinical trials in Brazil is comparatively very low which also contributes to the increase in clinical trials. The geographical scenario of Brazil which makes it feasible for the big countries to get access makes it more prime for conducting clinical trials. Another factor that has contributed to the increase in the number of clinical trials is that the approval time for conducting clinical trials in Brazil is very less. Moreover, the improved ICH-GCP compliance helps to make it a target to conduct clinical trials in Brazil (Virk, 2010).

Philippines pose as a larger prospect to clinical trials market as there has been acts and mandates being formulated regarding the reporting and monitoring of clinical trials being carried out within the country. The fact that there is a huge pharmaceutical market in Philippines also makes it a larger prospect for clinical trials (Yathindranath, et al., 2014). The per capita expenditure of government in Philippine was less than \$140 because of which clinical trials provide them with an alternative way to getting health services (Frost; , Sullivan;, 2016).

Objective

The main General objective of study is:

- i) To investigate the state of responsiveness of international clinical trials in Philippines, India and Brazil.
- ii) To investigate whether clinical trials in host countries respond more to host country needs or to the needs of the USA.

The Specific objectives of study are:

- i) Gather information on illness being addressed by clinical trials in the three countries from 2007 to 2016.
- ii) Gather top causes of death or injury based on YLD in India, Brazil and Philippines from 2007 to 2016.
- iii) Gather top causes of death or injury based on YLL in India, Brazil and Philippines from 2007 to 2016.
- iv) As a comparator, gather information on top causes of death or injury based on YLD and YLL on the default market, i.e. The US.
- v) Compare and see if clinical trials are less, as, or more responsive to the needs of the host countries (India, Brazil and Philippines) than the default pharmaceutical market (i.e. US)

Literature Review

Clinical trials are being done all over the world but in recent times the trend has changed to these trials being carried outside US (National Library of Medicines, 2018). There are many clinical trials being conducted all in different countries all over the world. Clinicaltrials.gov gives the details information on those. India is a major contributor to clinical trials from Asia with 148 of them in between 2005 to 2011 (Agency, 2013, p. 19). An article done to assess whether the clinical trials done in India were in line with the health care needs or not concluded that the clinical trials were not in line with the health care needs (Chaturvedi, Gogtay, & Thatte, 2017).

The paper also said that country should strengthen its sources so that the selection of participant is more equitable across the nation. The research looked at all the clinical trials in its registry i.e. Clinical trial registry India (CTRI) and was compared with the global burden of disease (DALY) from Global Health Estimates (2014) summary table of WHO. This paper done in India only compares between DALY and the clinical trials registered in their registry whereas the thing that makes it different from what is already been done is that we will compare YLL and YLD with the clinical trials. This makes it more in-depth than the previously done paper. The other fact that it is not just done for one country rather three different countries are being looked at gives it a more boarder perspective and opens to a greater possibility of understanding more things.

Another past paper that talks about the responsiveness of clinical trials in a way is the paper done by Ricardo Eccard da Silva and co. The paper “Globalization of clinical Trails: ethical and regulatory implications” covers the responsiveness aspect of clinical trials. The paper covers the fact that there is increase in number of clinical trials being conducted in low and middle-income nations (Silva, Amato, Guilhem, & Garbi Novaes, 2016). The paper focuses on the fact that there has been increase in the number of clinical trials that has been being conducted in developing countries but with the increase in the number it also means that ethical aspect is being neglected. It concludes that even though the increase in number of clinical trials means more opportunity for the people to take part in it but having said that it also means that ethical question related mainly to ensuring the integrity, welfare and safety of the participant everything needs to be discussed. The paper focuses on these points so that participants are kept safe. This paper touches on the responsiveness aspect of things. Though this paper just touches on the

responsiveness part it doesn't include the burden of disease but only discusses on the increase in number of clinical trials. Something different that this paper includes what the other doesn't is the fact that it is articulated with relation to the DALY and more than that it is more in-depth as it digs deep into comparing the clinical trials with YLL and YLD.

The paper on Drugs on neglected diseases initiative by Bernard Pecoul talks about the clinical trials for different health problems not focusing as per the need of patient (Pecoul, 2016). It talks about the current system for biomedical innovation not being able to deliver adapted and affordable technologies which lacks innovation of and access to tools related to health and it is not well documented. The paper talks about the past recognition of these disease being local to poor country is not just confined to those nations but also moving on to all over other nations too regardless of disease area or income classification. The experiment was done in five public research institutions from India, Brazil, Kenya, Malaysia, France and WHO/TDR which was in response to the frustration of being exposed to medicines that were not very effective against the health problem that were found in these countries, were highly toxic and even were unavailable to the people of these nations. The research comes to a concrete evidence that there is development of six adapted, affordable and non-parented treatments for the world's neglected diseases. The recommendations that the paper made were a series of progressive policy steps to re-orient the global biomedical system so that it responds to patient needs, particularly that the UN SG launch a political process to negotiate one or more binding global agreement on the financing prioritization, co-ordination and norms required to enable the discovery, development and delivery of and equitable access to innovations of public health importance (Pecoul, 2016). This paper does provide prospect on how the need of the people are not met although the number of clinical trials has increased and provides insight on how the problem can be resolved. Even then there are some aspects that it doesn't touch which will be dealt with this paper. Bernard focuses on the neglected diseases but then this paper focuses on health problems that are the main issues of Brazil, India and Philippines. Neglected disease will have a different look into it compared to the major health issues of the nation so the current paper will have a completely different idea in a sense that it will deal with major issues. Meaning that it will be more focused

on the major problem of the nation and can be related to the responsiveness of the clinical trials being conducted in these countries.

Journal publication looking at the “Published randomized clinical trials in Sub-Saharan Africa (SSA) focuses on high-burden disease but are frequently funded and led by high income nations” concludes that the randomized clinical trials carried out in SSA were highly funded and led by institutions from High Income Countries (Diakou, Ntoumi, Ravaud, & Boutron, 2017). Even though the paper finding talks about the RCTs focusing on the health problems with high burden, but it also gives focus on the fact that some other health problems that have high burden are neglected. The paper also found out that the RCTs were more focused on the acute health problems and only a few of the were focused on the more chronic health problems. Paper tries to explain a portion of what this paper is trying to look at like the influence of high-income nations on the clinical trials carried out in low- and middle-income nations. But what the paper only focuses on clinical trials whereas this paper focuses on all the clinical trials done over a certain period.

This research paper will give broader idea on how different the responsiveness of clinical trials is in Brazil, India and Philippines in comparison to United States of America with regards to the number of clinical trials in these countries and global burden disease, more specifically YLL and YLD.

Methodology

Research Design

The research is a quantitative study as the analysis and interpretation will be conducted based on numbers drawn from various sources and compared to understand the responsiveness regarding the clinical trials.

Type of Data

The study will be based on secondary data. Major clinical trials done to cover the illness in Brazil, India and Philippines will also be studied to access the trials. It is done so that we can see if the clinical trials are related to the illness in these countries. The data regarding the Years of life lost due to disability (YLD) and Years of life lost (YLL) will be collected from the healthdata.org site which has all the data for these categories. The information will be collected for the period of 10 years that is from 2007 to 2016. The site provides graphical as well as numerical data for the burden of disease for all the countries in this world. From this site we will take data for our specific country to study. Regarding the clinical trials being done in the countries under study we will be extracting data from Clinicaltrials.gov which has all the registered clinical trials for all the countries. For the comparison purpose we will also be taking the same information for USA. Health problems contributing to YLL and YLD of USA will be extracted from the same source so that we can see if they do have any influence on the clinical trials carried out in the host nations. It is a site which has all the records for progress of clinical trials that are being carried out in the world. It even gives the phase that the research is in which would help for the study.

Measures

The data that will be taken for this study is from valid source. The data for this study will be taken from healthdata.org and clinicaltrials.gov. The study will mainly focus on the YLL and YLD of the chose countries which being India, Brazil and Philippines. The data regarding YLL and YLD will be taken from healthdata.org whereas the data for clinical trials will be taken from clinicaltrials.org.

Disability Adjusted Life Years (DALY) is the sum of years of life lost due to premature death and years of life lost due to disability for people living with health problem or its consequences **Invalid source specified..** The paper looks at DALY and the explanation is totally based on these factors. The factor that will be compared is mainly YLL, YLD along with the clinical trials done in those country.

YLL simply means the total value which is derived from subtracting age at death from the longest possible life expectancy for a person at that age for that country **Invalid source specified..** YLD simply means the years of life lived in less than idle life. It is measured by multiplying the prevalence of that health problem with disability weight of the same **Invalid source specified..** These factors will be used to see the scenario of the country understudy. This will give the real problem and real need of the country under study and give us the real idea of the country.

Number of clinical trials and programs that are being done will give us idea about the actual programs that are being in these countries. The data for this variable will be derived from healthdata.org.

Data Extraction

There are two sets of data that was extracted from two different sites as mentioned above. Talking about the data extraction regarding the YLL and YLD regarding the host nations and the comparative nation which was USA. The data was extracted from healthdata.org which is an official site for the data regarding global burden of disease.

For YLDs of all the countries under study, there was an easy option to select the YLD and as per the nation and year data was downloaded which was an excel format. But since the data entry or database was being created in SPSS the thus downloaded excel format was translated into the format in SPSS. In excel file downloaded from the site the data was not in accordance with the highest impact. To find out the health problem with the most impact on YLD the data was arranged in a descending order meaning the highest value being shown at the first and that being followed by other lower values. In this way the top 10 major health problem was identified for each of the nation under study. After that the health problems along with its value was entered in SPSS format.

Regarding YLLs, it was not as simple compared to YLD. For the extraction of YLLs, in the healthdata.org site, advance setting had to be used. Under advance setting and under measures there was the option of YLLS from where we got the data for all the nations under study for the 10 years of study. Like YLDs, data was extracted in excel format from the site and then was arranged in accordance with the decreasing value. Doing that meant we had our top 10 health problems for YLLs for all the nations.

Other variable which is very crucial for the study was extracted from Clinicaltrials.gov. It is an official site for all the clinical trials that are being done all over the world. This site has records of all the clinical trials with what phase the clinical trials is being carried out as well. For the extraction of clinical trials required for this study advance search setting had to be used. In the advance search setting few criteria had to be entered like the country and year for the number and type of clinical trials. After doing so all the clinical trials were shown which had details about the clinical trials with the health problem it focused on. All the clinical trials were again extracted to excel with all the categories. After that only the category stating the health problem under study were extracted and then it was arranged alphabetically. As it was alphabetically arranged, we could have all the similar ones together. With that we could tally the number of clinical trials that addressed a health problem. After that we had a dataset with health problems and yearly total number of clinical trials done regarding the same. This was done for all the nations under study.

Data Analysis

Not much analysis has been done regarding the use of statistical tools but most of the information has been done through tables and bar diagrams. Descriptive information of all the host nations with regards to YLL, YLD and clinical trials were done through tables and bar diagrams.

To show the trend of YLL, YLD and clinical trials for all the nations under study a table was created with the health problems that contributed to these variables. Along with that a bar diagram to pictorially show the trend of how the impact of health problem has changed through the years of study can be seen properly. A different table for the clinical trials was also shown so that the

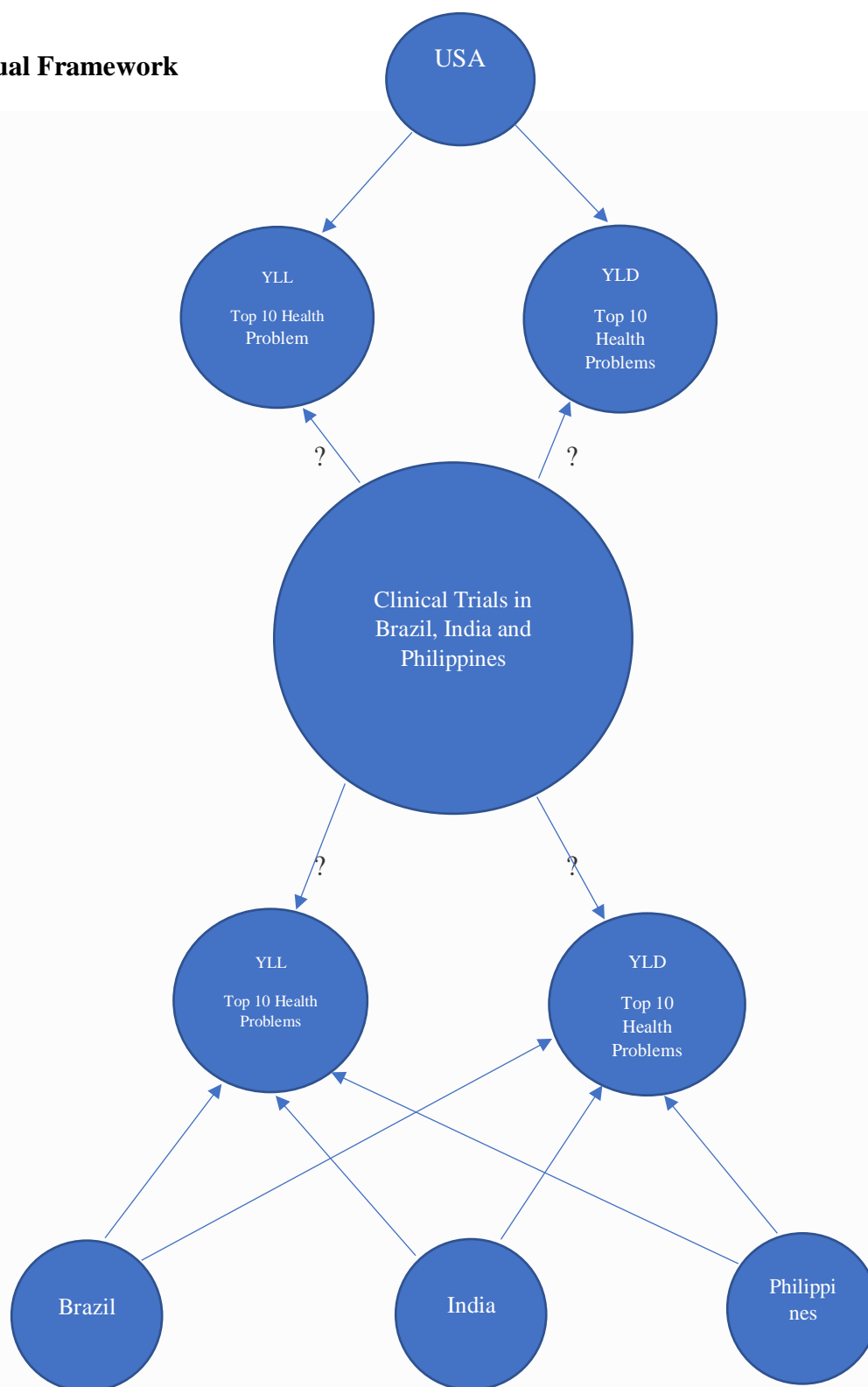
difference in health problem addressed by clinical trials and YLL, YLD could be seen. So, for the descriptive measure all the information's are being represented and can be easily be interpreted.

