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Efficacy of Oxford-AstraZeneca (ChAdOx1 CoV-19) vaccine against Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) cases, hospital admissions, type of variants, and deaths

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Abstract. – OBJECTIVE: The Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) epidemic has instigated enormous damage to the global healthcare system and economies. A large number of vaccines have been developed. However, confidence in any COVID-19 vaccine is essential for its sustainable success. The present study aimed to investigate the efficacy of the Oxford-AstraZeneca (ChAdOx1 CoV-19) vaccine against SARS-COV-2 cases, hospital admissions, type of variants and deaths.

MATERIALS AND METHODS: This study recorded data using electronic platforms PubMed, Web of Science, World Health Organization, US-Food and Drug Authorities-FDA, Facts sheets, and Pharmaceutical Websites. Initially, 278 articles and reports were identified, and after revising the abstracts, 39 studies, clinical trials and organizations, reports were selected for a detailed analysis.

RESULTS: The efficacy of the Oxford-AstraZeneca COVID-19 vaccine against symptomatic COVID-19 cases after the first dose was 60.59% (p=0.00001) and after the second dose was 66.84% (p=0.00001). The highest efficacy was against the Alpha variant 58.80% (p=0.00001) and the lowest efficacy was against the Beta variant 30.83% (p=0.00001). However, the overall efficacy against the SARS-CoV-2 variants after the first dose was 49.20%. The highest efficiency of SARS-CoV-2 variants after the second dose against the Beta (B.1.351) variant was 90.34% (p=0.00001), while the lowest efficacy was against the Omicron (B.1.1.529) variant 46.46% (p=0.00001), with overall efficacy against SARS-CoV-2-2 variants after the second dose 73.73%. The highest efficacy against emergency admission was 94.42% (p=0.00001), while the lowest efficacy was 86.57% (p=0.00001), with overall efficacy against ICU, hospital, and emergency admissions after the second dose was 87.74%. Furthermore, the efficacy of the Oxford-AstraZeneca vaccine against deaths after the second dose was 87.44% (p=0.00001).

CONCLUSIONS: The efficacy of the Oxford-AstraZeneca COVID-19 vaccine against symptomatic COVID-19 cases, various variants, ICU, and emergency admissions, and against deaths was high. The present study results provide valuable insights for healthcare workers, policymakers, and researchers about the precise efficacy levels against symptomatic cases, hospitalization, and mortality across the diverse populations and age groups.

Key Words:
Oxford-AstraZeneca, Efficacy, SARS-CoV-2, COVID-19 pandemic.

Introduction

The Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) outbreak, also known as the COVID-19 pandemic, has caused an unprecedented public healthcare and economic crisis worldwide. The outbreak originated in Wuhan, Hubei Province in December 2019 and was declared a global pandemic on 11th of March, 2020, by the World Health Organization. The virus spread globally, causing over 768.18 million cases and 6.94 million deaths as of June 20, 2023[1].

The difficulty in controlling COVID-19 is attributed to its high transmission rate, which allows rapid spread from person to person, lack of symptomatic cases which makes it difficult to identify and isolate patients, and a long incubation period of 2 weeks during which an infected person may spread it to others[2]. The emergence of the Omicron SARS-CoV-2 new variant has different biological and epidemiological characteristics making it more contagious than other variants[3].

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The more infectious mutated variants, such as the delta and Omicron variants, have further complicated efforts to control the pandemic by limiting the vaccine's effectiveness[4].

While facing all these challenges, the medical community tirelessly worked round-the-clock to develop several types of vaccines. The SARS-CoV-2 virus has surface spike proteins (S-protein) through which it binds to the host angiotensin-converting enzyme 2 (ACE2). Antibodies produced against the vaccine bind to the S-protein, preventing its attachment and endocytosis by the host cells, neutralizing the virus[5]. The several types of vaccines currently available include mRNA vaccines Pfizer-BioNTech and Moderna, viral vector vaccines Janssen and AstraZeneca, and inactivated vaccines Sinovac and Bharat Biotech's Covaxin[6].

The Food and Drug Administration (FDA) issued emergency authorization for COVID-19 vaccines in December 2020[7]. The global coverage of COVID-19 vaccines currently stands at around 70% of the total population. Despite the progress made in vaccine affordability and distribution, low- and middle-income countries are still particularly affected by limited access, with only 32.3% of the total population receiving at least one vaccine dose. This contrasts with high-income countries, where over 74.8% of the population has been fully vaccinated[8]. The World Health Organization has called for more equitable access to vaccines, highlighting international cooperation's importance in addressing this global challenge[9].

The Oxford-AstraZeneca vaccine, also known as Covishield, is an adenoviral vector vaccine primarily distributed in India, Brazil, and the United Kingdom[10]. Of the two billion doses administered, two-thirds have been distributed through COVAX facility[11]. This vaccine has several advantages over other COVID-19 vaccines, hence favored in LMICs. It is easier to transport, and store compared to other vaccines, which require ultra-cold storage temperatures. Additionally, it is cheaper to produce and purchase, making it more accessible with limited resources. Although safety and side effects analysis are not a prime objective of this study, there have been concerns regarding reports of thrombosis with thrombocytopenia syndrome in individuals who have received the AstraZeneca vaccine[12].

