

Economic Impact of Clinical Research to Research Centers and Opportunity Cost for the Reimbursement System in Turkey

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Abstract

Introduction: Clinical research is a key component of drug development with a significant economic value. It has been reported that the development of a new molecule requires 10 - 15 years and costs almost \$1.3 billion. Around 75% of the cost is spent on the Phase I-IV clinical research process. This study aimed to show the economic value of clinical research in Turkey. **Methods:** Clinical trial budgets were estimated from the raw data of the Report of Istanbul Medical Faculty Clinical Research (ITFKAR). In the research, the estimated cost of drugs used in the clinical trials for the Turkish reimbursement agency (SGK) was calculated to show the cost of medicines acquired through clinical research. **Results:** The total budget for sponsored pharmaceutical research was \$107 million in Turkey, and the government saved close to \$311,096,130 during 2006-2010, due to not reimbursing the patients for the drugs in the clinical trials. **Conclusion:** Despite the limitations of the study, the findings are unique for Turkey. The results can lead to revisiting the importance and economic value of clinical trials in Turkey.

Keywords

Clinical Research, Economic Impact, Reimbursement, Research Centers, Opportunity Cost

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1. Introduction

Clinical trials are the researches conducted human subjects who are healthy volunteers or patients. Clinical trials investigate the efficacy and safety of drugs, medical devices, diagnostic tools, and treatment techniques used for prevention, diagnosis, treatment, or reducing symptoms in humans. Clinical trials are fundamentally different from clinical practice. In clinical practice, proven and routine treatment is used. However, evidence must be collected in clinical trials for treatment to become routine.

The process of obtaining evidence has been standardized in past years with specific rules. Today, the primary drug-focused process in clinical trials commences with defining a molecule in the laboratory. Pre-clinical studies, in which the toxicity and efficacy of the molecule are monitored, are then performed on the defined molecule.

It has been reported that the development of a new molecule requires 10 - 15 years and costs almost \$1.3 billion, with 75% of the cost is spent on Phase I-IV clinical research [1]. In addition to being among the prerequisites for development of a medicine, clinical trials have a big economic value in themselves.

According to a Research America report, \$136 billion was spent for clinical research in 2011 in the United States (US). Of this figure, \$77.5 billion was spent by the private sector, and the pharmaceutical industry spent the biggest share on clinical research, \$38.5 billion [2]. A study conducted for Poland found that the annual budget for clinical research in Poland was \$258 million [3]. The United Kingdom Medical Investigations Council (UKMIC) provides £250 million support for translational studies [4]. In Australia, \$650 million is spent for clinical research each year [5]. In Turkey, pharmaceutical companies made a \$44 million investment in clinical research in 2012, according to the Association of Research Based Pharmaceutical Companies (AIFD—Arastirmaci İlac Firmaları Dernegi) report [6]. The report also claimed that the future of clinical research will positively affect the population of Turkey, the largest population in the region. The number of Research and Development (R&D) centers will increase in Turkey, and the share of R & D should be increased in the national gross budget to the level of developed countries. It was stated that R & D budget is expected to increase to 3% of the Gross Domestic Product (GDP) in 2023 [6].

There may be an opportunity cost or hidden benefit of clinical research for the reimbursement agencies. The opportunity cost may depend on the treatment cost for patients participating in the clinical trials, which are covered by the sponsor of the clinical trials. For this hypothesis, it could be said that if the patient is included in the clinical trial, the cost of treatment is covered by the sponsor, freeing the resources of the public sector. There is not any published analysis on this estimated opportunity cost in the literature.

The aim of this study was to investigate the economic impact of clinical research to the research centers and the opportunity cost for the reimbursement system in Turkey.

2. Methods

The raw data from files of clinical studies approved by the ethics committee of Istanbul University during 2006-2010 were included in this study. Only clinical studies on adult patients and controls from internal branches were included: internal medicine, neurology, oncology, cardiology, psychiatry, anesthesiology, pneumology, dermatology, rheumatology, and infectious diseases. Pediatric studies were excluded, as there is insufficient regulation of pediatric clinical investigations, which might affect have affected the study results.

2.1. Calculation of the Impact of Clinical Studies on the Budget of Clinical Research Centers

It has been accepted that the whole budget estimated from the reviewed files were spent on the studies. Similarly, it has been accepted that the number of patients was not changed during the studies. Thus, approved budgets can be accepted as drug investment for the approval year. Exchange ratios used were as follows: Euro/US \$, 1.3; US\$/Turkish Lira (TL), 1.6; and Euro/TL, 2.0 for 2008.

