Productivity of Clinical Trials Conducted at the Gulf Cooperative Council

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Abstract

Objectives: Clinical trial productivity has not been investigated in the Gulf Cooperation Council (GCC) region, including Oman, Saudi Arabia, United Arab Emirates (UAE), Qatar, Bahrain, and Kuwait. We aim to assess the productivity of clinical trials conducted in the GCC region. Specifically, we aim to estimate the number of clinical trials conducted and estimate the proportion of clinical trials conducted in the GCC countries published in peer-reviewed journals.

Methods: The clinical trials registry of the U.S. National Library of Medicine (NLM) was searched for clinical trials conducted from January 2000 to October 2019. The productivity was assessed by the publication status of the trials in the registry and through the search in Medline indexed journals. Results: A total of 682 trials were found from the GCC region, with an overall trend of 4.1 trials each year. However, the clinical trial productivity from our area contributes to only 0.37% of the trials globally. When comparing the raw data, Saudi Arabia shows the highest proportion by contributing 66.6% of the clinical trials from the region (p < 0.001). Oman contributed 3.5%. After normalization to population, Qatar shows to be the highest with 42.78 trials per million. A total of 238 trials were conducted before 2016, of which 46.6% were published. Conclusion: Saudi Arabia is the leading country in clinical trial productivity in the
GCC region. Countries should utilize the triple helix model to a partnership with industry and improve their contribution to science.

**Keywords:** Productivity; Clinical Trials; Publication; Oman; Gulf Cooperative Council.

**Advances in knowledge:**
- This is bibliometric analysis research that focuses on the productivity of clinical trials conducted in the Gulf Cooperative Council (GCC) countries and compares them and the possible reasons behind the fluctuation in their productivity.

**Application to patient care:**
- Clinical trials are essential for patient care. This study will help researchers and policymakers to have a proper future planning and conduction of clinical trials in GCC countries, especially Oman.

**Introduction**

Clinical trials are extremely crucial in delivering the best health care system. Their main goal is to assess the impact of interventions and measure the effectiveness and safety to ensure better healthcare.¹

The contribution to clinical trials from GCC countries has not been well studied. This information is needed for proper future planning of research funding. A small number of studies have been conducted addressing this question. A study was conducted to estimate the clinical trials in behavioral sciences in the Arab Gulf States from 2010 to 2018. The leading country that contributes the most to this area in GCC countries is Saudi Arabia. Moreover, there were only 16 trials conducted during the study period, which is considered low compared to the geographical location that includes over 93 million people.² Most of the studies have shown that Saudi Arabia is the major contributor of research output in the Arabian Gulf Region.³⁴⁵⁶⁷ When the publication is normalized for population size, Kuwait shows the highest research output and Qatar was the second.³⁶ Oman shows a significant increase in the publication productivity from 1990 to 2005. Still, no information is available after this period.³
Overall, the research outcome from the gulf region is increasing throughout the years. The publication registered in PubMed doubled between 1988-1997 and 1998-2007. Nevertheless, we still lag behind other countries even when the publication is normalized for population size despite being in the high-income rank.

This study aims to assess the productivity of clinical trials conducted in the Gulf Cooperation Council (GCC) countries, including Oman, Saudi Arabia, United Arab Emirates (UAE), Qatar, Bahrain, and Kuwait. Specifically, we aim to estimate the number of clinical trials conducted, classify the stages of clinical trials, assess the trend, and estimate the proportion of clinical trials conducted in the GCC countries published in peer-reviewed journals.

Methods
Study design
This study is a retrospective bibliometric analysis of all clinical trials conducted in the GCC region from January 2000 to October 2019. The data were collected from the U.S. NLM (https://clinicaltrials.gov/) clinical trial registry database. Productivity was assessed using the publication status of these trials in the registry and searching the publication of these trials in the Medline indexed journal.

