Title	Evidence Summary: Efficacy and Safety of Approved COVID-19 Vaccines
Code	28122020LMKC
Requestor Area	COVID-191 Keralty Public Health Crisis Committee
Name	COVID-191. Keralty Public Health Crisis Committee
Answer Date	30122020

Question:

1. What is the evidence for the efficacy and safety of Pfizer-Biontech's BNT162b2, Moderna's mRNA-1273, and Oxford University / AstraZeneca's ChAdOx1/ AZD1222 vaccines in preventing SARS-CoV-2 coronavirus infection (COVID-19)?

Research question

Populations	Healthy population (specific characteristics of each study)
Interventions	Vaccines: Biontech BNT162b2 - Pfizer mRNA-1273 by Moderna ChAdOx1/ AZD1222
Comparators	Placebo
Outcomes	• - Symptomatic SARS-CoV-2 infection confirmed by laboratory • - Hospitalization for COVID-19 • - Death from all causes • - Asymptomatic SARS-CoV-2 infection • - Serious adverse events • - Degree of reactogenicity ≥3

Introduction:

The SARS-CoV-2 (COVID-19 disease) pandemic is the most critical issue facing humanity in 2020, and its impact is expected to last for some time to come. Scientific research has rapidly attempted to curb the pandemic's magnitude, with no successful outcome to date for treatment of COVID-19 disease. From these vaccines, 339 studies were recorded in ClinicalTrials(1). For three of these vaccines, preliminary results have been formally and informally reported with promising results, including the ChAdOx1 vaccine developed by the University of Oxford and AstraZeneca, the BNT162b2 vaccine from Pfizer-Biontech, and the mRNA-1273 vaccine from Moderna (2) because of such news and the position of several countries to initiate population-based vaccination programs. It is necessary to know the available evidence on these vaccines' efficacy and safety against the SARS-CoV-2 virus, which is why we carried out this review.

The Oxford vaccine consists of a Chimpanzee adenovirus vector of deficient replication ChAdOx1, which contains the glycoprotein antigen's gene of the structural surface SARS-CoV-2(3).

The U.S. Food and Drug Administration (FDA) has granted emergency use authorizations (EUAs) for two COVID-19 vaccines:

On December 11, 2020, Pfizer-BioNTech BNT162b2 vaccine COVID-19

On December 19, 2020, for the Modern COVID-19 vaccine (mRNA-1273) to prevent symptomatic COVID-19 in people ≥18 years.

On December 30, 2020, the U.K. government accepted the recommendation of the Medicines and Healthcare products Regulatory Agency (MHRA) to authorize the emergency use of the ChAdOx1 nCoV-19 coronavirus vaccine in the U.K.

Technology Description

Vaccination is a simple, safe, and effective way to protect against some diseases by administering antigenic material to stimulate the immune system, leading to adaptive immunity to a pathogen(4). Vaccines activate the body's natural defenses to learn to resist specific infections and strengthen the immune system. In a vaccine, its effectiveness and adverse effects depend not only on the active ingredient but also on adjuvants, preservatives, stabilizers, inactivators, antibiotics, diluents, and other substances. Traditional vaccine technologies are based on killed/inactivated, and live/attenuated virus vaccine approaches. New killed/inactivated virus vaccination strategies include antigen, protein, and peptide subunit vaccines. Unique live/attenuated virus vaccination strategies include live virus modified vaccines, vaccinated animal markers/differentiators, vectors, and nucleic acids(5).

Methodology:

A Systematic Rapid Review (Manual de Revisions Sistemáticas Rápidas. Global Institute for Clinical Excellence. 2019)

Eligibility criteria

Search of information

A systematic search of the literature was conducted with no time limit until December 28, 2020, for studies that met the following inclusion criteria:

- Population, intervention, comparison, outcomes according to the PICOT question.

- Studies: randomized clinical trials (RCT) in humans

- Publication format: we took studies available into account. We did not consider studies published only in abstract form because the information reported is incomplete to evaluate its methodological quality. The studies' results may also change significantly between the initial presentation in a scientific event and the final publication.

- Publication status: studies published in indexed journals, in the press, or gray literature.

- Results report: studies that reported individual effect estimates for each primary research that was attributable to the comparison of interest and at least one outcome.

Sources

- We direct the search to randomized clinical trials (RCTs). The terms COVID 19, SARS-Cov2, and vaccine were used to search PubMed and Google Scholar

The search syntaxes used can be found in Annex 1. We include specific filters to restrict the RCT search. The number of references identified in the literature search is summarized using the PRISMA flowchart, Annex 2.

