REVIEW

# Pharmacological interventions to prevent Covid-19 disease: A rapid review

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## Summary

The aim of this rapid review was to determine the effectiveness of pharmacological interventions (excluding vaccines) to prevent coronavirus disease 2019 (Covid-19) or reduce the severity of disease. A systematic search of published peer-reviewed articles and non-peer-reviewed pre-prints was undertaken from 1 January 2020 to 17 August 2021. Four randomised controlled trials (RCTs) and one non-RCT were included; three trials (two RCTs and one non-RCT) tested ivermectin with or without carrageenan. While all reported some potential protective effect of ivermectin, these trials had a high risk of bias and the certainty of evidence was deemed to be 'very low'. One RCT tested bamlanivimab compared to placebo and reported a significantly reduced incidence of Covid-19 in the intervention group; this trial had a low risk of bias however the certainty of evidence was deemed 'very low'. The fifth RCT tested casirivimab plus imdevimab versus placebo and reported that the combination of monoclonal antibodies significantly reduced the incidence of symptomatic and asymptomatic SARS-CoV-2 infection, viral load, duration of symptomatic disease and the duration of a high viral load; this trial was deemed to have a low risk of bias, and the certainty of evidence was 'low'. The designations 'low' and 'very low' regarding the certainty of evidence indicate that the estimate of effect is uncertain and therefore is unsuitable for informing decision-making. At the time of writing, there is insufficient high quality evidence to support the use of pharmacological interventions to prevent Covid-19.

**KEYWORDS**
coronavirus, Covid-19, drug intervention, prevention, prophylaxis, SARS-CoV-2

# 1 | INTRODUCTION

On 11 March 2020, the World Health Organization (WHO) declared the coronavirus (Covid-19) outbreak a pandemic.[1] Pharmacological prevention of Covid-19 (i.e., prior to infection with severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2], not treatment of Covid-19 following infection with SARS-CoV-2) could be an important intervention, especially in the context of vaccine hesitancy, inequitable access to such and variants of concern. However, the risk-benefit of such interventions must be evaluated.[2] On 2 March 2021, the WHO published a recommendation against the use of hydroxychloroquine for individuals who do not have Covid-19. The panel acknowledged that in light of this recommendation, this area is no longer a research priority and that resources devoted to clinical research should be oriented to evaluate other more promising interventions.[3] As such, the aim of this rapid review was to determine the effectiveness of pharmacological interventions (excluding hydroxychloroquine and vaccines) in the community, prior to a diagnosis of Covid-19, to prevent Covid-19 disease.

# 2 | MATERIALS AND METHODS

A detailed report of the methods is provided in the protocol.[4] In summary, a systematic search of published peer-reviewed articles and non-peer-reviewed pre-prints was undertaken from 1 January 2020 to 17 August 2021; no language restrictions were applied. Titles, abstracts and full texts of potentially eligible papers were single screened based on the inclusion and exclusion criteria.[4] Eligible study designs were randomised controlled trials (RCTs) and non-RCTs; outcomes of interest were laboratory-confirmed diagnosis of Covid-19 or symptomatic infection. Data extraction and quality appraisal of included studies were completed by a single reviewer and checked by a second reviewer. Data extraction was completed using a standardised data extraction form. Quality appraisal of RCTs was completed using the Cochrane risk of bias tool version 2,[5] while ROBINS-I tool[6] (Risk of bias in non-randomised studies of interventions) was used for non-RCTs. A modified version of Grading of Recommendations Assessment, Development and Evaluation (GRADE), that is, using GRADE in situations of emergencies and urgencies during the Covid-19 pandemic, was used to evaluate the certainty of evidence by outcomes.[7]

# 3 | RESULTS

Five controlled trials (four RCTs[8-11] and one non-RCT[12]), were included; see Figure 1 for a preferred reporting items for systematic reviews and meta-analyses flow diagram of included studies.

Two RCTs and one non-RCT tested oral ivermectin, alone or in combination with a barrier nasal spray, using different dosing schedules. One RCT tested bamlanivimab, and another RCT tested REGEN-COV (casirivimab and imdevimab). Table 1 provides a description of the controlled trials included in this rapid review.