The literature on the efficacy of AstraZeneca is still lacking and more studies are needed to be conducted on the topic. In this study, we aimed to examine the effectiveness of the AstraZeneca vaccine against COVID-19 infection, ICU admissions, hospitalizations, and mortality. The analysis includes data from studies conducted worldwide on heterogeneous populations and considered factors such as dosing strategies and efficacy against various variants. By providing important data regarding the effectiveness of the AstraZeneca vaccine, this study provides valuable insights that can aid policymakers, public health officials, and healthcare providers in making informed decisions about vaccine deployment and vaccine prioritization strategies. It will also pave the way for future research and guide the development of effective public health interventions to combat the COVID-19 pandemic.

Materials and Methods

The present study was conducted in the "Department of Physiology, College of Medicine, King Saud University, Riyadh, Saudi Arabia".

Selection of Studies and Data Collection

The data were collected using electronic platforms such as PubMed, Web of Science, and other evidence-based websites, including the World Health Organization, US Food and Drug Authorities-FDA, and AstraZeneca Fact Sheets, Pharmaceutical Company Websites. We filtered the data using the key terms SARS-CoV-2, COVID-19 vaccine, Oxford-AstraZeneca, effectiveness, efficacy, ChAdOx1, AZD1222, and Vaxzevria. From the 278 results, after screening, we identified 142 articles and reports. After going through the abstracts, finally, 39 studies[13-51] were selected for a detailed analysis and discussion (Figure 1). These studies included phase 2/3 randomized control trials, real-world studies, and observational studies evaluating the effectiveness of the Oxford-AstraZeneca vaccine.

Inclusion and Exclusion Criteria

There were no limitations on study design, type, or publication language. We included studies with a heterogeneous population with no limitation on the age or gender of participants, variants of COVID-19, comorbidities, and baseline serological status. The types of outcomes measured the efficiency of the Oxford-AstraZeneca vaccine against precise disease endpoints, including symptomatic COVID-19 infection, ICU admission, and all-cause mortality. For each outcome, we did not take the time from vaccine ad-

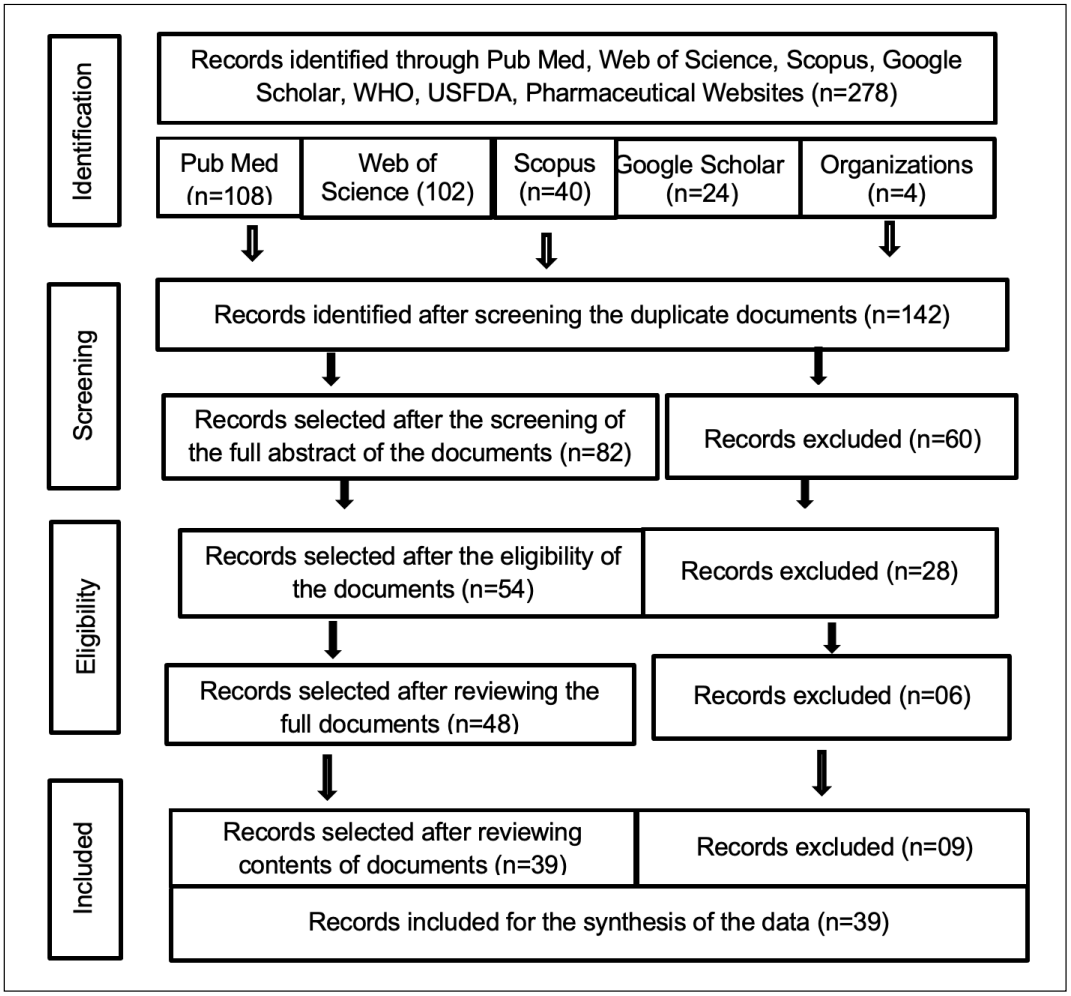

Figure 1. PRISMA Flow Diagram for the selection of documents.