Screening, selection, and extraction

Two reviewers screened the total number of references identified in the search by examining the titles and abstracts against independently predefined eligibility criteria. From the group of pre-selected references, a selection of studies was made. The reviewers verified that each study met the eligibility criteria by reading each publication in full text.

The reviewers carried out the extraction of the estimates of effect for the comparison and critical outcomes from what was reported in the synthesis articles. Data extraction accuracy was controlled by evaluating the consistency of the estimates included in the evidence tables against the results presented in the included articles. We summarized the findings narratively through evidence profiles, including interpreting the statistical significance of the reported effects.

Quality assessment

We evaluate the quality of the evidence through GRADE profiles (6), and table 1 summarizes the results.

Outcomes

Search results, screening, and selection

Annex 2 shows the search results, screening, and selection of evidence for this systematic review. Through the search in the identified databases, 44 documents were detected. They were initially reviewed by title and abstract; later, a complete reading of those that met the selection criteria was performed. Based on the articles' reading, eight articles/reports were included and described in the present review.

Synthesis of the evidence

Table 1 describes the summary of scientific evidence from the 31 studies included in this rapid review, which evaluate the efficacy and safety of Biontech-Pfizer's BNT162b2; Moderna's mRNA-1273; and Oxford University / AstraZeneca's ChAdOx1/ AZD1222 vaccines versus their comparators/placebo for preventing SARS-CoV-2 coronavirus infection (COVID-19), in terms of critical outcomes for decision-making.

Efficacy

Pfizer-BioNTech and Moderna vaccines reduced laboratory-confirmed cases of symptomatic COVID-19 compared to placebo, with vaccine efficacy of 95.0% (95% CI 90.3% to 97.6%) and 94.1% (95% CI 89.3%, 96.8%), respectively (7-10).

In the trial evaluating the Pfizer-BioNTech vaccine, hospitalization for COVID-19, five events occurred, all in the placebo group. The vaccine efficacy against hospitalization with COVID-19 was 100% (95% CI -9.9% to 100%)(7,8). While with the Moderna vaccine, there were ten hospitalization events, 9 in the placebo group and 1 in the vaccine group, with an 89% vaccine efficacy (95% CI: 13% to 99%)(9,10).

The Oxford University Phase I/II vaccine clinical trial included(11) 1,077 healthy participants randomly assigned to either the nCoV-19 ChAdOx1 vaccine group or the control vaccine group, except for participants who were enrolled in the booster group. In the nCoV-19 ChAdOx1 group, antibodies to the SARS-CoV-2 peak protein peaked on day 28 (median 157 ELISA units (E.U.), IQR 96-317; n = 127) and remained elevated until day 56 (119 EU, 70 -203; n = 43) in participants who received only one dose, increasing to a median of 639 EU (360-792) on day 56 in the ten participants who received a booster dose. Fatigue and headache were frequent reactions among participants in the ChAdOx1 nCoV-19 group and reported muscle pain, malaise, chills, and fever.

For the nCoV-19 ChAdOx1 vaccine, several reports were made from phase I/II discriminating primary from secondary outcomes. For phase I/II the clinical trial included 88 healthy participants between 18 and 55 years old, randomized to receive a single dose of the vaccine (5×1010 viral particles of ChAdOx1 nCov-19) or the control vaccine. Follow-up was conducted on days 7, 14, 28, and 56 after vaccination. IgM and IgA antibodies were increased, reaching a maximum level on day 14 and 28, respectively. IgE similar to that of SARS-CoV-2 convalescent patients was also found. IgG increased between day 28 and 56 after vaccination ($p<0.001$)(12)

Other preliminary results from the University of Oxford's Phase I/II clinical trial of the ChAdOx1 nCoV-19 vaccine included 52 participants aged 18-55 years with initial standard doses assigned to a low-dose or standard-dose booster of the vaccine within 56 days of the first dose. There was no difference in IgG titers at 14 days after the second dose between those who received the booster at 28 days (geometric mean titer (GMT): 35990; 95% confidence interval (CI): 24,408-53,068)(13)

The preliminary report of phase II/III clinical trial on vaccine safety and immunogenicity of the University of Oxford-AstraZeneca(14) included 560 healthy adults (18 years or older) from clinical centers in the United Kingdom, randomized to a low dose of vaccine (2.2 × 1010 viral particles), to the standard dose (3.5-6.5 × 1010 viral particles) and the control vaccine comparator group. We stratify the groups by age.