2.2. Calculation of the Impact of Clinical Studies on Reimbursement Systems

Among the reviewed files, the top four specialty fields with the highest number of studies were selected. In these fields, the top three studies with the highest number of patients were included in the calculations. If the same molecule was investigated in different studies among the top three, then the study with the different molecule was added to the list. In total, clinical studies of at least three molecules were included in the calculation. Only

direct drug costs were included, and other expenses were excluded. For the calculation of drug costs, discounted reimbursement figures of the Social Security Administration (SGK-Sosyal Güvenlik Kurumu) for licensed products were used. If not licensed and imported via the Turkish Chamber of Pharmacists (TEB—Türk Eczacıları Birliği), the prices of the SGK imported drug list were used. Calculations were performed with the drug prices dated 07/06/2013 and abroad drug prices dated 03/06/2013 [7] [8]. Discount ratios dated 01/03/2013 were used for calculating the discounts for the reimbursement [9]. Average per patient opportunity cost was calculated for each field. To do this, total cost was divided by the total number of patients. Total and per capita savings of the state in clinical drug studies were calculated. Average per capita drug cost savings in clinical studies were multiplied by the number of patients in Turkey; thus, estimated drug cost savings for the SGK from the clinical studies was calculated. When we transform costs in TL to US dollars, the exchange ratio was taken as US\$/TL, 1.95. The obtained figures were translated to 2008 figures by using a 3% annual discount rate, to compare to clinical research budgets at the median year 2008 [10].

3. Results

During 2006-2010, 937 non-drug and 209 drug study applications were submitted by the Istanbul Faculty of Medicine to the Istanbul University Ethical Committee. Of the drug studies, 174 were industry-sponsored, and 23 were academic in nature. Industry-sponsored drug research mostly originates in internal medicine and oncology departments (**Figure 1**).

Due to legal regulations, the Istanbul University Committee of Ethics was the most active ethical committee during that period. Therefore, it is stated in the Istanbul University Clinical Research Report that the applications during that time may represent most of the Turkey-wide industry-sponsored research [11]. According to this hypothesis, industry-sponsored drug clinical studies planned to include 14,370 patients during 2006-2010. Of these patients, 1294 were planned to participate to clinical studies in the Istanbul Faculty of Medicine. In light of these data, it can be determined that the Istanbul Faculty of Medicine provided 9% of the patients who planned to participate in clinical studies throughout Turkey. Industry-sponsored drug studies showed a tendency to increase until 2009, and then they dramatically reduced in 2009. A potential explanation may be the uncertainty resulting from legal issues (**Figure 2**).

Based on data from the Istanbul University Committee of Ethics, most of the clinical research patients came from neurology departments during 2006-2010 in Turkey. Considering the Istanbul Faculty of Medicine, most of the patients came from internal medicine and cardiology departments. Istanbul Faculty of Medicine provided clinical research patients to industry-sponsored studies, mostly from the oncology department.

It has been found that the average duration of industry-sponsored drug studies was 587 days. The longest study

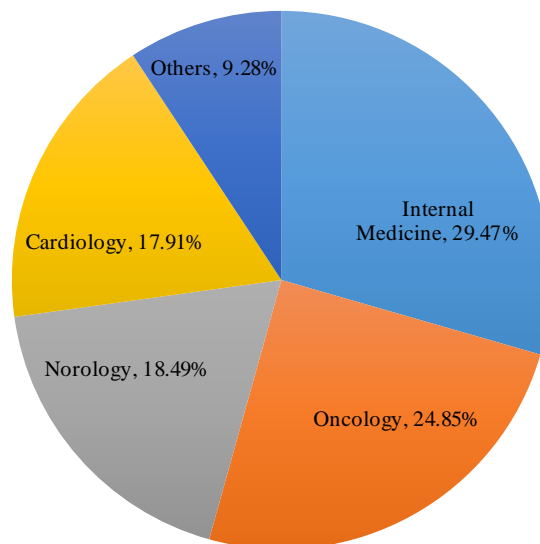


Figure 1. Distribution of all drug researches based on clinics. Cardiology, 17.91%; neurology, 18.49%; oncology, 24.85%; internal medicine, 29.47%; other, 9.28%.