ministration into account. Instead, the maximum effect, regardless of the time from dose administration, was included in the data set. When there were vaccine effectiveness results available for both the entire sample and subgroups (such as different age groups or time intervals), we focused on extracting data from the full sample. However, we also included separate data from subgroups when applicable or full data was not available. Additionally, we collected basic information about the studies (such as year of publication, author, title, country, format, and study design), as well as details about vaccine doses, the timing of outcome assessments since vaccination, and the type of variant. The outcomes were separated into one or two doses administered where available. When measuring AstraZeneca booster dose efficacy, we only included studies with full primary series homologous vaccine schedule data. We also measured the effectiveness of the vaccine against various variants, including Alpha (B.1.1.7), Beta (B.1.351), Gamma (P.1), Delta (B.1.617.2), and Omicron (B.1.1.529), B.1.128. For studies where the specific data on variants were not available, the variant that was a majority in that population or cohort at that specific period was considered for analysis. For each outcome, we extracted the 95% confidence interval (CI) as reported by the authors when available.

Statistical Analysis

The data were collected and arranged in an Excel worksheet. The data were rechecked by another team member before analysis. The statistical analyses were performed using "Review Manager 5.4.1". The overall efficacy of the Oxford-AstraZeneca COVID-19 vaccine with 95% confidence intervals (CIs) was estimated using the Mantel-Haenszel method[50]. A value of $p < 0.05$ was considered as the level of significance. The

Cochrane Chi-squared test was used to evaluate heterogeneity among articles, with a $p < 0.05$ indicating the existence of heterogeneity. To estimate the impact of heterogeneity on the meta-analysis, the I^2 value was calculated. I^2 values ≥ 50% and $p < 0.05$ indicated a moderate to high degree of heterogeneity among pooled studies. A fixed-effect design was used when $I^2 < 50\%$ and $p > 0.05$; otherwise, a random-effects model was adopted"[51].

Results

The studies recruited samples from over 13 countries, including the UK, Brazil, Scotland, Spain, India, Hungary, Argentina, Malaysia, Sweden, the US, Chile, Peru, and South Africa. Out of the total studies analyzed, data on double dose were only included in 16 studies, data on single dose only were included in 5 studies, and data on both the first and second dose were reported in 11 studies, only 4 studies reported data specifically related to booster doses. Data on the alpha variant were reported in 11 studies, data on the delta variant were available in 10 studies data on the beta variant were reported in 4 studies, data on the Omicron variant were reported in 3 studies, data on the zeta variant were reported in one study, and data on the B.1.128 variant were reported in 1 study. The data on efficacy against hospitalization were available in 14 studies, data on efficacy against death were collected from 10 studies, and data on efficacy against ICU admission were collected from 4 studies. The vaccine effectiveness met WHO guidelines for adequate protection at baseline, reaching 70% for the first dose and 60% for the second dose.

Efficacy Against Symptomatic COVID-19 Cases

First dose

Eight studies (Figure 2) reported the vaccine efficacy of the Oxford-AstraZeneca COVID-19 vaccine against symptomatic COVID-19 after the first dose. The Cochran's Q test and I^2 statistic revealed significant heterogeneity (Q-value=386.71, p=0.00001, I^2=98%), so a random model was used. The forest plot analysis showed that the overall efficacy against symptomatic COVID-19 after the first dose was significantly higher; 60.59%, p=0.00001 (Figure 2).

Second Dose

Sixteen studies (Figure 3) demonstrated the vaccine efficacy of the Oxford-AstraZeneca COVID-19 vaccine against symptomatic Covid-19 after the second dose. The Cochran's Q test and I^2 statistic revealed significant heterogeneity (Q-value=449.93, p=0.00001, I^2=97%), so a random model was used. The forest plot analysis showed that the overall efficacy against symptomatic COVID-19 after the second dose was significantly higher; 66.84%, p=0.00001 (Figure 3).

Vaccine Efficacy Against SARS-CoV-2 Variants

First dose

Twelve studies (Figure 4) reported the vaccine efficacy of the Oxford-AstraZeneca COVID-19 vaccine against SARS-CoV-2 variants after the first dose. The Cochran's Q test and I^2 statistic revealed a significant heterogeneity (p<0.05,

