

Productivity of Clinical Trials Conducted in the Gulf Cooperative Council Region

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ABSTRACT: Objectives: This study aimed to assess the productivity of clinical trials in the Gulf Cooperation Council (GCC) region, including Oman, Saudi Arabia, United Arab Emirates, Qatar, Bahrain and Kuwait and to address the existing research gap. Specifically, this paper aimed 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 US National Library of Medicine 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 the region contributes to only 0.37% of the trials globally. When comparing the raw data, Saudi Arabia showed the highest proportion, contributing 66.6% of the clinical trials from the region ($P < 0.001$), while Oman contributed 3.5%. After normalisation to population, Qatar was found to be the highest contributor, 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 in the GCC should utilise the triple helix model to form partnerships with the industry and improve their contributions to science.

Keywords: Productivity; Clinical Trial; Publications; Oman; Gulf Cooperation Council.

ADVANCES IN KNOWLEDGE

- A total of 682 clinical trials were conducted in the Gulf Cooperative Council (GCC) countries.
- Clinical trial productivity from the region was only 0.37% of the trials conducted globally.
- Saudi Arabia showed the highest proportion, contributing with 66.6% of the clinical trial from the region.

APPLICATION TO PATIENT CARE

- Clinical trials are essential for patient care. This study will help researchers and policymakers ensure proper future planning and conduct of clinical trials in GCC countries, especially Oman.

CLINICAL TRIALS ARE EXTREMELY CRUCIAL in delivering the best healthcare system. Their main goal is to assess the impact of interventions and measure the effectiveness and safety to ensure better healthcare.¹ This information is needed for proper future planning of research funding.

The contribution to clinical trials from Gulf Cooperation Council (GCC) countries has not been well-studied. Nonetheless, a small number of studies have been conducted addressing this question. For instance, a study was conducted to estimate the clinical trials in behavioural sciences in the Arab Gulf States from 2010 to 2018. It found that the GCC country that contributes the most to this area was 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 other studies have shown that Saudi Arabia is the major contributor of research output in the Arabian Gulf region.^{3–7} When the publication was normalised for population size,

Kuwait showed the highest research output with Qatar coming second.^{3,6} Whereas, 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 publications registered in PubMed (National Library of Medicine, Bethesda, Maryland, USA) doubled between 1988–1997 and 1998–2007.⁸ Nevertheless, the GCC still lags behind other regions, even when publications are normalised for population size and despite being in a high-income rank.⁷

This study aimed to assess the productivity of clinical trials conducted in GCC countries, including Oman, Saudi Arabia, United Arab Emirates (UAE), Qatar, Bahrain and Kuwait. Specifically, this research aimed 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 and published in peer-reviewed journals.

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Methods

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 US National Library of Medicine (NLM) clinical trial registry database.⁹ Productivity was assessed using the publication status of these trials in the registry and searching the publication of these trials in MEDLINE-indexed journals.

The search was focused on studies conducted in the GCC countries using the clinical trials registered in the NLM. To focus on interventional studies (clinical trials), the search needed to be narrowed-down using the advance search feature. Moreover, the study results were assigned to include all trials registered either with or without results. The starting date of '01/01/2000' and an undefined completion date was taken to list all the trials registered at the time of searching, which was October 2019. Furthermore, clinical trials were retrieved from each country individually using the 'on map' feature.

To assess the publication from each country, Python software foundation, Version 3.0, (Python™, Wilmington, Delaware, USA) was used to automate the search for publications in peer-reviewed journals. After obtaining the 'National Clinical Trial (NCT)' number for each trial from the NLM, Selenium WebDriver was used to search the 'NCT' number in the MEDLINE database with the help of PyAutoGUI (Python™), an 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 process gave a more accurate result and minimised missing data due to slow or interrupted connection. All the trials conducted after 2015 were excluded to provide a reasonable time for the trials to be published. Furthermore, a study was considered not published whenever there was a trial run before 2015, and this was not published.

Continuous variables were described using means, while categorical variables were described using frequencies and percentages. In addition, a bar chart was used 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. The independent t-test was used to compare between two independent groups.¹⁰ Finally, the t-test was used to compare the number of trials from each year. Using Statistical Package for the Social Sciences (SPSS), Version 24.0 (IBM Corp., Armonk, New York, USA), the data retrieved from the search was graphically represented and analysed accordingly using the bar chart. Then, the same was done to know how many trials were published from each country.