The first RCT of ivermectin, by Chahla et al.,[9] was conducted in Argentina, and individuals participated in the study from October to December 2020. The intervention group comprised 117 healthcare workers and administration staff, mean age 39.6 years ($\pm$9.4). The control group comprised 117 healthcare workers and administration staff, mean age 38.4 years ($\pm$7.4). The intervention group received ivermectin orally (12 mg every 7 days) and iota-carrageenan nasal spray six sprays per day for 4 weeks, plus standard biosecurity care and personal protective equipment (PPE). The control group received standard biosecurity care and PPE only.[9] The number of subjects diagnosed with Covid-19 was lower in the intervention group; 4/117 (3.4%) compared with 25/117 (21.4%) in control group ($p = 1.10^{-5}$). The odds of being diagnosed with Covid-19 was lower in the treatment group (adjusted odds ratio [aOR] 0.11, 95% confidence interval [CI] 0.03–0.33; adjusted for comorbidity, age, sex and designation (healthcare vs. non healthcare)[9]; see Table 1.

The second RCT of ivermectin, by Shoumann et al.,[8] was conducted in Egypt between June and July 2020. The aim of the study was to evaluate prophylactic use of ivermectin in asymptomatic family close contacts of patients with Covid-19. In the intervention arm, contacts received two doses of ivermectin according to their body weight on the day of diagnosis of the index case (day 1) and again at day 3. The weight adjusted dose was 15 mg per day for those with a body weight of 40–60 kg, 18 mg per day for those with a body weight of 60–80 kg and 24 mg per day for those with a body weight greater than 80 kg.[8] The control group received no treatment. During 2 weeks follow-up, 15 contacts (7.4%) had developed Covid-19 symptoms in the intervention group compared to 59 (58.4%) in the control group (these are further broken down into mild, moderate and severe symptoms for each group). Multivariate analysis (adjusted for index case severity, age, sex, any comorbidity) showed that ivermectin had a protective effect (aOR 11.45, 95% CI 4.44–29.48; $p < 0.001$)[8]; see Table 1.

The non-RCT of ivermectin, by Hector et al.,[12] was conducted in Argentina from 1 June to 1 August 2020. The study population included 788 healthcare workers in the intervention arm and 407 healthcare workers in the control arm. To be eligible for inclusion, healthcare workers had to be involved in the care of Covid-19 patients and have a negative reverse transcription polymerase chain reaction at the time of enrolment.[12] Those in the intervention arm received four sprays of carrageenan (0.17 g/spray carrageenan) followed by one drop of ivermectin (0.6 mg/ml). This was repeated five times daily for 2 weeks. The intervention group also received PPE; those in the control arm used PPE only. During 3 months follow-up, the infection rate in the control group was 58.2%; compared to no infections (0%) in the intervention group[12]; see Table 1.

