Evaluating quantity and quality of literature focusing on health economics and pharmacoeconomics in Gulf Cooperation Council countries

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Objective: To evaluate the quality and quantity of health economic researches published until the end of 2017 in G.C.C. and to identify the factors that affect the quality of studies.

Method: Studies were included according to predefined inclusion and exclusion criteria. The quantity was recorded, and the quality was assessed using the Quality of Health Economic Studies (QHES) instrument.

Results: Forty-nine studies were included. The mean (SD) quality score of all studies was 57.83 (25.05), and a high number of reviewed studies (47%) were evaluated as either poor or extremely poor quality.

The factors that affect the quality of studies with statistical significance were, the type and method of economic evaluation, the economic outcome was the objective of the research, author`s background, the perspective of the study, health intervention and source of funding.

Conclusion: The use of economic evaluation studies in G.C.C was limited. Different factors that affect the quality of articles such as performing a full economic evaluation and choosing societal perspective were identified. Strategies to improve the quality of future studies were recommended.

KEYWORDS: Pharmacoeconomics, health economics, QHES, Gulf Cooperation Council, quality, quality of literature

1. Introduction

The importance of pharmacoeconomics and health economics has recently been highlighted. There has been an increase in published research in this field and a number of landmark publications, such as those done by Newhouse JP,[1] Buxton MJ et al.[2] and Cutler DM and Reber S.[3]. The utility of this research has also been realized, with the outcomes aiding optimal decision-making in medicines and medical services, ultimately improving cost-effective choices in the health sector .[4]

However, despite the potential use of these publications, this depends substantially on the quality of the research. There have been concerns about the quality of some health economics studies published in the medical literature, with some published material being categorized as poor quality.[5-7] Poor or inferior quality research not only is not helpful, but it provides confusion and casts doubt on other research, and thus it is imperative that studies are evaluated

for their ability to meet quality criteria.[8] Pharmacoeconomics and health economics are relevant to all regions, including economically growing countries such as the Gulf Cooperation Council (G.C.C) countries. G.C.C countries are a group of countries that locate in the Middle East, overlooking the Arab Gulf Peninsula in a region of the largest oil producing area in the world. It consists of 6 countries that are similar in culture, habits, environment and economy. They are The Kingdom of Saudi Arabia (K.S.A), The United Arab Emirates (U.A.E), the State of Kuwait, The Sultanate of Oman, the State of Qatar and the State of Bahrain, with a total population of 47 million and a Gross Domestic Product (GDP) of 1.6 trillion, averaging to 33.3 thousand dollar GDP per capita.[9]

The G.C.C has recently observed extraordinary growth in the GDP, if the healthcare market alone is considered, there has been an annual rise at rate of 11% from approximately US$25.6 billion in 2010 to US$43.9 billion in 2015.[10]

While the role of the economic evaluation in decision-making in developed countries was established in the early 1970s, only recently have these practices started to be used in countries like the G.C.C. However, the importance of these practices has been known for some time, providing economic evidence in support of decisions on licensing, pricing, reimbursement and formulary additions.[8]

To date, there has been no analyses conducted of the economic evaluation studies emerging from G.C.C, and there is still little information about the health and pharmacy economics studies in the region. Also, the current economic downward due to a reduction in Oil`s price and increasing population in the region so, it is imperative to evaluate the studies that originate in this region, for quantity and quality, in order to make future recommendations for research and to ensure that the studies being utilized for decision-making for medicines and medical services are based on sound evidence.

The present study's objective aimed to evaluate the quality and quantity of health economic evaluations that are emerging from the G.C.C countries, published until the end of 2017. A comparative description of the studies characteristics was also conducted to identify factors affecting the quality of research in the future.

2. Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines for conducting systematic reviews were employed.[11] A literature search was carried out between September 2, 2017, and January 1, 2018, to identify all published health economics and pharmacoeconomics evaluation research from the countries of the G.C.C in English. The search was conducted in Pub Med and used the following index terms used in search were: "cost", "budget", "fee", "health", "pharmacy", "economics", "health economics", "pharmacoeconomics", "cost-effectiveness", "cost-benefit", "cost-utility", "cost minimization" AND "Arabian Gulf countries", " Gulf cooperation council", "G.C.C. countries", "Saudi Arabia", "KSA" , "United Arab of Emirates", "UAE", "Kuwait", "Qatar", "Bahrain", "The Sultanate of Oman", "Oman". The index terms used were searched utilizing "AND" to combine keywords listed. References of retrieved articles were considered for relevant articles that may have been missed.

2.1 Article selection and inclusion criteria

The title and abstract of all retrieved articles were reviewed for relevance, if there were uncertainty about the papers; the full text article was retrieved and read for relevance. Research that was written in the English language and published up until the end of 2017 were included. Studies needed to specifically state that (one or more of) their aims/objectives were related to health-related economic analysis or cost analysis. The research should focus on health economics in one of the G.C.C countries and should be an original (Primary source) research article where the full text was available.

2.2 Data Collection and Classification

Each article was examined carefully, and detailed information about the journal and article were entered in defined data collection tool.

Information about the journals in which each study was published was collected; journal's location and scope of a journal if it is medical oriented or other such as health management, economic or business. The access of journal was classified into open access and paid journal.

Extensive data about each published article were collected; the total number of authors, country and background of the first author information were obtained from the affiliation of each study, year of publication of study and the study period. Source of funding and location of study data was collected.The geographical location of the study was classified into sub-national, national and multinational.

The detailed information regarding the economic analysis conducted in each study, was the method of economic evaluation clearly stated the objective, type of costs included, type of currency used. Articles were classified according to the perspective of economic information if it was reported or not. A perspective refers to the point of view from which an economic analysis is performed; the five most common perspectives that are often cited within pharmacoeconomic studies are: institutional, third party, patient, governmental or societal.[12]

Furthermore, articles were categorized as full economic evaluation if they meet the requirements defined by Drummond et al.[4]; cost-effective analysis (CEA), cost-benefit analysis (CBA), cost-utility analysis (CUA) and cost-minimization analysis (CMA). Articles that did not meet Drummond et al. requirements were classified as partial economic evaluations; cost description (CD), cost analysis (CA) and cost of illness (COI).

The primary health intervention discussed in the article was also examined. The health intervention of each study was classified into five categories according to the intervention covered in the study as health technology for new technology, public health if a disease and

healthcare expenditure were discussed, pharmaceutical if drug or molecule was covered, service if new or old service was assessed and surgery.

