

Sofosbuvir with daclatasvir and the outcomes of patients with COVID-19: a systematic review and meta-analysis with GRADE assessment

Ahmad Fariz Malvi Zamzam Zein ^{1,2}, Catur Setiya Sulistiyana,^{1,2}
Wilson Matthew Raffaello,³ Arief Wibowo,⁴ Raymond Pranata ^{3,4}

¹Department of Internal Medicine, Faculty of Medicine Universitas Swadaya Gunung Jati, Cirebon, Indonesia

²Department of Internal Medicine, Waled General Hospital, Cirebon, Indonesia
³Faculty of Medicine Universitas Pelita Harapan, Tangerang, Indonesia

⁴Department of Cardiology and Vascular Medicine, Faculty of Medicine Universitas Padjadjaran, Rumah Sakit Umum Pusat Hasan Sadikin, Bandung, Jawa Barat, Indonesia

Correspondence to

Dr Ahmad Fariz Malvi Zamzam Zein, Universitas Swadaya Gunung Jati, Cirebon 45132, Indonesia; fariz_zein_dr@yahoo.com

Received 12 April 2021
Accepted 21 May 2021

ABSTRACT

Purpose This systematic review and meta-analysis aimed to evaluate the effect of sofosbuvir/daclatasvir (SOF/DCV) on mortality, the need for intensive care unit (ICU) admission or invasive mechanical ventilation (IMV) and clinical recovery in patients with COVID-19.

Methods We performed a systematic literature search through the PubMed, Scopus and Embase from the inception of databases until 6 April 2021. The intervention group was SOF/DCV, and the control group was standard of care. The primary outcome was mortality, defined as clinically validated death. The secondary outcomes were (1) the need for ICU admission or IMV and (2) clinical recovery. The pooled effect estimates were reported as risk ratios (RRs).

Results There were four studies with a total of 231 patients in this meta-analysis. Three studies were randomised controlled trial, and one study was non-randomised. SOF/DCV was associated with lower mortality (RR: 0.31 (0.12, 0.78); $p=0.013$; $I^2: 0\%$) and reduced need for ICU admission or IMV (RR: 0.35 (0.18, 0.69); $p=0.002$; $I^2: 0\%$). Clinical recovery was achieved more frequently in the SOF/DCV (RR: 1.20 (1.04, 1.37); $p=0.011$; $I^2: 21.1\%$). There was a moderate certainty of evidence for mortality and need for ICU/IMV outcome, and a low certainty of evidence for clinical recovery. The absolute risk reductions were 140 fewer per 1000 for mortality and 186 fewer per 1000 for the need for ICU/IMV. The increase in clinical recovery was 146 more per 1000.

Conclusion SOF/DCV may reduce mortality rate and need for ICU/IMV in patients with COVID-19 while increasing the chance for clinical recovery.

Protocol registration PROSPERO: CRD42021247510.

INTRODUCTION

COVID-19 remains one of the most prevalent diseases globally despite the best effort to contain them.¹ Although most patients have mild–moderate clinical symptoms, a significant proportion of them developed lethal acute complications.^{2–4} Optimal medications for COVID-19 remained poorly defined, and many completed trials showed negative results.⁵

SARS-CoV-2 is a positive-sense single-stranded RNA virus that relies on RNA-dependent RNA-polymerase (RdRp) for viral replication.⁶ Sofosbuvir/daclatasvir (SOF/DCV) is a direct-acting antiviral drug that has been shown to inhibit RdRp of hepatitis C virus (HCV).^{7,8} Preclinical studies

indicate the potential activities of SOF and DCV on SARS-CoV-2 RdRp, although the mixed results.^{9,10} Several clinical studies indicate the potential benefit of SOF/DCV in patients with COVID-19.^{9,11,12} These drugs have relatively mild side effects and are affordable. Thus, it can be used as a routine treatment if proven to be effective.^{9,13} This systematic review and meta-analysis aims to evaluate the effect of SOF/DCV on mortality, the need for intensive care unit (ICU) admission or invasive mechanical ventilation (IMV) and clinical recovery in patients with COVID-19.

MATERIALS AND METHODS

This is a Preferred Reporting Items for Systematic Reviews and Meta-Analyses compliant systematic review and meta-analysis. This study is registered in PROSPERO (blinded for peer review).