One RCT, by Cohen et al.,[10] that compared bamlanivimab to placebo was conducted in the USA from 2 August 2020 to 20 November 2020, with data collected up to 13 January 2021. The study population included residents and staff of 74 skilled nursing
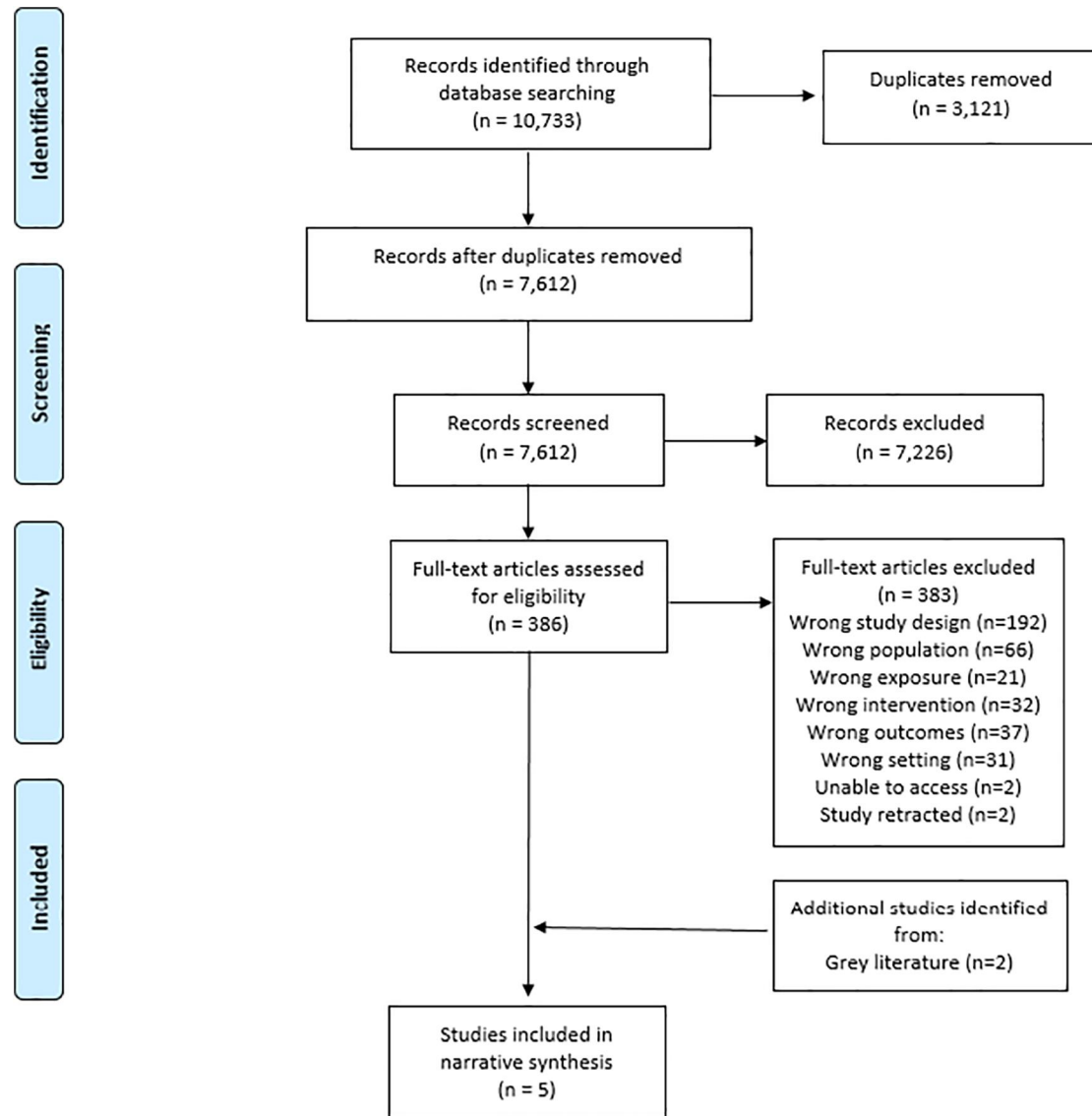
**FIGURE 1** Preferred reporting items for systematic reviews and meta-analyses flow diagram of included studies

and assisted living facilities in the US, with at least one confirmed SARS-CoV-2 index case. In total, $n = 966$ participants were included in the prevention cohort ($n = 300$ residents and $n = 666$ staff). In the residents group, 161 received a single intravenous infusion of bamlanivimab, 4200 mg (intervention group) and 139 received placebo. In the staff group, 323 received the same intervention, and 343 received placebo. The evaluation period was 8 weeks, with follow-up to 24 weeks[10] In the overall prevention population, bamlanivimab significantly reduced the incidence of Covid-19 in the intervention group ($n = 484$) compared with the placebo group ($n = 482$). The incidence of Covid-19 was 8.5% in the intervention group versus 15.2% in the control group (OR 0.43, 95% CI 0.28–0.68); $p < 0.001$. Disaggregated results (for residents and staff separately) showed that the reduction in incidence was statistically significant in residents only. The incidence of Covid-19 was 8.8% in the intervention group versus 22.5% in the control group (OR 0.20, 95% CI 0.08–0.49; $p < 0.001$), compared with 8.4% versus 12.2% in the intervention and

control groups, respectively for staff (OR 0.58, 95% CI 0.33–1.02; $p = 0.6$)[10]; see Table 1.