Apart from the descriptive part of the result one more thing was done to point if the clinical trials do address health problems of the nations under study or not. This paper tried to see if top 10 health problems contributing to YLL and YLD for the nations under study were common with top 10 health problems contributing to the same for a country for comparison which was USA. The top 10 health problems for the host nations and USA were compared to see if there were any health problems that were exclusive to host nations meaning the health problems that were only found in host nations and not in USA. This was done for all the host nations which gave us an idea of how exclusive health problems were and when these health problems were matched with the clinical trials then we would have an idea if there was an influence.

The general idea behind finding the exclusive health problems along with the clinical trials done regarding the same was that if the exclusive health problem are the ones that had most clinical trials done then that would mean clinical trials do focus on the need of the nations. Whereas if the exclusive health problems didn't have many clinical trials done on them but the ones that were common to the comparative nation then that would mean there is an influence in clinical trials being carried out.

Scope of Study

The increase in the number of clinical trials globally has made the study on this scenario very appropriate and relevant in the present context. The results from this research paper provides a scenario that can be investigated more detail with more research. It provides a baseline for broader study to explain more of the pull and push factors in what the result shows. It gives a broader perspective on whether the clinical trials do address the gravest needs of low and middle-income nations.

Conceptual Framework**Figure 1 Flowchart showing the conceptual framework of the research**

The above figure gives the conceptual framework of the whole research paper. The general idea of how and what the research paper is looking at is represented by the figure above. From the above figure we can see that the focus for the paper are YLL, YLD and clinical trials of all the countries that are being studied. The other thing that needs to be focused on in the figure is the arrow and the direction of the arrowhead. The question mark in the figure is the thing that the paper looked at. What it means is to see if the clinical trials in host nations are addressing the Top 1 health problems contributing to YLL and YLD of the host nations. The other one is if the YLL and YLD of USA does have any influence on the clinical trials done in the host nations.

Theoretical Framework

This paper focuses on the Human Development Approach theory which is the basis for discussion for the results of this paper. So, the human development approach will be elaborated on this section of the paper. While discussing the Human Development Approach we will talk about the ideas developed by Amartya Sen which was the Capability Approach. Capability approach was also the base for development of Human Development Approach. The human development approach mainly focuses on emphasizing the enhancement of freedom for every human being and the agenda of not leaving anyone out (UN, 2016).

Talking about where this approach comes from and what it talks about, we will have to have a look at the history development of the approach. The term Human development was brought into the context in 1970s with the proposal of second UN Development (Hirai, 2017). There were primarily ten policy measures to enhance the economic and social progress. But the concept of human development approach has been ever so evolving. If we must see the progression and evolution of the priorities that the approach has focused on, we can go through it from 1970 and then to 1990s onward.

Primarily the concept of Human Development Approach initiated by UN was to improve the human resource, but it was in a narrow sense. It meant that people were treated as the means to carry out development measures which is very similar to the concept of human resource (Hirai, 2017). After that the concept evolved during the early 1980s which focused on reduction of poverty and this were carried out World Bank. The change in the concept meant that it took human resource to a different level and focused on human resource as a goal (Hirai, 2017). Then again, the focused shifted towards improvement in human capacities which was done during the 1980s and was mainly focused by UNDP and NSRT (North-South Roundtables). Their main idea was that human resource was the main center for overall development (Hirai, 2017). In late 1980s CDP (Committee for Development Planning/Committee for Development Policy) was more focused on expanding the human capabilities. The concepts of Roundtable and CDP were quite similar but then CDP's concept focuses on the process of expansion which was based on the work of Amartya Sen (Hirai, 2017). From 1990 onwards the concept of Human Development

Approach has not changed that much but has had more objectives included to it. The changes have been made or more focused by UNDP. The things that concept has added regarding it were people's choice and substantive freedom along with the pre-existing concept of expansion of human capacities.

The main idea or the concept of this approach is giving importance to the development of human resource through different means available. All the changes in the concepts even though kept on evolving their point of focus was to improve human development even though their focus was different and their way of doing it was a bit different from each other. The main thing that the human development approach focuses on is the promotion of things that motivate for the human concern. It also tries to see the gap that can be between the theory in paper and the actual implementation and practice but during all of this it also tries to avoid the impact of powerful nations and the influence they can have on the whole thing (UN, 2016).

This paper tries to look at whether the clinical trials that are being carried out in the host nations does address the gravest needs. Since the clinical trials are done to improve the health of people all over the world, the use of human development approach is very appropriate to discuss the results with. All the concepts that human development approach focuses on, the main priority has always been the expansion of human capabilities and focuses on empowering people through programs that focus on health and education which would ultimately lead to development. The other thing that makes it very appropriate theory to be used for this paper is the fact that it also tries to see the gap that can be there between the theory in paper and the actual implementation and practice but during all of this it also tries to avoid the impact of powerful nations and the influence they can have on different aspect of health and other dimensions of human development (UN, 2016).

Capability approach complies with two main normative claims among which one is claims that primary importance is to attain well-being and the other one is the freedom of a person to achieve well-being is their own capability which is their real opportunity and the things that they value to do (Robeyns, 2016). The main core thinking of Sen's capability approach talks about two type of capability which is "being and doing". This in broader sense means that a person is provided with two capabilities one being the things that a person can do on their own and the other being the things that they can do with the situation that they have been provided with. With this core concept we can also connect it with the main of attaining healthy status (GAsper, 1997).



Findings

Whilst looking into the data of past 10 years for the countries under study that being India, Philippines and Brazil, all the clinical trials and health problems contributing to DALY were explored which will be further explained in later half of the paper. Further on, the paper will be divided into two sections to explain the scenario and context in a better manner. First half of this section will be more of a descriptive results and other half more of an analytical part.

The descriptive part will depict the trend of health problems contributing to YLL and YLD for the last 10 years. We will be able to see which health problem has had the most effect in which year in which country. Moreover, it will also investigate which health problem was mainly focused on for that country with respect to the clinical trials carried out. All of these will be done through the tables derived from the data extracted from online sites mentioned above.

Other half of this paper will try to investigate the exclusiveness of the health problems. While doing so it will also try to see whether the health problems that are exclusive to country has as many clinical trials. By doing so what this paper tries to do is to see if the clinical trials do focus on the health problems that are exclusive to the country or is it more focused on the health problems that are more concurrent to high income nations.

Descriptive Analysis

Moving on with the descriptive explorations of 10 years long trend of health problems contributing to YLL and YLD in India, Brazil and Philippines. The tables and diagrams from this point onwards will try to portray all the leading causes of YLL and YLD in the study country and relate them with clinical trials conducted in the same. Now looking at the trend of YLL and YLD of Brazil from 2007 to 2016.

Table 1 Trend of YLL for the past 10 years in Brazil

S.N.	Top 10 Disease	2007	CT	2008	CT	2009	CT	2010	CT	2011	CT	2012	CT	2013	CT	2014	CT	2015	CT	2016	CT	TT
1	Cardiovascular Disease	19	9	20	3	20	30	20	57	20.1	36	20.2	40	20.3	46	20.4	51	20	40	21.1	44	337
2	Neoplasm	14	5	14	8	14.2	11	14.4	7	14.6	4	14.9	4	15.1	8	15.3	9	15.6	11	15.8	14	379
3	Neonatal Disorder	10	1	8.5	1	8.2	2	7.8	2	7.55	2	7.2	0	6.9	0	6.5	1	6.1	0	5.8	2	456
4	Diarrhea	7.1	1	6.9	1	6.7	3	6.5	1	6.4	0	6.3	1	6.1	1	6	2	5.9	0	5.88	0	502
5	Diabetes	5.6	33	5.8	22	6	26	6.1	25	6.33	45	6.4	33	6.59	26	6.7	35	6.8	33	7	22	535
6	Chronic Respiratory Disease	3	6	3.2	4	3.2	3	3.2	8	3.29	4	3.2	9	3.3	4	3.35	4	3.4	4	3.5	4	617
7	Cirrhosis	2.9	2	3	2	2.9	0	3	4	3	1	3	2	3	2	3.1	1	3.1	2	3.2	1	497
8	HIV	2.7	16	3	9	2.7	7	2.7	7	2.6	11	2.6	11	2.6	7	2.5	9	2.5	3	2.5	7	542
9	Neurological Disease	2.3	12	2.4	4	2.5	0	2.6	6	2.7	5	2.8	5	2.9	13	3	5	3.1	15	3.2	14	567
10	Digestive Disease	1.9	3	2	5	2	0	2	5	2	5	2.1	3	2.1	7	2.1	6	2.1	6	2.2	2	578

TREND OF TOP 10 HEALTH PROBLEMS OF BRAZIL WITH REGARDS TO YLL (2007-2016)

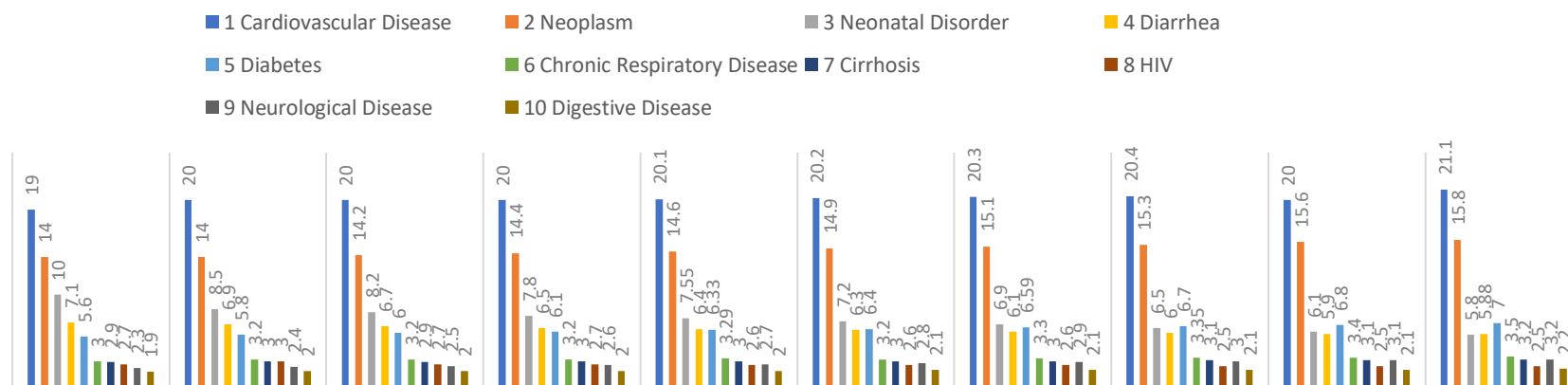


Figure 2 Bar Diagram showing the Trend of YLL in Brazil

Scenario of Brazil

Over the period of 10 years from 2007 to 2016 we can see in the table that cardiovascular disease has been the leading contributor to YLL in Brazil. About 20% of the total YLL is due to cardiovascular disease and it has consistently been the major impactor through the 10 years. Other 9 health problems contributing to YLL in Brazil from 2007 to 2016 were Neoplasm, Neonatal Disorder, Diarrhea, Diabetes, Chronic Respiratory Disease, Cirrhosis, HIV, Neurological Disease and Digestive Disease. Among all the clinical trials carried out for cardiovascular disease there were only 9 in 2007, 3 in 2008, 30 in 2009, 57 in 2010, 36 in 2011, 40 in 2012, 46 in 2013, 51 in 2014, 40 in 2015 and 44 in 2016. Similarly, for Neoplasm there were 5,8,11,7,4,4,8,9,11,14 number of clinical trials done from 2007 to 2016. For Neonatal Disorder the number of clinical trials done from 2007 to 2016 were 1,1,2,2,2,0,0,1,0,2 respectively. Diarrhea being the fourth contributor had 1,1,3,1,0,1,1,2,0,0 clinical trials done regarding the same from 2007 to 2016. Diabetes had 33,22,26,25,45,33,26,35,33 and 22 clinical trials done in response from 2007 to 2016. Similarly, Chronic Respiratory Disease had 6,4,3,8,4,9,4,4,4,4 number of clinical trials done. Cirrhosis had only a few clinical trials done which being 2,2,0,4,1,2,2,12,1 from 2006 to 2017. HIV didn't have that much of an impact on the YLL but regarding the clinical trials there were 16,9,7,7,11,11,7,9,3,7 done during the same time frame. Neurological Disorder is the ninth contributor for YLL, and it had 12,4,0,6,5,5,13,5,15,14 number of clinical trials done for the same. Last but not the least contributor which is Digestive Disease has had 3,5,0,5,5,3,7,6,6,2 number of clinical trials done. Cardiovascular and neoplasm have been top 2 major contributors all over the 10 years of study period but with other 8 health problems, they have been in increasing and decreasing order. As we go down the table, we can see that even if the health problem doesn't have major impact on YLL the number of clinical trials done are relatively more compared to the health problems that have had more impact. For example, HIV, which is very low in the table, has more clinical trials done on it compared to other health problems that are major impactors regarding YLL.