Search strategy and study selection

We performed a systematic literature search through PubMed, Scopus and Embase using the terms ‘(SARS-CoV-2 or 2019-nCoV or COVID-19) and (sofosbuvir or daclatasvir or Sofosbuvir/daclatasvir)’ from the inception of databases until 6 April 2021. Screening of title/abstracts were performed by two independent authors. The eligibility of the articles was assessed based on the inclusion and exclusion criteria. Discrepancies that arose were resolved by discussion.

Inclusion and exclusion criteria

Studies that match the following criteria were included: (1) randomised controlled trials (RCTs) or observational studies in patients with COVID-19, (2) comprise of SOF/DCV arm and a control arm and (3) reporting either (a) mortality or (b) the need for ICU admission or IMV or (c) clinical recovery.

Studies that match one of the following criteria were excluded: (1) conference papers, (2) abstract-only publications, (3) review articles and (4) commentaries. We did not impose any language restriction for this systematic review.

Data extraction

Two authors independently extracted data from the studies for the first author, study design, country of origin, setting of the study (inpatients or outpatients), details and dosing of the intervention group, details and dosing of the control group, sample size,



© Author(s) (or their employer(s)) 2021. No commercial re-use. See rights and permissions. Published by BMJ.

To cite: Zein AFMZ, Sulistiyana CS, Raffaello WM, et al. *Postgrad Med J* Epub ahead of print: [please include Day Month Year]. doi:10.1136/postgradmedj-2021-140287

age, gender, diabetes, chronic obstructive pulmonary disease, chronic kidney diseases, cardiovascular diseases and the laboratory values, including haematology parameters and liver and renal functions. Discrepancies were resolved by discussion.

Risk of bias assessment

We used the Cochrane Risk of Bias Assessment for RCTs¹⁴ and Newcastle-Ottawa Scale (NOS).¹⁵ NOS comprises of selection, comparability and outcome. Cochrane Risk of Bias Assessment assessed the possibility for selection, performance, detection, attrition, selective reporting and other biases. Discrepancies during the process were resolved by discussion. Grading of Recommendations Assessment, Development and Evaluation framework was used to determine the certainty of evidence.

Intervention and outcome

The intervention group was SOF/DCV, defined as 400mg SOF and 60mg DCV to treat COVID-19. The control group was the standard of care or placebo set by each trial/studies. The primary outcome was mortality, defined as clinically validated death. The pooled effect estimate was reported as risk ratio (RR). The secondary outcomes were (1) the need for ICU admission or IMV and (2) clinical recovery. Clinical recovery was defined as resolution of fever ($\leq 37.2^{\circ}\text{C}$) with a normal respiratory rate (≤ 24 breaths/min) and oxygen saturation ($\geq 94\%$) without the need for supplementary oxygen therapy for at least 24 hours or can be discharged from the hospital based on clinical improvement. The pooled effect estimate was reported as RRs.

Statistical analysis

DerSimonian Laird random-effects meta-analysis was used to calculate the pooled RRs for mortality, need for ICU admission/IMV and clinical recovery in the SOF/DCV compared with the control group. P values (two-tailed) of ≤ 0.05 were considered statistically significant. To evaluate heterogeneity, we used Cochran's Q test and I^2 statistics; I^2 values above 50% and p value below 0.10 indicate significant heterogeneity. Sensitivity analysis was performed for outpatient studies. STATA V.16.0 was used to perform the statistical analysis.

RESULTS

Baseline characteristics

There were four studies with a total of 231 patients in this systematic review and meta-analysis (figure 1).^{9 11 12 16} Three studies were RCT, and one study was non-randomised (table 1).

SOF/DCV and outcomes

SOF/DCV administration was associated with reduced mortality (RR: 0.31 (0.12, 0.78)], $p=0.013$; I^2 : 0%, $p=0.400$) (figure 2). Use of SOF/DCV was associated with reduced need for ICU admission or IMV (RR: 0.35 (0.18, 0.69), $p=0.002$; I^2 : 0%, $p=0.700$) (figure 3). Clinical recovery was achieved more frequently in the SOF/DCV (RR: 1.20 (1.04, 1.37), $p=0.011$; I^2 : 21.1%, $p=0.284$) (figure 4). Sensitivity analysis by removal of outpatient setting (Roosbeh *et al*¹⁶ 2021) showed that SOF/DCV

