

## Original Article

## Clinical Research Infrastructure in Turkey: a Pilot Strengths, Weaknesses, Opportunities, Threats Analysis

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### Abstract

**Objective:** The purpose of the study was to evaluate the infrastructure facilities of clinical trial units in Turkey to create descriptive information and perform a pilot strengths, weaknesses, opportunities, and threats (SWOT) analysis that describes the strengths to match them with the opportunities and aims to reduce weaknesses and threats.

**Methods:** This study was conducted using the data provided by nine clinical trial units within the scope of a collaboration agreement signed with Turkish Clinical Research Infrastructure Network between April 2013 and December 2016, using a survey created and applied with Google Forms application. Descriptive statistics was used to summarize infrastructure and capacity questions. Mean and median were calculated to interpret the current data. A pilot SWOT analysis was performed to evaluate the clinical research environment in Turkey.

**Results:** The number of clinical trials conducted varied over a wide range among the units. Most trials were conducted in the area of pediatrics, with the least number of trials being conducted in the area of endocrinology. Most units conducted national single-center trials with public funds. Physicians were mostly involved in clinical trials, and the number of nonprofessional healthcare personnel was limited. Application to the Ethics Committees and MoH was the most provided service among clinical trials units, where monitoring was the least provided service. None of the units had quality certification. A wide range of evaluations and suggestions concerning the clinical trial environment in Turkey was provided in this pilot SWOT analysis.

**Conclusion:** As these weaknesses and threats with the data, provided by the units, are consistent with the concerns expressed by the national policy makers, suggestions expressed in the survey to improve the clinical research capacity and environment in Turkey should be considered for future actions.

**Keywords:** Clinical trial unit, clinical research infrastructure, SWOT analysis

### INTRODUCTION

The number of clinical trials conducted in Turkey is increasing. From 2011 to 2016, the total number of clinical trials increased by almost 2.3 fold, from 978 to 2233. In addition, Turkey's rank increased from 36<sup>th</sup> to 31<sup>st</sup> on the global scale for the total number of clinical trials conducted per country (1). While regulations, human resources, and infrastructures of Turkey are considered promising for further development of clinical research, this development potential has not been realized as expected (2). The current status and weaknesses have been expressed by several government agencies and nongovernmental organizations, as summarized below:

- The lack of applied or clinical research capacity in universities (3).
- The lack of academic activities of the faculty, such as designing projects in cooperation with the industry, patenting, and providing commercialization services (3-5).
- Insufficient infrastructure to design and conduct multidisciplinary projects in universities (3, 5).
- Inefficient working of the Technology Transfer Offices (3-6).
- The lack of partnership among public sector, industry, and universities regarding Research and Development (R&D) activities and production (3-5).
- The frequent legislative changes without transition periods (3, 4).

- The absence of capacity to produce revenue from patent rights to improve the global competitiveness of Turkey (3, 4).
- The lack of specialty trainings and recruitments to ensure a qualified labor force (3-5).
- Allocation of limited financial resources for R&D activities and lack of R&D quality owing to inefficiency (3-5).
- The lack of clinical trial units in Turkey (2, 3).
- Negative approach of the public to participate in clinical trials (3, 4).
- Need for transparency in the application and assessment processes of the ethics committees and regulatory authority (2).
- The absence of standards for clinical trial site agreements and approval processes (2).
- The need for nonindustrial sponsors (2).
- The absence of regulation for rare diseases and orphan drugs (2).
- Inefficient and outdated scope of training programs for clinical trials (2).
- The lack of data infrastructure for clinical research coordination (6).
- The lack of incubation and innovation units for medical device development (7).
- The need for a legal framework for intellectual property rights (5, 7).
- Insufficient capacity of accredited analysis and testing laboratory services (5, 7).
- The absence of national biobanks and related legal framework (5).

To overcome the above mentioned weaknesses and problems, clinical research experience, capacity, and proposals of units, which play a direct role in clinical trials, are important (8). A clinical trials unit is defined as "an entity composed of an administrative component and one or more clinical research sites that contribute to a network by conducting clinical trials" (9).