No difference was reported between IgG antibodies on the 28th day after vaccination between low-dose and standard-dose groups, although they decreased with age. Similar findings were reported for IgG antibody titers, except that they did not vary with age after the booster vaccine. There was also no difference in anti-RBD antibodies. Antibody titers were higher on day 42 in participants who received the booster vaccine. However, there was no difference by age group. For almost all participants, neutralizing antibody titers were reported by day 14 after the booster vaccine (<99%).

The Oxford-AstraZeneca University vaccine's overall efficacy was 70.4% (CI 95.8%: 54.8 to 80.6). There were ten cases hospitalized for COVID-19, 21 days after the first dose, all in the placebo group; two were classified as severe COVID-19, including one death(15).

Adverse events (serious)

Pfizer-BioNTech vaccine: The number of serious adverse events was comparable between the vaccine group and the placebo group in the two studies (Phase II/III: intervention group: 126/21621, 0.6% vs. placebo group:111/21631, 0.5%; Phase II: intervention group 1/24, 4.2% vs. placebo group 0/18, 0.0%)(16)

Modern vaccine: The number of serious adverse events was comparable between the vaccine and placebo groups (RR 0.96, 95% CI 0.77 to 1.20)(9.10)

Oxford vaccine: In the Phase I/II report, moderate to severe systemic adverse reactions within seven days of vaccination was found to be more frequent with the first dose (moderate: 51.9%, severe: 19.2%) than with the booster (moderate: 19.2%, severe: 3.8%) (13)
The preliminary report of phase II/III clinical trial (October 26, 2020) reported 13 non-vaccine serious adverse events, which occurred in all groups(14).

Grade Reactogenicity ≥3

In the reports found for the Pfizer-BioNTech vaccine, grade reactions ≥three were few. However, the cases occurred more frequently in the vaccine groups than in the placebo groups(7,8).

Modern vaccine: Grade ≥3 was associated with vaccination (RR 4.93, 95% CI 4.55-5.34). Approximately 22% of vaccine recipients and 4% of placebo recipients reported local or systemic grade reactions ≥three after the first or second dose(9,10).

In the preliminary report of the Oxford University Phase I/II vaccine trial, it reported that 28.8% of participants (15/52) presented systemic reactogenicity with pyrexia following vaccination (13)

Mortality

Reporting of deaths from all causes was rare, with two events in the Pfizer-BioNTech vaccine group and 4 in the placebo group (R.R.: 0.50, 95% CI: 0.09, 2.73)(7,8). In the trial evaluating the Modern vaccine, six events occurred in the vaccine group and 7 in the placebo group (R.R.: 0.86; 95% CI: 0.29, 2.55)(9.10)

Asymptomatic infection

Pfizer-BioNTech vaccine: no report in studies found

Modern vaccine: Vaccination with one dose was associated with a lower risk of asymptomatic SARS-CoV-2 infection, defined in a post-hoc analysis as detection of SARS-CoV-2 DNA by polymerase chain

reaction (PCR) test on the day received the second dose and reported no symptoms of COVID-19 between dose one and dose 2 (R.R.): 0.37, 95% CI 0.20, 0.68), among people who were seronegative for SARS-CoV-2 at baseline(9,10).

Oxford Vaccine: Efficacy of the vaccine against asymptomatic transmission was 59% in the group that received a half-dose followed by a standard dose (seven cases among 1120 participants versus 17 cases among 1127 participants in the control group), but only 4% in the group that received two standard doses (22 among 2168 participants versus 23 among 2223 for the control) (15)

Table 1. Synthesis of scientific evidence on comparative clinical efficacy and safety

Population: Participants with heterogeneity of sex, age (≥16 years), and ethnicity