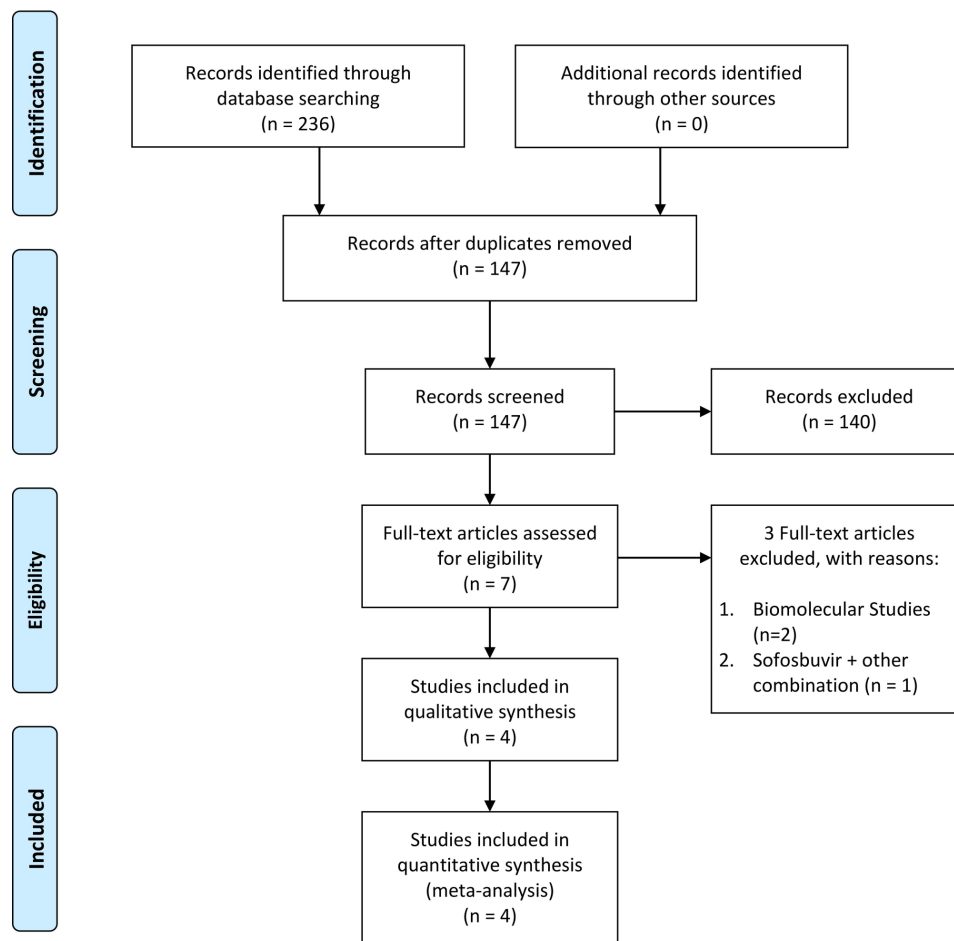


Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses flowchart.

Table 1 Baseline characteristics of the included studies

	Eslami <i>et al</i> ¹¹ 2020	Abbaspour Kasgari <i>et al</i> ¹² 2020	Roozbeh <i>et al</i> ¹⁶ 2021	Sadeghi <i>et al</i> ⁹ 2020
Study design	Open-label parallel	RCT	RCT	RCT
Trial registration number	IRCT20200324046850N2	IRCT20200328046886N1	IRCT20200403046926N1	IRCT20200128046294N2
Country of origin	Iran	Iran	Iran	Iran
Setting	Inpatients	Inpatients	Outpatients	Inpatients
COVID-19 severity	Severe	Moderate	Unclear	Moderate/severe
Sample size	35 vs 27	24 vs 24	27 vs 28	33 vs 33
Intervention	400 mg SOF and 60 mg DCV	400 mg SOF and 60 mg DCV+600 mg ribavirin	400 mg SOF and 60 mg DCV+HCQ	400 mg SOF and 60 mg DCV+SOC
Control	600 mg ribavirin	600 mg ribavirin+HCQ+400 mg iopinavir and 100 mg ritonavir two times per day	HCQ	SOC
Age (years)	61	53	45	60
Male (%)	51	37	47.3	51.5
Diabetes (%)	27.4	29.2	–	42.4
COPD (%)	9.6	2.1	–	–
CKD (%)	3.8	–	–	–
CVD (%)	23.1	23	–	–
Haemoglobin (g/L)	120	120	–	120
WBC ($\times 10^9/L$)	7.6	6.3	–	8.5
Lymphocyte ($\times 10^9/L$)	1.2	–	–	1.3
AST (IU/L)	30	26	–	35
ALT (IU/L)	23	22	–	32
Creatinine (mg/dL)	1.1	0.9	–	1
Risk of bias	NOS: 7 out of 9	Low–moderate	Low–moderate	Low–moderate
Funding	Abadan Faculty of Medical Sciences	Mazandaran University of Medical Sciences	Vice-Chancellor for Research at Mazandaran University of Medical Sciences	Digestive Disease Research Institute of Tehran University of Medical Science