In this study, a pilot survey among clinical trial units, which signed the collaboration agreement with Turkish Clinical Research Infrastructure Network (TUCRIN), was implemented to evaluate the current clinical research capacity and environment in Turkey with respect to clinical trials units.

## METHODS

Ethics committee approval was granted by Dokuz Eylul University Ethics Committee for Non-Interventional Studies (2015/17-32, July 9, 2015). This study was conducted with data that were voluntarily provided by nine clinical trial units within the scope of the collaboration agreement signed with TUCRIN between April 2013 and December 2016 (Table I). The data were provided via a survey with primary objectives of (a) setting partnerships in multinational clinical trials and (b) improving the national clinical research environment according to the objectives of TUCRIN (10).

The survey was designed to obtain descriptive information regarding clinical trial units and a strengths, weaknesses, opportunities, and threats (SWOT) analysis of clinical research in Turkey. Open-ended, closed-ended, and multiple choice questions were used. These questions covered the topics of the number of clinical trials, characteristic of volunteers, research areas and types, types of sponsors, research staff, services provided by units, quality management system, and a SWOT analysis sec-

**Table I. Clinical trial units that have a signed collaboration agreement with Turkish Clinical Research Infrastructure Network**

Erciyes University Center for Good Clinical Practice
Gaziantep University Center for Good Clinical Practice
Istanbul University School of Medicine, Department of Pharmacology, Drug Research Unit
Ankara University School of Medicine, Department of Internal Medicine, Division of Hematology
Hacettepe Technopolis Technology Transfer Center
Dumlupinar University
Kocaeli University, Clinical and Experimental Research Center
İzmir Katip Celebi University Health Research and Practice Center
Ankara University School of Medicine, Department of Histology and Embryology

**Table 2. The top five study types that were conducted by CTUs (n=9)**

Type of Studies	Frequency (%)
<b>Interventional studies</b>	
Phase IV studies	4 (44.4)
Vaccine studies	4 (44.4)
Phase II studies	3 (33.3)
Phase III studies	3 (33.3)
Bioavailability and bioequivalence studies	2 (22.2)
<b>Observational studies</b>	
Drug studies	3 (33.3)
Genetics studies	3 (33.3)
Epidemiological studies	3 (33.3)
Medical device studies	2 (22.2)
Cell transplantation studies	2 (22.6)

CTU: clinical trial unit

tion. A survey covering these questions was created with online Google Forms application in Turkish. The online survey invitation was sent to the unit representatives with an email link after a brief telephone interview. The survey is currently available online on the TUCRIN website (<http://tucrin.deu.edu.tr>) with open access for further collaborations (<https://goo.gl/UFD0hZ>).

Descriptive statistics was used to summarize infrastructure and capacity questions. Mean and median (min-max), as measures of central tendency, was calculated to interpret current data. Data, including research areas, services provided by units, and research types, were expressed as frequencies and percentages. Google Docs application was used for data analysis. SWOT analysis data were interpreted by two investigators for relevance and were summarized as a narrative list. According to the privacy policy of the survey declared and bilaterally agreed, the collected data from clinical trial units were pooled and anonymously presented.

## RESULTS

The median number of clinical trials conducted per unit in the previous year was 12 (2-60), whereas the median number of currently ongoing clinical trials was 10 (1-59). Research participants of the units included both healthy volunteers and patients. Most

clinical trials conducted focused on five main areas, including pediatrics, genetics and molecular biology, neurology and psychiatry, cardiology, and oncology and hematology, whereas no unit was involved in clinical trials for rare diseases.