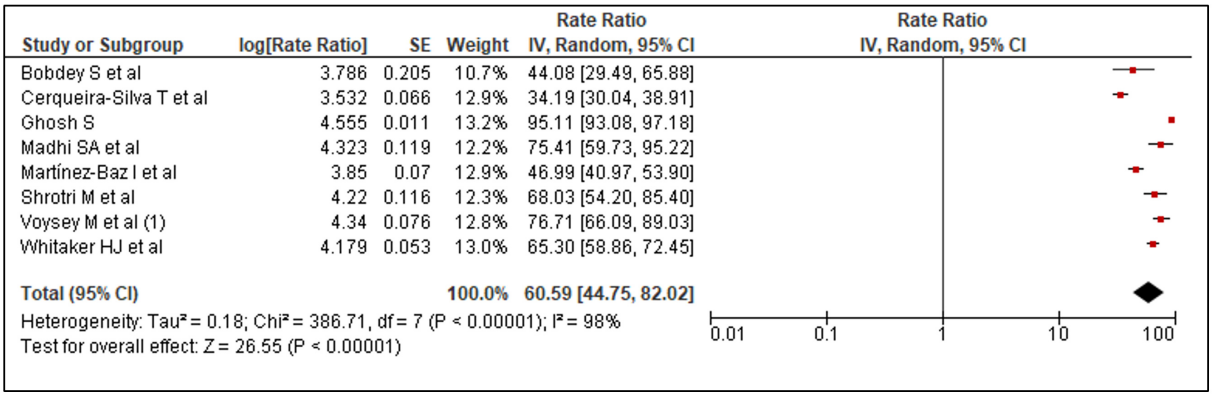

Figure 2. Efficacy of Oxford-AstraZeneca COVID-19 vaccine against symptomatic COVID-19 patients after the first dose.

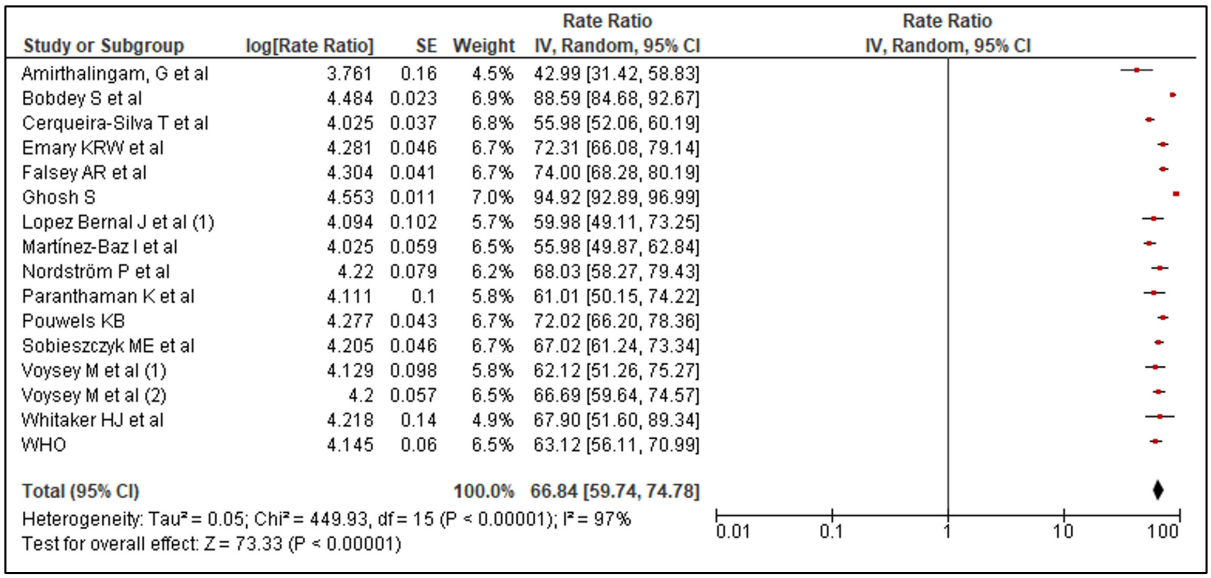

Figure 3. Efficacy of Oxford-AstraZeneca COVID-19 vaccine against symptomatic COVID-19 patients after the second dose.

*I*²=50%), so a random model was used. The forest plot analysis showed that the highest efficacy was against the Alpha variant (58.80%, $p<0.00001$), while the lowest efficacy was against the Beta variant (30.83%, $p<0.00001$). The overall efficacy of the Oxford-AstraZeneca COVID-19 vaccine against the SARS-CoV-2 variants after the first dose was 49.20% (Figure 4).