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; DCV, daclatasvir; HCQ, hydroxychloroquine; NOS, Newcastle-Ottawa Scale; RCT, randomised controlled trial; SOC, standard of care; SOF, sofosbuvir; WBC, white blood cells.

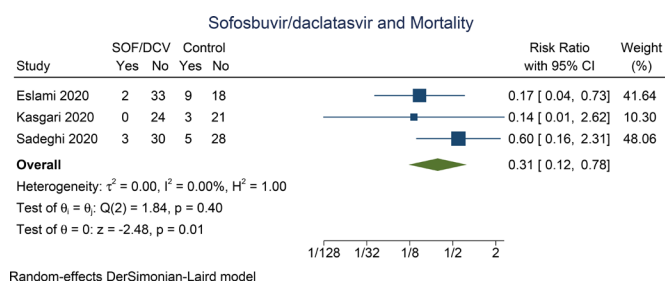
use in in-hospital setting was associated with increased clinical recovery (RR: 1.23 (1.08, 1.40), $p < 0.001$; I^2 : 0.3%, $p = 0.367$).

Risk of bias assessment

The risk of bias assessment of individual studies indicates low–moderate risk of bias (figure 5) (table 1).

Certainty of evidence

There was a moderate certainty of evidence for the mortality and need for ICU/IMV outcome, and a low certainty of evidence for clinical recovery (table 2). The absolute risk reductions were 140 fewer per 1000 (from 178 fewer to 45 fewer) for mortality and 186 fewer per 1000 (from 234 fewer to 89 fewer) for the need for ICU/IMV. The increase in clinical recovery was 146 more per 1000 (from 29 more to 278 more).



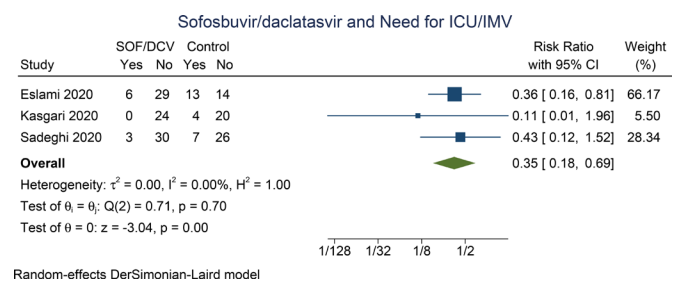
Random-effects DerSimonian-Laird model

Figure 2 Sofosbuvir/daclatasvir (SOF/DCV) and mortality.

DISCUSSION

This meta-analysis indicates that SOF/DCV use may reduce the mortality rate and need for ICU/IMV in patients hospitalised with moderate–severe COVID-19. The overall clinical recovery rate was also achieved more frequently in patients receiving SOF/DCV, especially in hospitalised patients.

This pooled analysis has low heterogeneity, which indicates small risk of inconsistency. The CI does not cross the imprecision threshold. Large study effects were demonstrated for mortality and the need for ICU/IMV outcomes. However, all included studies originated from a single country (Iran). Additionally, all studies have small sample size and positive results except for one in ‘clinical recovery’ outcome. One of the study that was excluded during the systematic literature search, uses a combination of SOF/ledipasvir, the open-label randomised clinical trial on 82 patients with mild–moderate COVID-19 indicates no



Random-effects DerSimonian-Laird model

Figure 3 Sofosbuvir/daclatasvir (SOF/DCV) and the need for intensive care unit admission (ICU) or invasive mechanical ventilation (IMV).

