Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

Efficacy and safety of Paxlovid for COVID-19:a meta-analysis

To the Editor:

We read with interest a recent article reported by Wang Y et al. [1]. The authors reported a case of COVID-19 rebound in a severe COVID-19 patient during long term (20 days) treatment of Paxlovid. Paxlovid is a recommended treatment for mild-moderate COVID-19 and risk factors for severe disease. With wide-spread use of Paxlovid, there have been case reports of individuals experiencing virologic rebound. Hence, meta-analysis of the efficiency and safety of Paxlovid in patients with COVID-19 is of great importance.

An extensive literature search was performed in PubMed, Web of Science, EMBASE, and Cochrane Library to find all for relevant studies published from December 1, 2021, to September 20, 2022. We screened the references of the retrieved studies and restricted the language of the search to English. Following keywords were used in the search: Paxlovid (nirmatrelvir/ritonavir) and COVID-19 (SARS-CoV-2, SARS2, SARS Coronavirus 2, Coronavirus Disease 2019, 2019-nCoV, 2019 Novel Coronavirus). The inclusion criteria were as follows: (1) the article reported the clinical results of Paxlovid, including the total number of participants and the specific number of deaths, hospitalization, rebound or adverse events; (2) English language. The exclusion criteria were as follows: (1) irrelevant to the research direction, (2) no relevant data, (3) case reports, (4) review papers, (5) repeated articles.

The analysis was conducted using the Review Manager statistical software, version 5.3. A binary controlled study was used to calculate the number of deaths, hospitalization, rebound or adverse events. Odds ratio (OR) and 95% confidence interval (CI) were used to assess the effect in a whole random-effects meta-analysis model. The I^2 and P value was used to quantify the heterogeneity of the effects among the included studies.

A total of 13 studies involving 186,306 patients were identified in the final analysis, and the detail of the included studies are shown in Table 1 [2-14]. Three studies described the rebound of COVID-19 patients in Paxlovid group and control group. The overall OR of rebound among COVID-19 patients in the Paxlovid vs. control group was 0.99 (95% CI, 0.28–3.57; I^2 =59%), $P = 0.99$ (Fig. 1A). Five studies described adverse events in Paxlovid group and control group. The overall OR of adverse events among COVID-19 patients in the Paxlovid vs. control group was 1.07 (95% CI, 0.49–2.34; I^2 =90%), $P = 0.87$ (Fig. 1B). There is no significant difference of rebound and adverse events in Paxlovid group and control group.

In addition, we analyze the efficacy of Paxlovid on death and hospitalization for COVID-19 patients. Seven studies described the death of COVID-19 patients in the Paxlovid group and control group, and seven studies described the hospitalization of COVID-19 patients. Our study showed that the overall OR for death and hospitalization among COVID-19 patients in the Paxlovid vs. control group was 0.22 (95% CI, 0.11–0.45; I^2 =93%), P <0.0001. The result indicates that the Paxlovid treatment is effective for patients with COVID-19, reducing the mortality or hospitalization rate by 78% (Fig. 1). Subtype analysis shows that the OR of mortality for COVID-19 patients in the Paxlovid vs. control group was 0.12 (95% CI, 0.04–0.36; I^2 =42%), $P = 0.0001$, indicating an 88% reduction in mortality. The OR of hospitalization for COVID-19 patients in the Paxlovid vs. control group was 0.32 (95% CI, 0.13–0.75; I2 =95%), $P = 0.009$, a 68% reduction in hospitalization rate.

In conclusion, our research shows that Paxlovid for COVID-19 is effective and safe. COVID-19 rebound is not unique to Paxlovid. There is no significant difference of rebound in Paxlovid group and control group. There has been more attention to COVID-19 rebounds following Paxlovid treatment, which may be attributable to more people being treated with Paxlovid. However, the phenomenon of rebounds following Paxlovid treatment reinforces the importance of testing for individuals with recurrent symptoms after Paxlovid treatment.

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Declaration of Competing Interest

All authors report that they have no potential conflicts of interest.

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Table 1
Basic information of the included studies.

Study	Events	Paxlovid Group		Placebo group	
		Events (n)	Total (n)	Events (n)	Total (n)
Dryden-Peterson S, 2022[2]	Death	0	6036	39	24,286
	Hospitalization	40	6036	223	24,286
Ganatra S, 2022[3]	Death	0	1130	10	1130
	Hospitalization	10	1130	23	1130
Hammond J, 2022[4]	Death	0	697	9	682
	Hospitalization	5	697	44	682
	Adverse events	476	1109	525	1115
Hedvat J, 2022[5]	Death	0	28	3	75
	Hospitalization	3	28	23	75
Pfizer; 2021[6]	Death	0	607	10	612
	Hospitalization	6	607	41	612
	Adverse events	10	607	40	612
Saravolatz LD, 2022[7]	Death	0	1039	12	1046
	Hospitalization	8	1039	66	1046
	Adverse events	67	1039	22	1046
Wong CKH, 2022[8]	Death	31	890	83	890
Yip TCF, 2022[9]	Hospitalization	172	4921	1931	83,154
Dai EY, 2022[10]	Rebound	3	11	1	25
Wang L, 2022[11]	Rebound	609	11,270	204	2374
Li HY, 2022[12]	Rebound	2	258	3	244
Anderson AS, 2022[13]	Adverse events	23	990	17	980
Yan GF, 2022[14]	Adverse events	2	5	7	30

