



Original article

The Characteristics of Clinical Studies Submitted to the Saudi Food and Drug Authority from 2009 until 2020



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ABSTRACT

Background: Clinical trials are crucial in contemporary evidence-based medicine for discovering new treatments for diseases. Their registration in a registry increases the transparency in the dissemination of knowledge about clinical research. It is essential to understand the activity of clinical trials in a country, thus identifying research gaps.

Objective: This study, therefore, aims to describe the clinical trial activity since the inception of clinical trials' administration and national clinical trials' registry within the Kingdom of Saudi Arabia (KSA).

Method: A descriptive study was conducted by reviewing all clinical studies that have been registered during 2009 and June 2020. The inclusion criterion was all phases of the clinical trials registered in the national registry during that period. Data analysis was done using descriptive statistics.

Results: Since 2009, 352 studies have been registered. However, a total of 333 studies with complete data was included in the analysis. A total of 80 sponsors funded the clinical studies in the KSA. The majority of the clinical studies are funded by multinational pharmaceutical companies. Oncology (13.81%) and diabetes (11.71%) were the most common therapeutic areas and constituted the largest proportion of the overall studies. 44% were phase 4 and 40% were phase 3 studies.

Conclusion: With a population approaching 34 million, the number of clinical trials in the KSA is not sufficient. Since the inception of the clinical trial's administration and SCTR, the emphasis has been on phase 3 and phase 4 clinical studies. The most studied therapeutic areas were oncology and diabetes. Many clinical studies in the KSA were sponsored by multinational pharmaceutical companies.

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1. Introduction

Clinical trials (CTs) are reflected as a significant method for evolving new treatments and on condition that access to possibly effective drugs that are still under exploration (Al-Rawashdeh

et al., 2019). Clinical trials are recognized as an important type of study design in the spectrum of translational research and it is perilous to advancing patient care (Wichman et al., 2021; Ali et al., 2017). They are essential to evaluate the safety and efficacy of medications. Meanwhile, their outcomes can influence clinical practice, thereby improving patient care (Shim et al., 2005). Despite the improvement in the Kingdom of Saudi Arabia (KSA) economy, there was an increase in the burden of chronic diseases (Saqib et al., 2018). The strategic objectives of vision 2030 focused on improving healthcare services and scientific research (Gamee, 2018). Clinical research in the KSA has made progressions during the last few years. Saudi researchers have contributed to the medical literature by piloting different types of research, including investigator-initiated CTs and international multicenter-sponsored CTs (Jamjoom et al., 2015; Al-Rawashdeh et al., 2019). The number of clinical trials in any country reflects the advancement of a healthcare system (Ali et al., 2017). The KSA contributed

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to only 0.2% of the total number of clinical trials conducted worldwide.

Trial registries were set up to progress transparency, remove repetition, improve responsiveness and avoid unused. Many trials certainly do not reach the point of patient registration due to countless reasons (Vellinga et al., 2021). According to the Declaration of Helsinki, it is mandatory to register clinical trials in a publicly accessible database before initiating the recruitment of the study participants (Vellinga et al., 2021; World Medical, 2013). Likewise, the registration of all clinical trials is a scientific, ethical, and moral responsibility (Organization, 2020). The registration of the prospective clinical trials in a registry increases the transparency in the dissemination of the information about clinical research (Vellinga et al., 2021; Ali et al., 2017). The registration of the clinical trials is also a prerequisite for publication as per the International Committee of Medical Journal Editors (DeAngelis et al., 2004; Aslam et al., 2013).

There is a paucity of data regarding the characteristics of clinical studies registered in the administration of clinical trials and the Saudi Clinical Trials Registry (SCTR). Saudi Food and Drug Administration (SFDA) established clinical trials administration and SCTR in 2009 and 2013, respectively (Bawazir et al., 2014; Ali et al., 2017; Alsultan et al., 2020). The prime responsibilities of the clinical trial administration are to evaluate the protocols of clinical trials and amendments, conduct inspections based on the Good Clinical Practice, and maintain SCTR (Bawazir et al., 2014; Alsultan et al., 2020). SCTR is currently a comprehensive database of all clinical trials in the KSA (SFDA). Since 2013, sponsors and researchers must register their clinical trials using the electronic portal of the SCTR (Alsultan et al., 2020). A previous study in the KSA reported the findings from ClinicalTrials.gov which is managed by the National Library of Medicine at the National Institute of Health in the United States (Zarin and Keselman 2007). In addition, this registry does not include all clinical trials which is the major limitation of this registry (Califf et al., 2012). Therefore, it necessitates exploring the clinical trial activity based on the registry of the KSA and perform a comprehensive evaluation of the national trial's portfolio.

The authority maintains an online database of submitted studies in the Kingdom. This study aims to describe the submitted studies to the SFDA over the last ten years. This study provides an opportunity to shed light on the status of research in the Kingdom. It will help identify the gaps where more research is needed. Consequently, the study can give the government, pharmaceutical companies, hospitals, and universities a chance to plan for improvements, minimize the burden of barriers, and identify opportunities for collaboration. Consequently, these efforts will increase the number of studies being conducted and maximize the benefit gained.

2. Methods

2.1. Study design and data source

It is a descriptive cross-sectional study based on 11 years of clinical studies record available in an online clinical trials platform of the SFDA from 2009 to June 2020. The data included the following information about each study: title, phase, protocol number, study drug, study site, sponsor, and the status of study (completed, rejected, terminated, or ongoing). We also constructed a set of additional variables. Using the DrugBank[®] database, we created variables such as therapeutic category, city, and province. The provinces were based on the thirteen administrative regions in the KSA, including Riyadh, Makkah, Madinah, Qassim, Eastern Region, Asir, Abha, Tabuk, Hail, The Northern Border, Jazan, Najran, Al - Baha, and Al-Jouf. The variable of the sponsor was further classified into government, private, local, or international sponsors. Government-sponsored studies include those sponsored by the SFDA, disease centers, government hospitals, and government universities. Private-sponsored studies include pharmaceutical companies, private hospitals, and private universities in the Kingdom.