2.3 Assessing the quality of the included article

Quality of health economic studies instrument (QHES) was used as a grading system for quality of the studies included as previously described in Offman J et al.[13] The QHES is a rating instrument that provides a score out of a maximum of 100 points based on 16 question criteria. The total points based on the criteria are then totalled, and a final score classifies each study according to 5 categories[13]; extremely poor (score ≤24), poor (25≤score<50), fair (50≤score≤74), good (75≤score<100) and excellent quality (score=100).

2.4 Statistical analysis

A mean of the quality scores for each study was calculated, and standard deviation (SD) was calculated across study characteristics. Descriptive statistics were used to measure the distribution of all variables and an independent t-test used to determine if there was a significant difference in the mean quality of studies by dichotomous variables (country of author, country of journal, scope of journal, type of economic evaluation, background or experience of first author, journal access and if economic evaluation was clearly stated in the objective). A one way Analysis of Variance (ANOVA) test was used to test the statistical significance of the difference in the mean quality of studies by variable had more than two categories (Perspective of study, the source of funding, a method of economic evaluation, country of study and primary health intervention). The Pearson correlation coefficient was used to determine the relationship between quality score and sample size, number of authors and publication's year. All statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) version 18. A p-value of <0.05 was considered statistically significant.

3. RESULTS

In total, the literature search identified 4066 articles as shown in table 1. After careful reading of the abstracts and titles, 992 were excluded due to duplication which yields 3074 articles. After a detailed examination of these articles 3025 studies were excluded, 1.4% of excluded studies were not full text (n=44), 2.1% of excluded studies were not an original study (n=64), 57.7% of excluded studies were not economic evaluation analysis (n=1744), 22.7% of excluded studies were not on G.C.C (n=688), 16% of excluded studies were not on health-related (n=484), and one excluded study was not in English (Figure 1). The articles included were retrieved solely from Pubmed database, although references for each included article were examined carefully to find any health economic or pharmacoeconomics literature from G.C.C., however, no additional articles were added. Finally, 4**9** published studies that met with inclusion criteria where included [14-6**2**] (Table 2).

3.1 Studies characteristics

3.1.1 Publication characteristics

The majority of studies (n= 34) were published in international journals[14,17-19,21,24,25,27-30,35-43,45-48,50-54,57-61] and the remaining 15 studies were published in journals based in G.C.C. countries. [15,16,20,22,23,26,31-34,44,49,55,56,62] Thirty seven studies were published in medical journals, [14-20,22-26,28-33,36,38,40,41,44,46,49,50,52-62] 7 in non-medical journals[21,27,34,35,37,39,48] and only 5 studies were published in health/medical economics journals [42,43,45,47,51] (Table 3). Forty two studies published in open access journals [14,16,18-47,49-51,55-58,60-62] while 7 studies published in paid access journals [15,17,48,52-54,59] (Table 3). The earliest study was published in 1991[14] and the most recent study was published in December 2017.[62] The majority studies were published in 2016 [49-56] (Figure 2).

3.1.2 Primary author characteristics

The mean (SD) number of authors per study was 4.20 (2.97) (range,1-18), in 45 studies the main authors were residing in the same country of study[14-24,26,28-32,36-59,61,62] and only in 4 studies the main authors were residing in countries outside the G.C.C. [25,27,35,60]; these included Canada,[25] USA ,[27] UK[35] and Poland.[60] The primary author in 40 of the included studies (81.6%) had a medical or clinical background [14-24,26-30,32-34,36-47,49,51,53,55-59,61] , compared with 4 studies were the primary background was health economics [48,52,60,62], 3 studies were public health was the primary background[35,50,54] and 2 studies were the primary background was of nonmedical origin.[25, 31]

3.1.3 Geographical location of data collection

Thirty four studies were national, [14,15,18-24,26,29-34,38-41,45-50,51-55,59-62] 9 studies were sub-national (where they covered cities of interest in a country)[16,28,36,42,44,50,56-58] and 6 studies were multinational.[17, 25, 27,35,37,43]

Eighteen of the studies published were based on data from Saudi Arabia, [15,16,23,26,28,31,34,36,39,44,47,53,56-59,61,62] 11 studies on data originating from Oman, [18-22,33,38,39,49,55] 7 studies with data from the United Arab of Emirates,[24,29,40,42,43,50,60] 5 studies from Qatar, [30,45,488,52,54] 3 studies were published on Kuwait [14,37,51] and one study published on Bahrain[45] (Figure 3).

3.1.4 Funding sources

Thirty-four studies stated they did not receive any funding to conduct the research [14-17,19-23,26-28,30-33,36,38-40,44-46,50,51,53,55-59,62] Six studies were funded by government organizations,[18,24,34,35,37,41] 6 studies were funded by the pharmaceutical industry [25,29,42,47,60,61] and 3 studies were funded by non-profit organizations.[48, 52,54]

3.1.5 Condition characteristics

The majority of studies (35[71.4%]) did not state the pharmacoeconomics perspective. [14-17,19,22-37,39,41,43,45,49-51,53-59] Ten (20.4%) studies were from the provider perspective, [18,20,21,42,44,46,48,52,60,62] 3 studies (6%) were from the society perspective [38,40,61] and one study (2%) was from the patient perspective .[47] Forty two (85.7%) studies were published in open access journals [14,16,18-47,49-51,55-58,60-62] whilst 7 (14.3%) studies published in paid access journal [15,17,48,52-54,55] (Table 3).

Twenty one studies did not investigate a specific disease. [14,16,17,19,20,23,26,28,33,35,39,41,43,45,49,52,53,55,56,59] Overall, 20 diseases were investigated over 27 studies. Diabetes [24,41,54,60] and rotavirus were investigated in 4 separate studies.[21,25,38,61] Asthma was investigated in 2 studies. [32,42] Each of the following conditions were investigated by a single study: neonatal hip instability,[15] epilepsy,[18] thyroid function,[22] acute gastroenteritis,[29] trauma,[30] deep vein thrombosis,[34] uveitis,[36] invasive aspergillosis,[37] mitral valve disease,[40] infection,[44] acute tonsil pharyngitis,[46] osteoarthritis,[47] hyperlipidemia,[48] refractory chronic urticaria,[51] heart failure,[57] diabetic retinopathy,[58] and mental health.[60]

Nineteen studies focused on public health, [16,18,21,24,25,29-32,35,36,38,41-43,45,53,54,57] 12 studies on services, [14,20,22,26,27,34,46,49,50,55,56,59] 12 on pharmaceutical products, [17,20,23,39,44,47,48,51,52,60-62] 5 on health technology [28,33,37,40,58] and one study on surgery. [15]

3.2 Trends in Economic Evaluation studies

There were 40 partial [14-37,39,42,43,45,46,49-59] and 9 full economic studies; of the latter there were 4 CEA,[40,48,60,61] CBA,[41] three CUA[37,47,62] and one CMA.[44]

The economic evaluation was stated clearly as a primary outcome in 37 studies [14, 15, 18-22, 24, 26, 30-33, 35, 38-52, 54, 56-62] (Table 3).