The raw data collected cannot be used to compare GCC countries' productivity, as it will not serve as a fair comparison unless normalised. After all, countries with different population sizes and expenditures are expected to have different research productivity. Normalising the productivity rates to the population size or the expenditure allows comparing these rates between countries. Therefore, the data was normalised using population size and gross domestic product (GDP) for each country. The average population size was obtained 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.¹¹

Results

The search strategy retrieved 752 trials, of which 55 were duplicates and 15 were found to have missing data and thus excluded. Therefore, a total of 682 trials were included in this analysis. On the other hand, there were 185,285 trials registered and conducted

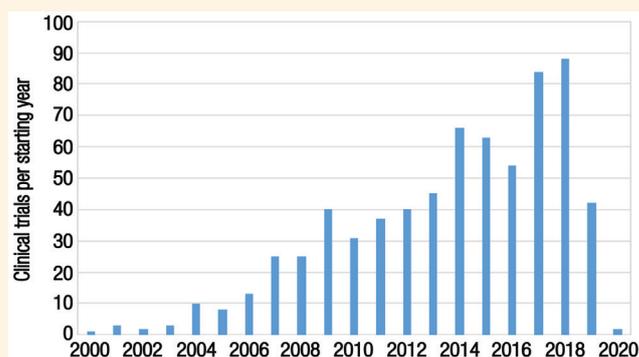


Figure 1: Trend of clinical trials conducted in the Gulf Cooperative Council countries between 2000 and 2019.

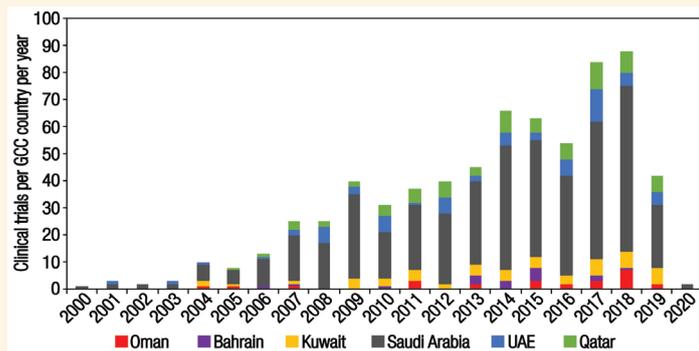


Figure 2: Clinical trials from each Gulf Cooperative Council country every year (2000–2020). UAE = United Arab Emirates.

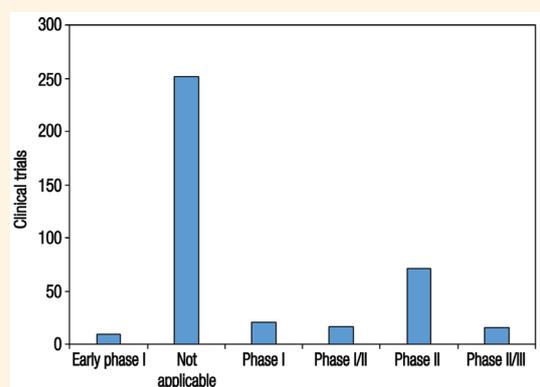


Figure 3: Distribution of clinical trials as per the phase when obtained from the clinical trials registry

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.

The overall trend of the trials was increasing over the study period by an average of 4.1 trials each year (0.6%), albeit with some fluctuation [Figure 1]. Saudi Arabia showed the highest proportion among all the GCC countries, contributing 66.6% of the

clinical trials, which is statistically different from the other GCC countries ($P < 0.001$). In contrast, Bahrain contributed 2.5%, which is the lowest in this region. Qatar, UAE, Kuwait and Oman contributed 10.3%, 9.7%, 7.3% and 3.5%, respectively [Figure 2].

To avert the bias of population size on the publication from each country, the trials from each country were normalised for the population size [Table 1]. After normalisation, Qatar was found to be the highest contributing country (42.776 trials 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 normalised for GDP, Saudi Arabia showed the highest productivity at 0.92 trial per 1 billion USD, followed by Bahrain (0.73 per 1 billion USD) and Qatar (0.64 per 1 billion USD). The UAE showed the lowest productivity when normalised for GDP (0.24 per 1 billion USD). Oman scored the second before last with 0.49 trials per 1 billion USD [Table 1].