2.2. Inclusion and exclusion criteria

We included all phases of the clinical trials registered during 2009 and June 2020. We did not include studies with the rejection

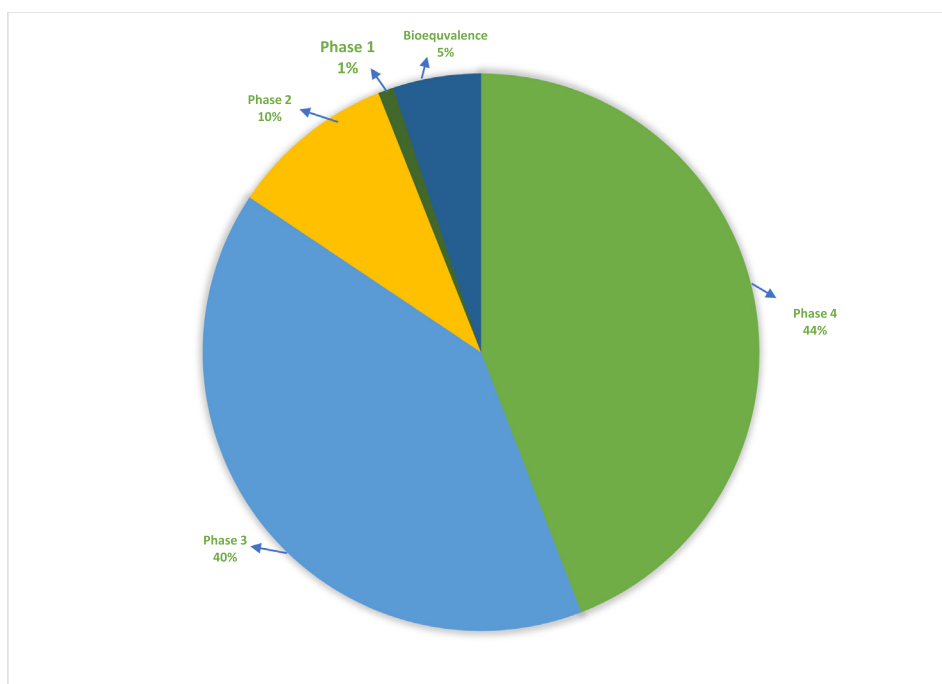


Fig. 1. Phases of the studies submitted to the Saudi Food and Drug Authority between 2009 and 2020 after excluding rejected studies (N = 333).

Table 1

Sponsors of the studies submitted to the Saudi Food and Drug Authority between 2009 and 2020 (n = 333).

Sponsors	n (%)
Novartis	44 (13.21)
SANOFI	39 (11.71)
Roche	23 (6.91)
AstraZeneca	15 (4.5)
Bayer	15 (4.5)
King Abdullah International Medical Research Center	15 (4.5)
Saudi Food and Drug Authority	14 (4.2)
King Faisal Specialist Hospital & Research Center	11 (3.3)
Eli Lilly	8 (2.4)
MSD	8 (2.4)
Jamjoom Pharmaceuticals	6 (1.8)
Janssen-Cilag International NV	6 (1.8)
King Abdullah Medical City, Makkah	6 (1.8)
AbbVie	5 (1.5)
Alexion	5 (1.5)
Boehringer Ingelheim	5 (1.5)
GSK	5 (1.5)
King Fahad Medical City	5 (1.5)
Merck Serono	5 (1.5)
Pfizer	5 (1.5)
novo nordisk	5 (1.5)
Bristol-Myers Squibb	4 (1.2)
Celgene	4 (1.2)
Tabuk Pharmaceuticals	3 (0.9)
Albireo Pharma	2 (0.6)
Alcon	2 (0.6)
ApoPharma	2 (0.6)
Astellas	2 (0.6)
BioMarin Pharmaceutical Inc.	2 (0.6)
Eagle Pharmaceuticals	2 (0.6)
General Department of Research and Studies, Ministry of Health	2 (0.6)
Intarcia Therapeutics	2 (0.6)
King Abdulaziz City for Science and Technology	2 (0.6)
King Saud Medical City	2 (0.6)
MEDIS Laboratories	2 (0.6)
McMaster University	2 (0.6)
Prince Mutaib bin Abdullah Chair for Biomarkers Research on Osteoporosis	2 (0.6)
SPIMACO ADDWAEIH	2 (0.6)
Southwest Oncology Group	2 (0.6)
The Australian and New Zealand Intensive Care Research Centre, Monash University, Australia	2 (0.6)
Acerta Pharma	1 (0.3)
Africa Middle East Cancer Intergroup	1 (0.3)
Allergan	1 (0.3)
Amgen	1 (0.3)
Arab Company for Pharmaceutical Products	1 (0.3)
Archigen Biotech Limited	1 (0.3)
Bellicum Pharmaceuticals	1 (0.3)
Biogen	1 (0.3)
Dilaforette AB	1 (0.3)
Hikma Pharmaceuticals	1 (0.3)
International Cancer Research Group	1 (0.3)
Kaleido Biosciences	1 (0.3)
King Abdulaziz University	1 (0.3)
King Abdulaziz University Hospital	1 (0.3)
King Fahad Hospital of the University	1 (0.3)
King Fahad Specialist Hospital-Dammam	1 (0.3)
King Saud University	1 (0.3)
Leo Pharma	1 (0.3)
London School of Hygiene & Tropical Medicine	1 (0.3)
Lundbeck	1 (0.3)
Mast Therapeutics	1 (0.3)
Mundipharma	1 (0.3)
National Plan for Science and Technology	1 (0.3)
Northern Area Armed Forces Hospital	1 (0.3)
Octapharma	1 (0.3)
Onxeo	1 (0.3)
Prince Mohammad Bin Abdulaziz Hospital	1 (0.3)
Prince Salman Center for Disability Research	1 (0.3)
Saud Al Babbain Cardiac Center	1 (0.3)
Saudi Ajal	1 (0.3)
Servier	1 (0.3)
Shire Human Genetic Therapies	1 (0.3)
Sunnybrook Health Science Center	1 (0.3)
The Canadian Heart Research Centre	1 (0.3)

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Table 1 (continued)

Sponsors	n (%)
The Saudi center for Organ Transplantation	1 (0.3)
The University of Queensland, Australia	1 (0.3)
Thrombosis Research Institute	1 (0.3)
Umm Al Qura University	1 (0.3)
University of Sydney	1 (0.3)
Vifor Pharma	1 (0.3)

status due to the unavailability of the study details required for the analysis.