3.3 Quality score of studies

The mean (SD) quality score of all 49 studies was 57.83 (25.05) and ranged from 15 to 100. Six studies were of an extremely poor quality, [15,22,27,28,53,59] 17 studies were classified as poor quality, [16,17,19,20,23,26,30,31,34,36,37,43,45,46,55,56,58] 14 studies were of fair quality, [14,24,25,29,32,33,35,39-42,49,50] 9 studies were of good quality, [18,21,38,44,45,46,47,57,60] and 4 studies were scored as excellent quality.[47,48,61,62]

3.4 Factors affecting the quality of studies

3.4.1 Country of origin

When country of origin was factored into the scoring, the mean (SD) quality score by country was Qatar 68.6 (24.42), U.A.E 66.42 (18.5), Kuwait 62 (33.4), Oman 60.09 (22.52), Saudi Arabia 53.16 (29.53), and Bahrain 43 (0). Summaries of the mean score as per countries are as shown in (Figure 4). There were no significant differences found when the scores were compared based on country of origin.

3.4.2 Method of evaluation

A higher quality score of studies was significantly associated $(p<0.05)$ with the type of economic evaluation used (full evaluation was higher), whether economic outcomes were stated in primary objectives of the study (whereby if this was stated as a primary objective the resulting quality of the study was higher) and the method of economic evaluation used (CUA resulted in the highest quality studies).

3.4.3 Publication and author characteristics

The quality of studies affected by the training of first author and the source of the funding but it was not affected by country of the journal, the scope of the journal, country of the author, or the number of authors. There was a positive correlation (r=0.276) between the number of authors and the quality of study as the number of authors increases, the quality of study was found to increase.

A positive correlation was also shown with respect to year of publication (r=0.256), where the most recent studies had better scores than older studies. The only negative correlation (r=0.042) was seen in sample size and quality score (Table 3).

4. Discussion

Research surrounding health economics is becoming more valued, and used to assist in decision-making in regards to health services, and thus quality and assurance of this data are paramount. This review was the first study to collectively examine the research on health economics that is originating from G.C.C countries. The primary objective was to assess the quantity, characteristics and quality of these studies and to provide recommendations for future research. The recommendations should help to inform future research that is emerging from G.C.C countries, in addition to any country that may be publishing such data.

This review found several interesting findings in regards to the quantity and characteristics of the research that is being published on this topic. Firstly, the number of studies on health economics originating from G.C.C has increased with time, especially after 2007 and peaked in 2016. This could be reflective of the increased importance of cost, cost of care, increase the prevalence of orphan diseases and increase the use of new expensive medicines and hence why it is of utmost importance moving forward to ensure quality studies are emerging. However, despite the increase in quantity, the number of studies published from this region is low when compared to other countries. Even when the absolute number of health economic evaluation studies based in Saudi Arabia (which has the highest number in G.C.C.) was compared with studies centered in the United Kingdom, Australia, the United States, and Canada, where economic analyses are formally used in health policy formulation, the numbers were still low.[4,63-66] The number was low even when compared to studies published in other developing countries, such as Korea (n = 45),[67] Zimbabwe (n=26)[68], Thailand (n = 41)[69] and Nigeria (n = 44).[70] In addition, there was a lack of studies focusing on pharmaceutical products (24.5%). These findings reflect the use of economic evaluation studies in decision-making in the region,

and these results of this review call for more research to be conducted in this region. However, this may reflect there is no requirement for submission economic data as a part of drug regulatory process in all countries of G.C.C, and thus in order for there to be a larger focus on this topic, change at a policy level may be required.

Despite this literature review being based in G.C.C. countries, most of the studies were published in international journals, based outside the region. This may reflect the absence of well-established journals in the G.C.C. region, especially in health. However, this trend in publication may have a negative implication, as many people in G.C.C countries may not have access to these international journals. This finding was found to a lesser extent in Saudi Arabia and Oman where many of their studies were published in journals of the same country.

Another major finding of this study was the high degree of poor quality research that has been published, based on the criteria of the QHES tool. In this current review, the majority of reviewed studies (47%) were poor and extremely poor quality and only 18% were good quality and 6% were excellent quality. These findings are in line with the results of research by Walker and Fox-Rushby [71] and Lee et al, [67] who also found a limited supply of good quality economic evaluation studies in developing countries. Based on the small number of publications found, it appears that health policies and plans in G.C.C are being made without sound economic evaluation data, which confirms findings by Maynard.[72] This is not a problem isolated to developing countries; Adams et al.[5] evaluated completeness of economic analysis in randomized clinical trials that published in the United States. The findings from this research were that the mean quality score of published trials was 0.32 on a scale of 0 to 1. Moreover, Udvarhelyi et al[6] explored whether published research using CEA and CUA in the United States adhered to basic analytic principles; the study found that the overall performance was only fair.

Lastly, Gerard K[7] was validating the potential benefit in policy terms of studies that have used CUA in the United Kingdom, and results revealed studies' technical execution was often of poor quality.