Search strategy
Our search was focused on studies conducted in the GCC Countries. We used the clinical trials registered at the U.S. NLM (https://clinicaltrials.gov/). In addition, as we were focusing on the interventional studies (clinical trials), we needed to narrow our search using the advance search feature to include that. Moreover, the study results were assigned to include all trials registered either with or without results. The starting date “01/01/2000” and the completion date were undefined as we were looking for all the trials registered at the search time, which was 16th October 2019. Furthermore, clinical trials were retrieved from each country individually using the “on map” feature.
Assessing clinical trials productivity

To assess the publication from each country, we used Python software foundation version 3.0 (Available at http://www.python.org) to automate the search for publications in peer-reviewed journals. After obtaining the “NCT” for each trial from the U.S. NLM (https://clinicaltrials.gov/), “Selenium automated webdriver” was used to search the “NCT” number in Medline database with the help of Pyautogui automated graphical user interface that assists image recognition. Moreover, the system was programmed to wait until the results appeared, identify them, and then return them to be saved. This gives a more accurate result and makes minimizes missing data due to slow or interrupted connection. We excluded all the trials conducted after 2015 to provide a reasonable time for the trials to be published. Therefore, we considered it not published whenever there is a trial run before 2015, and it is not published.

Statistical analysis

Continuous variables were described using means, while categorical variables were described using frequencies and percentages. In addition, we used the bar chart to assess the trend of the trials conducted each year, publication per country per year, and the publication trend from each country. The average rate of publication was estimated by dividing the total clinical trials over the study period. We used the independent t-test to compare between two independent groups. Finally, we used the t-test to compare the number of trials from each year. Using the “graph” function in IBM SPSS software (IBM Corp. Released 2016. IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY: IBM Corp), we graphically represented the data retrieved from the search and analyzed it accordingly using the bar chart. Then the same was done to know how many trials were published from each country.

We cannot use the raw data collected to compare Arabian Gulf countries' productivity as it will not serve as a fair comparison unless normalized. Countries with different population sizes and expenditures are expected to have different research productivity. Normalizing the productivity rates to the population size or the expenditure allows comparing these rates between countries. Therefore, we normalized our data using population size and Gross Domestic Product (GDP) for each country. We obtained the average population size over the study period from the Population
Division of the Department of Economic and Social Affairs of the United Nations Secretariat. In addition, the average GDP over the study period was obtained from the United Nations Department of Economics and Social Affairs, Statistics Division.\(^\text{11}\)

**Results**

The search strategy retrieved 752 trials, of which 55 were duplicates, and 15 were found to have missing data and were excluded. Therefore, a total of 682 trials were included in our analysis. On the other hand, there were 185,285 trials registered and conducted worldwide during the same study period. Therefore, the contribution from GCC countries represented 0.37% of trials conducted worldwide. Furthermore, out of the trials conducted before 2016, there were 111 published, representing 46.6% publication productivity.

**Clinical trials over time and by country**

Our study focused on the clinical trials conducted during the period between 2000 and 2019. The overall trend of the trials was increasing over this period by an average of 4.1 trials each year (0.6%) but with some fluctuation (**Figure 1**). Saudi Arabia shows the highest proportion among all the GCC countries by contributing 66.6% of the clinical trials, statistically different from the other GCC countries ($p < 0.001$). On the other hand, Bahrain contributed 2.5%, which is the lowest in this region. Qatar, UAE, Kuwait, and Oman contribute 10.3%, 9.7%, 7.3%, and 3.5% respectively. The contribution of each GCC country over time is shown in **Figure 2**.

**Normalization for population size and Gross Domestic Product**

To avert the bias of population size on the publication from each country, we normalized the trials from each country for the population size (**Table 1**). After normalization, Qatar was found to be the highest contributing country (42.78 Trial Per Million Population [PMP]), followed by Kuwait (16.969 PMP) and Saudi Arabia (16.846 PMP). Oman scored the lowest among the GCC countries (7.796 PMP). When normalized for Gross Domestic Products (GDP), Saudi Arabia showed the highest productivity 0.92 trial per 1 billion USD, followed by Bahrain 0.73 and Qatar 0.64. UAE showed the lowest productivity when normalized for GDP (0.24 per 1 billion USD). Oman scored the second before last with 0.49 trials per 1 billion USD (**Table 1**).
Publication trend for each country and subject covered

Most of the GCC countries had higher than average publication productivity (46.6%) except for Saudi Arabia and Bahrain. Saudi Arabia had a total of 154 trials that were conducted before 2016. The published trials represented 43.5% of the total trials conducted at that period in the country. In addition, the published trials from Bahrain represented 20% of the trials conducted during the study period. In contrast, the publication productivity from Qatar, Oman, United Arab Emirates and Kuwait represented 57.7%, 60%, 51.7% and 52.9%, respectively. The clinical trials from the GCC countries covered a wide range of specialties. The clinical trials in oncology showed the highest subject covered in this region and contributed 15.5% of all the trials from this region. In Oman, the clinical trials in hematology were the highest, contributing 50% of the trials conducted in Oman.