period was 1296 days in a dermatology study, whereas the shortest study period was 455 days in an anesthesiology study. During 2007-2010, annual reports of the Istanbul Faculty of Medicine confirm that the mean number of patients per 100,000 patients included in industry-sponsored drug research was 3.94 [12] [13]. In Turkey, this figure (Figure 3) may be 1.23 as calculated from study data and the number of patients obtained from the Ministry of Health. [14]

3.1. General Budgets of Clinical Research and Economic Impact to Research Centers

According to this study, during 2006-2010, the total budget of industry-sponsored drug research in Turkey was \$107 million. This figure is in accordance with the 2023 Report of Drug Future published by AIFD [6]. For the same years, drug consumption in Turkey was \$44 billion, based on IMS Health Corporation (IMS) data that suggests that only 0.2% of the total drug sector budget was allocated to drug research in Turkey (Figure 4).

During 2006-2010, when the mean budgets of industry-sponsored drug research in Turkey are taken into consideration, neurology studies had the largest budget with \$72.555.994. In addition, there was a clear difference with respect to other specialties. The mean budgets of industry-sponsored drug research in the Istanbul Faculty of Medicine was \$9.735.323.

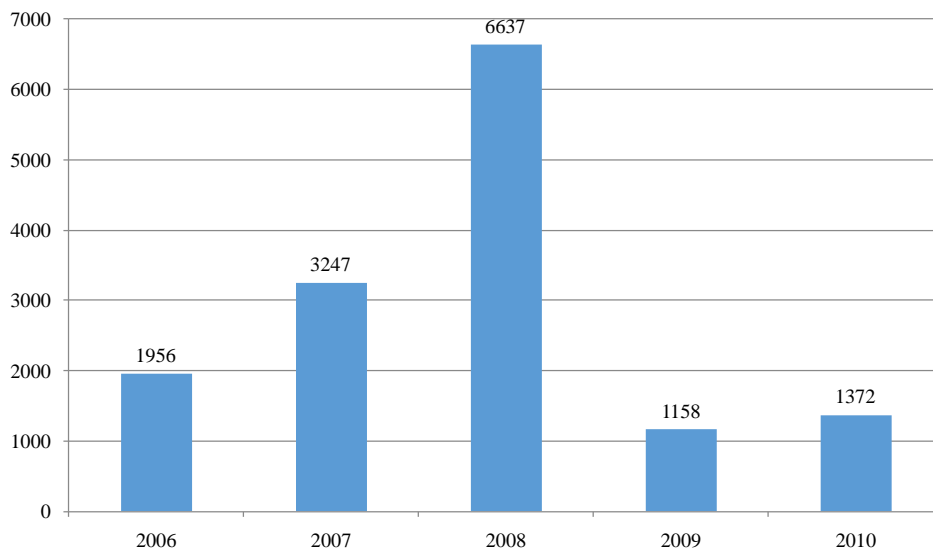


Figure 2. Patient numbers included clinical trials per year in Turkey.

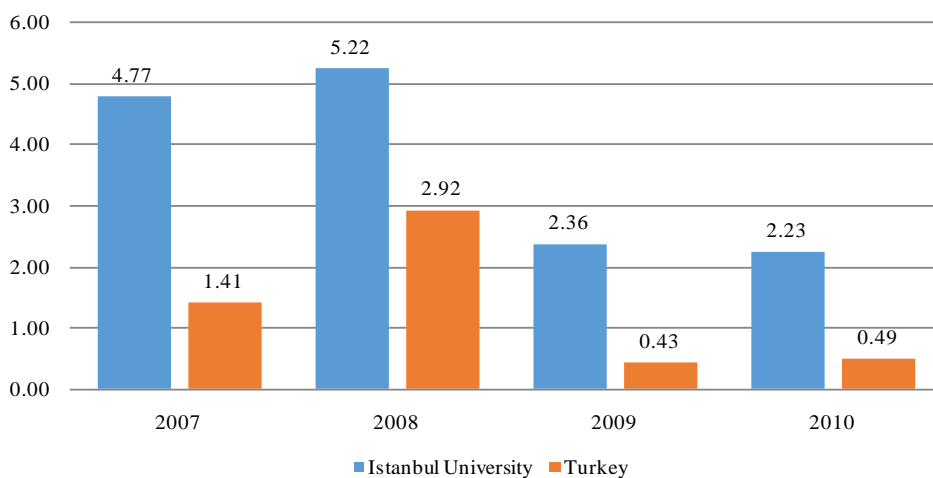


Figure 3. The numbers of patients per 100,000 patients included in industry-sponsored drug research in Istanbul University & Turkey.