Most of the reviewed studies in this review were partial economic evaluations; this may reflect the lack of experience of economic studies in the region. Partial economic evaluation measures the program or disease cost, but does not involve a comparison with alternative options and does not relate costs to outcomes.[4] The COI was the most frequently used type (40%) of partial economic analysis used. Only 18% of studies conducted a full economic evaluation and 12% of studies used modeling techniques in the analysis. The CEA was the most frequently used method in the full economic evaluation analyses conducted within this review. Similarly, Teerawattananon et al.[69] in Thailand found that CEA was the most popular (full economic) study type in Thailand and Lee et al. in Korea.[67]

The quality of studies was significantly affected by seven publication factors; firstly, the type of economic evaluation used, studies with a full economic evaluation were statistically better quality. Secondly, when the primary objective of the study was economic evaluation, the research also achieved a statistically higher quality score. Thirdly, the QHES was statically significant with the method of economic evaluation used, whereby the highest score was achieved in the studies that applied CUA and CEA methods in their analyses. Fourthly, the background or experience of the primary author as studies whose primary author`s background was in health economics or public health achieved a statistically higher score, and this finding could be due to people with health economic background are more skillful in designing economic analysis. Fifthly, quality of studies was statistically significant with the perspective of the study where studies were done from a societal perspective were statistically better in quality,

the reason behind that could be; social perspective a wide financial perspective which takes into account all alternative of resources. Sixthly, when the health intervention was a pharmaceutical, the quality of studies was statistically the best due to most of the pharmaceutical intervention studies are conducted by pharmaceutical companies who are recruited expertise in economic evaluation. Lastly, the source of funding has a significant impact on the quality of studies, as studies were funded by non-profit organization achieved better quality than were self-funded, government or pharmaceutical companies.

However, the quality of studies was not affected significantly by the scope of the journal, contrary to what was reported by Neumann et al.[73] and Gerard K,[74] who found that medical journals have a higher chance of publishing poor quality studies.

It is clear that Qatar had the highest mean of the quality score, but this could be due to it has a small number of studies including the research by Al-Badriyeh D et al.[48] whose study is one of four studies that got 100 points on the quality score.

Also it must be mentioned that there is a possibility of conflict of interest in some included studies as they received funding from pharmaceutical companies such as Merk & Co,[25] Merk Sharp and Dohme (MSD),[29] GlaxoSmithKline (GSK),[42,61] Pfizer[47] and Janssen Pharmaceutical NV.[60] Qatar Foundation was the only nonprofit organisation which supported three studies.[48, 52,54]

5. Recommendations

Increase health costs and spending in G.C.C provide an urgent impetus for high quality and good quantity of health economic research emerging from the G.C.C to help decision maker to take a valuable decision in health resource allocation. This study has found that there is a great need for improvement in both the quantity and quality of economic evaluation analysis in G.C.C.

There are several strategies that can be implemented to improve quality of evaluations originating from this (and other) region. For example, incorporation of health economics or pharmacoeconomics expertise in the research team will have an impact on designing good quality studies. Moreover, setting economic evaluation as a primary objective of the research and using the full economic evaluation type, especially CUA or CEA as the method of analysis. Thinking more laterally, an example is to increase education of the topic of health economics and pharmacoeconomics in the undergraduate and postgraduate courses. Increasing knowledge surrounding the most appropriate methodology and practice to conduct these analyses will without any doubt improve understanding by future researchers.

Furthermore, by ensuring that cost-effectiveness studies were one of the requirements for registration of medicines or medical services for enlisting them in national health insurance this should have a positive effect the in development of economic evaluation in G.C.C. countries. This change could emphasize the need and importance of these evaluations in the decision-making process.

Finally, by establishing health economics and pharmacoeconomics department in governmental health authorities, national health insurance and government hospitals will allow these organizations to conduct economic evaluation studies as a part of the usual process. It is important if this is to occur to use established methodological guidelines and processes that will

help standardise future economic analyses. Ultimately, these factors will aid in establishing standardised unified pharmacoeconomic guidelines and legislation by G.C.C.

6. Limitations

This study has some limitations. The search was conducted in one database (Pub Med) which can increase the chance of missing published articles, however, to combat these reference lists were examined to ensure that other relevant studies were identified. Furthermore, some articles did not obviously describe their methods, which made it is difficult to categorize outcomes.

7. Conclusion

The number of economic evaluation studies in the period between 1991 and end of 2017 was limited in G.C.C countries. Many of the studies that have been published are of poor quality; this quality can be improved by Incorporation of health economics or pharmacoeconomics expertise in the research team and performing a full economic evaluation and choosing either CUA or CEA as the economic evaluation method. In addition, economic outcomes should be one of the primary objectives of the nstudy and analysis should be from societal perspective . Actions need to be taken to improve quality and quantity of pharmacoeconomics analysis and health outcome research and to promote the use of health economics discipline in decision-making policy, registration and reimbursement of medicines in this region.

8. Key Issues

- This study to evaluate the quality and quantity of health economic research published in Gulf Cooperation Council countries till 31-12-2017.
- The majority of Pharmacoeconomic/ Health economic researches in Gulf Cooperation Council countries were poor and extremely poor in quality based on Quality of Health Economic Studies instrument (QHES).
- Main factors that influence the quality of Pharmacoeconomic/ Health economic researches were identified.

9. Acknowledgments

10. Conflict Of Interest

The authors have indicated that they have no conflicts of interest regarding the content of this article.

Table 1: Number of search results by key term without duplication

Key term	Arabian Gulf countries	Gulf cooperation council	G.C.C. countries	Saudi Arabia	KSA	United Arab of Emirates	UAE	Kuwait	Qatar	Bahrain	The Sultanate of Oman	Oman
Cost	17	19	0	60	40	81	6	71	153	35	16	45
Budget	1	1	1	10	5	2	0	10	4	6	1	4
Fee	0	3	0	40	25	1	0	8	87	13	8	35
Health	80	51	1	100	49	569	124	88	95	151	159	185
Pharmacy	6	7	1	22	22	146	3	45	22	15	16	50
Economics	8	14	0	4	2	8	1	11	1	1	0	0
Health economics	6	12	0	15	7	6	0	7	0	1	0	0
Pharmacoeconomics	1	0	0	3	2	2	0	5	2	0	0	0
Cost-effectiveness	1	1	0	41	21	2	0	2	7	3	0	9
Cost-benefit	0	2	0	10	3	3	0	16	6	0	0	1
Cost-utility	0	0	0	5	1	0	0	1	2	0	0	0
Cost minimization	0	0	0	2	0	0	0	1	0	0	0	0
Total	120	110	3	312	177	820	134	265	379	225	200	329

Table 2: Articles included in the present study (n=49)

Study (First author`s name)	QHES	The conclusion of included studies	Method of economic evaluation
Baraka A, et al.[14]	68	Cross-matching blood by the technicians contributed to 54.4% of the total working hours. This reflected a yearly loss of 25000.00 USD	CD
Al-Umran K.[15]	15	Cost-effectiveness of running a diagnostic program for CDH was found.	CD
Al-Dawood KM.[16]	36	In 1995 occupational injuries equated to 18.3% of total injuries reported. This led to high cost of medical fees, human suffering and a decrease in productivity.	COI
Abou-Auda HS.[17]	41	The cost of unused medicines in KSA and other Gulf countries was US$150 million	CD
Al Zakwani I, et al.[18]	77	The newer drugs contribute to a high degree of total cost and therefore their additional benefit needs to be vigourously assessed.	COI
Al Khabori M, etal.[19]	44	Ear care guidelines should take into consideration how earwax can affect hearing difficulties and put a strain on resources.	COI

