ABSTRACT

The aim of this study is to make an analysis based on the different literature sources about the benefits and risks of conducting clinical trials in human medicine. A clinical trial is defined as a controlled trial in humans of new drugs, devices, therapy or diagnosis, or comparisons of currently approved drugs, devices, therapy or diagnosis, to assess the safety, efficacy, benefits, costs, side effects, and / or results. Such studies can be conducted within the frame of industry to developed protocol (referred to as a "sponsor-initiated clinical trial") or protocol developed by the researcher ("investigator initiated clinical trial"). These studies most often carried out in connection with the new drug of phases I, II, III or IV, although they may be designed for the sole purpose to collect and analyze the data for the approved drugs or devices, in order to contribute to the medical knowledge for the treatment of a disease or medical condition. Clinical trials are usually financed by pharmaceutical companies and are an important part of the safety and efficacy of the drug or device to obtain approval from the institutions, with the final goal of selling the product on the market. Any such process is associated with benefits and risks to this conclusion reach authors working in the field, as the most common benefits are: obtaining access to new treatments that are not yet available to the public, receiving expert medical care and the patient has an active role in their own health care, but also helped others with similar diseases by contributing to medical research. Last but not least is the economic benefit for society and the individual patient. Risks, according to the authors, there may be unpleasant, serious or even life-threatening side effects of treatment, processing data is not always effective, the study may require a lot of time traveling to the place of the analysis, patients may need and hospital stay or more complex application of the test product, which would...
harm him via normal lifestyle. Costs not covered by public health insurance, at least not in full also helped others with similar diseases by contributing to medical research.

**KEYWORDS:** Clinical trial, benefit, risk, medicine.

**INTRODUCTION**

Clinical trials follow very strict scientific and ethical standards that protect participants in terms of their health, safety and integrity of their privacy.[1, 2, 3] Each clinical trial of a new treatment or a new way to provide already existing treatment must be approved by the appropriate agency for medicines in a given country, the hospital or clinic where the study is conducted, as well as by the relevant central ethics committee. In the institutional ethics Committees(LEC) are engaged health professionals and representatives of the community that protect clinical trial participants.

Choosing to participate in a clinical trial is an important personal decision. In taking that decision the patients should consult with their doctors about the possible benefits and risks. The aim of this study is to make an analysis based on the different literature sources about the benefits and risks of conducting clinical trials in human medicine.

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**Potential benefits**

When the experimental treatment is studied in comparison with the standard treatment, it is possible that participant will not receive the new treatment being tested. However, the
participant will receive the best standard treatment. On the other hand, if the new treatment is effective, participants in the study will be the first to benefit from it. In training for that clinical research and accession to it, the patient actively participates in decisions that affect his life. This can be personally empowering related to the research process.

The participant can benefit from extra care related to tracking his condition, and has a chance to help others suffering from a disease. Patients and principal investigator have the chance to raise awareness about early detection, diagnosis and screening, supportive treatment and prevention, which can lead to better results in therapy. Screening for inclusion of participants in the study may encourage them to continue to review regularly, which can lead to an overall improvement in their health. New drugs or treatments under study are not always better than or as good as standard. May have unintended side effects and a more enhanced effect when compared with standard drugs or treatments. Although the new drug or treatment may have benefits, it may not be appropriate for each participant, as the standard treatment and may not be effective for all suffering from a given disease.

Participants who fall within the standard treatment as a control, can not take advantage of such benefits as those who receive the new treatment, if it is determined that it is more effective. Last but not least is the commitment of time and by researchers, and by patients.  

**MATERIALS AND METHODS**

It's done a literature search in the database PubMed, Google Scholar, Scopus as the most important publications are discussed in this review. The key word for literature search are clinical trials, benefits, risks, risk-benefit ration, patients’ choice.