During 2006-2010, when the mean budgets of industry-sponsored drug research in the Istanbul Faculty of Medicine was reviewed in study phase groups, Phase III studies had the largest budget (Figure 5). However, when the mean budget per study is taken into consideration, Phase II studies had larger mean budget. Similarly, the largest average budget per patient occurred in Phase II studies (Figure 6).

3.2. The Opportunity Cost of Clinical Research for Reimbursement Systems

Treatment of a patient participating in a clinical trial is covered by the sponsors; thus, the SGK, the reimbursement agency, provides savings. We estimated this opportunity cost, which depends on the drug cost savings.

It was observed that the four most-studied fields were oncology, neurology, internal medicine, and cardiology. It has been found that the biggest share belong to oncology clinics, in terms of SGK drug opportunity cost. The total number of patients in the largest three studies was 252.

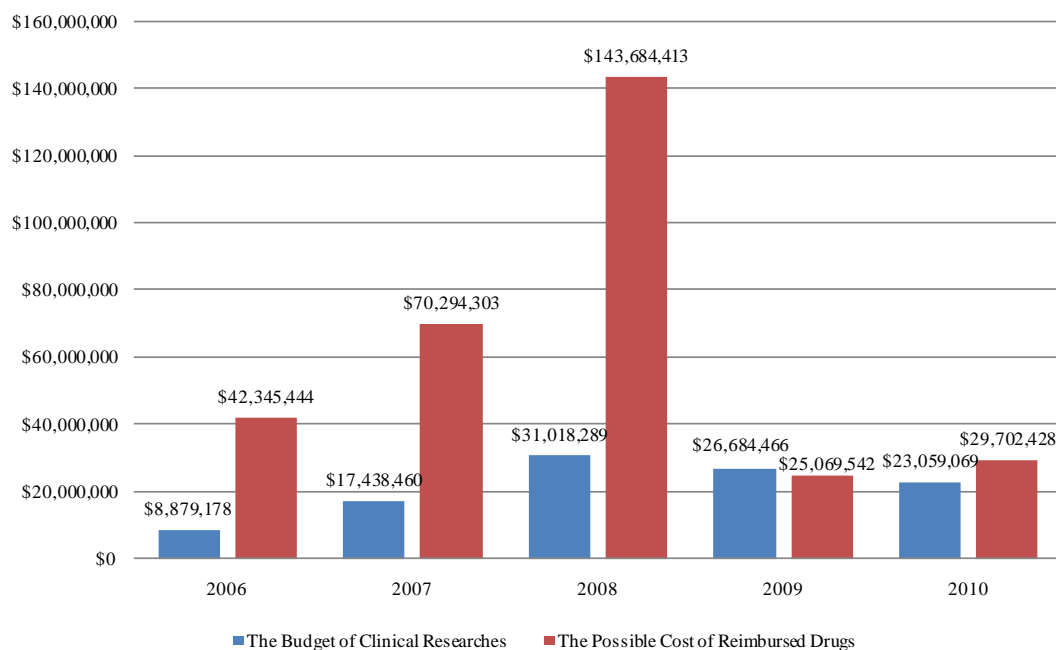


Figure 4. Total annual budgets of industry-sponsored drug researches in Turkey according to submissions to İstanbul Faculty of Medicine Ethics Committee and comparison of possible cost savings from SGK perspective.