Study (First author`s name)	QHES	The conclusion of included studies	Method of economic evaluation
Al-Siyabi K, et al.[20]	46	In Oman patients were requested to return any medication that was not used by them. The total sum equated to 20,140 Omani Riyal. Most of these medications were for cardiovascular or infectious diseases, which were also the most expensive medications	CA
Al Awaidy SA, et al.[21]	84	A vaccination programme may substantially reduce the cost spent on treating rotovirus in Oman, the study showed that the total cost spent by the Omani government was US791,817 annually in outpatient and US$1.8million in outpatient and hospital settings, respectively.	COI
El Shafie K, et al.[22]	21	In patients presenting with neck swelling, thyroid function tests are necessary. Restraint should be used in those with just fatigue or palpitations.	CD
Alsultan_MS, et al.[23]	38	A waste of resources was evident in terms of IV PPI use in patients in the non-ICU setting, receiving treatment for stress-ulcer prevention for these patients, which as a result put a burden on the total budget of the health .	CA
Al-Maskari F, et al.[24]	71	Healthcare resources to reduce the impact of DM, including DM care guidelines, screening for complications and better management may assist in reducing the cost. This study found that the cost of DM was heightened in disease progression with complications, and a large proportion of this cost was due to hospitalisations.	COI
Khoury H, et al.[25]	52	A vaccination programme may substantially reduce the cost spent on treating rotavirus in the Middle East and North Africa This vaccine must have a broad and consistent serotype coverage to account for the variety of strains seen in these regions.	COI
Study (First author`s name)	QHES	The conclusion of included studies	Method of economic evaluation
Al Saran K, Sabry A.[26]	42	KSA shows that the treatment cost for a hemodialysis patient is below the cost in the industrialized world.	COI
Khaliq AA.[27]	21	Saudi Arabia is fronting obstacles in many different aspects so they can manage to develop a successful health care infrastructure which is not unique .this can be accomplished by implementing strategies that can lead them to accomplish their target.	CD
Alameddine M, Nassir A.[28]	24	Urine Cytology test shouldn't be used as a diagnostic strategy for Urothelial cancer patients except in certain conditions.	CD
Howidi M, et al.[29]	74	Children who are below five years old and acquired gastroenteraitis affected their parents on a productivity scale causing at least one day off and an average loss of $64 USD.	COI
Tuma MA, et al.[30]	42	Occupational injuries happening on construction sites such as falling from height is the most crucial source of trauma, which causes a high weight on the health care system budget.	COI

Alhowaish AK, et al.[31]	43	The forecasted cost for the national healthcare for DM is going to exceed US$0.87 billion including both direct and indirect costs	COI
Al-Busaidi NH, et al.[32]	70	MOH expenditure for asthma medications is considered low compared to the high expenditure for inpatient and emergency visits Better asthma control can correlate with a positive impact on the total expenditure for the MOH.	COI
Khan SY, et al.[33]	64	The study suggests that laparoscopic surgery is more expensive versus open-appendectomies, but it is still safe and doesn't rise the morbidity nor the hospitalization time.	CA
Algahtani F, et al.[34]	46	Low molecular weight heparin to treat deep vein thrombosis aree cost effective and provide no difference in outcomes.	CA
Alkhamis A, et al.[35]	65	Health finance reform in GCC countries could substantially improve the efficicency and equitable nature of spending in healthcare services, and may reduce out of pocket spending.	CD
Bawazeer AM, et al.[36]	42	Only 2 of the whole patients with Anterior uveitis were Human leukocyte antigen B27 presented in the study. taking into consideration that Human leukocyte antigen B27 cost is around 1000 Saudi riyal, so requesting Human leukocyte antigen B27 test for all uveitis patients seems not to be cost effective	CD
Study (First author`s name)	**QHES**	The **conclusion of included studies**	**Method of economic evaluation**
Ahmad S, et al.[37]	26	PCR assay's based method for identifying (34-Bp tandem repeat/L98H) mutations is easy to run, available in most laboratories, with short processing time and low cost.	CD
Al Awaidy ST, et al.[38]	97	Pentavalent Rotavirus vaccination has a significant impact on lowering of Rotavirus Gastrointestinal disease burden in Oman. This intervention is cost effective from both payer prospective and societal prospective. Application of universal vaccination will reduce parental work loss resulted from Rotavirus gastroenteritis attacks in children.	CUA
Al Balushi K, et al.[39]	*50*	Oman emergency department drug prescribing behavior showed that Non-steroidal anti-inflammatory drugs were the most prescribed followed by cardiovascular disease medication, then respiratory and finally gastrointestinal. The highest expenditure for a drug class was Anti-Infective drugs.	CD
Mihaljevic T, et al.[40]	63	Although Robotically assisted metal valve repair surgery's cost is considered high, it still offers lowest postoperative cost, fastest return to work, and high clinical benefit. To be cost effective this procedure should be applied in volume centers.	CEA