Subject covered in clinical trials from each country

Oncology was the most subject covered in Saudi Arabia. However, when looking at each country, we can find that other subjects were covered (Table 2).

Distribution of clinical trials per phase and trials status

Clinical trials obtained from the U.S. NLM were categorized by phases. Moreover, we can see that most of the trials obtained were phase 3 and phase 4 (Figure 3). We retrieved 682 trials from the NLM registry, (49%) were completed and (22%) were still recruiting (Table 3).

Discussion

It is essential to conduct clinical trials to enhance and develop the health care system in our countries and deliver the best healthcare option to the patient. Moreover, it is also needed to make evidence-based decisions and have a cost-effective intervention suitable for patients in the GCC countries. When assessing the productivity of clinical trials, it is important to include factors that enable and limit the execution of clinical trials. We, therefore, planned to evaluate the productivity using the information available in clinical trial registries.

The number of clinical trials from GCC countries has been increasing throughout the years. However, there was some fluctuation in the years 2010 and 2016. Knowing that, we are still
lagging behind the other countries as our contribution is only 0.37% of the total clinical trials worldwide. Alemayehu *et al.* studied the barriers to conducting clinical trials in developing countries. Common barriers include lack of financial and human capacity, ethical and regulatory system obstacles, lack of research environment, operational barriers and competing demands.\textsuperscript{13} Moreover, a bibliometric analysis was done to study the global clinical research by the anesthesia department by Madhav Swaminathan *et al.*, listed the top 34 countries with 20 or more publications, and countries from the GCC region were among them. The mean publication per million population was (18.65) in only anesthesia departments in 6 years period. On the other hand, publication per million population in the GCC countries was only 16.6 in all specialties in the past 19 years.\textsuperscript{14}

Saudi Arabia has the highest number of clinical trials with a significant difference compared to the other GCC counties, while Bahrain has the lowest. After the normalization of the population size, Qatar has the highest productivity. Oman has the lowest productivity after normalization to the population size. When the raw productivity was normalized the GDP, Saudi Arabia had the highest productivity while UAE had the lowest. More than half of the trials are not yet published in peer-reviewed journals. Most of the trials in the region are in oncology. Trials in hematology are dominant in Oman.

There is an overall increasing trend in the number of clinical trials conducted in the GCC countries. This is expected given the growing trend in the GDP in these countries. Furthermore, the increased expenditure on research and development (R&D) has likely contributed to this. In addition, an increase in the population size and the increase in the number of hospitals and medical colleges in the study period have likely influenced the number of clinical trials conducted. A study by Al-Maawali *et al.* found a significant positive correlation between the number of publications and physicians.\textsuperscript{3} A study by Bredan *et al.* assessed the visibility of research from the Arab countries in the world biomedical literature over two decades (1988 to 1997 and 1998 to 2007). The publication from the Arab counties doubled in the second decade compared to the first. Moreover, the number of publications in PubMed increased by 50% between the two decades.\textsuperscript{8}
There was an overall increasing trend in the publication over time. However, the publication trend fluctuated in the years 2010 and 2016. This might result from the great recession affecting the global economy, including the GCC countries around 2007-2009. This crisis was observed in the biomedical field as a decline in clinical trials conducted after around two years of the crisis.

Saudi Arabia was the leading country in the total number of clinical trials among the GCC countries. That is expected from a country with relatively high population size and many medical colleges and hospitals, including many physicians. This finding is similar to all the studies assessing biomedical research in GCC countries, and the Middle East or Arab countries. Al-Maawali et al. found the same when comparing the productivity of biomedical research in GCC countries. The population size correlates with the number of hospitals, physicians, and healthcare expenditure, which are factors associated with clinical research productivity. This being said, other factors affect productivity in clinical research, as discussed later.