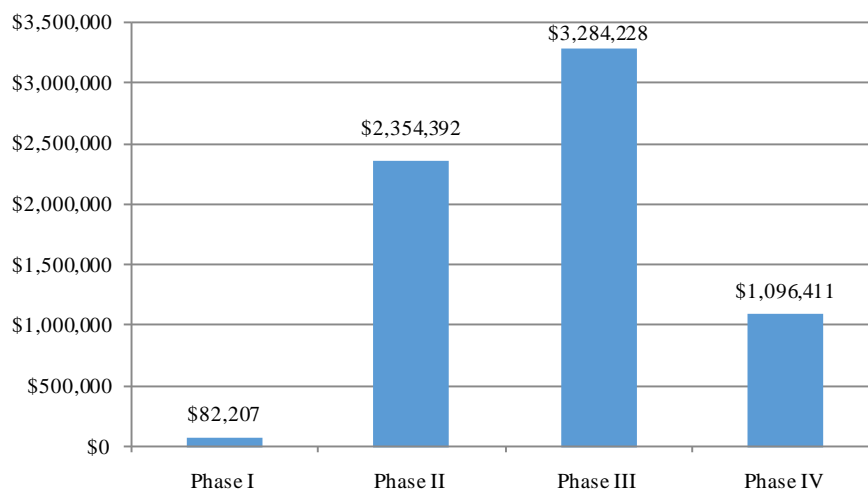


Figure 5. The mean budgets of industry-sponsored drug research in study phase groups.

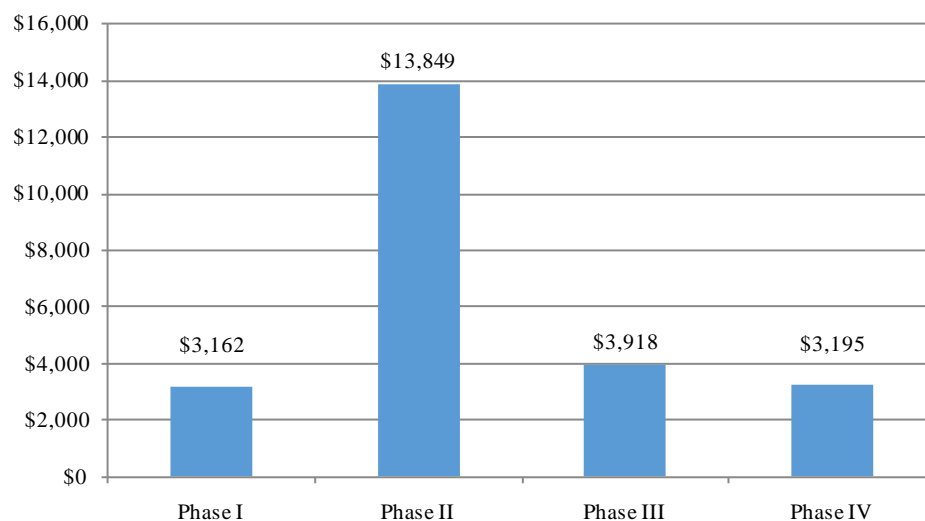


Figure 6. The mean budget per study in study phase groups.

In these oncology studies during 2006-2010, estimated SGK drug savings per patient was found to be \$44,784. When the total SGK opportunity cost from these three studies were calculated, total opportunity cost in oncology during 2006-2010 was \$11,285,652. Total estimated opportunity cost per study was \$3,761,884.

Studies conducted in neurology clinics had the second largest share of SGK drug opportunity cost. The total number of patients in the largest three studies was 984. In these neurology studies, during 2006-2010, estimated SGK unit drug savings per patient was found to be \$10.274. When the total SGK opportunity cost from these three studies were calculated, total opportunity cost in neurology during 2006-2010 was \$10,110,181. Total estimated opportunity cost per study was \$3,370,060.

Studies conducted in internal medicine clinics had the third largest share in SGK drug cost opportunity cost. The total number of patients in the largest three studies was 583. In these internal medicine studies, during 2006-2010, estimated SGK unit drug opportunity cost per patient was found to be €2,772. When the total SGK savings from these three studies were calculated, total opportunity cost in internal medicine during 2006-2010 was \$1,616,396. Total estimated opportunity cost per study was \$538,798.

Studies conducted in cardiology clinics had the fourth largest share in SGK drug opportunity cost. The total number of patients in the largest three studies was 940. In these cardiology studies, during 2006-2010, estimated SGK unit drug opportunity cost per patient was found to be \$702,810. When the total SGK opportunity cost from these three studies were calculated, total savings in cardiology during 2006-2010 was \$660,642. Total estimated opportunity cost per study in cardiology was \$220,214.

From oncology, neurology, internal medicine, and cardiology, a total of 18 studies and 2759 patients were included in this analysis. This figure (Figure 7) constitutes 19% of 14,370 patients included in clinical research during 2006-2010. In conclusion, based on the four clinics and the three studies with the highest number of patients, there was an estimated average SGK opportunity cost of \$25,211 per patient (Table 1).

