

Sunlight reduces COVID-19 risk: real-time meta-analysis of 6 studies

@CovidAnalysis, September 2026, Version 5 (V1 2022), c19early.org/sunmeta.html

Abstract

Significantly lower risk is seen for mortality, hospitalization, recovery, and cases. 6 studies from 6 independent teams in 4 countries show significant benefit.

Meta-analysis using the most serious outcome reported shows 39% [26-50%] lower risk. Results are similar for Randomized Controlled Trials.

No treatment is 100% effective. Protocols combine safe and effective options with individual risk/benefit analysis and monitoring. Sunlight currently has no early treatment studies. Two studies are ecological studies reporting results per specified increases in UVA/sunlight exposure. All data and sources to reproduce this analysis are in the appendix.

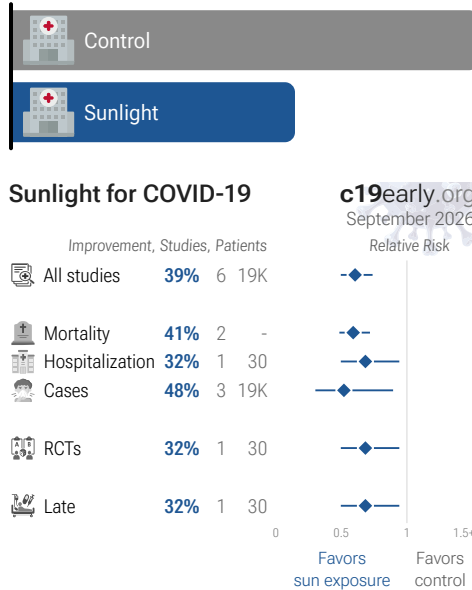
SUNLIGHT FOR COVID-19 — HIGHLIGHTS

Sunlight reduces risk with very high confidence for pooled analysis, high confidence for cases, and low confidence for mortality, hospitalization, and recovery.

35th treatment shown effective in December 2021, now with $p = 0.0000011$ from 6 studies.

Real-time updates and corrections with a consistent protocol for 226 treatments. Outcome specific analysis and combined evidence from all studies including treatment delay, a primary confounding factor.

Serious Outcome Risk



Sunlight for COVID-19

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Introduction

Other infections

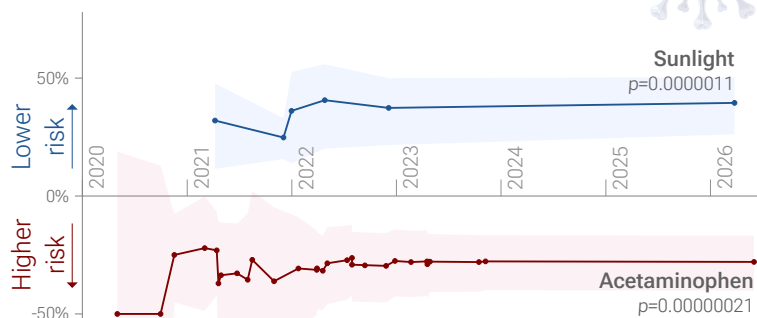
Efficacy with sunlight has been shown for influenza³⁻⁵.

Analysis

We analyze all significant studies reporting COVID-19 outcomes as a function of sunlight exposure. Search methods, inclusion criteria, effect extraction criteria (more serious outcomes have priority), all individual study data, PRISMA answers, and statistical methods are detailed in Appendix 1. We present random-effects meta-analysis results for all studies, studies within each treatment stage, individual outcomes, and Randomized Controlled Trials (RCTs).

Evolution of COVID-19 clinical evidence

Meta-analysis results over time



Preclinical Research

2 *in vitro* studies support the efficacy of sunlight^{6,7}.

Preclinical research is an important part of the development of treatments, however results may be very different in clinical trials. Preclinical results are not used in this paper.

Results

Table 1 summarizes the results for all studies, for Randomized Controlled Trials, and for specific outcomes. Fig. 2 shows a timeline of the results in sunlight studies. Fig. 3 plots individual results by treatment stage. Fig. 4, 5, 6, 7, and 8 show forest plots for random-effects meta-analysis of all studies with pooled effects, mortality results, hospitalization, recovery, and cases.