The fifth trial, by O'Brien et al.,[11] was a double-blind, placebo-controlled RCT of REGEN-COV (casirivimab and imdevimab), conducted at 112 sites in the United States, Romania, and Moldova. The trial had two parts: Part A involved participants who were reverse-transcriptase–quantitative polymerase-chain-reaction (RT-qPCR)-negative, and Part B involved those who were RT-qPCR-positive; the paper included in this rapid review described the results of Part A.[11] A total of 2067 participants had a confirmed SARS-CoV-2–negative RT-qPCR test, of which 1505 (72.8%) had no evidence of previous SARS-CoV-2 infection on serologic testing. These 1505 were randomly allocated to receive a subcutaneous injection of 1200 mg REGEN-COV ($n = 753$ participants) or placebo ($n = 752$ participants). Participants were followed up weekly and interviewed by study investigators to assess for signs and symptoms of Covid-19 and adverse events.[11] During 28-day follow-up, REGEN-COV

**TABLE 1** Description of controlled trials included in this rapid review

| Study characteristics | Population, Intervention, Comparator, Outcomes | Patient demographics | Primary outcome results |
|---|---|---|---|
| Author: Chahla[9] (pre-print)<br>Country: Argentina<br>Study design: RCT<br>Setting: Tucumán State Health System | Population: $n = 117$ (intervention group) and $n = 117$ (control group) healthcare workers and administration staff who were PCR negative at baseline<br>Intervention: Ivermectin orally (12 mg every 7 days) and iota-carrageenan nasal spray 6 sprays per day for 4 weeks plus standard biosecurity care and PPE<br>Comparator: Standard biosecurity care and PPE only<br>Outcomes:<br>- Covid-19 symptoms<br>- Covid-19 diagnosis | Intervention group: Mean age ($\pm$SD), 39.6 ($\pm$9.4) years; female, 65%.<br>Control group: Mean age ($\pm$SD), 38.4 ($\pm$7.4) years; female, 61%. | Covid-19 diagnosis<br>Intervention group, 4/117 (3.4%) versus control group 25/117 (21.4%); ($p = 1.10^{-5}$)<br>The probability of Covid-19 diagnosis was significantly lower in the intervention group, (OR 0.13, 95% CI 0.03–0.40, $p = 1.10^{-4}$) versus control group (OR 7.67, 95% CI 2.57–22.85, $p = 1.10^{-4}$).<br>When adjusted for comorbidity, age, sex and designation (healthcare vs. no healthcare), the probability of becoming ill with Covid-19 was significantly lower in the intervention group (aOR 0.11, 95% CI 0.03–0.33, $p = 1.10^{-4}$).<br>Covid-19 symptoms<br>Intervention group: 4 patients (mild)<br>Control group: 15 patients (mild); 7 patients (moderate); 3 patients (severe).<br>Safety outcomes<br>Adverse effects, they were not reported in any case. |
| Author: Hector[12]<br>Country: Argentina<br>Study design: Non-RCT<br>Setting: Four hospitals (data were collected from 1 June to 1 August 2020) | Population: $n = 788$ (intervention group) and $n = 407$ (control group) asymptomatic HCWs with negative PCR or rapid tests, involved in care of COVID-19 patients.<br>Intervention: 4 sprays of carrageenan (1 spray 0.17 g carrageenan) followed by 1 drop ivermectin (0.6 mg/ml). This was repeated 5 times daily for 2 weeks.<br>Comparator:<br>PPE only<br>Outcomes:<br>- Covid-19 diagnosis | Intervention: Mean age, N/R; male, N/R.<br>Control: Mean age, N/R; male, N/R. | Covid-19 diagnosis<br>Intervention group, 0% versus control group 58.2% ($p < 0.0001$).<br>Safety outcomes<br>Not reported. |
| Author: Shoumann[8]<br>Country: Egypt<br>Study design: RCT<br>Setting: Community | Population: $n = 203$ (intervention group) and $n = 101$ (control group) asymptomatic household family members in close contact with cases of Covid-19.<br>Intervention: Ivermectin weight adjusted dose was 15 mg per day for those with a body weight 40–60 kg, 18 mg per day for those with a body weight 60–80 kg and 24 mg per day for those with a body weight >80 kg.<br>Comparator:<br>No treatment.<br>Outcomes:<br>- Symptomatic Covid-19 (not all PCR-confirmed) | Intervention: Mean age, 40 years; male, 52.2%.<br>Control: Mean age, 38 years; male, 49.5%. | Symptomatic Covid-19:<br>- Intervention group:<br>15 (7.4%) overall<br>8 (53.3%) mild<br>6 (40%) moderate<br>1 (6.7%) severe<br>- Control group:<br>59 (58.4%) overall<br>31 (52.5%) mild<br>21 (35.6%) moderate<br>7 (11.9%) severe<br>The probability of symptomatic Covid-19 was significantly higher in the control group (OR 12.53, 95% CI 7.41–21.21) $p < 0.001$. When adjusted for index case severity, age, sex and any comorbidity the probability of symptomatic Covid-19 was significantly higher in the control group (aOR 11.45, 95% CI 4.44–29.48) $p < 0.001$.<br>Safety outcomes<br>Reported side effects were mild and reported in 11 (5.4%) contacts: |