When these figures are translated to 2008, it can be said that participation of one patient in a clinical study results in \$21,649 SGK opportunity cost. When the opportunity cost per patient in 2008 and the total of 14,370 patients who participated in clinical studies during 2006-2010 were considered, SGK opportunity cost may be \$311,096,130 during 2006-2010 from clinical researches.

The difference between direct drug opportunity cost and clinical research budgets reduced in the years 2009 and 2010. However, a \$107,079,461 total budget for clinical research during 2006-2010 and \$311,096,130 direct drug cost were calculated in our study (Figure 8 and Figure 9). Considering per patient or mean general budget, savings to the reimbursement system may be 4.4 or 2.9-fold of the clinical research investments. This shows the importance of clinical studies and their effect on a reimbursement system are far beyond the amount of direct budgets.

In addition, both direct investments in clinical research and SGK reimbursement savings show that clinical studies made a \$418,175,591 contribution to the Turkish economy during 2006-2010.

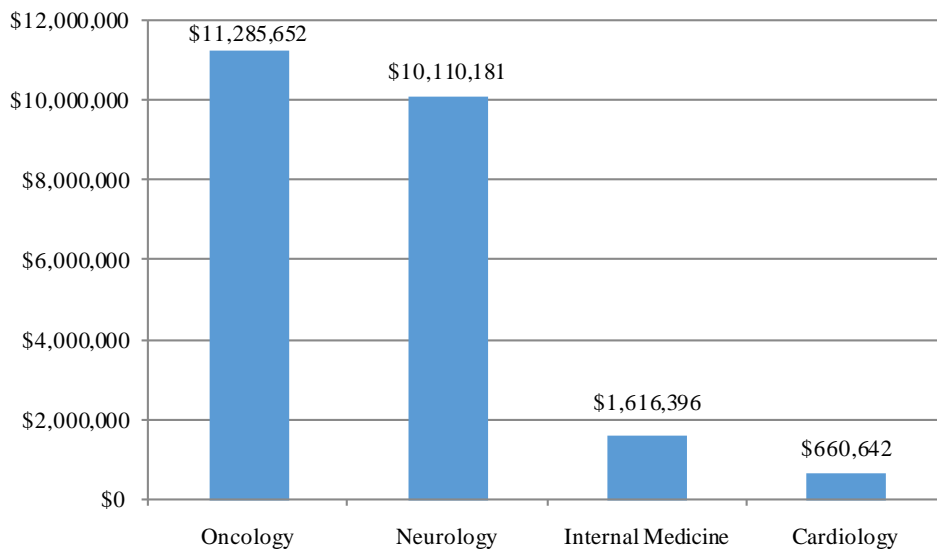


Figure 7. Total opportunity cost of social security institution in Istanbul university clinics from 2006 to 2010.

Table 1. Average social security institution drug opportunity-cost per patient included clinical trials.

Research clinics	2013 year US\$	2008 year (discounted) US\$
Oncology	147.847	126.961
Neurology	17.228	14.794
Internal Medicine	12.137	10.422
Cardiology	2901	2491
Mean	25.211	21.649