2.3. Ethical approval

The study was exempted by the Institutional Review Board of the King Saud University Medical City (E-20-5475).

2.4. Statistical analysis

Data analysis will be carried out using the SPSS software, version 21 (IBM, Armonk, NY: IBM Corp). We used descriptive statistics to report the results. The results were described as frequencies, percentages, median, and interquartile range.

3. Results

Since the inception of the clinical trials' administration and SCTR, 352 studies have been registered. The online database of the SFDA contains 249 studies (71%) with an ongoing status, followed by completed ($n = 62$, 18%), terminated ($n = 22$, 6%), and rejected ($n = 19$, 5%) studies. Subsequently, 19 studies with rejected status were excluded as they failed to meet the inclusion criteria. The reason for exclusion was the unavailability of data required for the analysis. Finally, a total of 333 studies were included in this study.

3.1. Overview of the included studies

Fig. 1 illustrates the phases of all included studies. Among the 333 studies, forty-four percent were phase 4 studies, followed by phase 3 (40%), phase 2 (10%), bioequivalence (5%), and phase 1 (1%) studies.

Table 1 shows the details of the sponsors. The studies included in this study were sponsored by 80 entities. More than two-thirds of the studies were sponsored by pharmaceutical companies and private hospitals (Table 1). Approximately 26% of the studies were government-sponsored. Novartis funded the most trials ($n = 44$, 13.2%) in the KSA. Other pharmaceutical companies such as Sanofi and Roche sponsored 39 and 23 studies, respectively (Table 1). In the KSA, a total of 13 sponsors (3.9%) were the national pharmaceutical companies. Out of 80 sponsors, nearly half of the sponsors funded only one clinical study. King Abdullah National medical Research Center ($n = 15$, 4.5%) and SFDA ($n = 14$, 4.2%) were the most common government sponsors (Table 1).

Fig. 2 depicts the study sites. The analysis demonstrated that studies were conducted at 740 study sites. A total of 186 studies (55.8%) were conducted in a single study site while the remaining ($n = 147$, 44.2%) were conducted as a multi-center study. Almost half of the study sites were located at King Faisal Specialist Hospital and Research Center Riyadh ($n = 82$, 11.08%), King Fahad Medical City Riyadh ($n = 72$, 9.73%), King Khalid University Hospital Riyadh ($n = 68$, 9.19%), King Abdulaziz Medical City National Guard Riyadh ($n = 67$, 9.05%), King Abdulaziz University Hospital Jeddah (6.76%) (Fig. 2).

Fig. 3 demonstrates that many studies were conducted in the Riyadh province (51.76%), followed by the Makkah (29.73%) and Eastern provinces (14%). Approximately 5% of the studies were conducted in other provinces (Fig. 3).

The therapeutic areas for the observational studies and registries are presented in Fig. 4. Table 2 shows that oncology (13.81%) and diabetes (11.71%) studies were the most numerous and constituted the largest proportion of the overall studies. Other common therapeutic areas were immune diseases (5.11%), hypertension (3.6%), thromboembolic diseases (3.3%), and viral diseases (3.3%). Appendix A shows the field of the studies for the top five centers in the KSA, where around 46% of the studies were conducted during the 11 years. Similarly, therapeutic areas such as oncology and diabetes were the most common in all the top 5 centers in the KSA.

4. Discussion

This cross-sectional study of registered clinical trials conducted by pharmaceutical companies and academic institutions such as universities and hospitals showed that the number of clinical trials is 352. On the contrary, a previous study based on the ClinicalTrials.gov (registry of the United States) reported 405 clinical studies in the KSA (Ali et al., 2017). As of November 2020, a total of 137, 020 studies are registered in ClinicalTrials.gov under the map of the United States that has reached 328 million population (trials.gov). The number is not sufficient in the KSA that has reached nearly thirty-four million population (GAFS, 2019).

This study found that majority of the studies were phase 3 and phase 4. The studies in these phases are conducted to assess the efficacy and safety of medications on a large population number (Suvarna, 2010). It shows the interest of the pharmaceutical companies in the later stage clinical trials as it allows the recruitment of a large number of study subjects with a diverse disease portfolio in a shorter period. In contrast, early-stage studies such as phase 1 studies generally require the recruitment of healthy study volunteers. Likewise, phase 1 studies do not provide direct therapeutic benefits to the study subjects (Louisa et al., 2012). Overall, 1% and 10% of studies were phase 1 and phase 2, respectively. A previous study in the US relatively reported a higher percentage of phase 1 (15.2%) and phase 2 (20.7%) trials than early-stage trials conducted in the KSA (Califf et al., 2012).

Although only 11% of the studies were rejected or terminated in the KSA during the last eleven years, it is imperative to discuss the reasons for their termination or rejection in an official report or guidance issued by the SFDA. Such communications may help sponsors in the future in increasing the quality of clinical trials. This study revealed that many studies were funded by an international pharmaceutical company. This trend is consistent with the results of the previous studies (Jamjoom et al., 2015; Ali et al., 2017). The benefits of the globalization of clinical research such as ethnic diversity decreased study cost, improved recruitment, and access to rare diseases may act as a stimulating force to increase the number of studies in our region (Nair et al., 2013). However, the international pharmaceutical companies must emphasize the Kingdom's specific healthcare needs, without con-