**T A B L E 1** (Continued)

| Study characteristics | Population, Intervention, Comparator, Outcomes | Patient demographics | Primary outcome results |
|---|---|---|---|
| | | | - Diarrhoea in 3 (1.5%)<br>- Nausea in 2 (1%)<br>- Fatigue in 2 (1%)<br>- Sleepiness in 1 (0.5%)<br>- Abdominal pain in 1 (0.5%)<br>- Heart burn in 1 (0.5%)<br>- Tingling and numbness in 1 (0.5%)<br>- Burning sensation in 1 (0.5%). |
| Author: Cohen[10]<br>Country: US<br>Study design: RCT<br>Setting: Skilled nursing and assisted living facilities | Population: $n = 966$ participants (666 staff and 300 residents) of 74 skilled nursing and assisted living facilities with at least 1 confirmed SARS-CoV-2 index case.<br>Intervention: Bamlanivimab, 4200 mg as a single intravenous infusion.<br>Comparator: Placebo<br>Outcomes:<br>Covid-19 diagnosis | Intervention group (residents): Median age (range), 76.0 (31–104) years; female, $n$ (%): $n = 95$ (59.0%).<br>Control group (residents): Median age (range), 75.0 (41–96) years; female, $n$ (%): $n = 84$ (60.4%).<br>Intervention group (staff): Median age (range), 43.0 (18–82) years; female, $n$ (%): $n = 260$ (80.5%).<br>Control group (staff): Median age (range), 42.0 (18–74) years; female, $n$ (%): $n = 283$ (82.5%). | Covid-19 diagnosis (overall):<br>Intervention group, 8.5% vs. control group 15.2%).<br>(OR 0.43, 95% CI 0.28–0.68); $p < 0.001$.<br>Covid-19 diagnosis (residents):<br>Intervention group, 8.8% vs. control group 22.5%).<br>(OR 0.20, 95% CI 0.08–0.49); $p < 0.001$.<br>Covid-19 diagnosis (staff):<br>Intervention group, 8.4% vs. control group 12.2%).<br>(OR 0.58, 95% CI 0.33–1.02); $p = 0.6$. |
| Author: O'Brien[11]<br>Country: US, Romania and Moldova<br>Study design: RCT<br>Setting: Community | Population: $n = 1,505$ (intervention group, $n = 753$ and comparator group, $n = 752$) previously uninfected household contacts of infected persons.<br>Intervention: Subcutaneous REGEN-COV at a total dose of 1200 mg (600 mg each of casirivimab and imdevimab which are monoclonal antibodies).<br>Comparator: Placebo<br>Outcomes:<br>- Symptomatic SARS-CoV-2 infection (RT-PCR confirmed)<br>- High viral load ($>10^4$ copies/ml)<br>- Duration of symptomatic RT-PCR confirmed SARS-CoV-2 infection (weeks)<br>- Duration of high viral load (weeks)<br>- Duration of symptomatic or asymptomatic RT-PCR confirmed SARS-CoV-2 infection (weeks)<br>- Symptomatic or asymptomatic SARS-CoV-2 infection (RT-PCR confirmed) | Intervention group: Mean age (range), 43.2 (12–87) years; male, $n = 333$ (44.2%).<br>Control group: Mean age (range), 42.7 (12–92) years; male, $n = 358$ (47.6%). | Symptomatic SARS-CoV-2 infection ($n$, participants)<br>Intervention versus placebo, $n = 11/753$ (1.5%) versus $n = 59/752$ (7.8%).<br>Relative risk reduction, 81.4%. (OR 0.17, 95% CI 0.09–0.33); $p < 0.001$.<br>High viral load ($n$, participants)<br>Intervention versus placebo, $n = 12/745$ (1.6%) versus $n = 85/749$ (11.3%).<br>Relative risk reduction, 85.8%. (OR 0.13, 95% CI 0.07–0.24); $p < 0.001$.<br>Duration of symptomatic SARS-CoV-2 infection (weeks)<br>Intervention versus placebo, $n = 12.9$ versus $n = 187.7$.<br>Relative difference versus placebo, 93.1%; $p < 0.001$.<br>Duration of high viral load (weeks)<br>Intervention versus placebo, $n = 14.0$ versus $n = 136.0$.<br>Relative difference versus placebo, 89.6%; $p < 0.001$.<br>Duration of symptomatic or asymptomatic SARS-CoV-2 infection (weeks)<br>Intervention versus placebo, $n = 41.0$ versus $n = 231.0$.<br>Relative difference versus placebo, 82.3%; $p < 0.001$.<br>Symptomatic or asymptomatic SARS-CoV-2 infection<br>Intervention versus placebo, $n = 36$ (4.8%) versus $n = 107$ (14.2%).<br>Relative risk reduction, 66.4%. (OR 0.31, 95% CI 0.21–0.46); $p < 0.001$. |