Most of the GCC countries had higher than average publication productivity (46.6%), except for Saudi Arabia and Bahrain. In Saudi Arabia, a total of 154 trials were conducted before 2016. However, the published trials represented 43.5% of the total trials conducted. In addition, the total published trials

Table 1: Clinical trials from each country after normalisation for gross domestic product per one billion and population per one million

Country	Average GDP per billion	Publication per GDP per billion	Average population size per million	Publication per million population
Oman	51.21	0.49	3.21	7.796
Bahrain	23.39	0.73	1.117	15.221
Kuwait	107.06	0.47	2.95	16.969
Saudi Arabia	491	0.92	26.95	16.846
Qatar	109	0.64	1.64	42.776
United Arab Emirates	270	0.24	6.924	9.532

GDP = gross domestic product.

Table 2: Most common subjects in clinical trials conducted in Gulf Cooperative Council countries

Country	n (%)	Subject
Oman	12 (48)	Haematology
Saudi Arabia	90 (19.8)	Oncology
United Arab Emirates	16 (24.2)	Endocrinology
Qatar	12 (17.1)	Endocrinology
Bahrain	3 (17.6)	Genitourinary
	3 (17.6)	Musculoskeletal
Kuwait	16 (32)	Endocrinology

from Bahrain represented 20% of the trials conducted during the study period. In contrast, the publication productivity from Qatar, Oman, UAE and Kuwait represented 57.7%, 60%, 51.7% and 52.9%, respectively.

Clinical trials from the GCC countries also covered a wide range of specialties. Oncology was the most frequently covered subject in this region, contributing towards 15.5% of all the trials. In Oman, clinical trials in haematology were the highest, contributing towards almost 50% of the trials conducted in the country [Table 2].

Clinical trials obtained from the NLM were categorised by phase. With respect to the GCC region, most of the research published focused on trials in phases 3 and 4 [Figure 3]. Of the 682 trials retrieved from the NLM registry, 49.1% were completed and 22.1% were still recruiting [Table 3].

Discussion

It is essential to conduct clinical trials to enhance and develop the healthcare systems and deliver the best healthcare option to patients. Moreover, it is also needed to make evidence-based decisions and create cost-effective interventions suitable for patients.¹² As such, when assessing the productivity of clinical trials, it is important to include factors that enable and limit the execution of clinical trials. Therefore, this study aimed 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, despite some fluctuation in the years 2010 and 2016. However, the region still lags behind other countries with a contribution of only 0.37% to the total clinical trials worldwide. Alemayehu *et al.* studied the barriers to conducting clinical trials in developing countries. They found that common barriers include lack of financial and human capacity, ethical and regulatory system obstacles, lack of research environment, operational barriers and competing demands.¹³ Moreover,

Table 3: Status of clinical trials conducted in the Gulf Cooperative Council countries as per the United States National Library of Medicine

Status	n (%)
Completed	335 (49.1)
Active, not recruiting	53 (7.8)
Enrolling by invitation	6 (0.9)
Not yet recruiting	22 (3.2)
Recruiting	151 (22.1)
Suspended	4 (0.6)
Terminated	28 (4.1)
Unknown status	77 (11.3)
Withdrawn	6 (0.9)
Total	682 (100)

a bibliometric analysis by Swaminathan *et al.* to study global clinical research by the anaesthesia departments listed the top 34 countries with 20 or more publications and found countries from the GCC region among them.¹⁴ While the mean publication in only anaesthesia departments globally was 18.65 PMP over the six-year period, publication in the GCC countries was only 16.6 in all specialties in the past 19 years.¹⁴

In this current research's analysis, Saudi Arabia had the highest number of clinical trials, with a significant difference compared to the other GCC countries, while Bahrain had the lowest. After normalisation of the results to account for population size, Qatar had the highest productivity, while Oman had the lowest productivity. When the raw productivity was normalised using the GDP, Saudi Arabia had the highest productivity while the UAE had the lowest. Furthermore, more than half of the trials have not yet been published in peer-reviewed journals. With respect to the specific subjects, most of the trials in the region were in the field of oncology, while trials in haematology were 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 GDP of 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 number of hospitals and medical colleges in the study period likely influenced the number of clinical trials conducted. This is echoed by Al-Maawali *et al.*, who found a significant positive correlation between the number of publications and physicians.³ Moreover, a study by Bredan *et al.* assessed the visibility of research from Arab countries in the world biomedical literature over two decades (1988–1997 and 1998–2007). It

found that publication from Arab countries doubled in the second decade, compared to the first. Moreover, the number of publications in PubMed increased by 50% between the two decades.⁸