**Table 3. The personnel involved in clinical trials**

	Median (Min–Max)
Principle investigator	10 (3–30)
Physician	4 (1–9)
Technical and support staff	2 (0–12)
Study nurse	2 (0–11)
Pharmacist	0 (0–5)
Statistician	0 (0–2)
Monitor	0 (0–15)

**Table 4. The top five services provided by clinical trial units (n=9)**

Services	Frequency (%)
Application to Ethics Committees and Ministry of Health	7 (77.8)
Data analysis	7 (77.8)
Clinical research design and preparation of protocol	6 (66.7)
Biological sample storage	6 (66.7)
Notification of adverse action and Pharmacovigilance	6 (66.7)

**Table 5. Strengths and weaknesses of current clinical research environment in Turkey and suggested actions for weaknesses**

Strengths	Weaknesses	Suggested Actions
1. Promoting the clinical trials by several funding programs (n=2)	1. The lack of dissemination of phase I and phase II studies	1. Dissemination of centers that might conduct study on phase I and phase II trials
2. Regulatory framework that is compatible with the European Union standards (n=4)	2. Insufficiency in consideration of clinical trials as an R&D activity	2. Planning a meeting with Ministry of Science, Industry and Technology and defining the frontiers
3. The high-potential healthy volunteers and patients (n=6)	3. Unstable regulatory environment	3. Providing a legal framework that is sustainable, accessible and transparent
4. The presence of qualified investigators (n=5)	4. Uncertainty in financial issues	4. The independent research budget managed by the investigator
	5. The lack of researcher motivation	5. Training of investigators whose primary goal is research
	6. The negative approach and insufficient knowledge of public (n=3)	6. Improving the communication with media and civil society organizations and engaging the public to research as a partner
	7. The lack of qualified research personnel	7. Creating the job description by Ministry of Health for research staff
	8. The lack of analytical centers	8. Establishing new analytical centers
	9. Insufficient number of qualified investigators	9. Optimizing the training frequency of investigators and providing sustainability
	10. The lack of ethics committee members specialized in clinical research	10. Academicians experienced in clinical research to be included in Ethics Committees
	II. Bureaucratic delays	
	12. Delays related to Ethics Committee procedures	
	13. Cutbacks in reimbursement	

R&D: Research and Development

Interventional and observational studies were conducted by the units, with the predominance of Phase IV and vaccine studies (Table 2). Of note, one unit also had experience with biosimilars studies. When the dissemination of clinical trials was assessed, 77.8% of units conducted national single-center trials, whereas 55.6% of units conducted multinational trials and national multicenter trials. Furthermore, 55.6% of units received industry funds for clinical trials, whereas 88.9% of units received public funds.

While principle investigators and physicians are the most encountered personnel involved in clinical trials, a limited number of study nurses, pharmacists, and technical staff participate in the study teams (Table 3).

The five most common services provided by clinical trial units are applications to the Ethics Committees and Ministry of Health, data analysis, clinical research design/preparation of protocol, biological sample storage, and adverse event reporting (Table 4).

Six units have implemented a quality management system, and five of these units have a quality management representative; nevertheless, none of the clinical trial units have a quality management system certificate.

**Table 6. Opportunities and threats of current clinical research environment in Turkey and suggested actions against threats**

Opportunities	Threats	Suggested Actions
1. Becoming a credible country at bioavailability and bioequivalence studies	1. The research process that takes a long time	1. Developing the expedited processes and integrating the online systems
2. A shift in tendency for clinical research from USA and Central Europe to Eastern Europe and Middle East	2. Increasing the competition due to global trends in the conduct of clinical trials	2. Providing the visibility and lobby strategies
3. Globalization and economic growth tendency of Turkey	3. Passing of the leadership to contract research organizations in the conduct of clinical trials	3. Undertaking of the leadership by investigator and investigator organizations
4. Conducting translational research	4. Success criteria such as commercial-based rapidity, result-orientation, and efficiency	4. Internalizing the universal values such as benefit for society and environment
5. Developing standards coordinated with the European Union adaptation process	5. Limited knowledge level about clinical trials	5. Increasing the participation in trainings
6. International collaboration possibilities among stakeholders (n=2)	6. Having studies of domestic pharmaceutical industry conducted in India	
7. R&D policy of the state (n=2)	7. Economic and administrative uncertainty in organizations	
8. The possibility of providing foreign currency inflow due to increase in analytical centers in Turkey		
9. Increasing tendency to the countries that provide reliable data (n=2)		
10. Increasing awareness about the importance of research (n=2)		
II. Less medical costs than USA and Western Europe		

R&D: Research and Development

According to the results of the SWOT analysis, most encountered "strengths" are reported as regulatory framework that is compatible with the European Union standards, high-potential healthy volunteers and patients, and presence of qualified investigators (Table 5). Other labeled "strengths," "weaknesses," "opportunities," and "threats" with suggested future actions that were matched with weaknesses and threats are also shown in Tables 5 and 6.