Abbreviations: aOR, adjusted OR; CI, confidence intervals; Covid-19, coronavirus disease 2019; HCW, healthcare worker; non-RCT, non-RCT; OR, odds ratio; PCR, polymerase chain reaction; PPE, personal protective equipment; RCT, randomised controlled trial; RT-PCR, reverse transcriptase PCR; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

significantly reduced the incidence of SARS-CoV-2 infection in the intervention group (1.5%) compared with the placebo group (7.8%) (OR 0.17, 95% CI 0.09–0.33); $p < 0.001$. Additionally, those in the intervention group had a significant reduction in SARS-CoV-2 viral load, duration of symptomatic SARS-CoV-2 infection, duration of high SARS-CoV-2 viral load ($>10^4$ copies/ml), duration of symptomatic or asymptomatic SARS-CoV-2 infection and incidence of symptomatic or asymptomatic SARS-CoV-2[11]; see Table 1.

The quality of the RCTs was appraised using the Cochrane Collaboration's tool for assessing risk of bias in randomised trials.[5] One RCT[8] of ivermectin was deemed to be at high overall risk of bias, while some concerns were identified for the other RCT.[9] Specific domains of concern were potential bias in the measure of outcomes and bias arising from the randomisation process. Furthermore, the trial by Chahla et al.[9] is published as a pre-print which means it has not yet been formally peer-reviewed and reported results may change following peer-review. Using Robins-I,[6] the non-RCT by Hector et al.,[12] was deemed to have a serious risk of bias, particularly in relation to the following domains: bias due to confounding, measurement of outcomes and selection of the reported result. The RCT of bamlanivimab by Cohen et al.[10] and the RCT of REGEN-COV by O'Brien et al.[11] were both deemed to be at low risk of bias; however, it is worth noting that the RCT by O'Brien et al. was funded by Regeneron Pharmaceuticals and others.