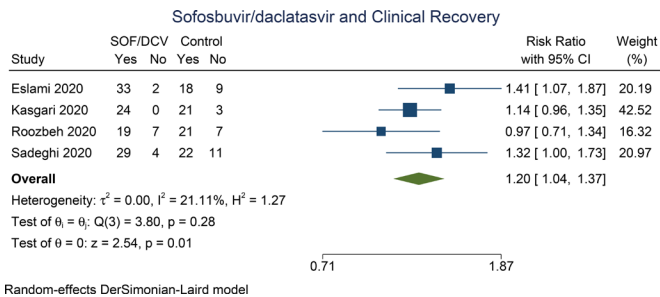


Figure 4 Sofosbuvir/daclatasvir (SOF/DCV) and clinical recovery.

benefit in terms of clinical response, duration of hospital and ICU stay and 14-day mortality, although it decreases the time to the clinical response.¹⁷

SARS-CoV-2 is a positive-sense RNA virus that highly relies on an RdRp for its replicating process.¹⁶ SOF/DCV has proven to inhibit the HCV replication effectively and potentially inhibit SARS-CoV-2 replication.¹⁸ Similar replication mechanism is demonstrated by other viral families, therefore, raising the possibility of using a particular antiviral regimen interchangeably, especially in the context of SARS-CoV-2 infections.¹⁶

Several key proteins have been identified in the replication of HCV, such as non-structural protein 5A (NS5A) and NS protein 5B (NS5B), which become a target of direct-acting antiviral activity of the SOF.¹⁸ Both HCV proteins NS5A and NS5B might share several similarities with SARS-CoV-2 proteins.¹⁸

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Kasgari 2020	+	+	-	+	+	+	+
Roozbeh 2020	+	?	+	+	+	?	+
Sadeghi 2020	+	?	-	+	+	+	+

Figure 5 Risk of bias assessment for randomised controlled trials.

Certainty assessment	Number of patients		Effect		Importance
	Number of studies	Study design	Risk of bias	Number of patients	
Mortality	3	Randomised trials	Serious*	17/84 (20.2%)	High
			Not serious	5/92 (5.4%)	Moderate
			Not serious	17/84 (20.2%)	Moderate
			Not serious	5/92 (5.4%)	Moderate
Need for ICU/IMV	3	Randomised trials	Serious*	24/84 (28.6%)	High
			Not serious	9/92 (9.8%)	Moderate
			Not serious	24/84 (28.6%)	Moderate
			Not serious	9/92 (9.8%)	Moderate
Clinical recovery	4	Randomised trials	Serious*	82/112 (73.2%)	High
			Not serious	105/118 (89.0%)	Low
			Not serious	82/112 (73.2%)	Low
			Not serious	105/118 (89.0%)	Low

* One study is not a randomised trial; two studies are open label.
 † All studies originated from a single country. Small-sample size with all positive studies.
 ‡ All studies originated from a single country. Small-sample size with all positive studies except for one.
 GRADE, Grading of Recommendations Assessment, Development and Evaluation; ICU, intensive care unit; IMV, invasive mechanical ventilation; RR, Risk ratio.

For instance, HCV NS5A is a multifunctional protein involved in HCV replication process and interferon signalling pathway. This protein resembles the non-structural proteins (nsp) 1–14 in SARS-CoV-2.¹⁹ HCV NS5B RNA polymerase might resemble RdRp of SARS-CoV-2, which is also known as nsp12.^{18 20} The SARS-CoV-2 nsp12 along with nsp7 and nsp8, which serve as its cofactor, catalyse the synthesis of viral RNA and thus playing an integral role in the replication of SARS-CoV-2.²¹ DCV binds to HCV NS5A and interferes with viral RNA replication and assembly and the production of inflammatory cytokines.^{18 22} In SARS-CoV-2, DCV shows an inhibition of viral replication and induction of interleukin-6 (IL-6) and tumor necrosis factor alpha (TNF-alpha), which play a significant role in cytokine storm.¹⁸

SOF is a nucleotide analogue that targets HCV RNA polymerase NS5B, therefore, preventing the addition of the next nucleotide and inhibiting RNA elongation.²³ The action of SOF is also extended beyond HCV as it also demonstrates similar antiviral activity against other viruses.^{24–26} In SARS-CoV-2, SOF serves as a competitive inhibitor and chain terminator of the SARS-CoV-2 RNA polymerase, which is well shown in an enzymatic assay.^{27 28} Structural superposition of the SARS-CoV-2 nsp12 with HCV NS5B was found to bind with SOF, therefore, showing its inhibitory effect.²³ This antiviral activity is retained possibly due to the preservation of RdRp structure among RNA viruses.²⁶

In silico, the potential activities of SOF/DCV against SARS-CoV-2 are well demonstrated.^{23 29} This discovery is reinforced by the finding of in vitro activity against SARS-CoV-2 demonstrated by SOF/DCV in Huh-7 and Calu-3 cells.¹⁸ Although current evidence is still lacking, to date, SOF/DCV is known for its good safety profile in treating HCV and shows a promising result against SARS-CoV-2.¹⁸ Therefore, further study is needed to elucidate the use of SOF/DCV in the treatment of COVID-19.