The bar diagram given helps to depict how the impact of health problems changes with time. Vertical axis shows the percent contribution of the health problems on YLL and the horizontal axis represents the year. We can also see the clinical trials that were carried out in the same year for the same health problem in the same table. Even though cardiovascular disease and neoplasm had so much effect on YLL the amount of clinical trials for them is not relevant in accordance with its impact but later it was given more priority along the year. Even though diabetes was not the biggest impactor regarding YLL but was the health problem which had most clinical trials carried out during the first two years of study time. We can also see the health problems that were focused on in the table below which is in accordance to the number of clinical trials done.

Table 2 Top 10 Health Problems Focused on by Clinical Trial

Yr	1 st Contributor	CT	2 nd Contributor	CT	3 rd Contributor	CT	4 th Contributor	CT	5 th Contributor	CT	6 th Contributor	CT	7 th Contributor	CT	8 th Contributor	CT	9 th Contributor	CT	10 th Contributor	CT	TT CTs
7	Diabetes mellitus	33	HIV	13	Hypertension	8	Obesity	7	Breast Cancer	9	Chronic Obstructive Pulmonary Disease	6	Schizophrenia	7	Anemia	4	Melanoma	4	Neoplasms	5	337
8	Diabetes	22	Health	15	Hepatitis	14	Obesity	13	HIV	9	Neoplasm	8	COPD	7	Arthritis	6	Chronic Respiratory Disease	4	Asthma	4	379
9	Cardiovascular	36	Diabetes	26	Hygiene	23	Retinal Detachment	12	Neoplasm	11	HIV	10	Health	8	Stroke	7	Pain	7	Breast Cancer	6	456
10	Cardiovascular	57	Diabetes	25	Hygiene	15	HIV	11	Obesity	10	Breast Cancer	9	Hepatitis	8	Neoplasm	7	Low back and Neck Pain	7	Oral Disorder	7	502
11	Diabetes	45	Cardiovascular	36	Arthritis	12	Hypertension	10	Breast Cancer	10	Obesity	9	Oral Disorder	8	Fibromyalgia	8	HIV	7	Health	6	535
12	Cardiovascular	40	Diabetes	33	Health	12	Arthritis	11	Asthma	11	HIV	11	Pain	11	Obesity	11	Chronic Respiratory Disease	9	Hypertension	8	617
13	Cardiovascular	46	Diabetes	26	Oral Disorder	11	Breast Cancer	10	Obesity	9	Neoplasm	8	Hypertension	6	Arthritis	6	Parkinson's Disease	6	Pain	5	497
14	Cardiovascular	51	Diabetes	35	Oral Disorder	12	Health	12	Obesity	11	Neoplasm	9	Low back and Neck Pain	9	Musculoskeletal	9	HIV	9	Breast Cancer	9	542
15	Cardiovascular	40	Diabetes	33	Pain	13	Oral Disorder	12	Hypertension	12	Obesity	11	Neoplasm	11	Neck Pain	9	Musculoskeletal	9	Asthma	8	567
16	Cardiovascular	44	Diabetes	22	Oral Disorder	15	Neoplasm	14	Obesity	12	Pain	12	Musculoskeletal	11	Asthma	10	Health	8	Parkinson's Disease	8	578

The table above shows the trend of clinical trials carried out over the period of 2007 to 2016. From the table we can see that the total number clinical trials done every year has been in increasing order apart from 2012. 2012 has the highest amount of clinical trials done whereas 2007 had the least. Now looking at the health problems and clinical trials, Diabetes and cardiovascular disease are the major health problems that were focused over the study period of 10 years. As shown in the table above we can see that there are so many health problems that had clinical trials done on and it also shows that apart from cardiovascular disease and Diabetes other health problems hasn't been consistently been focused on. Among all the clinical trials carried out for Low back problem there were only 2 in 2007, 3 in 2008, 5 in 2009, 7 in 2010, 4 in 2011, 3 in 2012, 3 in 2013, 9 in 2014, 9 in 2015 and 6 in 2016. Similarly, for Skin and Subcutaneous problem there were 1,3,3,4,1,1,3,2,2,2 number of clinical trials done from 2007 to 2016. For Sense organ Disease the number of clinical trials done from 2007 to 2016 were 2,4,1,5,3,2,4,3,3,2 respectively. Depression being the fourth contributor had 1,3,3,6,4,6,1,5,5,7 clinical trials done regarding the same from 2007 to 2016. Migraine had 1,0,0,1,2,1,1,1,1 and 2 clinical trials done in response from 2007 to 2016. Similarly, Anxiety had 1,2,0,4,3,3,2,3,3,3 number of clinical trials done. Musculoskeletal Disease had more clinical trials done which being 5,2,1,1,4,7,3,9,9,11 from 2006 to 2017. Dietary Iron Deficiency didn't have that much of an impact on the YLL but regarding the clinical trials there were 2,0,3,2,0,1,2,4,4,1 done during the same time frame. Diabetes is the ninth contributor for YLD, and it had 33,22,26,25,45,33,26,35,33 and 22 number of clinical trials done for the same. Last but not the least contributor which is Oral Disease has had 2,3,3,7,8,4,11,12,12,15 number of clinical trials done.

Now looking at the trend of YLD from 2007 to 2016 and the health problems focused by clinical trials. Low back problem has been the health problem that was a leading cause of YLD throughout the years of study. Looking down to other health problems, the impact that they had is not that more than each other. The percent of impact that the health problems had other than low back problems are very similar to each other. Oral Disease had the least impact on YLD on 2007 but over the period of 10 years diabetes and oral disease have been interchanging places for the least impactor on YLD. The top 10 health problems contributing to YLD of Brazil are Low Back Problem, Skin and Subcutaneous Problem, Sense organ Disease, Depression, Migraine, Anxiety, Musculoskeletal Disease, Dietary Iron Deficiency, Diabetes and Oral Disease.

Looking back at the Table 2, we can see that not most of the top 10 health problems impacting on YLD are not included in the top 10 health problems covered by clinical trials. But like the data from table 3 right around from 2013 more clinical trials were conducted on oral disorders. It can be observed on both the tables.

Table 3 Table 1 Trend of YLD for the past 10 years in Brazil

S.N.	Top 10 Disease	2007	CT	2008	CT	2009	CT	2010	CT	2011	CT	2012	CT	2013	CT	2014	CT	2015	CT	2016	CT	TT
1	Low Back Problem	11.6	2	11.7	3	12	5	12	7	12	4	12	3	12	3	12	9	12	9	12	6	337
2	Skin and subcutaneous problem	7.6	1	7.6	3	8	3	8	4	7	1	7	1	7	3	7	2	7	2	7	2	379
3	Sense organ Disease	7.5	2	7.6	4	8	1	7	5	8	3	8	2	8	4	8	3	8	3	8	2	456
4	Depression	6.9	1	6.7	3	6	3	6	6	6	4	6	6	6	1	6	5	6	5	6	7	502
5	Migraine	6.4	1	6.4	0	6	0	6	1	6	2	6	1	6	1	6	1	6	1	6	2	535
6	Anxiety	6	1	6	2	6	0	6	4	6	3	6	3	6	2	6	3	6	3	5	3	617
7	Musculoskeletal Disease	3.9	5	3.9	2	4	1	4	1	4	4	4	7	4	3	4	9	4	9	4	11	497
8	Dietary Iron Deficiency	3.6	2	3.5	0	3	3	3	2	3	0	3	1	3	2	3	4	3	4	3	1	542
9	Diabetes	3.1	33	3.1	22	3	26	3	25	2.5	45	2.3	33	2.3	26	2.4	35	2.4	33	2.4	22	567
10	Oral Disease	2.9	2	2.9	3	3	3	3	7	3	8	3	4	3	11	3	12	3	12	3	15	578

TREND OF TOP 10 HEALTH PROBLEMS OF BRAZIL WITH REGARDS TO YLD (2007-2016)

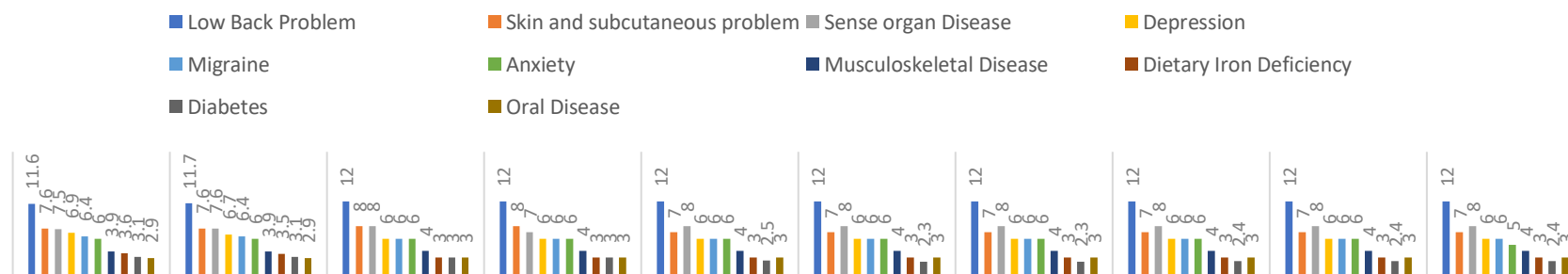


Figure 3 Bar Diagram showing the Trend of YLD in Brazil

The bar diagram given above shows the trend of impact that the health problems had on YLD over the 10 years of study time. In the figure, vertical axis represents the impact of health problem on YLC in percent whereas horizontal axis is for the year of study. The index for the colors of bars are also given in the figure itself so it will be easy to understand the figure. Bar diagram makes it easy to understand the trend as coz it represents the data in a pictorial way.

If we must compare the number of clinical trials with the percent of impact, we can see that even the top impactor doesn't have that many clinical trials. But the clinical trials for low back pain was increasing from 2014 onwards. Looking at the clinical trials the focus on oral disease had been increasing from 2013 compared to other health problems.

Table 4 Trend of YLL for the past 10 years in India

S.N.	Top 10 Disease	2007	CT	2008	CT	2009	CT	2010	CT	2011	CT	2012	CT	2013	CT	2014	CT	2015	CT	2016	CT	TT	
1	Diarrhea	25	8	24.9	5	24	11	23.1	17	22.1	10	19.2	9	20	9	19	5	18.1	9	17	3	254	
2	Neonatal Disorder	14.6	0	14.2	4	13.9	2	13.55	1	13	4	12	2	12	3	11.5	2	10.8	3	10	2	316	
3	Cardiovascular Disease	13	18	14	23	15	37	15.4	44	16.2	18	17	20	17.7	18	18.5	13	19	20	19.9	14	337	
4	HIV/AIDs	7.4	12	7.2	7	7.15	11	6.9	12	6.8	9	6.6	7	6.44	9	6.2	5	6.1	7	5.9	7	316	
5	Neoplasm	4.8	13	5	6	5.3	3	5.5	3	5.7	2	6	3	6.34	5	6.7	3	7.04	1	7.3	3	321	
6	Diabetes	3.3	41	3.4	33	3.61	63	3.77	51	3.96	55	4.1	29	4.33	39	4.5	22	4.7	27	4.8	15	299	
7	Chronic Respiratory Disease	2.7	2	5.2	1	5.41	2	5.57	2	5.6	4	5.7	2	5.9	1	6.2	2	6.5	2	6.8	4	258	
8	Digestive Disease	1.8	1	1.8	3	1.8	6	1.8	3	1.8	2	1.8	5	1.9	1	1.9	2	2	2	2	1	208	
																				1	1.6	1	214
																				2	2.2	6	217
TREND OF TOP 10 HEALTH PROBLEMS OF INDIA WITH																							

TREND OF TOP 10 HEALTH PROBLEMS OF INDIA WITH REGARDS TO YLL (2007-2016)