## DISCUSSION

The number of clinical trials conducted varied over a wide range of clinical trial units. Most clinical trial units have conducted national single-center trials, with most receiving public funds. It was also revealed that physicians were mostly involved in clinical trials, and the number of non-professional healthcare personnel was limited. Application to the Ethics Committees and Ministry of Health was the most provided service among clinical trials units. None of the clinical trial units had a quality management system certificate.

While the expertise of the units covered a wide range of disease areas, none of the clinical trial units had any experience with rare disease research. Rare diseases are of importance for public health and there is an ongoing need for national networks to support research on rare diseases

in Turkey (II). In this case, TUCRIN should involve units with rare disease experience for a better national representative.

Most clinical trials services were provided by the majority of units, whereas monitoring service was provided by only one unit, and the median number of monitors employed in the units is zero. The reason for this could be that study monitors are employed by sponsors and contract research organizations. Increasing number of clinical trials requires qualified research personnel performing monitoring activities. Government agencies and nongovernmental organizations could have an important role in organizing training programs for clinical monitoring in academic units (2). TUCRIN may also lead training efforts through university-industry partnership.

The evaluation of personnel involved in clinical trials also showed that there is a need for nonphysician personnel in the units. It is a remarkable point that the median number of statisticians employed in clinical trials units is zero. Statistics is considered to be a valuable contribution to research in optimizing the design, analysis and interpretation of results, and drawing conclusion. Clinical trial units should be supported by a department of biostatistics, or similar departments in their institutions (12). There should be a recommendation to prepare a job de-

scription for a statistician in the scope of research proposal and to include the salary of a statistician in grant proposals.

Most units have a quality management representative and their own quality documentation. However, none of them has a certificate for their quality management system. The units are aware of the need to have a quality system during the stages of clinical trials (13). ISO 9001 certification is applicable to all services provided by the units. The scope of the certification could include "The planning and management of clinical trials." This certification enables the units to obtain external recognition. Other benefits obtained by units could include improved image and service quality (14).

Similarities were found between the current status of clinical research infrastructure in Turkey and the identified weaknesses and threats of the current clinical research environment (Tables 5 and 6). The negative approach of the public to participate in clinical trials was a common answer as a weakness that is parallel with the current status of the clinical research infrastructure of Turkey. The lack of clinical research capacity, unstable regulatory environment, financial issues, inefficient training programs for clinical trials, insufficient research units, and lack of qualified research personnel were other similar points between the current status of clinical research infrastructure in Turkey and Tables 5 and 6. Furthermore, several funding programs for clinical trials, regulatory framework that is compatible with the European Union standards, and presence of qualified investigators are identified as strengths that show an inner inconsistency with the weaknesses of the current clinical research environment.

### Study Limitations

The data obtained from nine clinical trial units represents the scope of collaborations of TUCRIN, limiting the generalization of the study results to the whole clinical research infrastructure in Turkey. This limitation suggests the need for the evaluation of the clinical research capacity and environment in Turkey out of the TUCRIN scope.

In conclusion, as these weaknesses and threats with the data provided by the units are consistent with the concerns expressed by the national policy makers, suggestions expressed in the survey to improve the clinical research capacity and environment in Turkey should be considered for future actions. Continuous monitoring of the state of clinical research units in Turkey would also prove beneficial to identify ongoing needs. Stakeholders and policy makers participating in clinical research should continue to implement actions to strengthen the national clinical research infrastructure in Turkey.

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**Informed Consent:** N/A.

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