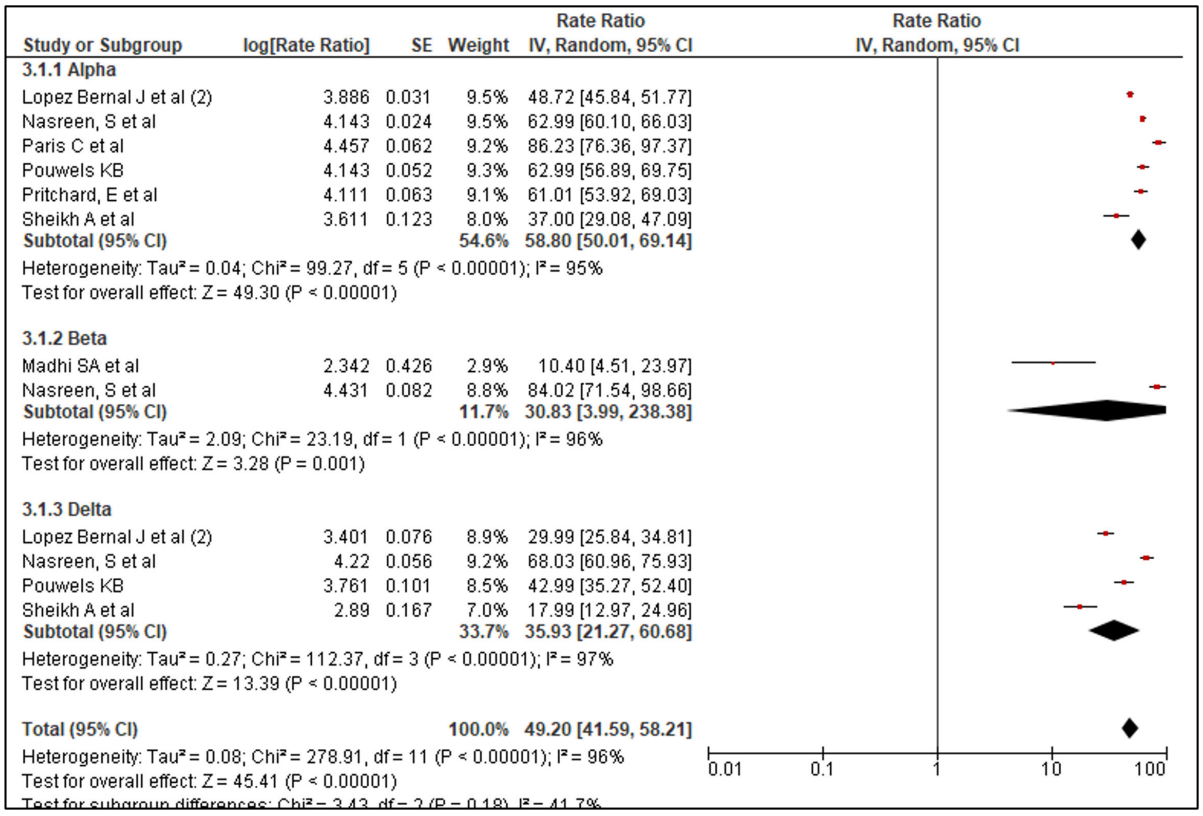

Figure 4. Efficacy of Oxford-AstraZeneca COVID-19 vaccine against SARS-CoV-2 variants after the first dose.

Second dose

Seventeen studies (Figure 5) reported the vaccine efficacy of the Oxford-AstraZeneca COVID-19 vaccine against SARS-CoV-2 variants after the second dose. The Cochran's Q test and I^2 statistic revealed a significant heterogeneity ($p<0.05$, $I^2>50\%$), so a random model was used. The forest plot analysis showed that the highest efficacy was against the Beta variant (90.34%, $p<0.00001$), while the lowest efficacy was against the Omicron variant (46.46%, $p<0.00001$). The overall efficacy of the Oxford-AstraZeneca COVID-19 vaccine against SARS-CoV-2 variants after the 2nd dose was 73.73% (Figure 5).

Efficacy Against ICU, Hospital, and Emergency Admissions

Second dose

Fourteen studies (Figure 6) reported the vaccine efficacy of Oxford-AstraZeneca COVID-19 vaccine against ICU, hospital, and emergency admissions after the second dose. The Cochran's Q test and I^2 statistic revealed a significant heterogeneity ($p<0.05$, $I^2>50\%$), so a random model was used. The forest plot analysis showed that the highest efficacy was against emergency admissions (94.42%, $p<0.00001$), while the lowest efficacy was against hospital admission (86.57%, $p<0.00001$). The overall efficacy of the