**RESULTS**

*Identification and Risk Assessment*

The concept of risk assessment is usually understood as referring to the combination of the probability and size of any future damage. In this view, the risks are considered to be "high" or "low" depending on whether they are likely to occur is higher or lower and that the damages are more or less serious. In research involving human risk is a basic organizing principle, a filter through which must pass the participants, while greater risks will be expected to include a larger or more extensive safeguards designed to reduce the possibility of occurrence of damage into the patient. Authors of the study on the topic noted that it is made relatively little progress in describing the criteria for risk assessment. In large part
this is due to the many difficulties inherent in classifying risk decisions, including difficulties associated with the adoption of risk in general,\textsuperscript{[4,10]} and other aspects such as objectivity, quantity, etc.\textsuperscript{[4,11]}

**Minimum risk and a greater minimum risk**

According to the general rule, the survey presents a minimal risk if "probability and extent of damage or discomfort to the patient in the study were not more themselves than those normally encountered in daily life, or during the execution of a routine physical or psychological examinations or tests."\textsuperscript{[4,12]} Although the concept of minimal risk remains controversial in the academic and scientific circles, it is widely used, according to the authors of the analysis, even though they think the assessment is strictly individual. For example, "typical" minimal risk encountered in daily life or in clinical care side effects or discomfort can be perceived differently by some individuals with certain diseases. It is important, therefore, to establish a practical level evaluation of minimal risk, a fact noted in the design of the clinical trials. This question is particularly affected when making clinical trials with children participants, usually to the design of the study included so-called "additional protection" risk to the patients.

The authors note that similar regulations for children, many research proposals relating to incapacitated adults use the concepts of minimal risk and a minor increase over minimal risk, especially in people with mental disorders in which introduce the concepts in three categories: (1) minimal risk; (2) a minor increase over minimal risk; and (3) greater than minimal risk (which covers risks more than a minor increase over minimal risk). The purpose of this tripartite division is to allow the protocols of studies involving only a minor increase over minimal risk to include only minimal additional protections.\textsuperscript{[4,13]}

**Benefits of conducting clinical trials**

Authors performing research on the topic, identify three types of potential benefits in elderly individuals participating in the clinical trials of medicines: (1) direct medical benefit of subjects; (2) indirect benefit of subjects; and (3) benefit for others. In several publications noted that if the direct benefits consistent definitions, namely, improving the condition of patients, easier and accessible administration of therapy, better social participation, etc., it is in indirect benefits, which speaks for "deviation from the routine, the participants the opportunity to meet with others and to feel useful, or greater access to professional care and support."\textsuperscript{[4,14]}
There is ongoing debate about whether the condition that the subjects receive reimbursement for their time and inconvenience a direct or indirect benefit of participation in research. Benefits of indirect financial incentives are in the strict sense, according to the authors. Principle that financial incentives must not exceed the "recovery" of the time and cost of the subject, so as not to create unnecessary motivation for participation is well established, but not always easy to implement. The problem is complex because healthy volunteers as well as participants with a particular disease may agree to participate in a clinical trial of drugs, because of the financial incentive. Payment must be adequate to justify the commitment of the participants with time and discomfort of carrying out the study itself, but not as much reason for taking unreasonable risks. Similarly, patients with a particular disease who do not have health insurance, may be "tempted" to join the study if it appears that otherwise can not get the provided medical care.

Many researchers distinguish and third category benefits - "other benefit" that concerns families, persons who care for the sick participants and society as a whole, especially in the context of future suffering from a disease. When, however, the study included invasive tests that do not create real possibility of direct benefit to the health of the subject, then this kind of benefit is "the most dramatic form of the conflict between the public interest in the conduct of important and promising research and the interests of potential object." In this case, the authors say that it is necessary risks and potential benefits to be as balanced.

The metaphorical nature of these conditions, according to many, explored the topic, draws attention to the difficulties in making accurate the Solution only in rare cases can apply quantitative methods of evaluation. There is another category of benefits, which the authors define as economic benefits from improved health. Australian researchers note that these benefits have helped Australia become the leading economy of the 21st century. There are a number of evidence to support this. Research conducted in the period between 1992-93 and 2004-05 shows that R & D in Australia has contributed to economic net benefit in the amount of approximately $ 29.5 billions. According to the same study notes that healthier people are more able to participate in the process in society and in the family and community life.