Intervention: Biontech-Pfizer BNT162b2

Comparison: Placebo

Critical Outcome	Study	Participants	Size of the effect	Certainty degree
Efficacy (hospitalization due to COVID-19) Polack, 2020 (7) Pfizer, 2020 (8)	RCT	Total 43,448 Intervention: 21,720 Placebo: 21,728 Population evaluation of effectiveness: 36621 Population security assessment: 37706	Intervention: 0/17399 (0.0%) Placebo: 5/17495 (0.0%) RR 0.00 (0.00, 1.10) 100% efficiency (-9.9% a 100%)	⊕⊕◯◯ LOW The short duration of follow-up (median two months) The population included in the RCT may not represent everyone ≥16. Imprecision due to the small number of events observed.
Efficacy (symptomatic COVID-19 confirmed by the laboratory) Symptomatic disease with SARS-CoV-2 RT-PCR positive, in seronegative adults, ≥seven days after the second dose Polack, 2020 (7) Pfizer, 2020 (8)	RCT	Total 43,448 Intervention: 21,720 Placebo: 21,728 Population evaluation of effectiveness: 36621 Population security assessment: 37706	Intervention: 8/17411 Placebo: 162/17511 Efficiency: 95.0%. (90.3% a 97.6%)	⊕⊕⊕⊕ HIGH Effectiveness is unlikely to change. The population included in the RCT may not represent everyone ≥16
Adverse reactions (severe) Polack, 2020 (7) Pfizer, 2020 (8)	RCT	Total 43,448 Intervention: 21,720 Placebo: 21,728 Population evaluation of effectiveness: 36621 Population security assessment: 37706	Intervention: 126/21621 (0.6%) Placebo: 111/21631 (0.5%) RR 1.14 (0.88 a 1.46)	⊕⊕⊕◯ MIDDLE It is not certain that rare serious adverse events were captured due to the median follow-up of 2 months. Imprecision due to the small number of events observed
Death from all causes (including serious adverse events or COVID-related) Polack, 2020 (7)	RCT	Total 43,448 Intervention: 21,720 Placebo: 21,728 Population evaluation of effectiveness: 36621 Population security assessment: 37706	Intervention:2/21621 placebo: 4/21631 RR 0.50 (0.09 a 2.73)	⊕◯◯◯ VERY LOW The denominator was not reported. Deaths from COVID-19 may not have had time to occur at a median follow-up of 2 months.

Pfizer, 2020 (8)				Imprecision due to the small number of events observed.
Reactogenicity, grade ≥3 (Any local reaction or systemic event after Dose 1 or 2) Polack, 2020 (7) Pfizer, 2020 (8)	RCT	Total 43,448 Intervention: 21,720 Placebo: 21,728 Population evaluation of effectiveness: 36621 Population security assessment: 37706	Intervention:364/4132 (8.8%) Placebo: 85/4124 (2.1) RR 4.27 (3.39 a 5.38)	⊕⊕⊕⊕ HIGH
Adverse reactions (serious) **Walsh, 2020(16)**	RCT Phase II	Total: 108 (healthy adults 18-55 years old Intervention: 90 Placebo: 18	Intervention:1/24 (4.2) Placebo: 0/18 (0.0) RR: 2.28 (0.10, 52.92)	N/A
Reactogenicity, grade ≥3 (Any local reaction or systemic event after Dose 1 or 2) Walsh, 2020(16)	RCT Phase II	Total: 108 (healthy adults 18-55 years old Intervention: 90 Placebo: 18	Intervention: 2/24 (8.3%) Placebo: 1/18 (5.6%) RR 1.50 (0.15 a 15.28)	N/A
Population: Participants ≥18 years **Intervention: Modern mRNA-1273** **Comparison: Placebo**				
Efficacy (hospitalization due to COVID-19) Moderna, 2020(9,10)	RCT	Total 30351 Intervention: 15184 Placebo: 15170	Intervention: 1/14134 (0.0%) Placebo: 9/14073 (0.1%) RR 0.11 (0.01 a 0.89 Efficiency 89%. (13% a 99%).	⊕⊕⊕◯ MIDDLE The population included in the RCT may not represent all individuals ≥18. Imprecision due to the small number of events observed.
Efficacy (symptomatic COVID-19 confirmed by the laboratory) Moderna, 2020(9,10)	RCT	Total 30351 Intervention: 15184 Placebo: 15170	Intervention:11/14134 (0.1%) Placebo: 185/14073 (1.3%) RR 0.06 (0.03 a 0.11) Efficiency: 94.1%. (89,3% a 96,8%)	⊕⊕⊕⊕ HIGH The population included in the RCT may not represent all individuals ≥18.
Asymptomatic infection	RCT	Total 30351 Intervention: 15184 Placebo: 15170	RR: 0,37 (0,20 a 0,68)	⊕◯◯◯ VERY LOW The available evidence is indirect because it represents 1)