Fig. 1. The beneficial effect of sunlight on the immune system is periodically considered to be a new discovery¹, but has long been known, for example Niels Ryberg Finsen received a Nobel Prize in 1903 for phototherapy².

	Relative Risk	Studies	Patients
All studies	0.61 [0.50-0.74] ****	6	10K
RCTs	0.68 [0.50-0.94] *	1	30
Mortality	0.59 [0.49-0.72] ****	2	0
Cases	0.52 [0.30-0.89] *	3	10K

Table 1. Random-effects meta-analysis for all studies, for Randomized Controlled Trials, and for specific outcomes. Results show the relative risk with treatment and the 95% confidence interval. * $p < 0.05$
**** $p < 0.0001$.

Timeline of COVID-19 sunlight studies (pooled effects)

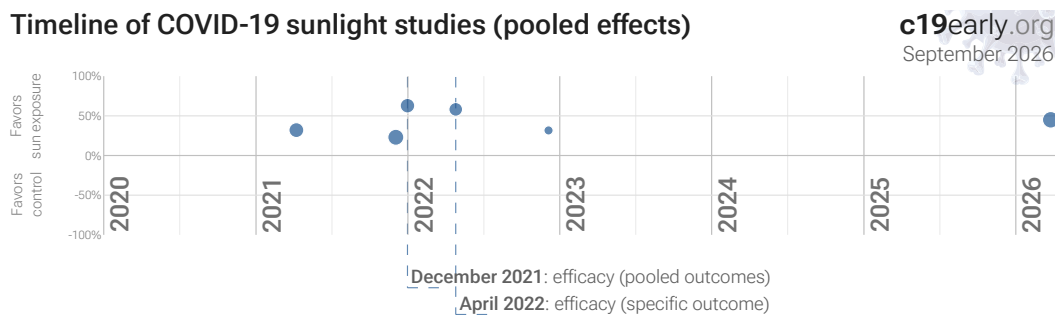


Fig. 2. Timeline of results in sunlight studies. The marked dates indicate the time when efficacy was known with a statistically significant improvement of $\geq 10\%$ from ≥ 3 studies for pooled outcomes and one or more specific outcome. Efficacy based on specific outcomes was delayed by 3.8 months, compared to using pooled outcomes.

Efficacy in COVID-19 sunlight studies (pooled effects)

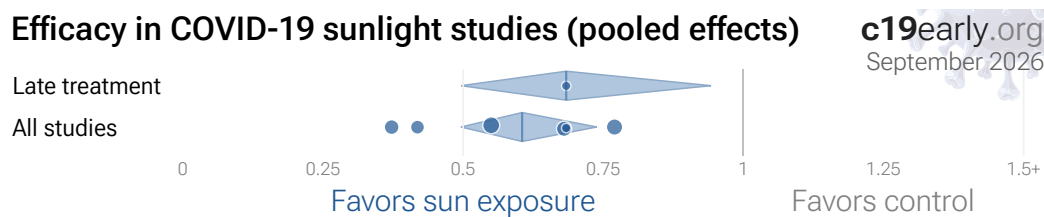


Fig. 3. Scatter plot showing the most serious outcome in all studies. The diamond shows the results of random-effects meta-analysis.