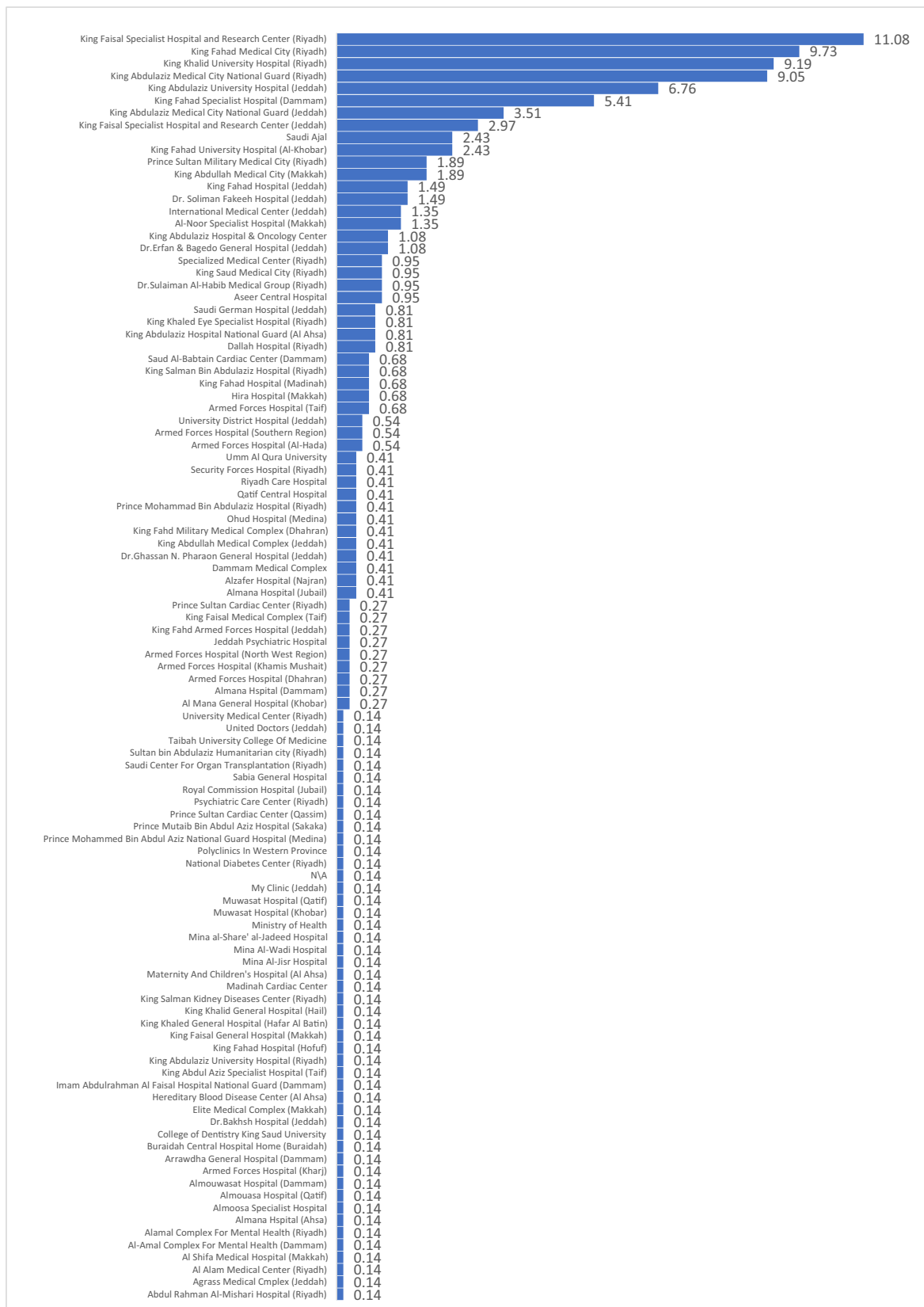


Fig. 2. The sites of the studies submitted to the Saudi Food and Drug Authority between 2009 and 2020 after excluding rejected studies (N = 333).

sidering it as an additional site for the recruitment of the study subjects (Weigmann, 2015).

This study demonstrated varying interests of the study sites in terms of the therapeutic areas. Likewise, the difference in thera-

peutic areas between hospitals is linked to the nature of the healthcare setting. In this study, specialist hospitals such as King Faisal Specialist Hospital and Research Center focused primarily on cancer and immune disorders. On the contrary, university

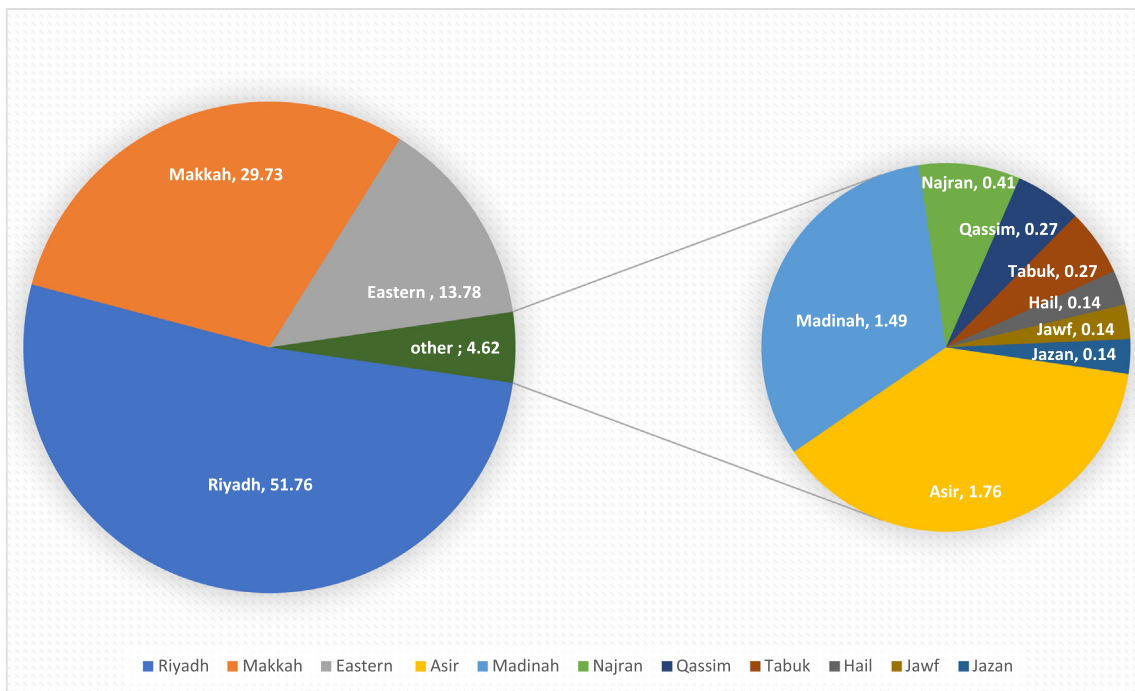


Fig. 3. The distribution of studies submitted to the Saudi Food and Drug Authority between 2009 and 2020 by the administrative regions after excluding rejected studies (N = 333).