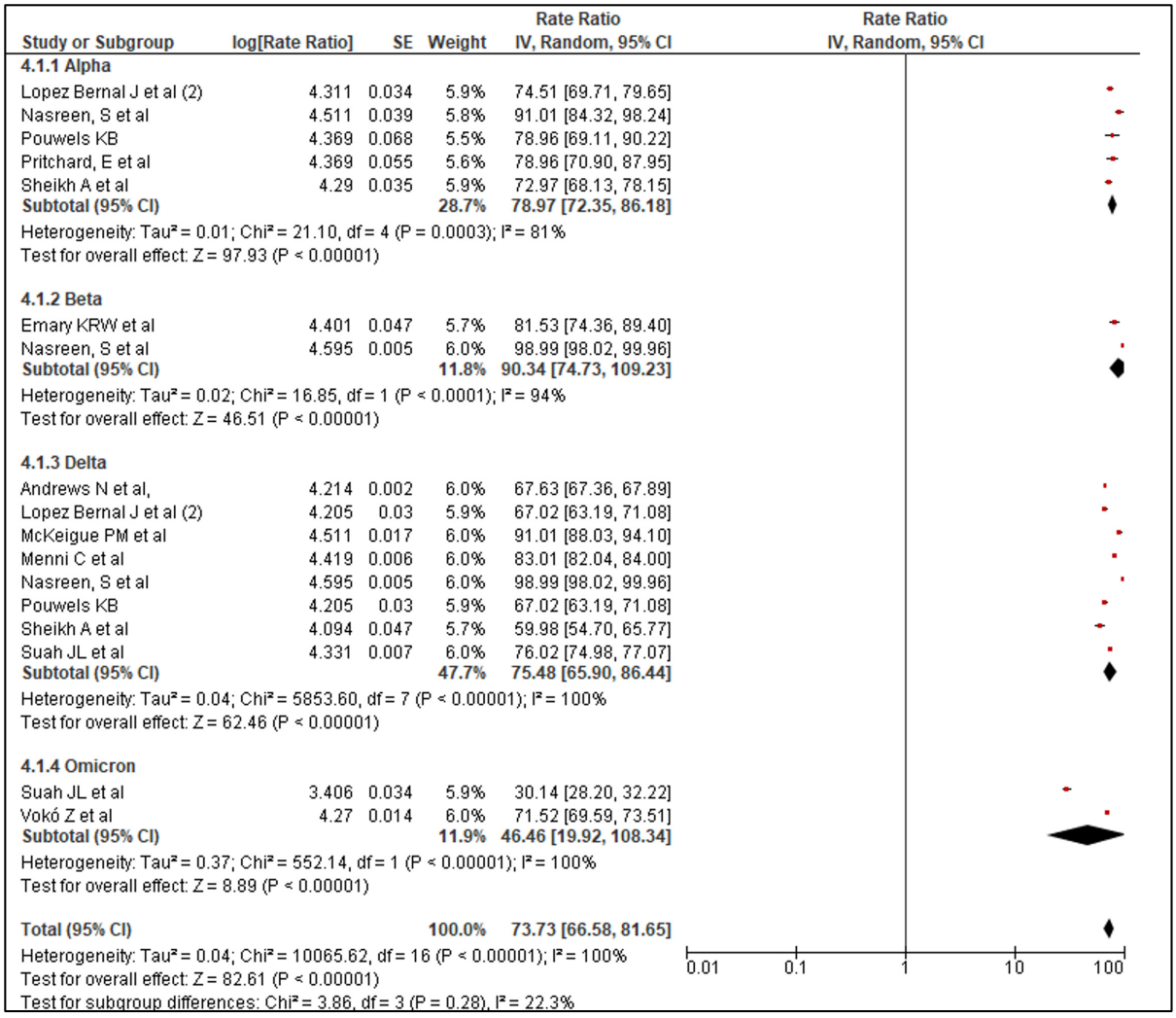

Figure 5. Efficacy of Oxford-AstraZeneca COVID-19 vaccine against SARS-CoV-2 variants after the second dose.

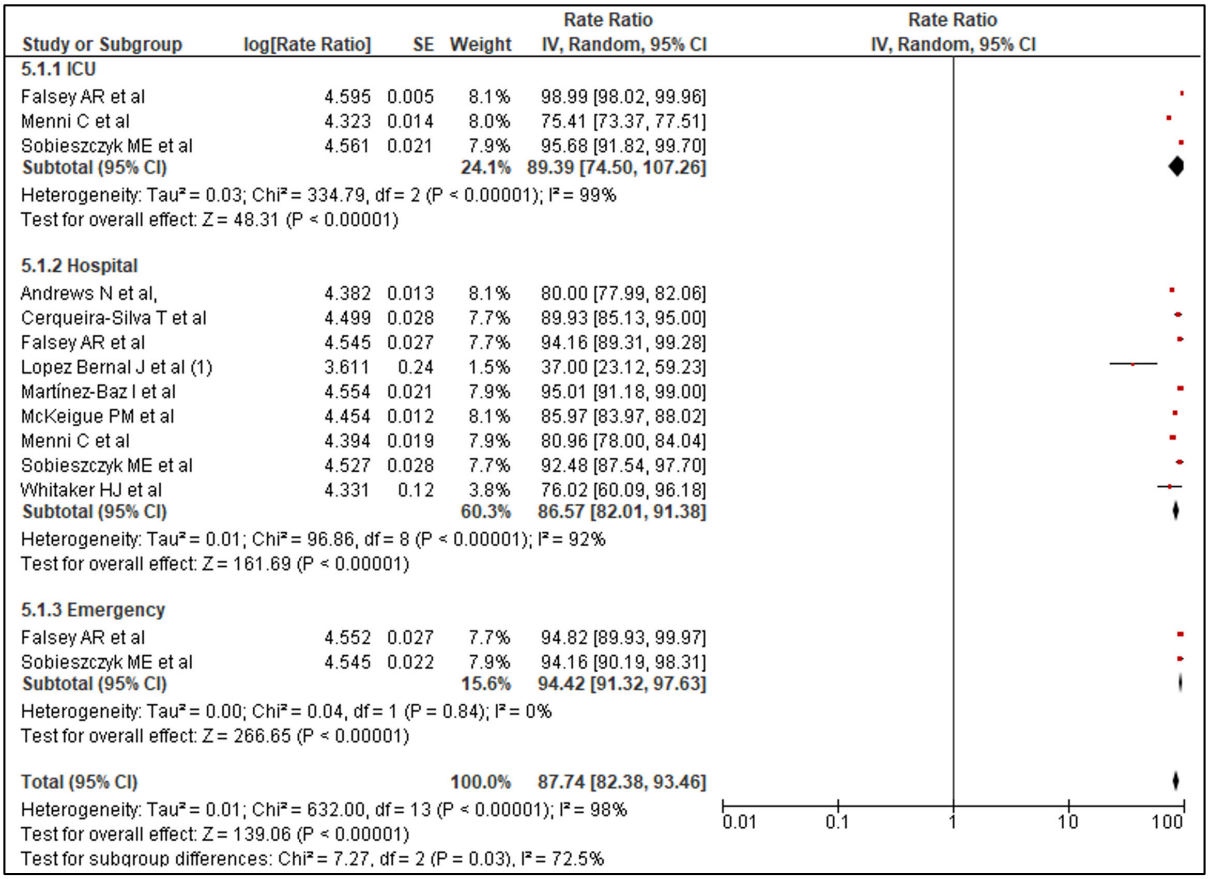

Figure 6. Efficacy of Oxford-AstraZeneca COVID-19 vaccine against ICU, hospital, and emergency admissions after the second dose.