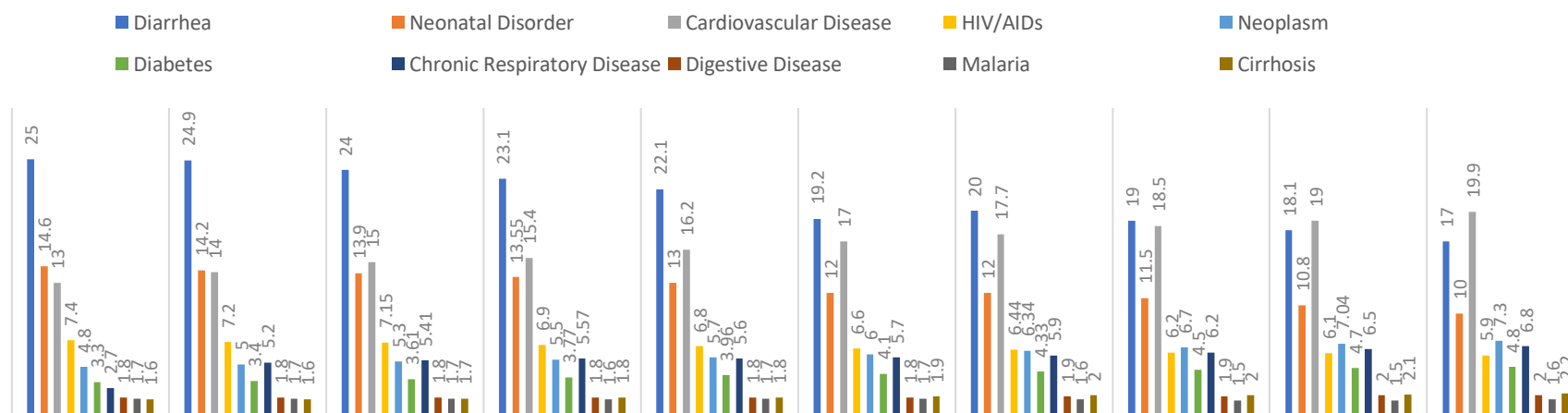


Figure 4 Bar Diagram showing the Trend of YLL in India

Scenario of India

Table no.4 shows the trend of health problems contributing to YLL of India from 2007 to 2016. Top 10 health problems contributing to YLL of India are Diarrhea, Neonatal Disorder, Cardiovascular Disease, HIV/AIDs, Neoplasm, Diabetes, Chronic Respiratory Disease, Digestive Disease, Malaria and Cirrhosis. Among all the clinical trials carried out for Diarrhea there were only 8 in 2007, 5 in 2008, 11 in 2009, 17 in 2010, 10 in 2011, 9 in 2012, 9 in 2013, 5 in 2014, 9 in 2015 and 3 in 2016. Similarly, for Neonatal Disorder there were 0,4,2,1,4,2,3,2,3,2 number of clinical trials done from 2007 to 2016. For Cardiovascular Disease the number of clinical trials done from 2007 to 2016 were 18,23,37,44,18,20,18,13,20,14 respectively. HIV/AIDs being the fourth contributor had 12,7,11,12,9,7,9,5,7,7 clinical trials done regarding the same from 2007 to 2016. Neoplasm had 13,6,3,3,2,3,5,3,1 and 3 clinical trials done in response from 2007 to 2016. Similarly, Diabetes had 41,33,63,51,55,29,39,22,27,15 number of clinical trials done. Chronic Respiratory Disease had only a few clinical trials done which being 2,1,2,2,4,2,1,2,2,4 from 2006 to 2017. Digestive Disease didn't have that much of an impact on the YLL but regarding the clinical trials there were 1,3,6,3,2,5,1,2,2,1 done during the same time frame. Malaria is the ninth contributor for YLL, and it had 1,2,0,1,1,1,1,1,1,1 number of clinical trials done for the same. Last but not the least contributor which is Cirrhosis has had 2,2,0,1,2,1,2,5,2,6 number of clinical trials done. Throughout the years of study Diarrhea has been the top most contributor of YLL for India but we can see that the number of clinical trials done for it is comparably not significant to its impact. But looking down the table we can see that the health problems that are sixth and seventh impactor has the most clinical trials done compared to any other health problems. The trend has been consistent throughout 10 years of study but there has been change in the ranks of health problems going down the table. Through the years Chronic respiratory disease has had more impact than diabetes but the number of clinical trials done were less.

Figure 4 given above is a bar diagram representation of trend of health problems contributing to YLL for India. Throughout the year we can see that the blue bar representing Diarrhea has been the major impactor. But looking down the years on 2016 we can see that the impact of diarrhea has gone down to cardiovascular disease. Cardiovascular disease took the top most impactor in the year 2016 which can also be seen that there always has been the increase in its impact on YLL.

Table 5 Top 10 Health Problems Focused on by Clinical Trials in India

Yr	1 st Contributor	CT	2 nd Contributor	CT	3 rd Contributor	CT	4 th Contributor	CT	5 th Contributor	CT	6 th Contributor	CT	7 th Contributor	CT	8 th Contributor	CT	9 th Contributor	CT	10 th Contributor	CT	TT CTs
7	Diabetes	41	Cardiovascular	18	Neoplasm	13	HIV	12	Chronic Periodontitis	10	Cirrhosis	4	Breast Cancer	4	Gingivitis	4	Asthma	4	Low back and Neck pain	4	254
8	Diabetes	33	Cardiovascular	23	Health	16	Schizophrenia	8	Sense Organ Disease	8	Depression	8	HIV	7	Neoplasm	6	Parkinson's Disease	6	Breast Cancer	5	316
9	Diabetes	63	Cardiovascular	37	Health	22	HIV	11	Lung Cancer	8	Schizophrenia	8	Diarrhea	6	Hypertension	6	Breast Cancer	5	Hepatitis	5	337
10	Diabetes	51	Cardiovascular	44	Health	15	HIV	12	Arthritis	8	Schizophrenia	8	Breast Cancer	6	Hepatitis	6	Hypertension	6	Infection	6	316
11	Diabetes	55	Health	19	Cardiovascular	18	Diarrhea	9	HIV	9	Depression	9	Arthritis	9	Hepatitis	7	Breast Cancer	5	Iron Deficiency	5	321
12	Diabetes	29	Cardiovascular	20	Health	12	Arthritis	9	Schizophrenia	7	HIV	7	Breast Cancer	5	Obesity	5	Asthma	4	Depression	4	299
13	Diabetes	39	Cardiovascular	18	Fasting	10	HIV	9	Hepatitis	6	Arthritis	6	Periodontitis	5	Dengue	5	Neoplasm	5	Breast Cancer	5	258
14	Diabetes	22	Cardiovascular	13	Sense Organ Disease	7	Pregnancy	6	Cirrhosis	5	Periodontitis	5	Hypertension	5	Low back and Neck Pain	5	HIV	5	Health	4	208
15	Diabetes	27	Cardiovascular	20	Periodontitis	8	HIV	7	Health	6	Hypertension	5	Arthritis	5	Pleurisy	5	Depression	4	Anemia	4	214
16	Diabetes	15	Cardiovascular	14	Periodontitis	10	HIV	7	Diarrhea	6	Cirrhosis	6	Pregnancy	5	Gingivitis	4	Breast Cancer	4	Asthma	4	217

Above table is the presentation of trend of clinical trials in India. It shows the health problem that has been focused on in India from 2007 to 2016. Diabetes has always been the health problem that has been primarily focused on by clinical trials in India. The second most focused health problem has been cardiovascular disease throughout the study period. From third onwards there are other health problems being focused. There has been change in the health problems being focused and the health problems were Neoplasm, Sense organ Disease, HIV, Cirrhosis, periodontitis, Asthma, Hepatitis, Diarrhea and some other health problems which can be seen in the table.

Table 6 Trend of YLD for the past 10 years in India

S.N.	Top 10 Disease	2007	CT	2008	CT	2009	CT	2010	CT	2011	CT	2012	CT	2013	CT	2014	CT	2015	CT	2016	CT	TT
1	Dietary Iron Deficiency	11	1	11	1	11	2	11	2	11	5	11	2	11	1	11	1	11	2	11	1	254
2	Sense organ Disease	8	2	8	8	9	3	9	3	9	4	9	3	9	5	9	7	9	3	9	3	316
3	Migraine	6	0	6	0	6	0	6	0	6	1	6	0	6	0	6	0	6	0	6	0	337
4	Low Back Problem	6	4	6	2	6	1	6	3	6	1	6	2	6	4	7	5	7	1	7	4	316
5	Skin and subcutaneous problem	6	2	6	8	6	4	6	3	6	4	6	4	5	5	5	7	5	4	5	3	321
6	Depression	5	2	5	8	5	2	5	1	5	9	5	4	5	1	5	2	5	4	5	1	299
7	Musculoskeletal Disease	5	1	5	1	5	1	5	1	5	1	5	1	5	1	5	1	5	2	5	2	258
8	Chronic Obstructive Disorder	4	18	4	23	4	37	4	44	4	18	4	20	4	18	4	13	4	20	4	14	208
9	Diabetes	3	41	3	33	3	63	3	51	3	55	3	29	3	39	3	22	3	27	3	15	214
10	Anxiety	3	0	3	1	3	0	3	0	3	1	3	0	3	1	3	1	3	0	3	1	217

TREND OF TOP 10 HEALTH PROBLEMS OF INDIA WITH REGARDS TO YLD (2007-2016)

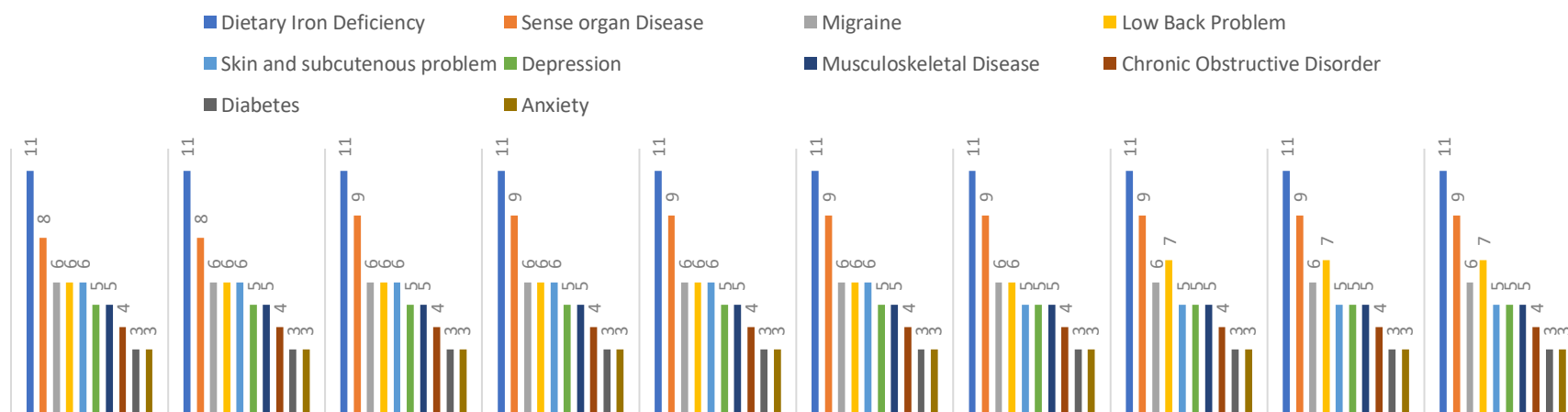


Figure 5 Bar Diagram showing the Trend of YLD in India

Table no.6 shows the trend of health problems contributing to YLD of India from 2007 to 2016. Top 10 health problems contributing to YLD of India are Dietary Iron Deficiency, Sense Organ Disease, Migraine, Low Back Problem, Skin and subcutaneous problem, Depression, Musculoskeletal Disease, Chronic Obstructive Disorder, Diabetes and Anxiety. Throughout the years of study Dietary Iron Deficiency has been the top most contributor of YLD for India but we can see that the number of clinical trials done for it is comparably not significant to its impact. Among all the clinical trials carried out for Dietary Iron Deficiency there were only 1 in 2007, 1 in 2008, 2 in 2009, 2 in 2010, 5 in 2011, 2 in 2012, 1 in 2013, 1 in 2014, 2 in 2015 and 1 in 2016. Similarly, for Sense organ Disease problem there were 2,8,3,3,4,3,5,7,3,3 number of clinical trials done from 2007 to 2016. For Migraine the number of clinical trials done from 2007 to 2016 were 0,0,0,0,1,0,0,0,0,0 respectively. Low back problem being the fourth contributor had 4,2,1,3,1,2,4,5,1,4 clinical trials done regarding the same from 2007 to 2016. Skin and subcutaneous problem had 2,8,4,3,4,4,5,7,4 and 3 clinical trials done in response from 2007 to 2016. Similarly, Depression had 2,8,2,1,9,4,1,2,4,1 number of clinical trials done. Musculoskeletal Disease had more clinical trials done which being 1,1,1,1,1,1,1,1,2,2 from 2006 to 2017. Chronic Obstructive Disorder didn't have that much of an impact on the YLD but regarding the clinical trials there were 18,23,37,44,18,20,18,13,20,14 done during the same time frame. Diabetes is the ninth contributor for YLD, and it had 41,33,63,51,55,29,39,22,27,15 number of clinical trials done for the same. Last but not the least contributor which is Anxiety has had 0,1,0,0,1,0,1,1,0,1 number of clinical trials done.