Another way of looking at the economic benefits for Australia is based on studies showing that companies conducting clinical trials of medicines in Australia pay taxes, buy goods on the spot, and that their activities stimulate and engage new jobs.
These benefits are confirmed by the authors studied these processes in other countries, such as Singapore is a regional leader in the field of biotechnology and pharmaceutical sector through the range of activities based on the support of biotechnology. In 2008 gross expenditure on R & D was $ 7.1 billion, equivalent to 2.77% of GDP.

China has increased its support for clinical research of medicines by 30% in recent years, only in the period of 2008-09 increased by a further 8% by 2010.\textsuperscript{5,17} In South Korea the government implements ambitious plans for the research, in 2012 invested 5% of GDP in R & D, including basic and clinical research on the therapeutic.\textsuperscript{5,18} Not least, the authors reported getting better developing this research in Brazil and India. As for the United States, only California in 2012 invested US $ 3.0 billion medical research in regenerative medicine and stem cell biology.\textsuperscript{5,6}

Here it should note that some authors describe the category financing of clinical trials with public funds or state funds, emphasizing some advantages - full disclosure and publicity of results in the conduct of such clinical trials (otherwise researchers lose their financial incentives) This brings an additional benefit for physicians and the scientific community in the implementation of new therapies. Another advantage is that this system of financing fewer resources are likely to be lost in the development of drugs that offer small net medical benefit compared to existing drug therapy already.\textsuperscript{7,19} Researchers will have less motivation to test drugs, especially at an early stage if they are not convinced of their added value. The authors of the analysis believe that publicly funded clinical trials of drugs led to a significant reduction in the number of non-priority research drugs receiving approval from the Medicines Agencies. This can lead to significant savings concerning the various phases of clinical trials.\textsuperscript{7} Moreover, the publicly-funded system is not contrary to studies funded by the pharmaceutical companies themselves. Although drugs covered by publicly funded programs are cheaper than those financed by private companies. However, if a pharmaceutical manufacturer is confident that its drug would offer significant advantages over existing ones, despite the refusal, for example, publicly funded contractors to pay for clinical trials, they will be free to do so with its own resources.

Another potential benefit of a system of clinical trials with public funding is that it eliminates the potential risk of improper payments to physicians for participating in drug trials. (Gardiner, 2004;Eichenwald and Colata, 1999a and Eichenwald and Colata, 1999b).
Authors concluded that a doctor who were paid as researcher in a clinical trial, is more likely to prescribe the company's drugs after his participation in the study.\cite{7,20} This higher propensity can be attributed to the fact that doctors who take part in these studies were more familiar with the company's products, but can be explained by the fact that participation in research is an effective mechanism encouraging doctors to prescribe specific drugs.\cite{7}

By eliminating any connection between the company, which is a manufacturer of a drug, and doctors who take part in research, the system of publicly funded research eliminates this potential for abuse of the process of testing. This should lead to lower costs of clinical trials, as payments should reflect the actual cost of the doctors. This would also eliminate the potential effects of "kickbacks" from pharmaceutical companies to physicians, according to the authors examining this topic.

Another aspect of the system of publicly funded clinical trials is the financing through international aid (eg the United States and other rich economic countries) to require developing countries to provide by state regulatory authorities to prevent generic competition for period exclusive, potentially raising the price of life-saving drugs at several hundred percent over the competitive market price (Hubbard and Lowe, 2004).

**DISCUSSION AND CONCLUSIONS**

Clinical trials of drugs are type of study "used" in human individuals to develop knowledge that can be applied to the benefit of society.\cite{21} Clinical studies are necessary for the progress of medicine, particularly for the discovery of new pharmaceuticals.\cite{22}

Clinical trials of drugs, besides its direct risks and benefits for the individual and indirectly contribute to such families and society as a whole, including impact on many sectors of the economy. This includes other sectors of health, contribution to the state budget and other sectors directly related to the market of clinical trials. In particular it is suitable cash flow to the tax and health systems.\cite{23}

According to the edition of Health consumer index from the middle of 2014 clinical trials would improve the quality standards of the work of doctors, particularly those who are at the beginning of his career, which reflects positively on the entire health system.\cite{23}
REFERENCES


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