6 sunlight COVID-19 studies

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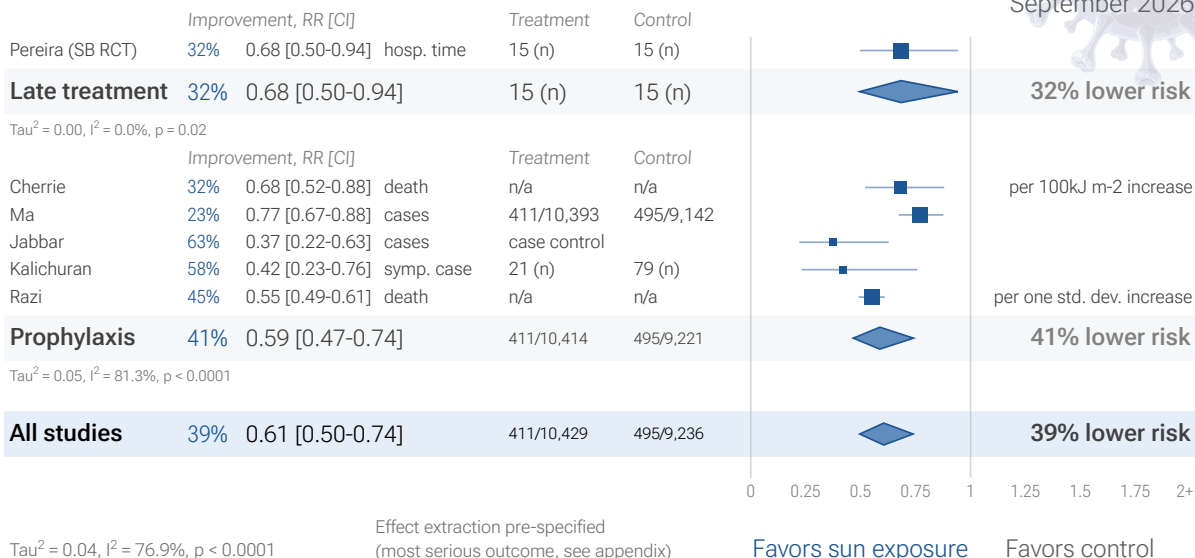


Fig. 4. Random-effects meta-analysis for all studies. This plot shows pooled effects, see the specific outcome analyses for individual outcomes. Analysis validating pooled outcomes for COVID-19 can be found below. Effect extraction is pre-specified, using the most serious outcome reported. For details see the appendix.

2 sunlight COVID-19 mortality results

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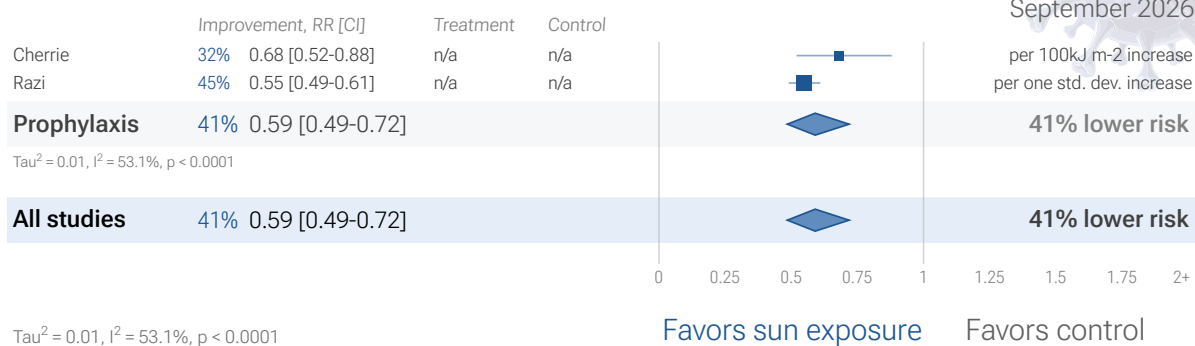


Fig. 5. Random-effects meta-analysis for mortality results.

1 sunlight COVID-19 hospitalization result

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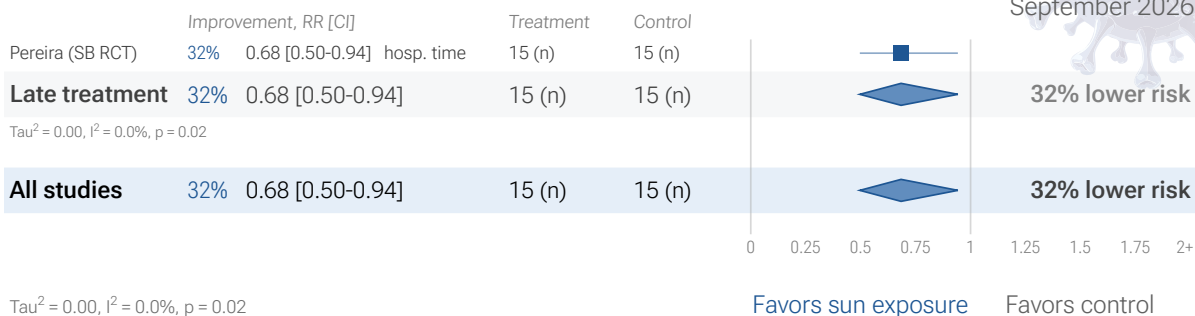


Fig. 6. Random-effects meta-analysis for hospitalization.