The limitations of this systematic review and meta-analysis were due to a small number and sample size of the studies.

Moreover, all studies originated from Iran, and it is not known whether it will be applicable to patients from other countries. Further investigation is needed to obtain a higher certainty of evidence.

CONCLUSION

SOF/DCV use may reduce mortality rate and need for ICU/IMV in patients with COVID-19 while increasing the chance for clinical recovery.

Twitter Raymond Pranata @RaymondPranata

Contributors AFMZZ, CSS and RP were involved in the conceptualisation and design of the manuscript. AFMZZ, CSS, AW, WMR and RP participated in data curation and investigation. RP performed data analysis, formal analysis and statistical analysis. AFMZZ, CSS and WMR drafted the manuscript. AW and RP reviewed and edited the manuscript.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

This article is made freely available for use in accordance with BMJ's website terms and conditions for the duration of the covid-19 pandemic or until otherwise determined by BMJ. You may use, download and print the article for any lawful, non-commercial purpose (including text and data mining) provided that all copyright notices and trade marks are retained.

ORCID iDs

Ahmad Fariz Malvi Zamzam Zein <http://orcid.org/0000-0001-7821-3813>

Raymond Pranata <http://orcid.org/0000-0003-3998-6551>

REFERENCES

- 1 WHO. Weekly epidemiological update - 2 March 2021, 2021. Available: <https://www.who.int/publications/m/item/weekly-epidemiological-update-2-march-2021>
- 2 Pranata R, Huang I, Raharjo SB. Incidence and impact of cardiac arrhythmias in coronavirus disease 2019 (COVID-19): a systematic review and meta-analysis. *Indian Pacing Electrophysiol J* 2020;20:193–8.
- 3 Lim MA, Pranata R, Huang I, et al. Multiorgan failure with emphasis on acute kidney injury and severity of COVID-19: systematic review and meta-analysis. *Can J Kidney Health Dis* 2020;7:205435812093857.
- 4 Pranata R, Huang I, Lim MA, et al. Delirium and Mortality in Coronavirus Disease 2019 (COVID-19) - A Systematic Review and Meta-analysis. *Arch Gerontol Geriatr* 2021;95:104388.
- 5 Siemieniuk RAC, Bartoszko JJ, Ge L, et al. Drug treatments for covid-19: living systematic review and network meta-analysis. *BMJ* 2020;45:m2980.
- 6 Chen Y, Liu Q, Guo D. Emerging coronaviruses: genome structure, replication, and pathogenesis. *J Med Virol* 2020;92:418–23.
- 7 Hessel MHM, Cohen AF, Rissmann R. Sofosbuvir and daclatasvir. *Br J Clin Pharmacol* 2016;82:878–9.
- 8 McCormack PL. Daclatasvir: a review of its use in adult patients with chronic hepatitis C virus infection. *Drugs* 2015;75:515–24.
- 9 Sadeghi A, Ali Asgari A, Norouzi A, et al. Sofosbuvir and daclatasvir compared with standard of care in the treatment of patients admitted to hospital with moderate or severe coronavirus infection (COVID-19): a randomized controlled trial. *J Antimicrob Chemother* 2020;75:3379–85.
- 10 Elfiky AA. Ribavirin, Remdesivir, sofosbuvir, Galidesivir, and tenofovir against SARS-CoV-2 RNA dependent RNA polymerase (RdRp): a molecular docking study. *Life Sci* 2020;253:117592.
- 11 Eslami G, Mousaviasl S, Radmanesh E, et al. The impact of sofosbuvir/daclatasvir or ribavirin in patients with severe COVID-19. *J Antimicrob Chemother* 2020;75:3366–72.
- 12 Abbaspour Kasgari H, Moradi S, Shabani AM, et al. Evaluation of the efficacy of sofosbuvir plus daclatasvir in combination with ribavirin for hospitalized COVID-19 patients with moderate disease compared with standard care: a single-centre, randomized controlled trial. *J Antimicrob Chemother* 2020;75:3373–8.
- 13 Hill A, Wang J, Levi J, et al. Minimum costs to manufacture new treatments for COVID-19. *J Virus Erad* 2020;6:61–9.
- 14 Higgins JPT, Altman DG, Gøtzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ* 2011;343:d5928.