Moderna, 2020 (9,10)				the testing of SARS-CoV-2 at one time, 2) the evaluation after one dose, and 3) a short follow-up period. Imprecision due to the small number of events that were observed.
Adverse reactions (severe) Moderna, 2020(9,10)	RCT	Total 30351 Intervention: 15184 Placebo: 15170	Intervention: 147/15385 (1.0%) Placebo: 153/15366 (1.0%) RR 0.96 (0.77 a 1.20)	⊕⊕⊕◯ MIDDLE The population included in the RCT may not represent all individuals ≥18.
Reactogenicity, grade ≥3 Moderna, 2020(9,10)	RCT	Total 30351 Intervention: 15184 Placebo: 15170	Intervention 3308/15376 (21.5%) Placebo: 671/15362 (4.4%) RR 4.93 (4.55 a 5.34)	⊕⊕⊕⊕ HIGH
Death from all causes Moderna, 2020(9,10)	RCT	Total 30351 Intervention: 15184 Placebo: 15170	Intervention: 6/15184 (0.0%) Placebo: 7/15165 (0.0%) RR 0.86 (0.29 a 2.55)	⊕◯◯◯ VERY LOW The population included in the RCT may not represent all individuals ≥18. Deaths from COVID-19 may not have had time to occur. Imprecision due to the small number of events that were observed.
Population: Participants ≥18 years **Intervention: ChAdOx1 / AZD1222 DE Oxford University / AstraZeneca** **Comparison: Placebo**				
Efficacy (hospitalization due to COVID-19) Voysey, 2020(15)	RCT	Total 11636 Intervention: 5807 Placebo:5829	10 cases all in the placebo group	⊕◯◯◯ VERY LOW The denominator was not clearly reported. The population included in the RCT may not represent all individuals ≥18. Imprecision due to the small number of events observed.
Efficacy (laboratory-confirmed symptomatic COVID-19) primary, 14 days after the second dose Voysey, 2020(15)	RCT	Total 11636 Intervention: 5807 Placebo:5829	Intervention: 30/5807(0.5%) Placebo: 101/5829 (1.7%) Efficiency: 70-4%. (54,8 a 80,6)	⊕⊕⊕◯ MIDDLE The population included in the RCT may not represent all individuals ≥18. Imprecision due to the small number of events observed.
Asymptomatic infection	RCT		**Half a dose:**	⊕⊕◯◯

Voysey, 2020(15)			**Intervention 7/ 1120 ( )** **Placebo: 17/ 1127()** **Efficiency: 59%.** **Two standard doses:** **Intervention: 22/2168** **Placebo: 23/2223** **Efficiency: 4%.**	LOW These data require additional confirmation (secondary results data) Imprecision due to the small number of events that were observed.
Death from all causes **Voysey, 2020**(15)	RCT	Total 11636 Intervention: 5807 Placebo:5829	One death in the placebo group	⊕◯◯◯ VERY LOW The denominator was not clearly reported. Deaths from COVID-19 may not have had time to occur during follow-up
Adverse Reactions (series) Universidad de Oxford(14)	ECA Fase II/III (reporte preliminar)	Total: 560 Intervención: Comparación:	Intervención: 13	The denominator was not clearly reported. Deaths from COVID-19 may not have had time to occur during follow-up.
Source: The data presented in this table come from the eight articles included and from the evaluation of the quality of evidence GRADE				

Conclusions

Available data indicate that the Pfizer-BioNTech and Modern vaccines effectively prevent symptomatic COVID-19 with a high certainty of evidence. The efficacy evaluated through the COVID-19 hospitalization outcome presented a serious concern for the Pfizer-BioNTech vaccine due to the short duration of follow-up (median two months). It is possible that the severe cases of COVID-19 that led to hospitalization may not have had time to occur at a median follow-up of 2 months.

For the Moderna vaccine at the outcome of the effectiveness evaluated through the hospitalization by COVID-19 presented a moderate certainty of the evidence because the follow-up period was also short. Additionally, hospitalization was determined in a subset of cases that met a definition of severe COVID-19 specified by the protocol and was not determined for all cases of COVID-19. Therefore, it is possible that hospitalizations for COVID-19 occurred in cases that did not meet specific criteria for severe COVID-19.

The Oxford University / AstraZeneca vaccine presented an acceptable safety profile and is effective against symptomatic COVID-19, with no hospital admissions or severe cases reported in the intervention group.