Study (First author`s name)	QHES	The conclusion of included studies	Method of economic evaluation
Al-Qadhi W, et al.[41]	62	Patient health questionnaire (PHQ2 and PHQ9 were equivocal) as a screening instrument for depression and their use in primary care has cost saving potential.	CD
Alzaabi A, et al.[42]	72	Due to the reported cases of asthma in Abu Dhabi in the emergency departments and the subsequent high expenditure there is a high burden on the healthcare budget. This data also indicates that asthma is not adequately controlled.,	COI
Hamidi S.[43]	32	This study suggests that there is an area of improvement in health policies in Abu Dhabi through switching from inpatient care to outpatient home care service and day surgery. Implementing cost constrain measures for pharmaceuticals. Finally focusing and funding of preventive care instead of curative care.	CD
Joosub I, et al.[44]	97	Mean total costs per day were not significantly different between imipenem/cilastatin and meropenem, which implies that the overall cost of treating moderate to severe infections is only affected to a small degree by the medications.	CMA
Al-Kaabi SK, et al.[45]	49	Gulf Cooperation Council expenditure for managing non-communicable diseases (cardiovascular disease, mental health, behavioral disorders, cancer, respiratory disease, and diabetes) was above the official targeted expenditure .The total bill for all these diseases were US$36.2 Billion.	COI
Study (First author`s name)	QHES	The conclusion of included studies	Method of economic evaluation
Al Alawi S, et al.[46]	43	Using Ceftriaxone in the Out Patient clinic in Bahrain for treating Acute Tonsillopharyngitis is considered safe, clinically effective ,and cost effective, with minimum Side effects and readmissions	CA
Nasef SA, et al.[47]	100	Osteoarthritis Patients who are above 65 years treated with Celecoxib with/without PPI co-therapy was found to be highly cost effective for medium and long term usage.	CUA
Al-Badriyeh D, et al.[48]	100	The study suggests that the dyslipidemic medications atorvastatin and pravastatin should be used as a first line therapy, while rosuvastatin to be used as an alternative option	CEA
Akhwand S, et al.[49]	71	Institutional 'Do Not Resuscitate' (DNR) policies may help to reduce healthcare costs and improve services. However, these need to be used with a careful assessment.	CD
Hamidi S, et al.[50]	60	Neuropsychiatric services were only covered in 18% of the insurance plan in Abu Dhabi. Out of this 18%, 33% were fully covered and 67% were required to co-pay .It is suggested that basic insurance plans should fully cover neuropsychiatric services.	CA
Al-Ahmad M, et al.[51]	92	Though omalizumab cost is high, it reduces Emergency and Outpatient cost due to its clinical effectiveness. In addition because it's safe, it will be more economic effective if it was self-administrated at home.	COI

Al-Badriyeh D, et al.[52]	86	Based on evidence of the multi indication PPI Scoring model. It was found that esomeprazole and rabeprazole are preferred as a first line treatment in Qatari government hospitals and this has the potential of lowering the hospital PPI expenditure by 15%.	CA
Maraiki F, et al.[53]	18	Using Plastic Bags for I.V mixture provide a benefit over I.V glass bottle which may reduce the cost without affecting the drug stability.	CA
Bener A, et al.[54]	66	The burden of diabetes in Qatar is larger than expected by International Diabetes foundation. Medication and diabetes mellitus complication is the main contributor of the cost. The increasing obesity with diabetes prevalence and need for medical treatment will drastically pressure the health budget.	COI
Islam SS, et al.[55]	37	The rate of Computed tomography increased by 67% between 2010 and 2014, which reflected on an up rise in the emergency department expenditure and a higher waiting time.	CA
Alawi MM, et al.[56]	46	A stewardship program for prescribing antimicrobial showed high safety, clinical and cost-effective as a preventive measure against Multi drug resistant infections.	CA

Study (First author`s name)	QHES	The conclusion of included studies	Method of economic evaluation
Salem K, et al.[57]	79	Congestive heart failure with reduced ejection fraction puts a large economic and disability load on one non-Organization for Economic Cooperation and Development Middle Eastern countries.	COI
Al-Otaibi H, et al.[58]	48	RETeval Screening device could be the first device to distinguish patients that require further investigation for high threating diabetic retinopathy due to its outstanding sensitivity.	CA
Hindawi S, et al.[59]	21	This study showed a deviation from the current policy instructing Universal testing and switching it to a Universal Leukodepletion with exception to donors from endemic or risky donors. This outcome due to the fact no donor was confirmed with a Human T-cell lymphotropic virus type1 and type 2 (HTLV1-HTLV2) from a pool of donors. If this is applied this will reduce the cost of tests without hindering the safety.	CD
Schubert A, et al.[60]	93	Treating with Canagliflozin 100mg /300mg is more clinically and cost effective when compared with Dapagliflozin 10 mg or Empagliflozin 10mg/25mg in a patient with type 2 diabetes mellitus.	CEA

Al-Aidaroos AY, et al.[61]	100	The Current Rotavirus vaccination is estimated to reduce the overall Rotavirus gastroenteritis burden by 65% over a life time with a reduction in outpatient and emergency visits by 87%. Cost neutrality is achieved if the price of vaccine per course is less than SAR 178.20.	CEA
Alsaqa'aby MF, et al.[62]	100	All disease-modifying drugs included in the study were not cost effective in treatment relapsing-remitting multiple sclerosis at willing to pay threshold $100,000, and the threshold should reach $300,000 to be cost-effective.	CUA

Table 3: Quality score and its relation to study characteristics

Study characteristics	No. Studies	Mean of QHES	SD	(P-Value)Statistical test
Country of journal				(0.241) independent *t*-test
Same country of study	15	51.46	24.56	
Outside the country	34	60.64	25.1	
Scope of journal				(0.574) independent *t*-test
Medical	37	56.67	24.2	
Other	12	61.41	28.32	
Country of the first Author				(0.994) independent *t*-test
Same country of study	45	57.96	25.97	
Outside	4	57.75	29.88	
Background or experience of the first author				(0.032)** independent *t*-test
Medical	40	54.22	24.61	
Other	9	73.88	21.33	
Geographic location of the study				
Sub national	9	56	23.09	
national	34	61.55	25.78	
multinational	6	39.5	16.67	
Country				(0.702) One way ANOVA
G.C.C.	4	44.75	18.62	
Bahrain	1	43	0	
Kuwait	3	62	33.4	
Qatar	5	68.6	24.42	
Saudi	18	53.16	29.53	
UAE	7	66.42	18.5	
Oman	11	60.09	22.52	
Source of funding				(0.008)** One way ANOVA
Government	6	57.83	28.77	
Pharmaceutical	6	81.83	19.14	
No fund	34	51.29	23.98	
Nonprofit organization	3	84	13.95	
Study perspective				(0.00)** One way ANOVA
Provider	10	79.8	20.03	
society	3	86.66	20.55	
Patient	1	100	0	
Study characteristics	**No. Studies**	**Mean of QHES**	**SD**	**(P-Value)Statistical test**