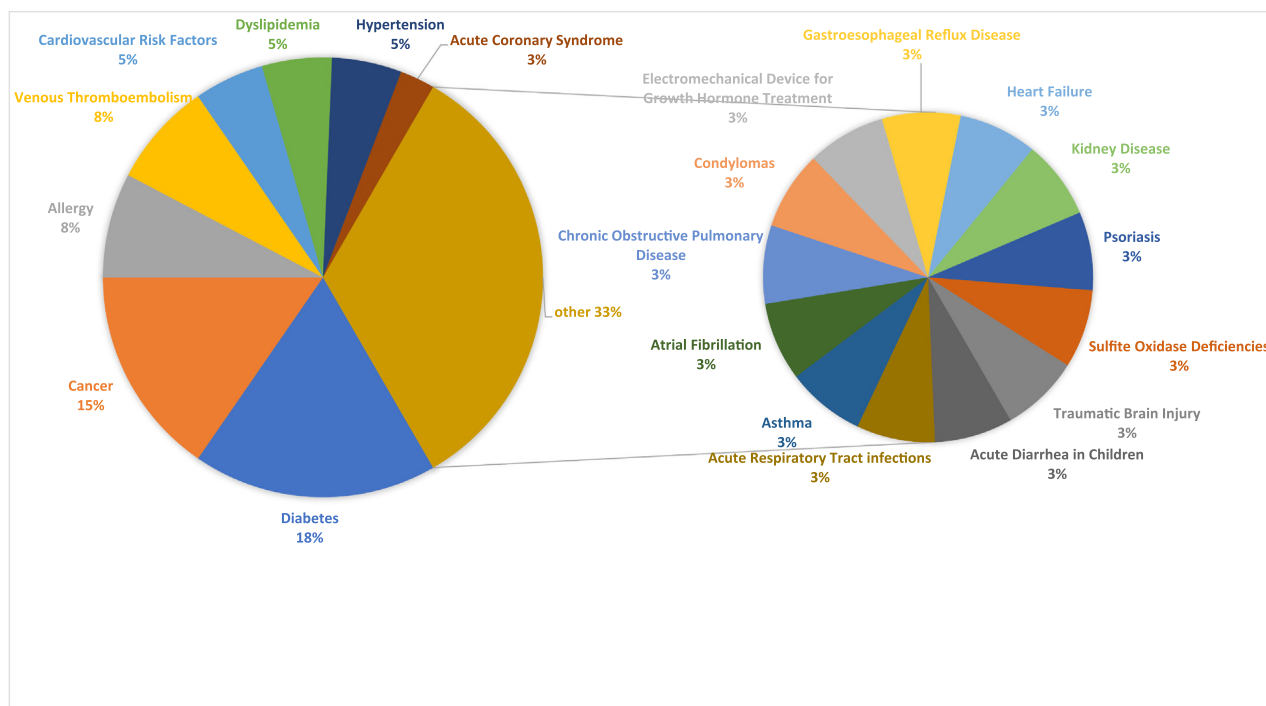


Fig. 4. The field of observational studies and registries submitted to the Saudi Food and Drug Authority between 2009 and 2020 after excluding rejected studies (N = 333).

hospitals, such as King Khalid University Hospital, had a diverse portfolio of therapeutic areas. This difference was also evident by the radar figures included in this study. Riyadh was found to be the epicenter of clinical studies as it also has significance as the capital of the KSA. Furthermore, this city excels with an abundance of renowned hospitals and skilled medical professionals. The review of therapeutic areas in the KSA showed that the top five

therapeutic areas included oncology, diabetes, immune diseases, hypertension, thromboembolic diseases, and viral diseases. These therapeutic areas are also consistent with the global orientation of the studies (Wu et al., 2015).

According to the global prevalence of diabetes, KSA ranked seventh, but only 11.7% of the studies were related to diabetes (Al Dawish et al., 2016). Generally, ethnicity and race significantly

Table 2

Therapeutic areas of the studies submitted to the Saudi Food and Drug Authority between 2009 and 2020 (n = 333).

Therapeutic areas	n (%)
AntiCancers	46 (13.81)
Antidiabetics	39 (11.71)
Observational Studies and registries	39 (11.71)
Immunosuppressants	17 (5.11)
Antihypertensives	12 (3.6)
Anticoagulants	11 (3.3)
Antivirals	11 (3.3)
Drugs for Macular Edema and Retinopathy	8 (2.4)
Vaccine	8 (2.4)
AntiAsthmatics	7 (2.1)
AntiBacterials	7 (2.1)
Drugs for Multiple Sclerosis	7 (2.1)
Interferons	7 (2.1)
Antirheumatics	6 (1.8)
Iron chelator	6 (1.8)
Antihypertensives for pulmonary arterial hypertension	5 (1.5)
Chron's Disease	5 (1.5)
Analgesic, Sedative	4 (1.2)
Antihyperlipidemics	4 (1.2)
Antiplatelets	4 (1.2)
Drugs for Conjunctivitis	4 (1.2)
Drugs for Eczema or Dermatitis	4 (1.2)
Drugs for Haemophilia	4 (1.2)
Drugs for Glaucoma	3 (0.9)
Drugs for Heart Failure	3 (0.9)
Drugs for Spinal Msucular Atrophy	3 (0.9)
General Anesthetics	3 (0.9)
Non-Steroidal Anti-inflammatory Drugs	3 (0.9)
Supplement	3 (0.9)
Ammonia Detoxicants	2 (0.6)
AntiSchizophrenics	2 (0.6)
Antifibrinolytics	2 (0.6)
Drugs for Anemia	2 (0.6)
Drugs for Heat Stroke	2 (0.6)
Drugs for Osteoporosis	2 (0.6)
Drugs for Progressive Familial Intrahepatic Cholestasis Types 1 and 2	2 (0.6)
Drugs for Vitamin D3 deficiency	2 (0.6)
Drugs for vasocclusive crisis in SCD	2 (0.6)
Morquio A Syndrome	2 (0.6)
Non-Steroidal mineralocorticoid receptor antagonists	2 (0.6)
Antidementia	1 (0.3)
Antidepressants	1 (0.3)
Antifungal	1 (0.3)
Antihyperthyroidism	1 (0.3)
Corticosteroids	1 (0.3)
Drugs for Fibrinogen Deficiency	1 (0.3)
Drugs for Glomerulonephritis	1 (0.3)
Others*	23 (6.5)

* It represents all remaining therapeutic areas that were studied only once.

impact the response of the body to the different drugs and treatments, which draws attention to the need for more studies in the KSA to explore the difference in response (Allmark, 2004; Taylor and Wright, 2005).