On the other hand, more than 40% of the participants who received the Pfizer-BioNTech vaccine were > 55 years old. This indicates that the participant population represents the population at greatest risk for COVID-19 due to the relatively older age. A 95% efficacy of the Pfizer-BioNTech vaccine in safely preventing COVID-19 in this population is very reassuring. However, the short follow-up time and lack of systematic testing for SARS-CoV-2 as part of the protocol leaves important questions unanswered regarding the vaccine's intermediate-term effectiveness, the potential for rare and serious side effects, and whether the vaccine can prevent asymptomatic transmission.

The ongoing concern related to asymptomatic infections is that people with these infections may continue to transmit the virus to others, despite being vaccinated unknowingly. Although asymptomatic infections are not a direct measure of disease transmission, researchers have seen information on this outcome as an indication of how much vaccines might affect the spread of COVID-19. For now, in the reports included in this review, we found information on this outcome from the Moderna and Oxford / AstraZeneca University vaccines that provided preliminary data on preventing asymptomatic SARS-CoV-2 infection. Regarding Moderna's vaccine, the SARS-CoV-2 PCR test results from nasopharyngeal swabs collected on the day of the second dose of vaccine indicated a lower risk of asymptomatic infection among vaccine recipients compared to placebo recipients. However, the certainty of the evidence for this outcome was very low. For the Oxford / AstraZeneca University vaccine, the vaccine's efficacy against asymptomatic transmission was 59% in the group that received half a dose followed by a standard dose, but only 4% in the group that received two standard doses. These data require further confirmation.

Regarding reactogenicity, there was no serious concern affecting the certainty of the estimates for both the Pfizer-BioNTech and the Modern vaccine; and, in addition, they were associated with a lower risk of death from any cause; however, the certainty of the evidence was very low.

According to the above, the Pfizer-BioNTech, Modern, and Oxford / AstraZeneca University vaccines are safe and effective. These data demonstrate that the known and potential benefits of the vaccines outweigh the known and potential harms of SARS-CoV-2 (COVID-19) coronavirus infection. Vaccine cohorts need to be followed up to check individuals' status to identify possible side effects and adverse events following vaccination against COVID-19.

Recommendations for health professionals

Providers and health care professionals should communicate consistent, complete, and clear information regarding benefits, risks, contraindications, safety issues, and warning and follow-up recommendations to persons receiving m COVID-19 RNA vaccines or their caregivers.

It should be explained that there is limited evidence regarding how much mRNA m COVID-19 vaccines can reduce transmission in the general population and how long protection lasts, so prevention and biosecurity guidelines should be strictly followed: use of masks, hand washing, a distance greater than 2 meters, avoid crowds, enclosed and unventilated spaces.

We should generate pharmacovigilance systems to identify and respond quickly to any adverse events that occur in a recipient after vaccination (LVRS), including vaccine administration errors, serious adverse events, and multisystemic inflammatory syndrome cases, cases of VIDOC-19 resulting in hospitalization or death. It is recommended that any other clinically significant adverse event be reported, even if it is not clear that it is associated with vaccination.

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Appendixes

Appendix 1. Evidence search reports in electronic databases.

Search type	Electrónica
Data Base	**PubMed**
Date	28/12/2020
Time Range	Sin restricción
Language	Sin restricción
Limits	**Clinical trials/Randomized Controlled Trial**
Search Strategy	"covid19"[All Fields] AND ("vaccin"[Supplementary Concept] OR "vaccin"[All Fields] OR "vaccination"[MeSH Terms] OR "vaccination"[All Fields] OR "vaccinable"[All Fields] OR "vaccinal"[All Fields] OR "vaccinate"[All Fields] OR "vaccinated"[All Fields] OR "vaccinates"[All Fields] OR "vaccinating"[All Fields] OR "vaccinations"[All Fields] OR "vaccination s"[All Fields] OR "vaccinator"[All Fields] OR "vaccinators"[All Fields] OR "vaccine s"[All Fields] OR "vaccined"[All Fields] OR "vaccines"[MeSH Terms] OR "vaccines"[All Fields] OR "vaccine"[All Fields] OR "vaccins"[All Fields]) (Oxford Vaccine): ("ChAdOx1"[Title/Abstract] OR "AZD1222"[Title/Abstract]) AND "vaccine"[Title/Abstract] AND ("sars-cov-2"[Title/Abstract] OR "covid-19"[Title/Abstract])
Number of references	41

Anexo 2. Diagrama PRISMA: flujo de la búsqueda, tamización y selección de estudios.