We can see throughout the study years that the number of clinical trials on it has not been more than maximum of 2. But looking down the table we can see that the health problems that are seventh and eighth impactor has the most clinical trials done compared to any other health problems. The trend has been consistent throughout 10 years of study but there has been change in the ranks of health problems going down the table. Through the years Chronic respiratory disease and Diabetes has had more impact than diabetes but the number of clinical trials done were less.

Figure 5 given above is a bar diagram representation of trend of health problems contributing to YLD for India. Throughout the year we can see that the blue bar representing Dietary Iron Deficiency has been the major impactor. Blue bar and organ bar have always had high scrapers meaning they have always been the leading of YLD in India.

Table 7 Trend of YLL for the past 10 years in Philippines

S.N.	Top 10 Disease	2007	CT	2008	CT	2009	CT	2010	CT	2011	CT	2012	CT	2013	CT	2014	CT	2015	CT	2016	CT	TT
	Cardiovascular																					72
1	Disease	19.8	3	20.3	3	20.09	6	21.6	3	22	9	22.3	3	22	1	22.9	3	23.3	1	23.5	6	
2	Diarrhea	16.6	1	16.5	0	16.1	0	15.6	0	15.6	1	15.6	0	14.5	0	14.4	0	12.9	0	13.5	0	84
3	Neonatal Disorder	12.6	1	12.1	0	11.8	1	11.56	0	11.3	2	11	2	10.7	1	10.7	0	10.5	0	10.2	1	84
4	Neoplasm	8.86	7	8.9	2	9	2	9.3	2	9.5	3	9.6	1	9.6	1	10.6	2	10.2	2	10.3	1	85
5	Diabetes	6.4	11	6.6	8	6.8	16	7	17	7.2	14	7.3	10	7.3	8	7.6	3	7.8	7	7.8	3	90
6	HIV/AIDs	6	0	6.01	0	5.86	0	5.6	0	5.6	0	5.4	0	5.3	0	5.3	1	5.2	0	5.1	0	75
	Chronic Respiratory																					
7	Disease	4.2	1	3.4	1	3.5	1	3.5	1	3.6	2	3.7	0	3.66	1	3.79	1	3.85	1	3.8	2	61
8	Digestive Disease	2	0	2	1	2	0	2	1	2	0	2	1	2	1	2	0	2.1	2	2.1	0	73
9	Cirrhosis	1.6	0	1.6	0	1.7	0	1.7	0	1.7	0	1.7	0	1.7	0	0.8	0	1.9	0	1.9	0	70
10	Malaria	1.2	1	1	2	1	0	1.5	0	1	0	1	0	1.1	0	1.1	0	1.2	1	1.3	0	48

TREND OF TOP 10 HEALTH PROBLEMS OF PHILIPPINES WITH REGARDS TO YLL (2007-2016)

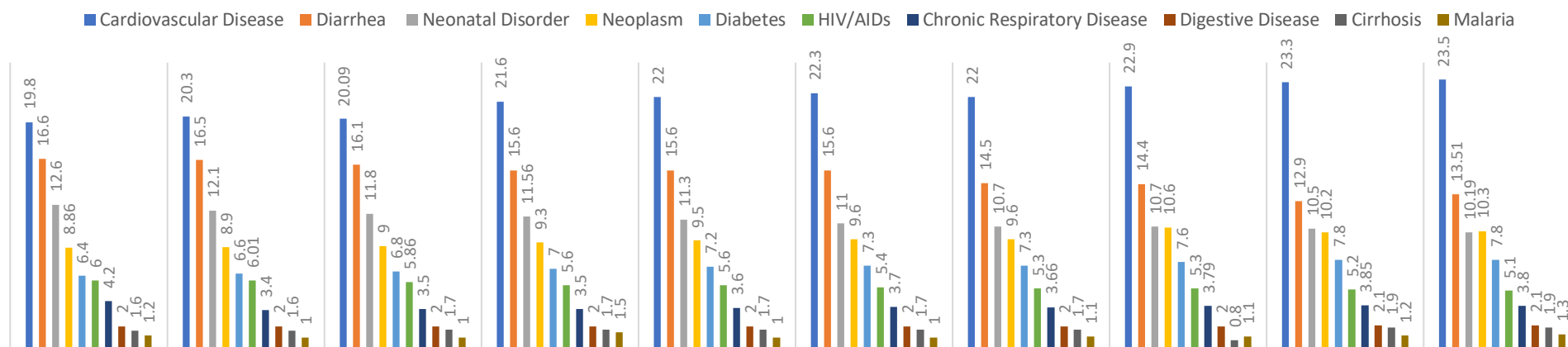


Figure 6 Bar Diagram showing the Trend of YLL in Philippines

Scenario of Philippines

Table no.7 shows the trend of health problems contributing to YLL of Philippines from 2007 to 2016. Top 10 health problems contributing to YLL of Philippines are Cardiovascular Disease, Diarrhea, Neonatal Disorder, Neoplasm, Diabetes, HIV/AIDs, Chronic Respiratory Disease, Digestive Disease, Cirrhosis and Malaria. Among all the clinical trials carried out for cardiovascular disease there were only 3 in 2007, 3 in 2008, 6 in 2009, 3 in 2010, 9 in 2011, 3 in 2012, 1 in 2013, 3 in 2014, 1 in 2015 and 6 in 2016. Similarly, for Diarrhea there were 1,0,0,0,1,0,0,0,0 number of clinical trials done from 2007 to 2016. For Neonatal Disorder the number of clinical trials done from 2007 to 2016 were 1,0,1,0,2,2,1,0,0,1 respectively. Neoplasm being the fourth contributor had 7,2,2,2,3,1,1,2,2,1 clinical trial done regarding the same from 2007 to 2016. Diabetes had 11,8,16,17,14,10,8,3,7 and 3 clinical trials done in response from 2007 to 2016. Similarly, HIV/AIDs had 0,0,0,0,0,0,0,1,0,0 number of clinical trials done. Chronic Respiratory Disease had only a few clinical trials done which being 1,1,1,1,2,0,1,1,1,2 from 2006 to 2017. Digestive Disease didn't have that much of an impact on the YLL but regarding the clinical trials there were 0,1,0,1,0,1,1,0,2,0 done during the same time frame. Cirrhosis is the ninth contributor for YLL, and there were no clinical trials done regarding this health problem. Last but not the least contributor which is Malaria has had 1,2,0,0,0,0,0,0,1,0 number of clinical trials done. Throughout the years of study Cardiovascular Disease has been the top most contributor of YLL for Philippines but we can see that the number of clinical trials done for it is comparably not significant to its impact. But comparing the number of clinical trials done for a health problem and the total number of clinical trials then the number doesn't look that insignificant. Going down the table we can see that the health problems that are fourth and fifth impactor has the most clinical trials done compared to any other health problems. The trend has been consistent throughout 10 years of study.

Figure 6 given above is a bar diagram representation of trend of health problems contributing to YLL for Philippines. Throughout the year we can see that the blue bar representing Cardiovascular Disease has been the major impactor and the trend also shows that its impact has been ever so increasing. Having a look at all the bar diagrams for 10 years of data we can see that every bar looks like each apart from on the year 2014 where Malaria had more impact than cirrhosis.

Table 8 Top 10 Health Problems Focused on by Clinical Trials in Philippines

YR	1 st Contributor	CT	2 nd Contributor	CT	3 rd Contributor	CT	4 th Contributor	CT	5 th Contributor	CT	6 th Contributor	CT	7 th Contributor	CT	8 th Contributor	CT	9 th Contributor	CT	10 th Contributor	CT	Total CTs
7	Diabetes	11	Cardiovascular	8	Neoplasm	7	Infections	6	Lung Cancer	5	Nausea and Vomiting	5	Breast Cancer	2	Embolism	2	Tetanus	2	Pertusis	2	72
8	Diabetes	8	Infection	6	Cardiovascular	5	Asthma	5	Hypertension	5	Depression	3	Alzheimer	3	Diphtheria	2	Parkinson's	2	Tetanus	2	84
9	Cardiovascular	17	Diabetes	17	Schizophrenia	5	Cancer	4	Tuberculosis	3	Hypertension	3	Venous Thrombosis	3	Hepatitis	2	Fatty Liver	2	Arthritis	2	84
10	Cardiovascular	17	Diabetes	17	Arthritis	5	Cancer	5	Hypertension	3	Schizophrenia	3	Tuberculosis	2	Hepatitis	2	Asthma	2	Anemia	2	85
11	Diabetes	14	Cardiovascular	10	Influenza	5	Asthma	4	Neoplasm	3	Dengue	3	Hypertension	3	Arthritis	3	Schizophrenia	3	Depression	3	90
12	Diabetes	10	Cardiovascular	9	Asthma	8	Schizophrenia	6	Dengue	3	Influenza	3	Epilepsy	2	Iron Deficiency	2	Presbyopia	2	Overactive bladder	2	75
13	Cardiovascular	9	Diabetes	8	Asthma	5	Musculoskeletal	4	Cerebral Palsy	4	Epilepsy	4	Muscle Spasticity	4	Pediatric	4	Urinary Bladder	3	Arthritis	2	61
14	Cardiovascular	5	Influenza	4	Diabetes	3	Pediatric	3	Prostate cancer	3	Schizophrenia	3	Neoplasm	2	Depression	2	Arthritis	2	Diphtheria	2	73
15	Cardiovascular	9	Diabetes	7	Arthritis	3	Iodine Deficiency	3	Asthma	3	Neoplasm	2	Anemia	2	Depression	2	Ulcerative colitis	2	Hemophilia	2	70
16	Cardiovascular	3	Diabetes	3	Cancer	3	Infection	3	Asthma	2	Pneumonia	2	Influenza	2	Arthritis	2	Hypertension	2	Anemia	2	48

Above table is the presentation of trend of clinical trials in Philippines. It shows the health problem that has been focused on in Philippines from 2007 to 2016. Diabetes was the health problem primarily focused on during 2007 and 2008 but from that cardiovascular disease has been the health problem of interest. The second most focused health problem has been cardiovascular disease, Diabetes, Influenzas and Infection changing from year to year. From third onwards there are other health problems being focused. There has been change in the health problems being focused and the health problems were Neoplasm, Asthma, Schizophrenia, Arthritis and cancer being some of the major health problems that were being focused on apart from the all-important ones.

Table 9 Trend of YLD for the past 10 years in Philippines

S.N.	Top 10 Disease	2007	CT	2008	CT	2009	CT	2010	CT	2011	CT	2012	CT	2013	CT	2014	CT	2015	CT	2016	CT	TT
1	Low Back Problem	11	1	11	0	10.7	1	9.52	1	10.5	1	10.6	0	10.6	1	9.6	2	10.8	1	10.8	1	72
2	Skin and subcutaneous problem/Headache	10	1	10.28	1	10.2	0	6.8	0	10.1	2	10	1	10	1	6.8	0	9.88	1	9.8	1	84
3	Sense organ Disease/Neonatal	9	0	8.7	1	8.7	1	3.06	2	8.8	1	8.8	1	8.8	0	2.9	0	8.9	1	8.9	1	84
4	Disorder	5	0	5.3	0	5.3	0	4.2	0	5.3	0	5.3	0	5.3	0	4.33	0	5.3	0	5.3	1	85
5	Migraine/Blindness	4	0	4.8	0	4.1	1	4.1	1	4.1	1	4.1	0	4.1	4	4.3	1	4.2	1	4.2	1	90
6	Disease	4	11	4.1	8	4.3	16	5.4	17	4.46	14	4.5	10	4.6	8	5.9	3	4.8	7	4.8	3	75
7	Diabetes	4	0	3.85	3	3.8	1	3.6	0	3.9	2	3.9	0	3.9	1	3.69	0	4	1	4	0	61
8	Depression	3	1	3.4	0	3.44	0	3	0	3.44	0	3.44	0	3.4	0	3	0	3.4	0	3.4	0	73
9	Anxiety Asthma/Age Related Disease/Intestinal	3	2	2.76	5	2.7	0	4.12	0	2.7	4	2.7	8	2.7	5	4.22	0	2.7	3	2.7	2	70
10	Nematod Chronic Obstructive Disorder	3	1	3	1	3	11	6.1	17	3.1	10	3.6	9	3.6	9	5.9	5	3.3	9	3.36	1	48

TREND OF TOP 10 HEALTH PROBLEMS OF PHILIPPINES WITH REGARDS TO YLD (2007-2016)

■ Low Back Problem
 ■ Migraine/Blindness
 ■ Depression
 ■ Chronic Obstructive Disorder
 ■ Skin and subcutaneous problem/Headache
 ■ Musculoskeletal Disease
 ■ Anxiety
 ■ Sense organ Disease/Neonatal Disorder
 ■ Diabetes
 ■ Asthma/Age Related Disease/Intestinal Nematod