Overall, the number of clinical studies in KSA does not meet the demand yet (Memish et al., 1990). Alemayehu et al. showed various obstacles decelerating the progress of clinical trials in developing countries, including lack of qualified research staff such as clinical coordinators, slow approval time, difficulty in recruitment of study subjects, and busy schedule of clinicians (Alemayehu et al., 2018). Other factors may also deter the progress of the clinical trials in the KSA such as inadequacy in data management, insufficient adherence to Good Clinical Practice, and the redundancy and delay of ethical approval by the study sites (Bawazir et al., 2014). Moreover, the lack of details on the website of the SFDA related to the inclusion criteria of the studies and reliance on the English lan-

guage can also affect the awareness of the public about ongoing and new studies, thereby decreasing the enrollment of human volunteers. In contrast, the availability of the results of studies will increase participation and make patients feel empowered to make their own medical decisions (Eichler and Sweeney 2018).

There are several opportunities despite the present challenges. As the total population of the KSA is estimated to be around 34 million reported by The General Authority for Statistics (GAFS 2019). The prevalence of chronic diseases such as obesity, diabetes, and hypertension is high (Ministry of Health 2013). It can help to recruit a large number of study subjects in a shorter time, thereby reducing the cost of the recruitment process (Al-Tannir et al., 2018). Meanwhile, researchers in the KSA and study participants have also shown a positive attitude towards the conductance of clinical trials (Al-Tannir et al., 2018; Gamee 2018). Besides, the Kingdom has numerous advanced hospitals and clinical professionals (Bawazir et al., 2014). These factors provide an ideal environment and are crucial for conducting clinical trials (Minisman et al., 2012). In the KSA, the government may also support clinical research through the implementation of an expedited approval process, uniform institutional review board process across the Kingdom, financial assistance, and a supportive research environment (Ali et al., 2017). Such efforts will eventually increase the total number and quality of the clinical trials, thus improving patient outcomes (Grossi et al., 2013).

5. Conclusion

With a population approaching 34 million, the conductance of the clinical trials within the KSA during the past 11 years has been rather paltry. Since the inception of the clinical trial's administration and SCTR, the emphasis has been on phase 3 and phase 4 clinical studies. Although many sponsors funded the clinical studies, almost half of the studies were sponsored by only seven entities. The most studied therapeutic areas were oncology and diabetes. Approximately 80% of the registered studies were conducted in the Riyadh and Makkah provinces. This study does not reflect the exact number of ongoing and completed studies in the KSA as the approval of phase 4 trials from the SFDA is not mandatory as per current regulations.

6. Strength and limitations

The strength of this study is the reporting of findings using the national registry of the KSA. The previous report in the KSA was entirely based on an international registry. This study also has certain limitations. This study is exclusively based upon the information available on the website of the SFDA. There is the possibility that other studies not registered could exist. There is also a paucity of important details about the ongoing clinical studies on the SFDA website such as the completion date of the trials, the nature of the study subject included, and the results of the studies.

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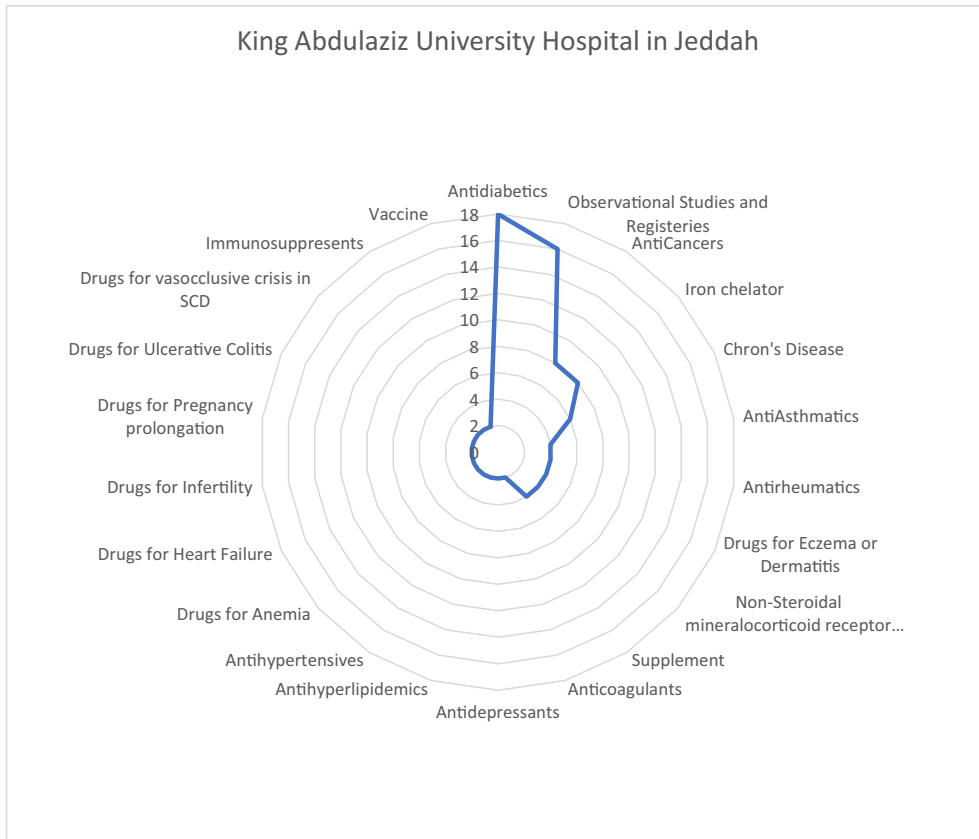
Declaration of Competing Interest