Oxford-AstraZeneca COVID-19 vaccine against ICU, hospital, and emergency admissions after the second dose was 87.74% (Figure 6).

Efficacy Against Deaths Due to COVID-19

Second dose

Six studies (Figure 7) reported the vaccine efficacy of the Oxford–AstraZeneca COVID-19 vaccine against deaths after the second dose. The Cochran's Q test and I^2 statistic revealed a significant heterogeneity (Q-value=94.02 p<0.00001, I^2=95%), so a random model was used. The forest plot analysis showed that the overall efficacy against deaths after the 2nd dose was significantly higher 87.44%, p=0<0.00001 (Figure 7).

Discussion

On 23rd November 2020, the Oxford-AstraZeneca vaccine was approved by the UK Medicines and Healthcare Products Regulatory Agency for emergency use authorization in the UK for the adult population of age >18 years. The recommended vaccine schedule involved administering two full doses 4-12 weeks apart. A pooled analysis from the UK and Brazil phase 3 trial showed that the overall vaccine efficacy was 70.4% in preventing COVID-19 symptomatic infection[13]. The present study provided updated primary efficacy results based on an extensive global literature of thirty-nine studies. This study goes beyond primary efficacy assessment and provides a breakdown of single *vs.* double vaccine doses and efficacy against multiple variants. In this study, high efficacy was observed following the administration of vaccine doses.

Since the declaration of a pandemic and worldwide emergency status, scientists have worked relentlessly to create effective vaccines that would not have major side effects. To ensure this, they have conducted multiple phase 2 and 3 trials. However, the data on the efficacy conducted in the controlled environment of these trials cannot be extrapolated

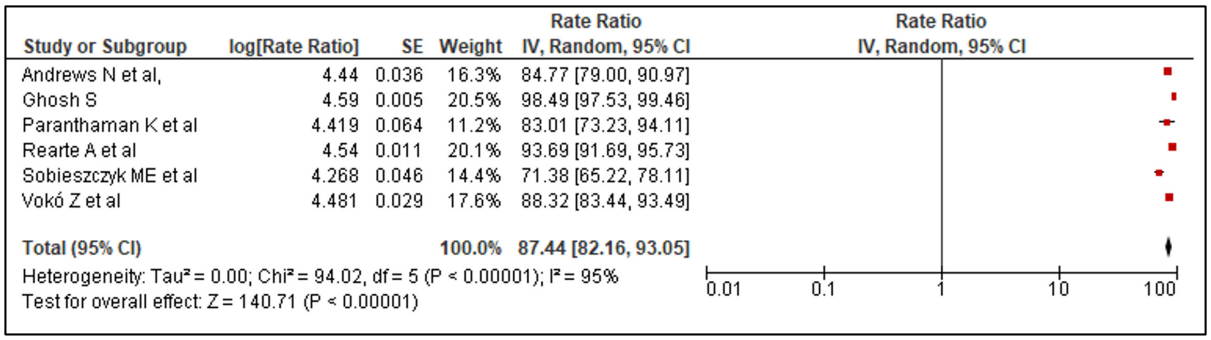

Figure 7. Efficacy of Oxford-AstraZeneca COVID-19 vaccine against deaths after the second dose.

to the general heterogeneous population. After the vaccines were issued worldwide, real-world trials were conducted to detect the efficacy and side effects. Initially, data were collected for the Pfizer vaccine, which is considered the vaccine with high efficacy, but it is also the most studied as compared to the Oxford-AstraZeneca vaccine, which only has a limited number of studies. In this study, we reported the efficacy of the Oxford-AstraZeneca vaccine after analyzing 39 different studies.

Meo et al[52] reported that Pfizer/BioNTech and Oxford-AstraZeneca vaccinations decreased the number of SARS-CoV-2 cases and deaths after the vaccination compared to before the vaccination campaign at country levels. This country-wide vaccination study demonstrated that vaccination is the best tool to combat such pandemics.

The World Health Organization (WHO) has established a specific threshold to define adequate COVID-19 vaccine effectiveness. The vaccines demonstrate the effectiveness of at least 70% against symptomatic infections and 90% against hospitalizations or mortality, with a lower 95% confidence interval (CI) of at least 50% and 70%, respectively. According to this threshold, Oxford-AstraZeneca proves to be effective against symptomatic COVID-19 infection with an efficacy of 70% and against hospitalizations with an efficacy of 90%[13,14]. The analysis conducted in this study presents compelling evidence supporting the efficacy of administering two standard doses of the vaccine. Our data is comparable to the single-blind randomized controlled trials[13] done in the UK (COV001, COV002), Brazil (COV003), and South Africa (COV005), which reported overall efficacy against symptomatic infection as 70.4% (95.8CI, 54.8-80.6%) after 2 full doses. Another large RCT phase 3 trial[15] done in the US, Peru, and Chile found a similar efficacy of 74.0% against symptomatic COVID-19 (95% CI, 65.3-80.5%).