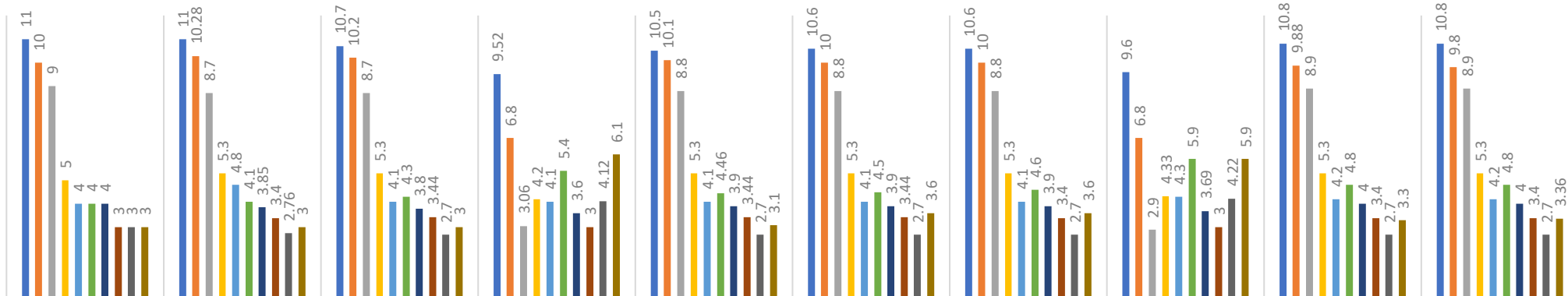


Figure 7 Bar Diagram showing the Trend of YLD in Philippines

Table no.9 shows the trend of health problems contributing to YLD of Philippines from 2007 to 2016. Top 10 health problems contributing to YLD of Philippines are Low Back problem, Skin and subcutaneous problem along with headache, sense organ disease, neonatal disorder, migraine, blindness, Musculoskeletal Disease, Diabetes, Depression, Anxiety, Asthma. There were more than 10 health problems that had impacts on the YLD on different years. Among all the clinical trials carried out for Low back problem there were only 1 in 2007, 0 in 2008, 1 in 2009, 1 in 2010, 1 in 2011, 0 in 2012, 1 in 2013, 2 in 2014, 1 in 2015 and 1 in 2016. Similarly, for Skin and Subcutaneous problem there were 1,1,0,0,2,1,1,0,1,1 number of clinical trials done from 2007 to 2016. For Sense organ Disease the number of clinical trials done from 2007 to 2016 were 0,1,1,2,1,1,0,0,1,1 respectively. Migraine being the fourth contributor had 0,0,0,0,0,0,0,0,0,1 clinical trial done regarding the same from 2007 to 2016. Musculoskeletal

Disease had 0,0,1,1,1,0,4,1,1, and 1 clinical trial done in response from 2007 to 2016. Similarly, Diabetes had 11,8,16,17,14,10,8,3,7,3 number of clinical trials done. Depression had very few clinical trials done which being 0,3,1,0,2,0,1,0,1,0 from 2006 to 2017. Anxiety didn't have that much of an impact on the YLD and similarly there were no clinical trials done regarding the same. Asthma along with Intestinal Nematode is the ninth contributor for YLD, and it had 2,5,0,0,4,8,5,0,3,2 number of clinical trials done for the same. The least contributor which is Chronic Obstructive Disorder has had 1,1,11,17,10,9,9,5,9,1 number of clinical trials done.

Throughout the years of study Low Back problem has been the top most contributor of YLD for Philippines but we can see that the number of clinical trials done for it is comparably not significant to its impact. But looking down the table we can see that the health problems that are sixth impactor has the most clinical trials done compared to any other health problems. The trend has been consistent throughout 10 years of study. The interesting fact we can see in the table is that there are no clinical trials being conducted for a health problem that was fourth most impactor. Apart from that looking in the table we can see that there were years where no clinical trials were conducted for the health problems in the list.

Figure 7 given above is a bar diagram representation of trend of health problems contributing to YLD for Philippines. Throughout the year we can see that the blue bar representing Low Back Problem has been the major impactor with skin and subcutaneous problem always running very closely.

Scenario of USA

YLL											
S.N.	Top 10 Disease	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
	Cardiovascular										
1	Disease	25.9	25.7	25.5	25.3	25.5	25	25	24.9	24.7	24.6
2	Neoplasm	25.3	25.5	25.8	25.9	25.8	25.8	25.6	25.5	25.4	25.4
	Maternal										
3	Disorder	2.8	2.7	2.5	2.4	2.4	2.3	2.3	2.3	2.2	2.1
	Chronic										
	Respiratory										
4	Disease	5.28	5.4	5.4	5.5	5.6	5.6	5.7	5.7	5.7	5.66
	Respiratory										
5	Infection	2.6	2.6	2.6	2.6	2.6	2.6	2.7	2.7	5.8	6.3
	Neurological										
6	Disorder	5	5.1	5.2	5.3	5.5	5.6	5.66	5.6	5.6	5.6
7	Diabetes	4.7	4.8	4.8	4.9	4.9	4.9	4.9	4.9	4.9	4.9
	Digestive										
8	Disease	4.8	4.8	4.6	4.7	4.7	4.7	4.8	4.8	4.7	4.6
9	HIV/AIDs	1.1	1	1	0.8	0.7	0.7	0.6	0.6	0.5	0.6
	Musculoskeletal										
10	Disorder	0.4	0.3	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4

Table 10 Trend of YLL for the past 10 years in USA

This table shows the top 10 health problems that had an impact on YLL of USA. We can see that cardiovascular disease has had the most impact on YLL of USA throughout the years of study. But during the recent years Neoplasm also has had more impact and overtakes cardiovascular disease for the top spot. Comparatively, the number of top 2 and other health problems is very big. The top 10 health problems contributing to YLL of USA were Cardiovascular Disease, Neoplasm, COPD, Neurological Disease, Diabetes, Digestive Disease, Maternal Disorder, Respiratory Infection, HIV/AIDs and Musculoskeletal Disease.

S.N.	Top 10 Disease	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
1	Low back pain	9.5	9.4	9.4	9.4	9.4	9.3	9.3	9.3	9.3	9.2
2	Headache Disorder	6.3	6.2	6.2	6.2	6.1	6.1	6	6	5.9	5.9
3	Depressive Disorder	5.8	5.77	5.7	5.7	5.6	5.6	5.5	5.5	5.47	5.4
4	Diabetes	4.7	4.9	5.2	5.3	5.4	5.44	5.47	5.48	5.4	5.4
5	Stroke	2.3	2.3	2.3	2.3	2.3	2.35	2.4	2.4	2.5	2.5
6	Anxiety	4.7	4.6	4.5	4.4	4.46	4.4	4.3	4.33	4.3	4.24
7	Chronic Obstructive Pulmonary Disease	4.4	4.4	4.5	4.9	4.5	4.6	4.6	4.6	4.66	4.66
8	Musculoskeletal Disorder	4.1	4.1	4.1	4.11	4.1	4.09	4.07	4.05	4.03	4.01
9	Neck Pain	3.8	3.8	3.87	3.9	3.9	3.9	3.95	3.9	3.98	4
10	Neonatal/Osteoarthritis	1.9	1.9	1.9	2	1.98	2	2	2	2.1	2.1

Table 11 Trend of YLD for the past 10 years in USA

Table no.11 shows the trend of health problems contributing to YLD of USA from 2007 to 2016. Top 10 health problems contributing to YLD of USA are Low Back problem, Headache Disorder, Depressive Disorder, Diabetes, Stroke, Anxiety, Chronic Obstructive Pulmonary Disease, Musculoskeletal Disorder, Neck Pain and Neonatal Disorder/ Osteoarthritis. There were more than 10 health problems that had impacts on the YLD on different years. Throughout the years of study Low Back problem has been the top most contributor of YLD for USA.

Top 10 Disease	2007	CT Ind	CT Brazil	CT Phil	2008	CT Ind	CT Brazil	CT Phil	2009	CT Ind	CT Brazil	CT Phil	2010	CT Ind	CT Brazil	CT Phil	2011	CT Ind	CT Brazil	CT Phil
Cardiovascular Disease	25.9	18	9	8	25.7	23	3	5	25.5	37	30	11	25.3	44	57	17	25.5	18	36	10
Neoplasm	25.3	13	5	7	25.5	6	8	2	25.8	3	11	0	25.9	2	7	2	25.8	2	4	2
Maternal Disorder	2.8	3	5	0	2.7	0	2	0	2.5	4	6	0	2.4	3	3	0	2.4	0	1	0
Chronic Respiratory Disease	5.28	1	6	1	5.4	1	4	1	5.4	2	3	1	5.5	2	8	1	5.6	4	4	0
Respiratory Infection	2.6	0	7	0	2.6	0	4	1	2.6	1	4	1	2.6	2	2	1	2.6	2	3	0
Neurological Disorder	5	10	11	3	5.1	24	15	8	5.2	14	10	6	5.3	12	20	2	5.5	17	9	4
Diabetes	4.7	41	33	11	4.8	33	22	8	4.8	63	26	16	4.9	51	25	17	4.9	55	45	14
Digestive Disease	4.8	1	3	0	4.8	3	5	1	4.6	6	5	0	4.7	3	5	1	4.7	1	3	0
HIV/AIDs	1.1	7	16	0	1	5	9	0	1	9	10	2	0.8	20	20	3	0.7	3	9	4
Musculoskeletal Disorder	0.4	1	5	0	0.3	1	2	0	0.4	1	1	0	0.4	1	1	1	0.4	1	4	1
Top 10 Disease	2012	CT Ind	CT Brazil	CT Phil	2013	CT Ind	CT Brazil	CT Phil	2014	CT Ind	CT Brazil	CT Phil	2015	CT Ind	CT Brazil	CT Phil	2016	CT Ind	CT Brazil	CT Phil
Cardiovascular Disease	25	20	40	9	25	18	46	9	24.9	13	51	5	24.7	20	40	9	24.6	14	44	3
Neoplasm	26	3	4	1	25.6	5	8	1	25.5	3	9	2	25.4	1	11	2	25.4	3	14	1
Maternal Disorder	2.3	1	4	0	2.3	1	2	0	2.3	8	2	1	2.2	1	4	0	2.1	6	5	0
Chronic Respiratory Disease	5.6	2	9	1	5.7	1	4	1	5.7	2	7	1	5.7	2	4	1	5.66	4	4	2
Respiratory Infection	2.6	1	8	0	2.7	0	2	0	2.7	1	5	1	5.8	1	5	1	6.3	4	5	2
Neurological Disorder	5.6	12	11	7	5.66	2	9	2	5.6	5	11	6	5.6	3	11	3	5.6	3	14	1
Diabetes	4.9	29	33	10	4.9	39	26	8	4.9	22	35	3	4.9	27	33	7	4.9	15	22	3
Digestive Disease	4.7	5	4	1	4.8	1	7	1	4.8	2	6	0	4.7	2	6	2	4.6	1	3	0
HIV/AIDs	0.7	9	11	2	0.6	5	9	1	0.6	7	19	3	0.5	5	11	2	0.6	2	14	2
Musculoskeletal Disorder	0.4	1	7	0	0.4	1	3	4	0.4	1	9	0	0.4	2	9	0	0.4	2	11	1

Table 12 Clinical trials of 3 host nations with response to YLL of USA

Table 12 is to see whether there is an influence of health problems of USA on the clinical trials that were done in the three host nations. The table shows the number of clinical trials for the health problems carried in the host nations as per health problems of USA. We can see that even if the health problems are related to USA there are so many clinical trials done regarding them. We can also make out another thing from this table that is the fact that the clinical trials of host nations are in sync with the health problems contributing to YLL of USA, what it means is that the health problem that has contributed the most in USA also has relatively more clinical trials done regarding the same. Even though down the line there are a few health problems that has more clinical trials done regarding them like Diabetes, but these are the most common and highly affecting disease that also might be a reason for having a greater number of clinical trials.

Top 10 Disease	2007	CT Ind	CT Brazil	CT Phil	2008	CT Ind	CT Brazil	CT Phil	2009	CT Ind	CT Brazil	CT Phil	2010	CT Ind	CT Brazil	CT Phil	2011	CT Ind	CT Brazil	CT Phil
Low back pain	9.5	4	2	1	9.4	2	3	0	9.4	1	5	1	9.4	3	7	1	9.4	1	4	1
Headache Disorder	6.3	0	0	0	6.2	0	0	0	6.2	0	0	0	6.2	0	0	0	6.1	0	0	0
Depressive Disorder	5.8	2	1	0	5.77	8	3	3	5.7	2	3	1	5.7	1	6	0	5.6	9	4	2
Diabetes	4.7	41	33	11	4.9	33	22	8	5.2	63	26	16	5.3	51	25	17	5.4	55	45	14
Stroke	2.3	2	2	1	2.3	3	5	1	2.3	5	8	2	2.3	2	4	0	2.3	1	7	1
Anxiety	4.7	0	1	1	4.6	1	2	0	4.5	0	0	0	4.4	0	4	0	4.46	1	3	0
Chronic Obstructive Pulmonary Disease	4.4	18	6	1	4.4	23	4	1	4.5	37	3	1	4.9	44	8	1	4.5	18	4	2
Musculoskeletal Disorder	4.1	1	5	0	4.1	1	2	0	4.1	1	1	1	4.11	1	1	1	4.1	1	4	1
Neck Pain	3.8	4	2	1	3.8	2	3	0	3.87	1	5	1	3.9	3	7	1	3.9	1	4	0
Neonatal/Osteoarthritis	1.9	0	1	1	1.9	4	1	0	1.9	2	2	1	2	7	15	9	1.98	3	14	4
Top 10 Disease	2012	CT Ind	CT Brazil	CT Phil	2013	CT Ind	CT Brazil	CT Phil	2014	CT Ind	CT Brazil	CT Phil	2015	CT Ind	CT Brazil	CT Phil	2016	CT Ind	CT Brazil	CT Phil
Low back pain	9.3	2	3	0	9.3	4	3	1	9.3	5	8	1	9.3	1	9	1	9.2	4	6	1
Headache Disorder	6.1	0	0	0	6	0	0	0	6	0	0	0	5.9	0	0	0	5.9	0	0	0
Depressive Disorder	5.6	4	6	0	5.5	1	1	1	5.5	2	2	1	5.47	4	5	1	5.4	1	7	0
Diabetes	5.4	29	33	10	5.47	39	26	8	5.48	22	35	3	5.4	27	33	7	5.4	15	22	3
Stroke	2.4	2	4	0	2.4	0	2	2	2.4	2	8	0	2.5	3	16	1	2.5	0	11	0
Anxiety	4.4	0	3	0	4.3	1	2	0	4.33	1	2	0	4.3	0	3	0	4.24	1	3	0
Chronic Obstructive Pulmonary Disease	4.6	20	9	0	4.6	18	4	1	4.6	13	7	1	4.66	20	4	1	4.66	14	4	2
Musculoskeletal Disorder	4.1	1	7	0	4.07	1	3	4	4.05	1	9	1	4.03	2	9	1	4.01	2	11	1
Neck Pain	3.9	2	3	0	3.95	4	3	1	3.9	5	8	2	3.98	1	9	1	4	4	6	1
Neonatal/Osteoarthritis	2	9	11	3	2	6	7	2	2	1	6	2	2.1	2	7	2	2.1	2	3	1