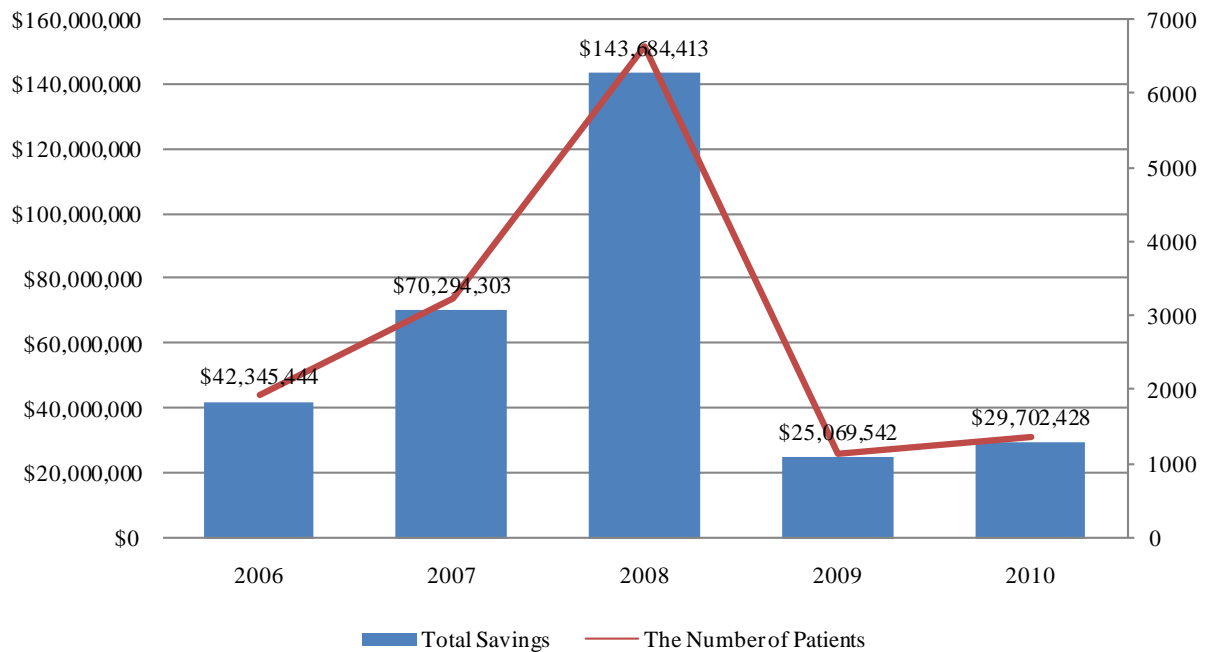


Figure 8. Drug opportunity cost and predicted number of patients from Social Security Institution perspective in industry-sponsored clinical trials in Turkey.

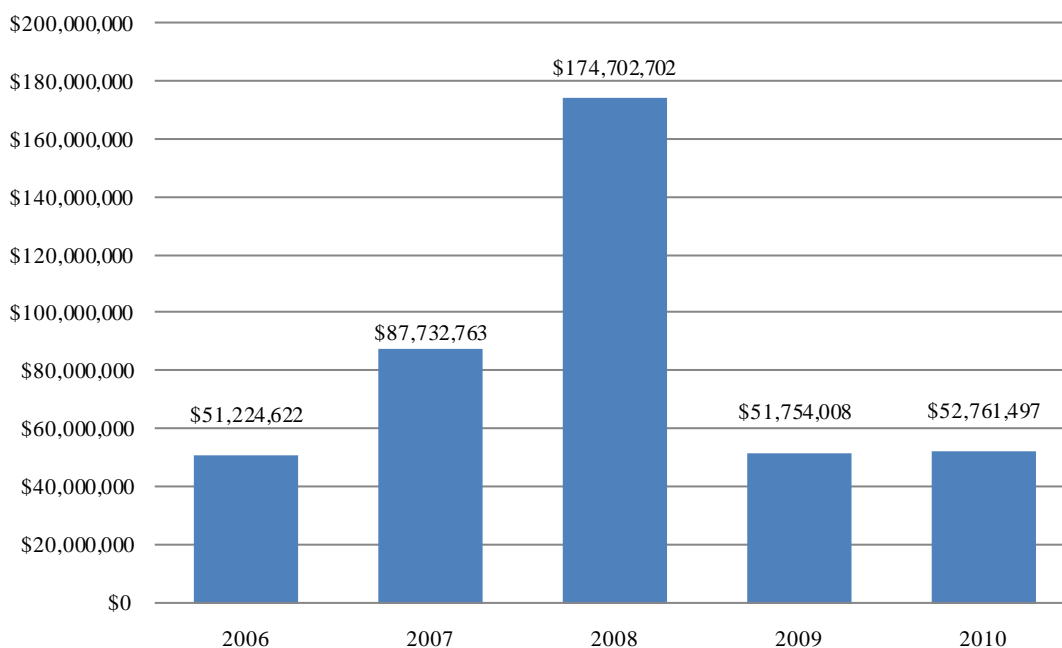


Figure 9. Economic contribution of industry-sponsored drug researches in Turkey.

4. Discussion

The analysis provided important data on industry-sponsored drug research. It has been considered that the data obtained from the Istanbul Faculty of Medicine Ethics Committee records may represent Turkish data, as the Committee received most of the submissions during 2006-2010, when it was one of the only active working committees due to legal regulations during those years [11].