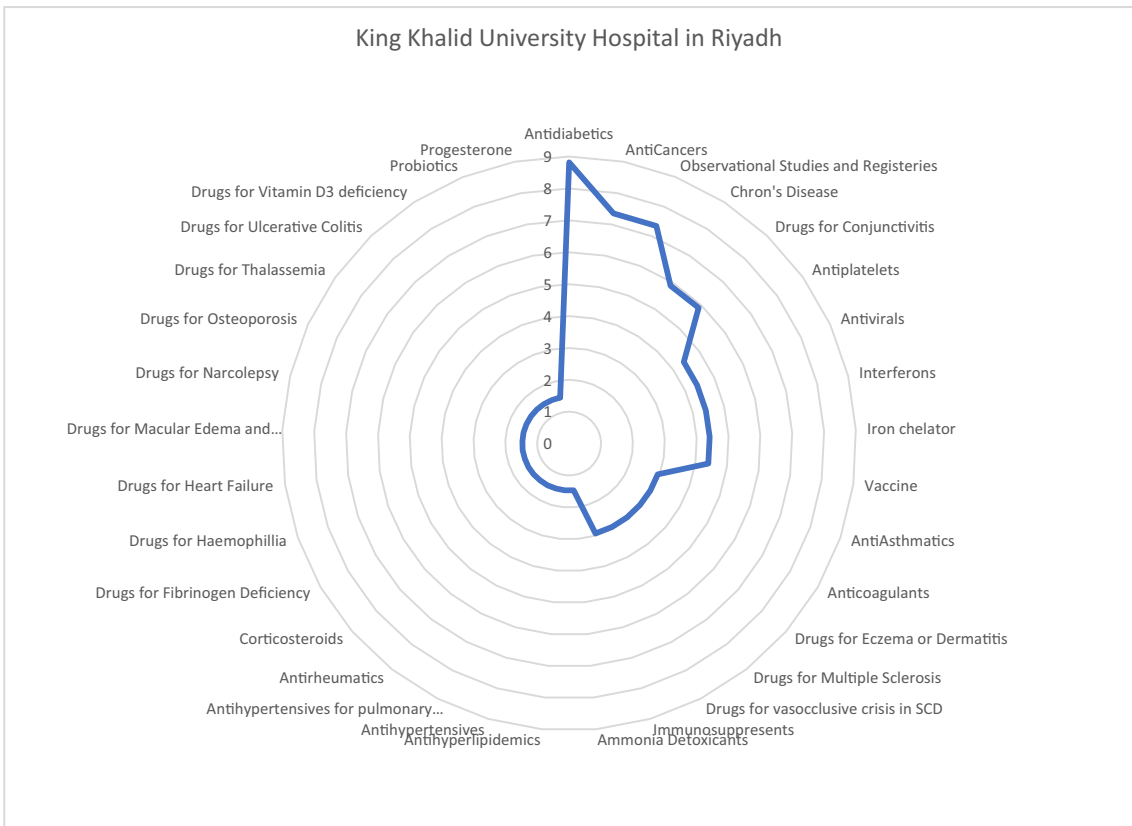
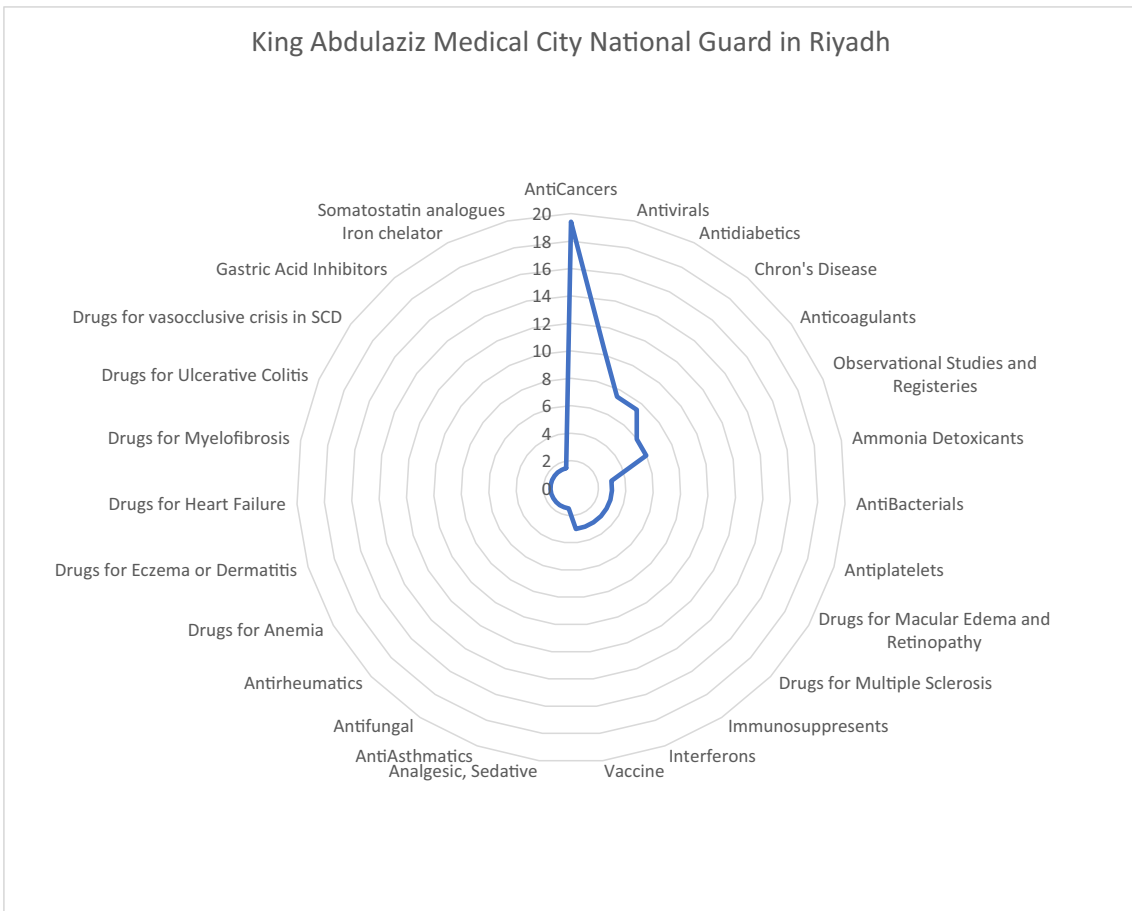
The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