Table 13 Clinical trials of 3 host nations with response to YLD of USA

Table 13 shows the number of clinical trials for the health problems carried in the host nations as per health problems of USA contributing to its YLD. We can see that even if the health problems are related to USA there are so relatively more clinical trials done regarding them. We can also make out another thing from this table that is the fact that the clinical trials of host nations are in sync with the health problems contributing to YLD of USA, what it means is that the health problem that has contributed to YLD of USA also has relative number of clinical trials done regarding the same in host nations. Even though down the line there are a few health problems that has more clinical trials done regarding them like Diabetes and Chronic Obstructive Pulmonary Disorder, but these are the most common health problem all around the world and highly focused ones.

Exclusiveness

Exclusiveness of India

YLL																					
Top 10																					
S.N.	Disease	2007	CT	2008	CT	2009	CT	2010	CT	2011	CT	2012	CT	2013	CT	2014	CT	2015	CT	2016	CT
1	Diarrhea	25	8	24.9	5	24	11	23.1	17	22.1	10	19.2	9	20	9	19	5	18.1	9	17	3
	Neonatal																				
2	Disorder	14.6	0	14.2	4	13.9	2	13.55	1	13	4	12	2	12	3	11.5	2	10.8	3	10	2
3	Malaria	1.7	1	1.7	2	1.7	0	1.6	1	1.7	1	1.7	1	1.6	1	1.5	1	1.5	1	1.6	1
4	Cirrhosis	1.6	2	1.6	2	1.7	0	1.8	1	1.8	2	1.9	1	2	2	2	5	2.1	2	2.2	6
			254		316		337		316		321		299		258		208		214		217

Table 14 YLL Exclusive Disease in India with clinical trials

The above table shows health problems that are exclusive to only India with respect to the health problems of USA. After crossmatching the health problems that contributed to YLL of USA with that of India the above table was formulated. As we can see from the list of 10 health problems only four of them were exclusive to India. The health problems that are exclusive to India were the first two and last two contributors to top 10 health problems contributing to YLL of India. Apart from the obvious which is the fact that only four of the health problems are exclusive we can also see that the clinical trials that were highly focused in the host country were the health problems that were not exclusive. Looking back at the table 4 we can see that the highest number of clinical trials were concentrated towards the middle table meaning that the health problems which were ranked from 3rd to 8th had most of the clinical trials. This also means that the exclusive health problems were not the main concern of Clinical trials.

YLD																					
Top 10																					
S.N.	Disease	2007	CT	2008	CT	2009	CT	2010	CT	2011	CT	2012	CT	2013	CT	2014	CT	2015	CT	2016	CT
1	Dietary Iron Deficiency	11	1	11	1	11	2	11	2	11	5	11	2	11	1	11	1	11	2	11	1
2	Sense organ Disease	8	2	8	8	9	3	9	3	9	4	9	3	9	5	9	7	9	3	9	3
3	Migraine	6	0	6	0	6	0	6	0	6	1	6	0	6	0	6	0	6	0	6	0
4	Skin and Subcutaneous Problem	6	2	6	8	6	4	6	3	6	4	6	4	5	5	5	7	5	4	5	3
		254		316		337		316		321		299		258		208		214		217	

Table 15 YLD Exclusive Disease in India with clinical trials

Here we can see the health problems that are exclusive to India with respect to YLD. Amongst the 10 health problems that were the major contributors to YLD of India only four of them were exclusive to India alone when being compared to the health problems that contributed to YLD of USA. Even though the clinical trials are supposed to focus on the health problems of the host country but from the table above we can clearly see that other than the above four exclusive health problems it was the health problems of USA that were being focused on. From the point of view of clinical trials, we can also say that the health problems that were mainly focused by clinical trials aren't the ones that are exclusive to host nation rather those were the disease that were also a major concern for USA.

Exclusiveness of Brazil

YLL																					
S.N	Top 10 Disease	2007	CT	2008	CT	2009	CT	2010	CT	2011	CT	2012	CT	2013	CT	2014	CT	2015	CT	2016	CT
Neonatal																					
1	Disorder	10	0	8.5	0	8.2	2	7.8	2	7.55	2	7.2	0	6.9	0	6.5	1	6.1	0	5.8	2
2	Diarrhea	7.1	1	6.9	1	6.7	3	6.5	1	6.4	0	6.3	1	6.1	1	6	2	5.9	0	8	0
3	Cirrhosis	2.9	2	3	2	2.9	0	3	4	3	1	3	2	3	2	3.1	1	3.1	2	3.2	1
		337		379		456		502		535		617		497		542		567		578	

Table 16 YLL Exclusive Disease in Brazil with clinical trials

Comparing the health problems contributing to YLL of Brazil and USA we can see the health problems that are exclusive to Brazil. Amongst 10 of the top health problems contributing to YLL of Brazil only three of them are exclusive. Just looking at the number of clinical trials among the exclusive health problems we can see that there aren't that much done regarding these. Major health problems that were focused by the clinical trials in host nation were common health problems of USA as well. Meaning the exclusive health problems do not have that many clinical trials among them.

YLD																					
Top 10																					
S.N.	Disease	2007	CT	2008	CT	2009	CT	2010	CT	2011	CT	2012	CT	2013	CT	2014	CT	2015	CT	2016	CT
1	Skin and subcutaneous Problem	7.6	1	7.6	3	8	3	8	4	7	1	7	1	7	3	7	2	7	2	7	2
2	Sense organ Disease	7.5	2	7.6	4	8	1	7	5	8	3	8	2	8	4	8	3	8	3	8	2
3	Migraine	6.4	1	6.4	0	6	0	6	1	6	2	6	1	6	1	6	1	6	1	6	2
4	Dietary Iron Deficiency	3.6	2	3.5	0	3	3	3	2	3	0	3	1	3	2	3	4	3	4	3	1
5	Oral Disease	2.9	2	2.9	3	3	3	3	7	3	8	3	4	3	11	3	12	3	12	3	15
		337		379		456		502		535		617		497		542		567		578	

Table 17 YLD Exclusive Disease in Brazil with clinical trials

Relatively, health problems contributing to YLD of Brazil has the greatest number of exclusive health problems compared to other host nations. Even though there aren't that many exclusive health problems the one that has had the most clinical trials done in the recent years is included. Other than that, the major impactor of YLD for Brazil is not one of the exclusive health problems.

Exclusiveness of Philippines

YLL																					
Top 10																					
S.N.	Disease	2007	CT	2008	CT	2009	CT	2010	CT	2011	CT	2012	CT	2013	CT	2014	CT	2015	CT	2016	CT
1	Diarrhea	16.6	1	16.5	0	16.1	0	15.6	0	15.6	1	15.6	0	14.5	0	14.4	0	12.9	0	13.51	0
	Neonatal																				
2	Disorder	12.6	1	12.1	0	11.8	1	11.56	0	11.3	2	11	2	10.7	1	10.7	0	10.5	0	10.19	1
3	Cirrhosis	1.6	0	1.6	0	1.7	0	1.7	0	1.7	0	1.7	0	1.7	0	0.8	0	1.9	0	1.9	0
4	Malaria	1.2	1	1	2	1	0	1.5	0	1	0	1	0	1.1	0	1.1	0	1.2	1	1.3	0
			72		84		84		85		90		75		61		73		70		48

Table 18 YLL Exclusive Disease in Philippines with clinical trials

Only four of the health problems from top 10 major contributors of YLL in Philippines are exclusive to the host nation. Looking at the table and comparing it with the table 7 showing top 10 major health problems contributing to YLL Philippines, we can see that the clinical trials focusing on health problems aren't exclusive. The exclusive health problems barely have any clinical trials done regarding the same. The maximum number of clinical trials done in a year for any of the exclusive health problems is two which is very little, furthermore we can also see that there are years where no clinical trials for the health problems were done.

YLD																					
S.N.	Top 10 Disease	2007	CT	2008	CT	2009	CT	2010	CT	2011	CT	2012	CT	2013	CT	2014	CT	2015	CT	2016	CT
1	Skin and subcutaneous problem/Headache	10	1	10.28	1	10.2	0	6.8	0	10.1	2	10	1	10	1	6.8	0	9.88	1	9.8	1
2	Sense organ Disease/Neonatal Disorder	9	0	8.7	1	8.7	1	3.06	2	8.8	1	8.8	1	8.8	0	2.9	0	8.9	1	8.9	1
3	Migraine/Blindness	5	0	5.3	0	5.3	0	4.2	0	5.3	0	5.3	0	5.3	0	4.33	0	5.3	0	5.3	1
4	Asthma/Age Related Disease/Intestinal Nematode	3	2	2.76	5	2.7	0	4.12	0	2.7	4	2.7	8	2.7	5	4.22	0	2.7	3	2.7	2
		72		84		84		85		90		75		61		73		70		48	

Table 19 YLD Exclusive Disease in Philippines with clinical trials

There were 10 health problems that had major impact on the YLD of Philippines but when compared to the similar facts of USA we can see that there are only 4 of them which are exclusive. Looking back at the top 10 health problems the health problem which had most of the clinical trials done on is not included here in the exclusive one. Also, from the table we can see that there are no clinical trials done for some of the health problems during some of the years.

Exclusiveness of USA

S.N.	Top 10 Disease	2007	CT Ind	CT Brazil	CT Phil	2008	CT Ind	CT Brazil	CT Phil	2009	CT Ind	CT Brazil	CT Phil	2010	CT Ind	CT Brazil	CT Phil	2011	CT Ind	CT Brazil	CT Phil
1	Maternal Disorder	2.8	3	5	1	3	1	3	0	2.5	5	9	0	2	3	3	0	2	1	3	0
2	Respiratory Infection	2.6	3	2	2	3	2	2	2	2.6	1	4	2	3	2	3	2	3	3	2	1
3	Musculoskeletal Disorder	0.4	1	5	0	0.3	1	2	0	0.4	1	1	1	0.4	1	1	1	0.4	1	4	1
Total CTs			254	337	72		316	379	84		337	456	84		316	502	85		321	535	90

Top 10 Disease	2012	CT Ind	CT Brazil	CT Phil	2013	CT Ind	CT Brazil	CT Phil	2014	CT Ind	CT Brazil	CT Phil	2015	CT Ind	CT Brazil	CT Phil	2016	CT Ind	CT Brazil	CT Phil
Maternal Disorder	2	2	9	0	2.3	2	8	1	2	8	6	1	2	8	6	0	2	6	10	1
Respiratory Infection	3	2	6	2	2.7	1	3	1	3	2	5	1	5.8	2	5	2	6	3	5	2
Musculoskeletal Disorder	0.4	1	7	0	0.4	1	3	4	0.4	9	3	1	0.4	2	9	1	0.4	2	11	1
Total CTs		299	617	75		258	497	61		208	542	73		214	567	70		217	578	48

Table 20 Health problem contributing to YLL and exclusive to USA with its corresponding Clinical trials in host nations

This table shows health problems that were exclusive to only USA when it was compared to the nations that were under study. When the health problems that contribute to YLL of USA were compared to the health problems contributing to the same of other nations under study then this table was formulated which only shows exclusive health problems. There were only 3 health problems that were exclusive to USA among the top 10 health problems that contributed to YLL. The health problems exclusive to USA were Maternal Disorder, Respiratory Infection and Musculoskeletal Disorder. This table also shows how many clinical trials were done in the host nations as per the health problems exclusive to USA. Even though these health problems were only exclusive to USA we can see that the clinical trials done regarding these in the corresponding host nations were relative enough. Even though when the clinical trials regarding the health problems were compared to the total it doesn't add up to that much but then it is relative significant.