According to this study, during 2006-2010, the total budget of industry-sponsored drug research was \$107 million. This figure is in accordance with the 2023 Report of Drug Future published by AIFD. For the same years, drug consumption in Turkey was \$44 billion based on IMS data, which suggests that only 0.2% of the total drug sector budget was allocated to drug research in Turkey. Besides the economic value of industry-sponsored clinical studies in terms of direct investment, another opportunity cost or savings comes from the payments of the cost of patient treatments by clinical research budgets rather than the SGK. For instance, the total budget of industry-sponsored drug research in Turkey was \$107 million. If those patients had been covered by SGK, the drug costs would be \$311,096,130. However, the SGK avoided this drug cost, as 14,370 patients participated in clinical studies covered by research budgets during 2006-2010. The average of the four highest research branches (oncology, internal medicine, cardiology, and neurology) resulted in \$21,649 drug cost savings per patient with participation in the clinical research in 2008. On the other hand, per patient clinical research investment during 2006-2010 was calculated as \$4,879. From a per-patient or general budget perspective, savings from the reimbursement system was 4.4 or 2.9 fold of direct clinical research investments. From this point of view, a benefit of clinical research comes from the estimated savings from the reimbursement system rather than investments. Thus, health authorities should take into account the reimbursement effect when planning incentives for increasing clinical research budgets.

In 2010, \$127 billion were spent for global drug R & D. Annual R & D investment of the drug sector in Turkey remains at a level of \$60 million and takes only a 0.039% share of global investments. Around the world, the ratio of drug R & D costs to national gross product in some countries varies from 0.53% to 0.03%. In Turkey, the ratio of drug R & D costs to national gross product is around 0.007%, which is quite low. On the other hand, in terms of drug expenses and drug clinical research investments, 2% of drug expenses is covered by clinical studies in Poland, whereas it is only 0.25% in Turkey [11]. If 1% of drug expenses was covered by clinical research, this would bring a \$160 million investment in Turkey in addition to an estimated \$704 million alternative savings from drug reimbursements.

In order to develop technology and/or new products in the pharmaceutical sector, the sector should be priori-

tized for R & D, such as in drug manufacturing. If Turkey develops the R & D area to a significant level, then the Turkish pharmaceutical sector may draw additional R & D investments [6].

Development of hospital infrastructure is important for the expansion of clinical investigations. Considering the shift of R & D studies to developing and important markets such as Turkey, necessary steps should be taken not to miss this opportunity in Turkey. To do this, in addition to governmental support, the number of researchers and research centers should be increased. Based on our findings, clinical research per hospital bed and per specialist physician are quite low. The number of participating patients is also lower than it should be.

Our study has several limitations. Approved studies were accepted as unchanged during the study period. When we calculate the annual number of patients or budgets, we took into consideration the submission date rather than completion or finalization of studies. In addition, only one rate of exchange was used for the period 2006-2010.

As the budgets were calculated in US dollars, and inflation rates were low for dollars, the effect of this assumption can be accepted as minimal. In the cost calculations, 2013 prices were used, and those figures were translated to 2008 prices by 3% annual reduction rate in the American dollar exchange rate. In this study, we included four specialty fields with the highest number of participating patients in 18 clinical investigations. The average drug costs of these studies were extrapolated to a general mean value. These 18 studies constituted 19% of all participants during 2006-2010. Thus, the data can be accepted as representative of the entire population of clinical studies.

In the economic dimensions of clinical research, this study generated initial data for Turkey. Obtained clinical research investment figures are in accordance with figures published by the sector. Therefore, despite the hypothetical nature of these data, they are important, as some part is parallel to sector publications, and there is a lack of data for some other parts.

Turkey has a unique position and critical potential for clinical research investments. An increasing population, relatively higher portion of unanticipated patients or healthy volunteers, candidate centers for clinical studies, and the number of educated staff stress the high potential for clinical research in the midterm and long-term. Our study showed that through public initiatives that may increase the number of clinical studies, benefits in many areas can be realized in Turkey. According to a published questionnaire, 69.5% of respondents stated that clinical research budgets could be reduced, due to a reduction in drug prices [15].

5. Conclusion

From this point of view, public decision-makers may provide an increase in the number of clinical studies through several regulations on pricing and reimbursement. Similarly, when planning clinical research of innovative products, besides adding Turkish centers into study centers, incentive regulations on licensing, pricing, or reimbursement may lead to a significant increase in clinical studies in Turkey. In this context, our study may be a good reference for health authorities.

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Note

All costs in this paper are specified in U.S. dollars, except where specified otherwise.

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