Not stated	35	47.88	19.4	
Method of economic evaluation				(0.000)** One way ANOVA
CBA	1	62	0	
CEA	4	89	17.64	
CUA	3	99	1.73	
CMA	1	97	0	
COI	16	62.06	17.76	
CD	13	38.23	19.7	
CA	11	48.36	17.32	
Type of economic evolution				(0.000)** independent *t*-test
Full	9	90.22	15.88	
Partial	40	50.55	20.59	
Was economic evaluation stated in objective?				(0.001)** independent *t*-test
yes	37	64.29	24.26	
no	12	37.91	15.41	
Health intervention				(0.001)** One way ANOVA
Health technology	5	45	19.33	
Public health	19	59.52	20.39	
Pharmaceutical	12	78.53	26.2	
Service	12	43.33	17.06	
Surgery	1	15	0	
Journal Access				(0.351) independent *t*-test
Opened access	42	59.21	23.34	
Paid access	7	49.57	34.69	
Sample size				(0.779) Pearson Correlation
Listed	40	57.62	25.11	
Not listed	9	58.77	26.23	
Pearson Correlation, r				-0.042
Number of authors				(0.055) Pearson Correlation
less than 5	32	52.12	23.71	
More than or equal 5	17	64.82	26.71	
Pearson Correlation, r				0.276
Year of Publication	49	57.83	25.05	(0.076) Pearson Correlation
Pearson Correlation, r				0.256

Lowest QHES=15 and highest QHES=100   ****p<0.05**

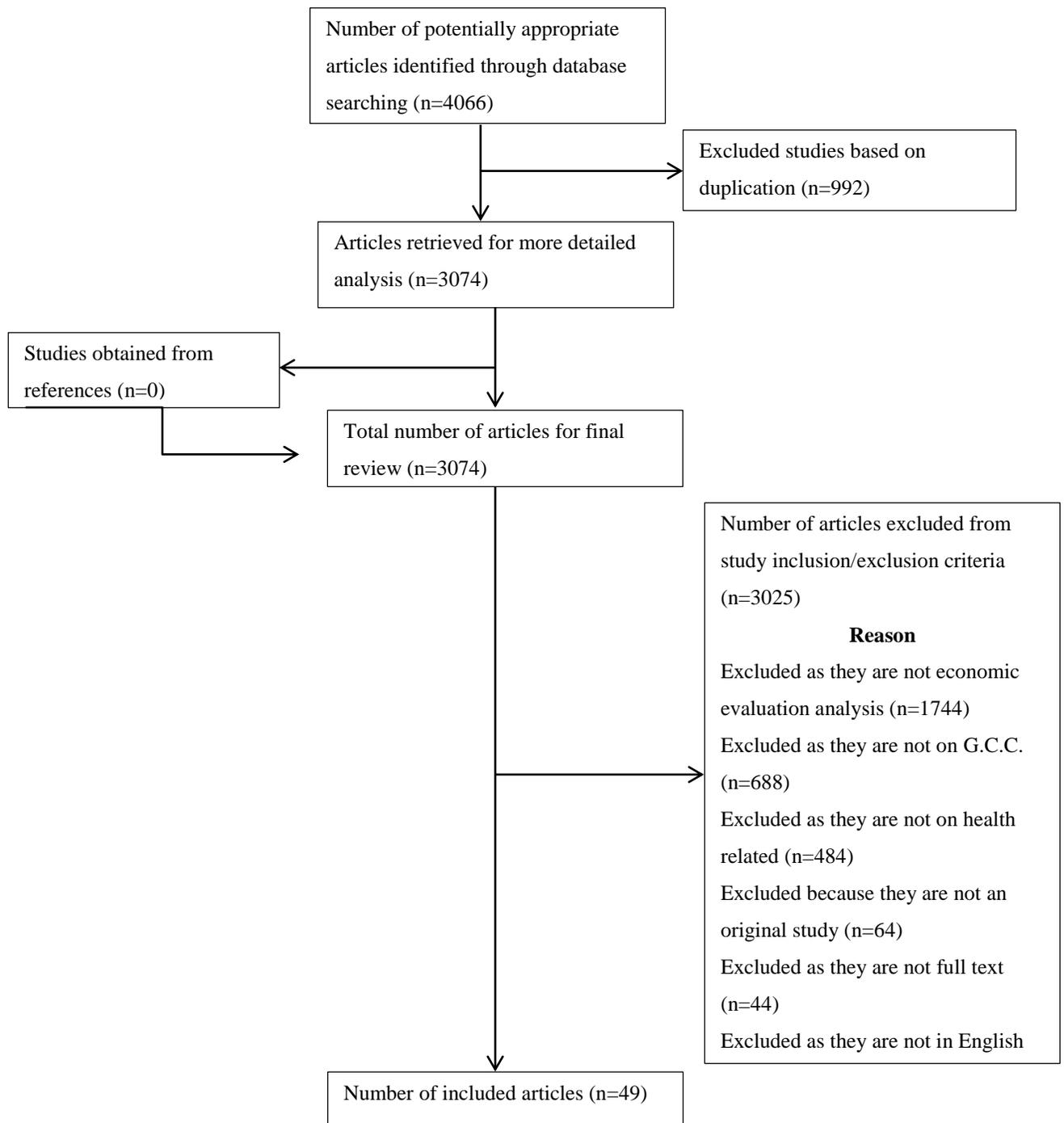**Figure 1: Study selection flow diagram (based on PRISMA guidelines).**

Number of potentially appropriate articles identified through database searching (n=4066)

Excluded studies based on duplication (n=992)

Articles retrieved for more detailed analysis (n=3074)

Studies obtained from references (n=0)

Total number of articles for final review (n=3074)

Number of articles excluded from study inclusion/exclusion criteria (n=3025)

Reason

Excluded as they are not economic evaluation analysis (n=1744)

Excluded as they are not on G.C.C. (n=688)

Excluded as they are not on health related (n=484)

Excluded because they are not an original study (n=64)

Excluded as they are not full text (n=44)

Excluded as they are not in English

Number of included articles (n=49)

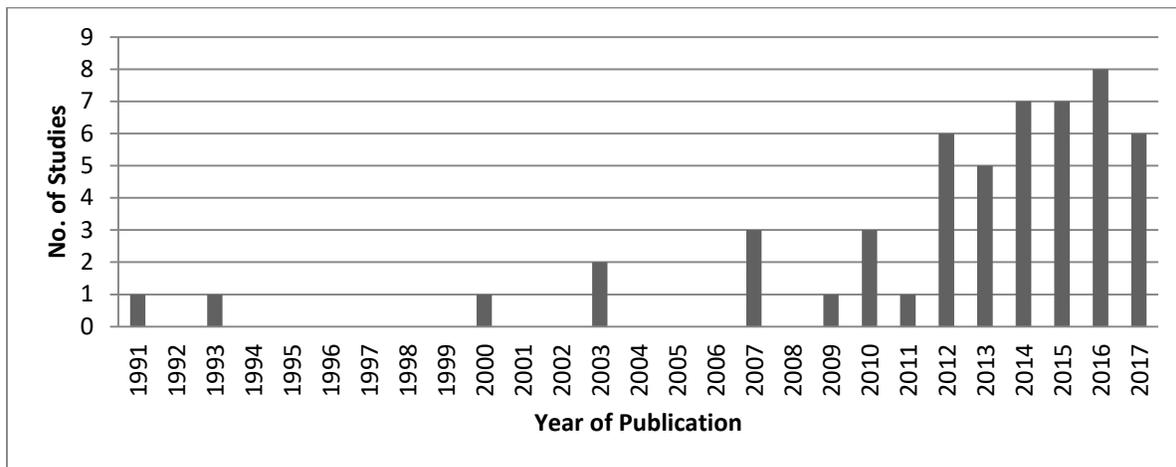**Figure 2: Number of published studies per year**