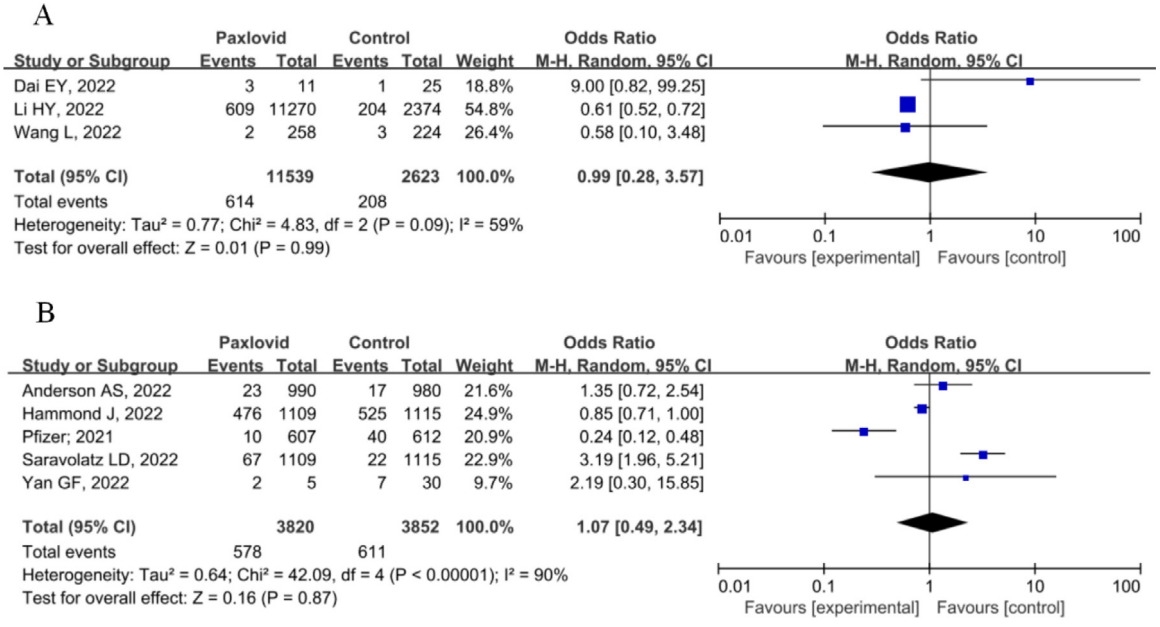

Fig. 1. Incidence of rebound (A) and adverse events (B) in Paxlovid group and control group.

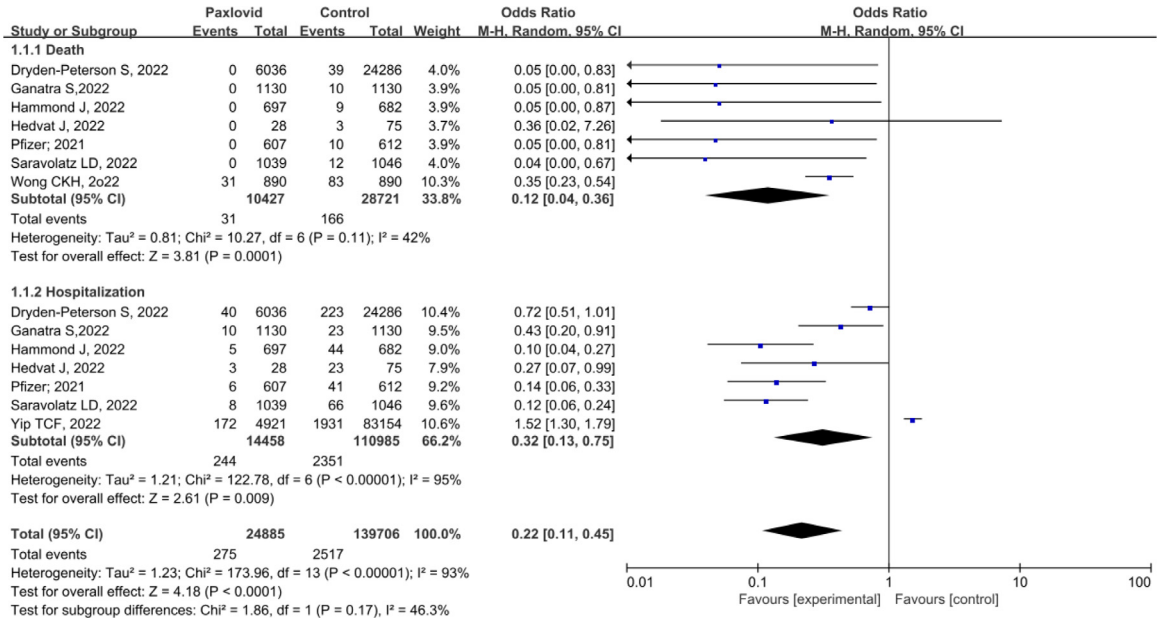

Fig. 2. Subgroup analysis: impact of Paxlovid on mortality and hospitalization rates of COVID-19 patients.

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