As such, there was an overall increasing trend in publication over time. However, the publication trend fluctuated in the years 2010 and 2016. These dips may have resulted from the great recession affecting the global economy, including the GCC countries around 2007–2009, which manifested 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. This is expected from a country with a relatively larger population and many medical colleges and hospitals, including many physicians. This finding is echoed by all other studies assessing biomedical research in GCC countries and the Middle East or Arab countries.^{3,5,6,8,15} For example, when comparing the productivity of biomedical research in GCC countries, Al-Maawali *et al.* found that population size correlated with the number of hospitals, physicians and healthcare expenditure, which are factors associated with clinical research productivity.³ This being said, other factors affect productivity in clinical research, which are discussed later in this discussion.

After normalisation for population size, Qatar shows the highest productivity in GCC countries. This finding can be explained by Qatar's early investment in building excellent biomedical research infrastructure and collaborating with many institutions with good research experience. For instance, Qatar Foundation (QF) was established in 1995 and has provided exciting R&D opportunities for the new generation since then. QF provided a link between universities, the government and industries for the advancement of R&D in Qatar. Li and Fang studied the impact of the triple helix model on research and productivity. This model involves universities, the government and industries that have an interactive relationship rather than a linear one to develop innovative systems in a country, including R&D.¹⁶ Rassi *et al.*, studied the medical research productivity in Arab countries in 2007–2016 and showed that Qatar had the highest research output PMP, not only among the GCC countries but also of all Arab countries.⁵ This supports this paper's finding as their study period is similar to that employed in this research and echoed by Al-kind *et al.* in the field of cardiovascular research.¹⁵

Oman scored the lowest in the number of clinical trials among the GCC countries. This was similar to findings from other research, even after normalisation for population size.⁵ The Research Council in Oman

was established in 2005 and made a difference in the productivity of research in general and in clinical trials [Figure 2]. Nonetheless, 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. In Oman, R&D expenditure (% of GDP) was reported to be 0.21961% in 2018.¹⁷ As low expenditure in R&D is a persisting issue, researchers and policymakers should collaborate to a greater degree to address this, given its impact on research productivity.

When the productivity was normalised to GDP, 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 spender on R&D until 2015.¹⁸ Since then, UAE has spent 0.895% of its GDP on R&D and is regarded as the highest spender since. This could explain why Saudi Arabia was found to be the highest, but it does not explain the finding in the case of UAE. To answer this inconsistency, 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 publications doubled in the lower-income group and tripled in the middle-income group, where it increased only slightly in the upper-income group, which is what can be seen in the case of UAE.⁸

Less than half (46%) of the registered clinical trials in the GCC region were published in peer-reviewed journals. The number of clinical trials published was expected to be higher as all these articles were completed before 2016; however, this might be explained by the bias toward biomedical research in general in the Arabian region.¹⁹

Oncology was found to be the most covered subject 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 and found a positive trend in oncology research from Saudi Arabia due to the increase in the number of cancer centres and practicing centre specialties. In addition, they compared the published papers during 2008–2012 and 2013–2017 and found a significant increase in the number of the publications in the second period ($P = 0.004$). Moreover, the international collaboration increased in the second period ($P = 0.001$).²⁰

Most of the clinical trials retrieved from the NLM were found to be in phases 3 and 4. Even though

the region's contribution to the trials worldwide is low, most of the trials are in their latest phases. A total of 335 trials registered with NLM were completed and only 115 (34%) trials had their result available in the NLM registry. As such, further investigation about the reasons behind such a finding is needed.

There are a few limitations to this study. The search was limited to only one database (ClinicalTrials.gov). Second, the selection of the clinical trials registry of the NLM over the WHO registry was made for several reasons: (1) the WHO registry was established after the NLM registry (2006 versus 2000); (2) the NLM is a comprehensive registry containing all important and relevant trials; and (3) the assumption was made that the trend found 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 main focus was the trend and not the absolute numbers. However, 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 retrieved. Moreover, only the quantitative aspects of clinical trials in this study were considered rather than the qualitative aspects. Nonetheless, to the best of the authors' knowledge, this paper is the first to address the clinical trial productivity in this period.

Conclusion

Healthcare 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 countries, while Oman scored lower than expected. In addition, Qatar showed promising results when normalising the raw data for population size. Countries in the GCC region should improve research infrastructure to attract more sponsored clinical trials and facilitate investigator-initiated trials.

AUTHORS' CONTRIBUTION

AA-H and MA-K conceptualised 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.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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