After normalization for population size, Qatar shows the highest productivity in GCC countries. Qatar invested early in building an excellent biomedical research infrastructure and collaborated with many institutions with good research experience. Qatar Foundation (QF) was established in 1995, and since then, it has provided an exciting opportunity for R&D for the new generation. Li and Fang studied the impact of the triple helix model on research and productivity. This model involves universities, government, and industries, where they have an interactive relationship rather than a linear one to develop the innovation system in a country including R&D. Rassi et al., studied the medical research productivity in the Arab countries in the period from 2007 to 2016 and showed that Qatar was the highest research output per 1 million people not only among the GCC countries but also of all Arab countries. This support our finding as their study period is close to what we did in this paper. This is again similar to the result by Al-kindi et al. in the field of cardiovascular research.

Oman scored the lowest in the number of clinical trials in GCC countries among the GCC counties. This was similar to what was found by others, even after normalization for population size. The Research Council in Oman was established in 2005, and it made a difference in the productivity of research in general and in clinical trials, as shown in Figure 2. The number of
clinical trials are still considered low compared to the other GCC countries. According to the world bank, this could be due to the lack of infrastructure for clinical trial research and the country's relatively low funding and expenditure in R&D. R&D expenditure (% of GDP) was reported to be 0.21961 in 2018. Low expenditure in R&D has been an issue, and researchers and policymakers should collaborate more to solve this, given its impact on productivity. 

When we normalized the productivity to GDP, we found that Saudi Arabia was the highest among the GCC countries and UAE was the lowest. According to the World Bank, Saudi Arabia spent around 0.898% of its GDP on R&D in 2011 and was considered the highest to spend on R&D until 2015. After that, UAE had an expenditure of 0.895% of its GDP on R&D and is regarded as the highest ever since. That could explain why Saudi Arabia was found to be the highest, but it does not explain the finding in the case of the UAE. Bredan et al. studied the visibility of Arab countries in the world biomedical literature. They divided the countries into three economic groups based on their per capita gross national products. It was noticed that the publication from the lower-income group doubled and tripled in the middle-income group, where it increased only slightly in the upper-income group, and that is what we see in the case of UAE.

We found that less than half (46%) of the registered clinical trials were published in peer-reviewed journals. The number of trials published was expected to be higher as all these articles were completed before 2016. This might be explained by the bias toward biomedical research in general from the Arabian Region.

Oncology was found to be the most subject covered in GCC countries. Moreover, this was expected to be influenced by the result from Saudi Arabia since they have the highest contribution among all GCC countries. Alghamdi et al. studied the oncology research over ten years. They found a positive trend in oncology research from Saudi Arabia due to the increase in the number of cancer centers and practicing center specialties. In addition, they compare the published papers during 2008-2012 and 2013-2017, and the number of the publications increased compared to the first period ($p=0.004$). Moreover, the international collaboration increased in the second period ($p=0.001$).
We found that most of the trials retrieved from the U.S. NLM were in phases 3 and 4. This is a good indicator. Even though our contribution to the trials worldwide is low, most of the trials are in their latest phases. We found 335 trials registered at NLM was completed and only (34%) 115 trials had their result available at the NLM registry. Further investigation about the reasons behind such a finding is needed.

There are many limitations to our study. First, the search was limited to only one database (ClinicalTrials.gov). Second, the selection of the clinical trials registry of the U.S. NLM over the World Health Organization (WHO) registry was for several reasons. Firstly, the WHO registry was established after the NLM registry (2006 versus 2000). Secondarily, the NLM is a comprehensive registry containing all important and relevant trials. Thirdly, the assumption is that the trend we find in studies from the NLM registry would be similar to that of the WHO registry. There is no reason to expect systematic differences between the two registries and the interest in the trend and not the absolute numbers. Information from other registries would improve the accuracy of observations and conclusions. Additionally, not all studies are registered, and this may also have limited the results we retrieved. Moreover, we viewed the quantitative aspects of clinical trials in this study rather than the qualitative aspects. We believe that we were the first to address the clinical trial productivity in this period.

**Conclusion**

Health care system delivery is strongly related to clinical trials. There is a positive trend in the productivity of clinical trials from the GCC countries. Saudi Arabia is the leading country in clinical trial productivity among the GCC counties, while Oman scored lower than expected. Qatar showed a promising result when normalizing the raw data for population size.