S.N.	Top 10 Disease	2007	CT Ind	CT Brazil	CT Phil	2008	CT Ind	CT Brazil	CT Phil	2009	CT Ind	CT Brazil	CT Phil	2010	CT Ind	CT Brazil	CT Phil	2011	CT Ind	CT Brazil	CT Phil
1	Stroke	2.3	2	2	1	2.3	3	5	1	2.3	5	8	2	2.3	2	4	0	2.3	1	7	1
2	Neck Pain	3.8	2	2	0	3.8	0	2	0	3.9	0	1	0	3.9	0	4	0	3.9	0	0	0
3	Neonatal/Osteoarthritis	1.9	3	11	1	1.9	6	13	4	1.9	5	6	3	2	10	17	8	2	10	15	4
Total CTs			254	337	72		316	379	84		337	456	84		316	502	85		321	535	90
	Top 10 Disease	2012	CT Ind	CT Brazil	CT Phil	2013	CT Ind	CT Brazil	CT Phil	2014	CT Ind	CT Brazil	CT Phil	2015	CT Ind	CT Brazil	CT Phil	2016	CT Ind	CT Brazil	CT Phil
	Stroke	2.3	2	4	1	2.4	1	2	2	2.4	2	8	1	2.5	3	16	1	2.5	1	11	0
	Neck Pain	3.9	1	2	0	4	1	1	0	3.9	1	2	0	4	1	1	0	4	2	2	0
	Neonatal/Osteoarthritis	2	12	25	3	2	10	8	2	2	6	10	3	2.1	5	17	3	2.1	5	7	3
Total CTs			299	617	75		258	497	61		208	542	73		214	567	70		217	578	48

Table 21 Health problem contributing to YLD and exclusive to USA with its corresponding Clinical trials in host nations

This table shows health problems that were exclusive to only USA when it was compared to the nations that were under study. When the health problems that contribute to YLD of USA were compared to the health problems contributing to the same of other nations under study then this table was formulated which only shows exclusive health problems. There were only 3 health problems that were exclusive to USA among the top 10 health problems that contributed to YLD. The health problems exclusive to USA were Stroke, Neck Pain and Neonatal Disorder plus Osteoarthritis. This table also shows how many clinical trials were done in the host nations as per the health problems exclusive to USA. Even though these health problems were only exclusive to USA we can see that the clinical trials done regarding these in the corresponding host nations were relative enough. Even though when the clinical trials regarding the health problems were compared to the total it doesn't add up to that much but then it is relative significant.

Looking at the exclusive health problems of all the host nations and that of USA, the thing that we can make out from this is the fact that even though there were few health problems that were exclusive to each of the host nations and USA, but the number of clinical trials done regarding the same were very significant.

Tables 14,16 and 18 represents the exclusive health problems contributing to YLL of the host nations under study. They also show the clinical trials for those exclusive health problems. From those data we can see that apart from one of the health problems that is Diarrhea which had relatively significant number of clinical trials done for it, ever other health problems just had one or two clinical trials done on it. This data was consistent throughout the study period for all the health problems. This was consistent even for the health problems contributing to YLD of the host nations. Tables 15,17 and 19 shows the data for the same where we can see that the number of clinical trials were comparatively very less and insignificant compared to the total number of clinical trials done in the same year.

Now, looking at the table for exclusive health problems contributing to YLL of USA we can see that even though these were the health problems that were exclusive to USA there were relatively significant number of clinical trials done for those in the host nations. For most of the health problems exclusive to USA there were relatively a greater number of clinical trials done in Brazil than any other host nations. But not just that the number of clinical trials for other exclusive health problems were relatively consistent and higher than the clinical trials done for the health problems that were exclusive to their own nation. From all these data we can see that the exclusive health problems of USA were focused on by clinical trials done in three of the host nations. But when it comes to exclusive health problems of the host nations then it was very evident that there were not that many clinical trials done regarding them. From this we can say that the clinical trials were not responsive to the gravest needs of host nations. This can be said because when we looked at the clinical trials done in host nations and was cross matched with the exclusive health problems of USA, we could see that there were clinical trials focused on the health problems of USA. If the clinical trials do not focus on the health problems that were exclusive to host nations rather, they focus on the health problems exclusive to USA meaning the clinical trials do not address the gravest needs of the host nations.

Discussion

Having a look at the results from what this paper investigates and comparing it with the things that has already been conducted in the past regarding the same is the main aim of this part of the paper. There have not been many researchers conducted in the past for the similar topic but then there are papers that investigate different component of this paper.

This paper mainly looks at how responsive Clinical trials were regarding the top 10 health problems contributing to YLL and YLD of three different countries, India, Philippines and Brazil being those countries. From the result we found that only a few of the top 10 health problems were exclusive to the host countries. Only four of the ten health problems for India were exclusive for both YLL and YLD meaning most of the health problems were like that of our comparison country which was USA. When the clinical trials for these exclusive health problems were observed we could see that it was very few. Even though exclusive health problem was one of the major contributors to YLL of India the clinical trials done regarding the same was very less compared to that of the common ones. This also leads to a conclusion that the clinical trials done in India are not responsive or is a per the need of the country. This result is also supported by a paper done earlier by Chaturvedi and co which found out that the clinical trials done in India were not in line with the healthcare (Chaturvedi, Gogtay, & Thatte, 2017). The research looked at all the clinical trials in its registry i.e. Clinical trial registry India (CTRI) and was compared with the global burden of disease (DALY) from Global Health Estimates (2014) summary table of WHO. The paper was only limited with the clinical trials registered in their own country whereas this line included all the clinical trials registered globally. Even if the registered clinical trials were different in two of the studies the results from both were quite similar. Which also kind of boosts the result of this paper too and backs up the result of papers done in the past for the same topic.

Another part of the result that isn't directly focused on the by the paper but is a part that's affected by all the increase in number of clinical trials done in these host nations is the ethical aspect. From the results of this paper we can see that the clinical trials in host nations have been increasing specially in Brazil where the clinical trials are comparatively higher than in other host nations. Even though there is an increase in the clinical numbers when we look at the responsiveness and as per the need aspect of it, we can see that it's not the same deal. From the results we can see

that from top 10 health problems contributing to YLL of Brazil only 3 of them are exclusive to Brazil which means 7 of them are common to the comparative country. Not just that the exclusive health problems have merely any clinical trials done regarding them. Even though it doesn't mean that the clinical trials are not responsive or as per the need or not but the fact that these 3 health problems are a few from the top 10 contributors and have relatively significant impact on the YLL does mean the opposite. This result is quite like the result from one of the papers done previously. One of the researches that talks about the responsiveness of clinical trials in a way is the paper done by Ricardo Eccard da Silva and co. The paper "Globalization of clinical Trails: ethical and regulatory implications" covers the responsiveness aspect of clinical trials. The paper covers the fact that there is increase in number of clinical trials being conducted in low and middle-income nations (Silva, Amato, Guilhem, & Garbi Novaes, 2016). The paper focuses on the fact that there has been increase in the number of clinical trials that has been being conducted in developing countries but with the increase in the number it also means that ethical aspect is being neglected. It concludes that even though the increase in number of clinical trials means more opportunity for the people to take part in it but having said that it also means that ethical question related mainly to ensuring the integrity, welfare and safety of the participant everything needs to be discussed. These things are also backed up by this paper as there should be more clinical trials that focus on the need of the people, their needs and things that affect them rather than things that are influenced by some other country. Also, the fact that when clinical trials are carried out then they should also take care of the ethical aspects.

Similar part of the paper was also focused by another paper which talks about the past recognition of these disease being local to poor country is not just confined to those nations but also moving on to all over other nations too regardless of disease area or income classification. The experiment was done in five public research institutions from India, Brazil, Kenya, Malaysia, France and WHO/TDR which was in response to the frustration of being exposed to medicines that were not very effective against the health problem that were found in these countries, were highly toxic and even were unavailable to the people of these nations. The research comes to a concrete evidence that there is development of six adapted, affordable and non-parented treatments for the world's neglected diseases (Pecoul, 2016). This fact is kind of mentioned by this paper when we

can see that the exclusive health problems for each of the host nations are very less and they even have a smaller number of clinical trials done regarding the same. Even when the exclusive health problems are the ones that contribute majorly to YLL and YLD they do not have that many clinical trials done regarding the same. It connects to the things mentioned by the paper by Drugs on neglected diseases initiative by Bernard Pecoul (Pecoul, 2016).

From results we can see that there are so many health problems that are so common to the health problems contributing to YLL and YLD of USA. Every nation under study had majority of the health problems that were common to the health problems of USA and then the health problems that were common were the ones that have more clinical trials done regarding the same than the ones that were exclusive to the host nations. From this we can conclude that these clinical trials are highly influenced by high income nations, in this case it being USA. This result from the paper is also backed up by the paper “Published randomized clinical trials in Sub-Saharan Africa (SSA) focuses on high-burden disease but are frequently funded and led by high income nations” which concludes that the randomized clinical trials carried out in SSA were highly funded and led by institutions from High Income Countries (Diakou, Ntouni, Ravaud, & Boutron, 2017). The paper also found out that the RCTs were more focused on the acute health problems and only a few of the were focused on the more chronic health problems. Even though the paper is only focusing on the RCTs carried out but the result from this paper can be backed up by the results of this paper. In this paper we can also see that the health problem that had more impact on the YLL and YLD of host nations they were not the health problems that were focused on by the clinical trials. There were clinical trials done for the health problems that were a problem and contributor to YLL and YLD of USA. With this paper the section looked at is bigger and wider than the paper done by Diakou and co. Furthermore, with all the results from the paper which is highly focused on the influence of high-income nations on the clinical trials being carried out on middle and low-income nations we can say that it doesn't address the gravest needs of nations under study. This is against the concept of Human Development Approach which focuses on finding the gap between the policy and implementation of programs to develop the capacity of human resource for an overall development and it tries to see if there is an influence of high-income nation. The part of the paper that discusses about the exclusiveness of health problems and the clinical trials

that focuses on those health problems shows that the clinical trials that were exclusive to the host nations didn't have that many clinical trials done to address them. Whereas on the contrary when the health problems that were exclusive to a high-income nation like USA was investigated then we could see that there were comparatively more clinical trials done for these diseases that too in the host nations. The exclusiveness section shows the link of clinical trial carried out in low and middle-income nations with the health problems contributing to YLL and YLD of high-income nations like USA. The main outcome that we derived from this exclusiveness section of the paper was the fact that there has been an influence of high-income nation on the clinical trials carried out on low and middle-income nations. That was one of the concepts of Human Development approach which was highly focused. If the clinical trials do not address and focus on the needs of countries, then it will not be towards human development rather it will be very one directional towards high-income nations. The sole aim of Human Development Approach was to develop human capabilities which means to empower and improve the health of human being so that they can have more opportunity and access to facilities eventually improving the health of everyone. So, this paper lights upon the shades that high-income nations are influencing the clinical trials that are being done in low and middle-income nations.

People do what they have things to do, if they have certain opportunity provided to them then only, they can get involved in those things to achieve what they want to achieve. This is one of the concepts of Sen's Capability approach which is core for the development of Human Development Approach. When people need certain health program or clinical trials to address a certain health problem then they will do things that they can and on the other hand if they do not have the opportunity then they cannot do those things. Similarly, with the clinical trials, if there are clinical trials done in a country that addresses the needs of the people then they provide them with opportunity to get rid of their health problems but if there are no opportunity provided to the people then they will not have the chance to make use of the same. So, addressing the health problems and making use of it is what makes a huge difference.

Study Limitations

The study is completely based on the secondary data which is the main drawback of the paper. The paper only looks at a fixed number of variables and over a certain period so the results of the paper cannot be generalized over all the countries out there. The results also might not be applicable for other variables and other indicators of study. The study period was not set to the present time which might also be a factor in the results not being appropriate for the current time or scenario.

Conclusion

Based on all the results drawn from the information provided in this paper after analyzing the data's extracted from the online sites clinicaltrials.org and healthdata.org we can address whether the clinical trials carried out in the host nations were responsive to the gravest need of host nations or not. Before directly going into the conclusion, talking about the descriptive section of the thesis we could see that there were so many health problems that contributed to the top 10 health problems contributing to YLL and YLD of the host nations as well as USA. Amongst the nations that were studied there were so many common health problems that contributed to YLL and YLD of all those nations. There were only a few health problems that were exclusive to the nations when compared to the health problems of USA. Even the trend of health problems for all the host nations and the nation that was used to compare we could see that for the total 10 years of study the contributors didn't change that much. The health problems that were the major contributors were mostly the same which were mostly non-communicable disease like cardiovascular disease and Diabetes but for India diarrhea was the most predominant contributor throughout the years of study.

Main part of the paper that shows whether the clinical trials do address the gravest needs of low and middle-nations is the exclusiveness section of the paper. From this section we can conclude that the clinical trials that are being carried out in middle and low-income nations are influenced by the major health problems of high-income nation which in this case is USA. From the exclusiveness table we could see that for the health problems that were exclusive to USA had relatively significant number of clinical trials being carried out in the host nations. On the other

hand, for the health problems that were exclusive to the host nations the number of clinical trials done were very little in number compared to the clinical trials done regarding other health problems. From this we can clearly conclude that the clinical trials hardly address the gravest needs of low and middle-income nations based on top 10 health problems contributing to YLL and YLD. Talking about the whole things with the human development approach we can say that even though the clinical trials done are to improve the health of people but the main idea of it not being influenced by high-income nations isn't being complied. For the sake of human development, the health problems that is a major problem in that nations should be addressed rather than being influenced by any country. Therefore, measures that ensure that clinical trials are not influenced by high-income nations and the fact that they address the needs of the host nations should be established and regularly monitored.

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