Figure 3: The Proportion of studies of each country in the total included studies
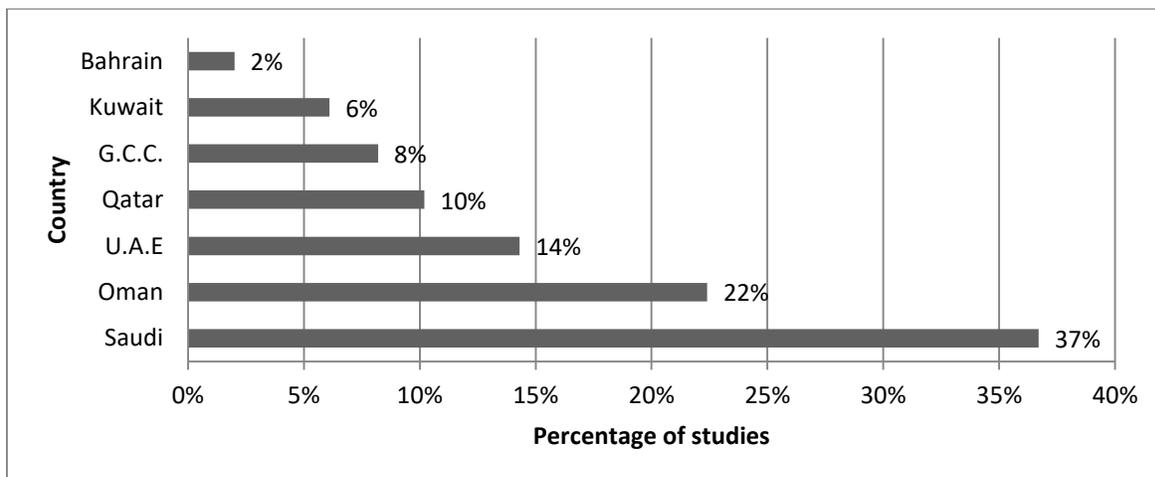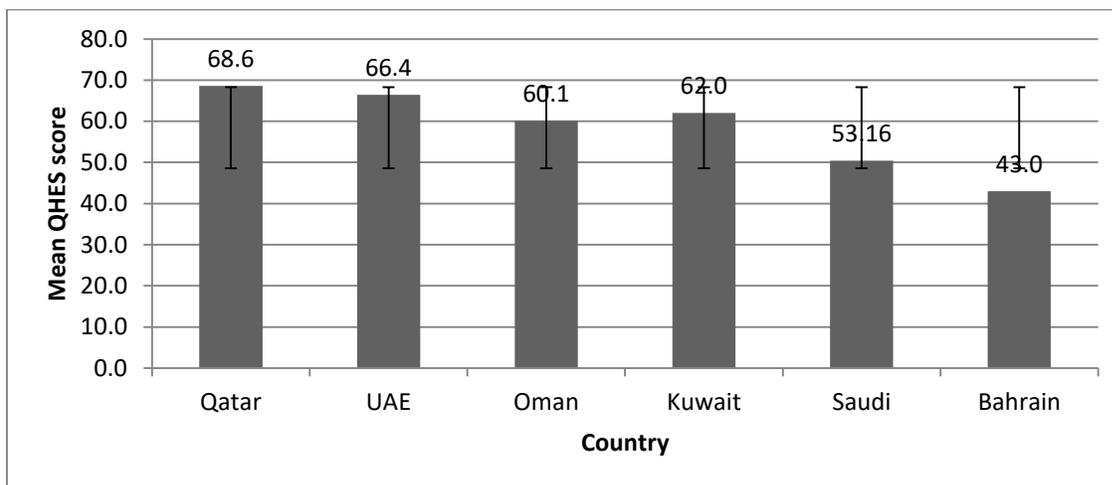
Figure 4: Summery of mean QHES per country

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Appendix

Quality of health economic studies instrument (QHES)

Question	Point	Yes	No
1 Was the study objective presented in a clear, specific, and measurable manner?	7		
2 Was the perspective of the analysis (societal, third-party payer, etc.) and reasons for its selection stated?	4		

3	Were variable estimates used in the analysis from the best available source (i.e., Randomized Controlled Trial – Best, Expert Opinion- Worst)?	8		
4	If estimates came from a subgroup analysis, were the groups pre specified at the beginning of the study?	1		
5	Was uncertainty handled by: 1) statistical analysis to address random events; 2) sensitivity analysis to cover a range of assumptions?	9		
6	Was incremental analysis performed between alternatives for resources and costs?	6		
7	Was the methodology for data abstraction (including the value of health states and other benefits) stated?	5		
8	Did the analytic horizon allow time for all relevant and important outcomes? Were benefits and costs that went beyond 1 year discounted (3-5%) and justification given for the discount rate?	7		
9	Was the measurement of costs appropriate and the methodology for the estimation of quantities and unit costs clearly described?	8		
10	Were the primary outcome measure(s) for the economic evaluation clearly stated and did they include the major short-term, long-term and negative outcomes?	6		
11	Were the health outcome(s) measures/scales valid and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used?	7		
12	Were the economic model (including structure), study methods and analysis, and the components of the numerator and denominator displayed in a clear, transparent manner?	8		
13	Were the choice of economic model, main assumptions and limitations of the study stated and justified?	7		
14	Did the author(s) explicitly discuss direction and magnitude of potential biases?	6		
15	Were the conclusions/recommendations of the study justified and based on the study results?	8		
16	Was there a statement disclosing the source of funding for the study?	3		
	Total points	**100**		

Source: Offman J et al. (2003) [13]