Using a modified version of GRADE,[7] the certainty of evidence for the use of ivermectin to prevent Covid-19 disease was considered 'very low'. All studies were downgraded for limitations due to research design, that is, non-blinded designs, inappropriate adjustment for confounding variables and premature stopping of the non-intervention arm in one RCT. Studies were also downgraded for imprecision due to small sample sizes (range 234–1195 participants) and short durations of follow-up (2–12 weeks). The certainty of evidence for the use of bamlanivimab to prevent Covid-19 disease was considered 'very low'. This RCT was downgraded for limitations due to research design (i.e., nasal swabs alone, which may have lower sensitivity than nasopharyngeal swabs, were obtained for subsequent SARS-CoV-2 detection during the evaluation and follow-up period) and imprecision due to small sample sizes (966 participants) and short durations of follow-up (24 weeks). The certainty of evidence for the use of REGEN-COV to prevent Covid-19 disease was considered 'low'. This RCT was downgraded for imprecision due to small sample sizes (1505 participants) and short durations of follow-up (28 days). The designations 'low' and 'very low' (regarding the certainty of evidence) indicate that the estimate of effect is uncertain and should not be relied upon to inform decision-making.

## 4 | DISCUSSION

This rapid review identified five controlled trials of pharmacological interventions to prevent Covid-19; additionally, 60 ongoing trials were identified, and the results of which are yet to be published. Three trials tested ivermectin for the prevention of Covid-19, either used alone or in combination with (iota) carrageenan nasal spray. Carrageenans have displayed viricidal effects in vitro against a range of different viruses including human rhinoviruses and the influenza virus.[9] In the US and EU, ivermectin is approved in humans for treatment of some parasitic worm infestations and skin conditions such as rosacea. While ivermectin has been shown to inhibit SARS-CoV-2 in vitro, the dose required to achieve adequate concentrations in the lungs to be effective against SARS-CoV-2, is much higher than currently authorised for use in other conditions.[13] In a living systematic review and network meta-analysis of pharmacological prevention of Covid-19, the authors concluded that the evidence for ivermectin with or without iota-carrageenan is very uncertain in relation to its ability to reduce the risk of Covid-19 disease and mortality.[2] This uncertainty is due to a serious risk of bias and very serious imprecision in the included trials. Moreover, the effect estimates are likely to change substantially with additional evidence from ongoing trials.[2]

Ivermectin has received substantial media coverage, based on observational studies suggesting a potential benefit in treatment and prophylaxis of Covid-19. However, there is a lack of evidence from rigorous RCTs to inform policy. Indeed, the trials[8,9,12] included in this rapid review do not change this, and in addition, safety outcomes were either poorly reported or not reported. The recent removal of an ivermectin trial pre-print from Research Square (a pre-print server) has drawn attention to the evidence base for the treatment.[14] Research Square have launched an investigation into the ethical concerns raised about the pre-print. Such concerns included plagiarism within the manuscript, duplication of patient records, inconsistencies between the raw data and that reported in the manuscript, the inclusion of patients who had died before the study's start date and reported numbers that seemed too consistent to have occurred by chance.[14]

At the time of writing, the US Food and Drug Administration (FDA) have advised against the use of ivermectin for the prevention or treatment of Covid-19. Similarly, the European Medicines Agency (EMA)[15] concluded that ivermectin cannot currently be recommended outside controlled clinical trials, and that rigorous RCTs are needed to determine if ivermectin is safe and effective for the prevention and treatment of Covid-19.