Main messages

- Sofosbuvir/daclatasvir (SOF/DCV) may lower mortality in patients with COVID-19.
- SOF/DCV was associated with significant reduction in the need for intensive care unit/invasive mechanical ventilation.
- SOF/DCV was associated with higher chance of clinical recovery.

Current research questions

1. Additional high-quality randomised controlled trials are required for definite conclusion.
2. Studies originating from other countries are required to increase the certainty of evidence.

What is already known on the subject

- SARS-CoV-2 relies on RNA-dependent RNA-polymerase (RdRp) for viral replication.
- Sofosbuvir/daclatasvir are direct acting antiviral drugs that have been shown to inhibit RdRp of hepatitis C virus.

- 15 Wells G, Shea B, O'Connell D. The Newcastle-Ottawa scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. *Ottawa Hosp Res Inst* 2000 http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp
- 16 Roozbeh F, Saeedi M, Alizadeh-Navaei R, *et al.* Sofosbuvir and daclatasvir for the treatment of COVID-19 outpatients: a double-blind, randomized controlled trial. *J Antimicrob Chemother* 2021;76:753–7.
- 17 Khalili H, Nourian A, Ahmadinejad Z, *et al.* Efficacy and safety of sofosbuvir/ ledipasvir in treatment of patients with COVID-19; a randomized clinical trial. *Acta Biomed* 2020;91:1–14.
- 18 Sacramento CQ, Fintelman-Rodrigues N, Temerozo JR. The in vitro antiviral activity of the anti-hepatitis C virus (HCV) drugs daclatasvir and sofosbuvir against SARS-CoV-2. *bioRxiv* 2020.
- 19 Gordon DE, Jang GM, Bouhaddou M, *et al.* A SARS-CoV-2 protein interaction map reveals targets for drug repurposing. *Nature* 2020;583:459–68.
- 20 Gao Y, Yan L, Huang Y, *et al.* Structure of the RNA-dependent RNA polymerase from COVID-19 virus. *Science* 2020;368:779–82.
- 21 Subissi L, Posthuma CC, Collet A, *et al.* One severe acute respiratory syndrome coronavirus protein complex integrates processive RNA polymerase and exonuclease activities. *Proc Natl Acad Sci U S A* 2014;111:E3900–9.
- 22 Smith MA, Regal RE, Mohammad RA. Daclatasvir: a NS5A replication complex inhibitor for hepatitis C infection. *Ann Pharmacother* 2016;50:39–46.
- 23 Jácome R, Campillo-Balderas JA, Ponce de León S, *et al.* Sofosbuvir as a potential alternative to treat the SARS-CoV-2 epidemic. *Sci Rep* 2020;10:9294.
- 24 Gan CS, Lim SK, Chee CF, *et al.* Sofosbuvir as treatment against dengue? *Chem Biol Drug Des* 2018;91:448–55.
- 25 Mesci P, Macia A, Moore SM, *et al.* Blocking Zika virus vertical transmission. *Sci Rep* 2018;8.
- 26 Dragoni F, Boccuto A, Picarazzi F, *et al.* Evaluation of sofosbuvir activity and resistance profile against West Nile virus in vitro. *Antiviral Res* 2020;175:104708.
- 27 Ju J, Kumar S, Li X. Nucleotide analogues as inhibitors of viral polymerases. *bioRxiv* 2020.
- 28 Gordon CJ, Tchesnokov EP, Woolner E, *et al.* Remdesivir is a direct-acting antiviral that inhibits RNA-dependent RNA polymerase from severe acute respiratory syndrome coronavirus 2 with high potency. *J Biol Chem* 2020;295:6785–97.
- 29 Beck BR, Shin B, Choi Y, *et al.* Predicting commercially available antiviral drugs that may act on the novel coronavirus (SARS-CoV-2) through a drug-target interaction deep learning model. *Comput Struct Biotechnol J* 2020;18:784–90.