Likewise, the initial dose of the AstraZeneca vaccine also demonstrated sufficient effectiveness, with a 67% efficacy against symptomatic COVID-19 infection. However, it is important to note that the data contributing to this efficacy rate is widely distributed, ranging from 34.2% (95% CI, 30.1-38.1) to a corrected vaccine efficacy of 95.13% two weeks after the first dose (with a range of 92.72-96.74). In our statistical analysis, we were able to identify a more reliable efficacy estimate. Despite this, our analysis suggests that further investigation is needed regarding the possibility of a single-dose regimen. Implementing a single-dose regimen could potentially reduce the burden on low- to middle-income countries in terms of vaccine purchase, distribution costs, and community acceptance. This could contribute to achieving a higher vaccination rate in the population, leading to herd immunity.

The Alpha variant emerged in the United Kingdom in late 2020. AstraZeneca's efficacy against this variant is the most studied, with most studies conducted in the UK and Scotland. A community-based study of the adult population >18 years in the UK showed vaccine efficacy of 79% against symptomatic infection after the second dose (56-90%) and 63% after the first dose (55-69%). This is in stark contrast to a prospective cohort study in Spain stating 50% efficacy against symptomatic COVID-19 (95% CI, 37-61%)[25].

The Delta variant, which emerged in late 2020 and quickly became the predominant variant in India, posed a significant challenge[27]. However, no specific data is available from India regarding the efficacy of the AstraZeneca vaccine against the Delta variant. The Delta variant gained dominance in the United States during the summer of 2021. However, the Omicron variant has now surpassed it as the predominant variant, according to estimates by the Centers for Disease Con-

trol and Prevention. While focusing solely on the Omicron variant in our study analysis, we found that the baseline levels of vaccine effectiveness did not meet the established criteria for vaccine efficacy. This is concerning, considering that the Omicron variant has been the dominant variant in some states for over a year now. Other studies have also indicated that the efficacy against the Omicron variant did not reach sufficient levels to effectively prevent infections or hospitalizations. However, the overall efficacy of the Oxford-AstraZeneca COVID-19 vaccine against symptomatic COVID-19 cases, variants against hospital admissions and deaths was appropriately good.

Study Strengths and Limitations

The study's strengths are the efficacy of Oxford-AstraZeneca COVID-19 vaccine was analyzed based on the worldwide large sample size and extensive literature. The efficacy data were from diverse sites targeting different ethnicities and countries, including the UK, Brazil, Scotland, Spain, India, Hungary, Argentina, Malaysia, Sweden, the US, Chile, Peru, and South Africa. In addition, this report goes beyond primary efficacy assessment and provides a breakdown of single *vs.* double vaccine doses and efficacy against multiple variants. Moreover, this study analysis provides valuable insights for healthcare workers, policymakers, and researchers, informing them about the precise efficacy levels against symptomatic infection, hospitalization, and mortality across diverse populations and age groups. Similar to other studies, this study has some limitations: trust and confidence in any COVID-19 vaccine is essential to its sustainable success, and efficacy is an important consideration, but still, such large sample-sized studies are needed to highlight more data from the developing nations for the better understanding of the efficacy of the vaccine.

Conclusions

The efficacy of the Oxford-AstraZeneca COVID-19 vaccine against symptomatic COVID-19 cases after the first dose was 60.59% and after the second dose was 66.84%. The highest efficacy was against the Alpha variant and the lowest efficacy was against the Beta variant. However, the overall efficacy against the SARS-CoV-2 variants after the first dose was 49.20%. The highest efficiency of SARS-CoV-2 variants after the second dose against the Beta variant was 90.34%, while the lowest efficacy was against the Omicron (B.1.1.529) variant at 46.46%, with overall efficacy against SARS-CoV-2-2 variants after the second dose 73.73%. The highest efficacy against emergency admission was 94.42%, while the lowest efficacy was 86.57%, with overall efficacy against ICU, hospital, and emergency admissions after the second dose was 87.74%, and efficacy of the Oxford-AstraZeneca vaccine against deaths after the second dose was 87.44%. This study provides updated efficacy results based on worldwide extensive literature-based data from the UK, Brazil, Scotland, Spain, India, Hungary, Argentina, Malaysia, Sweden, the US, Chile, Peru, and South Africa. In addition, this report goes beyond primary efficacy assessment and provides a breakdown of single *vs.* double vaccine doses and efficacy against multiple variants. Notably, higher effectiveness was observed following the administration of a double dose. The present study results provide valuable insights for healthcare workers, policymakers, and researchers about the precise efficacy levels against symptomatic cases, hospitalization, and mortality across diverse populations.

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Conflicts of Interest

No conflict of interest.

Ethics Approval

The data were recorded from publicly available data-based web sources and had no direct involvement of animals or humans; hence ethical approval is not required.

Informed Consent

Not required.

Availability of Data and Materials

The data may be provided on reasonable request.

Authors' Contribution

SAM, study concept, manuscript writing and editing. SA, literature review, data collection and data entry; NMB, data analysis, ASM, literature review and data checking.

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