The fourth trial identified was a RCT of bamlanivimab, a monoclonal antibody designed to attach to the spike protein of SARS-CoV-2 to prevent it from entering the body's cells.[10] This RCT was conducted in nursing homes and assisted living facilities in the US. The findings showed that bamlanivimab significantly reduced the incidence of Covid-19 in the overall prevention population (compared with placebo), but disaggregated results showed that this effect was only significant in the residents' subgroup, not the staff. The authors concluded that further research is needed to assess the preventive efficacy of this therapy.[10] On 9 November 2020, the US FDA issued an emergency use authorisation for the use of bamlanivimab monotherapy for mild to moderate Covid-19 in adults and paediatric patients (aged 12 years of age and older weighing at least 40 kg) who are at high risk for progressing to severe Covid-19 and or

hospitalisation.[16] However, in light of emerging variants of concern, this emergency use authorisation for bamlanivimab monotherapy was revoked (on 16 April 2021), due to concerns that these variants may be resistant to bamlanivimab monotherapy.[16] At the time of writing, the EMA and FDA have not given guidance on the use of bamlanivimab for prevention of Covid-19.

The fifth trial identified was a RCT of REGEN-COV (called Ronapreve in the UK), which is a combination of two neutralising monoclonal antibodies (casirivimab and imdevimab).[11] In outpatients with Covid-19, REGEN-COV has been shown to reduce the incidence of hospitalisations and death, reduce viral load and shorten the duration of symptoms.[11] As such, an emergency use authorisation for these agents (administered together) was granted by the FDA for the treatment of mild to moderate Covid-19,[17] and post-exposure prophylaxis of Covid-19 in individuals aged ≥12 years of age who are at high risk of severe Covid-19.[18] The trial included in this rapid review was conducted in participants without Covid-19, but who were at high risk of SARS-CoV-2 infection due to household exposure to a person with confirmed SARS-CoV-2 infection.[11] REGEN-COV was reported to be protective against SARS-CoV-2 infection during 28 days follow-up. Safety data showed that 20.2% (REGEN-COV group) and 29.0% (placebo group) had at least one adverse event; no participant reported any adverse events of special interest, and no one withdrew from the trial due to an adverse event.[11] On 20 August 2021, the Medicines and Healthcare Products Regulatory Agency in the UK approved Ronapreve (i.e., RENGEN-COV) for the treatment and prevention of acute Covid-19 in adults.[19] While the results for RENGEN-COV (i.e., Ronapreve) are promising; more data are required before such an intervention can be recommended for widespread prevention of Covid-19.

In addition to the controlled trials included in this rapid review, phase I RCT data were identified with respect to the safety of another monoclonal antibody, meplazumab. However, no Covid-19 outcomes were included, and it is unclear if it is intended that this agent would be used for the prevention of Covid-19.[20]

## 5 | LIMITATIONS

Rapid reviews have methodological limitations due to the time constraints involved. The included evidence for ivermectin, bamlanivimab and REGEN-COV was deemed to be of 'low' or 'very low' certainty, thus not suitable for informing changes in policy. Moreover, one trial was a pre-print and had not been formally peer-reviewed. This raises additional concerns about the overall quality and the potential for results to change prior to formal publication of these studies.

## 6 | CONCLUSION

This rapid review of available evidence is consistent with other international reviews, indicating insufficient evidence to support the use of any pharmacological interventions to prevent Covid-19. While Covid-19 vaccination is currently the most effective preventive strategy; additional measures for prevention of Covid-19 continue to be social distancing, hand hygiene, cough etiquette, mask wearing and avoidance of places where Covid-19 spreads more readily such as poorly ventilated and enclosed spaces.

## CONFLICT OF INTEREST

No conflict of interest declared.

## ETHICS STATEMENT

Ethics approval was not required for this study as it involved a review of the published literature.

## AUTHOR CONTRIBUTION

Karen Cardwell, Eamon O Murchu, Paula Byrne, Natasha Broderick, Kieran A. Walsh and Sinéad M. O'Neill scoped the question, constructed the systematic search, screened titles/abstracts and full-texts and completed the data extraction and quality appraisal. Karen Cardwell wrote the manuscript. All authors reviewed and contributed to the writing of the manuscript.

## PATIENT CONSENT

No patients were involved in this study.

## PERMISSION TO REPRODUCE MATERIAL FROM OTHER SOURCES

Not applicable.

## DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analysed in this study.

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