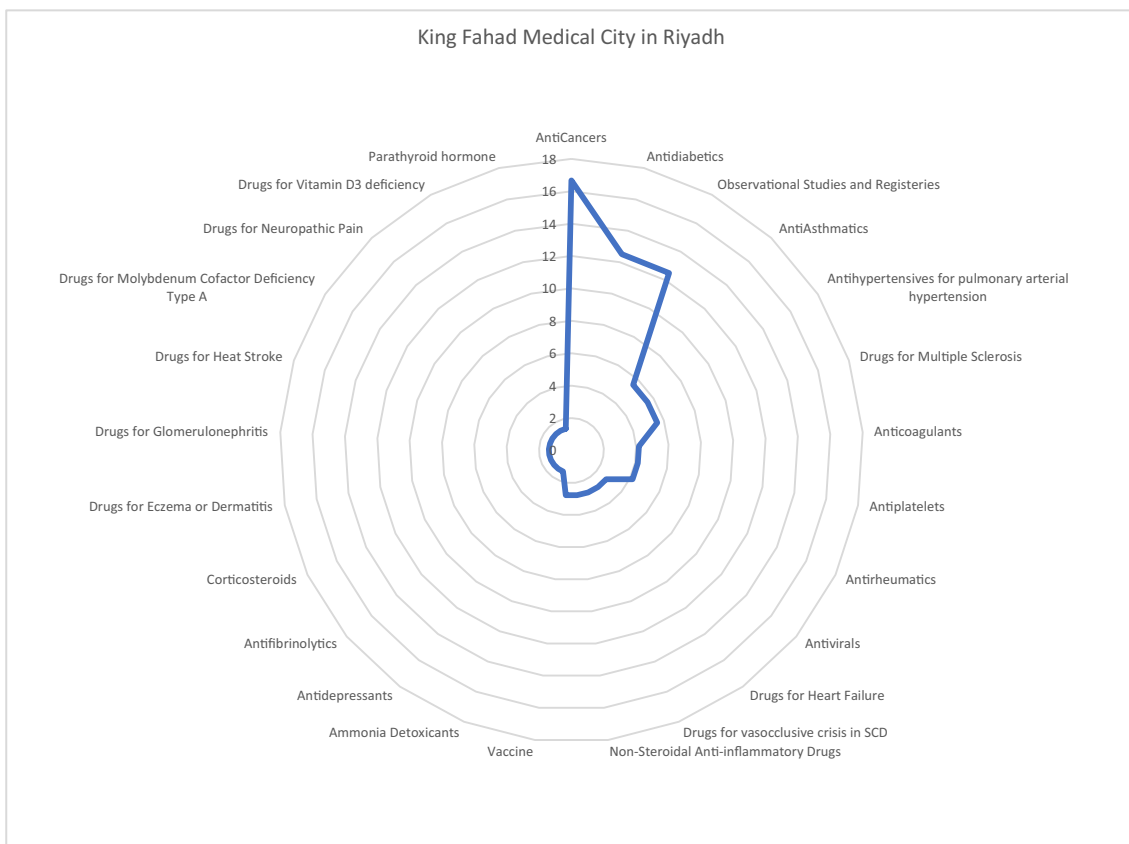
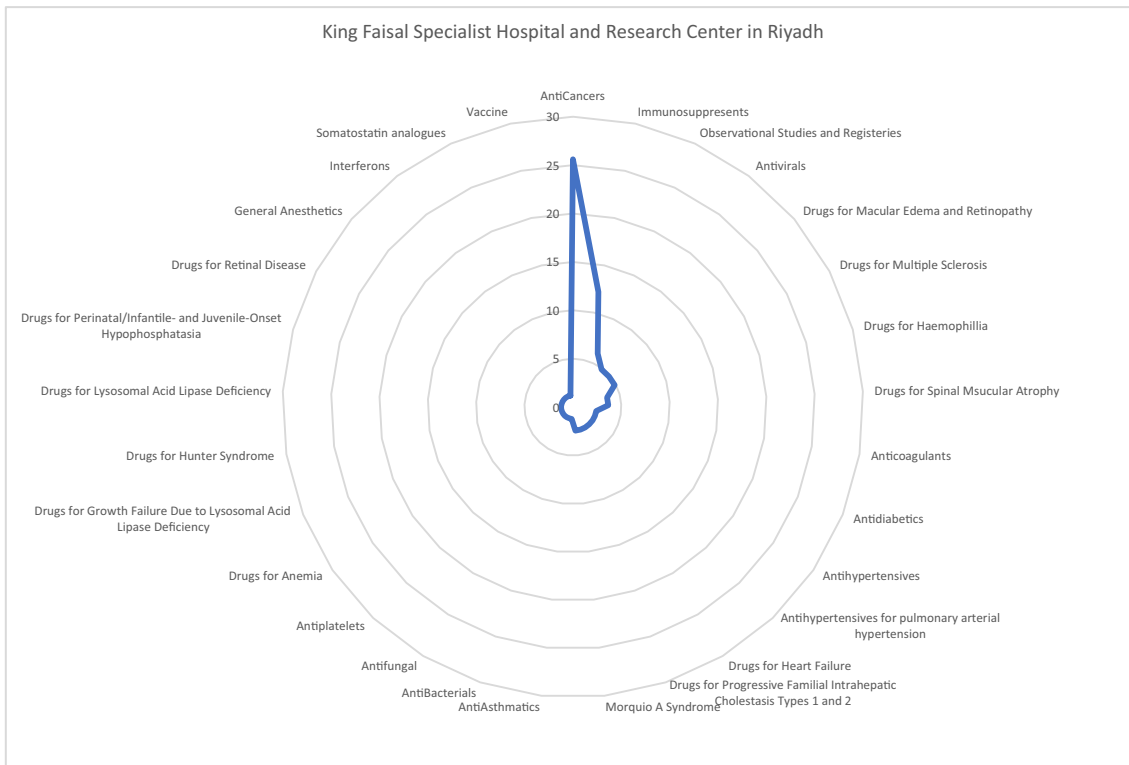
Acknowledgments

None.

Appendix A







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