**Conflict of Interest**

The authors declare no conflicts of interest.

**Funding**

No funding was received for this study.
Authors’ Contribution

AA-H and MA-K conceptualized and designed the study. MA-K and WR prepared the analysis plan. AA-H collected the data, conducted the data analysis and drafted the manuscript. MA-K and WR reviewed the initial draft. All authors approved the final version of the manuscript.

Acknowledgment

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**Figure 1.** The trend of the clinical trials conducted at the Gulf Cooperative Council between 2000 and 2019.

**Figure 2.** Clinical Trials from each country in each year.
<table>
<thead>
<tr>
<th>Country</th>
<th>Average Gross Domestic Product per billion</th>
<th>Publication per GDP per 1 billion</th>
<th>Average population size per million</th>
<th>Publication per million population (PMP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oman</td>
<td>51.21</td>
<td>0.49</td>
<td>3.21</td>
<td>7.796</td>
</tr>
<tr>
<td>Bahrain</td>
<td>23.39</td>
<td>0.73</td>
<td>1.117</td>
<td>15.221</td>
</tr>
<tr>
<td>Kuwait</td>
<td>107.06</td>
<td>0.47</td>
<td>2.95</td>
<td>16.969</td>
</tr>
<tr>
<td>Saudi Arabia</td>
<td>491</td>
<td>0.92</td>
<td>26.95</td>
<td>16.846</td>
</tr>
<tr>
<td>Qatar</td>
<td>109</td>
<td>0.64</td>
<td>1.64</td>
<td>42.776</td>
</tr>
<tr>
<td>UAE</td>
<td>270</td>
<td>0.24</td>
<td>6.924</td>
<td>9.532</td>
</tr>
</tbody>
</table>

**Table 1.** Clinical trials from each country after normalization for Gross Domestic Product (GDP) per 1 billion and population per 1 million

![Clinical trials per phases](image)

**Figure 3.** Distribution of the clinical trials as per the phase when obtained from the clinical trials registry
<table>
<thead>
<tr>
<th>Country</th>
<th>Frequency</th>
<th>Percentage</th>
<th>Subject</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oman</td>
<td>12</td>
<td>48%</td>
<td>Haematology</td>
</tr>
<tr>
<td>Saudi Arabia</td>
<td>90</td>
<td>19.8%</td>
<td>Oncology</td>
</tr>
<tr>
<td>UAE</td>
<td>16</td>
<td>24.2%</td>
<td>Endocrinology</td>
</tr>
<tr>
<td>Qatar</td>
<td>12</td>
<td>17.1%</td>
<td>Endocrinology</td>
</tr>
<tr>
<td>Bahrain</td>
<td>3</td>
<td>17.6%</td>
<td>Genitourinary</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>17.6%</td>
<td>Musculoskeletal</td>
</tr>
<tr>
<td>Kuwait</td>
<td>16</td>
<td>32%</td>
<td>Endocrinology</td>
</tr>
</tbody>
</table>

**Table 2.** The most subject covered in clinical trials conducted in the GCC countries.

<table>
<thead>
<tr>
<th>Status</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Completed</td>
<td>335</td>
<td>49.1%</td>
</tr>
<tr>
<td>Active, not recruiting</td>
<td>53</td>
<td>7.8%</td>
</tr>
<tr>
<td>Enrolling by invitation</td>
<td>6</td>
<td>0.9%</td>
</tr>
<tr>
<td>Not yet recruiting</td>
<td>22</td>
<td>3.2%</td>
</tr>
<tr>
<td>Recruiting</td>
<td>151</td>
<td>22.1%</td>
</tr>
<tr>
<td>Suspended</td>
<td>4</td>
<td>0.6%</td>
</tr>
<tr>
<td>Terminated</td>
<td>28</td>
<td>4.1%</td>
</tr>
<tr>
<td>Unknown status</td>
<td>77</td>
<td>11.3%</td>
</tr>
<tr>
<td>withdrawn</td>
<td>6</td>
<td>0.9%</td>
</tr>
<tr>
<td>Total</td>
<td>682</td>
<td>100%</td>
</tr>
</tbody>
</table>

**Table 3.** Clinical trials status as per the U.S NLM.