1 sunlight COVID-19 recovery result

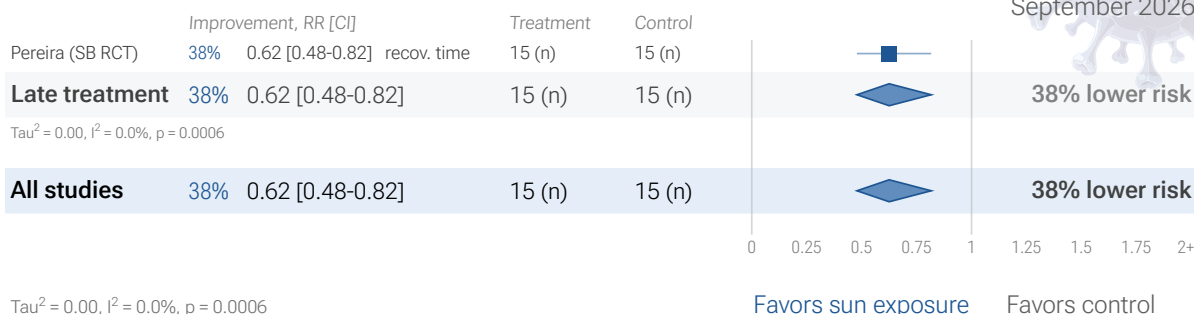


Fig. 7. Random-effects meta-analysis for recovery.

3 sunlight COVID-19 case results

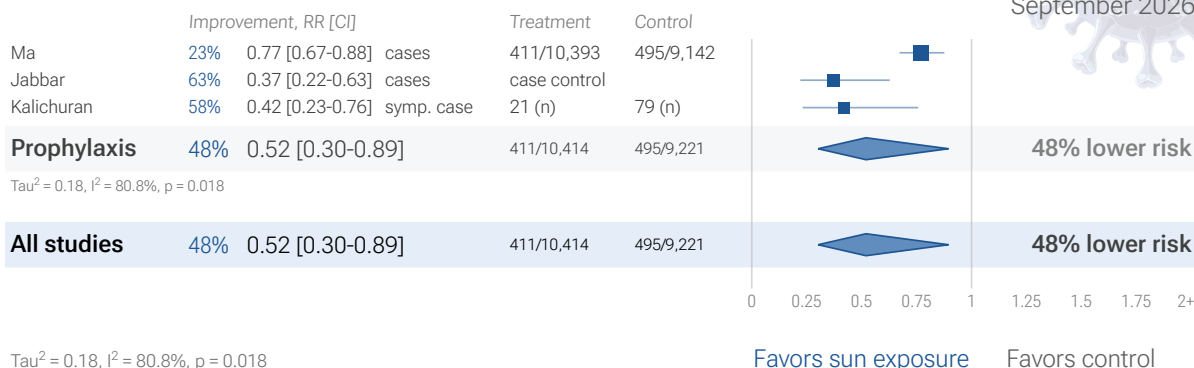


Fig. 8. Random-effects meta-analysis for cases.

Randomized Controlled Trials (RCTs)

Fig. 9 shows a forest plot for random-effects meta-analysis of all Randomized Controlled Trials. RCT results are included in Table 1. Currently there is only one RCT.

RCTs have many potential biases

RCTs help to make study groups more similar and can provide a higher level of evidence, however they are subject to many biases⁸, and analysis of double-blind RCTs has identified extreme levels of bias⁹. For COVID-19, the overhead may delay treatment, dramatically compromising efficacy; they may encourage monotherapy for simplicity at the cost of efficacy which may rely on combined or synergistic effects; the participants that sign up may not reflect real world usage or the population that benefits most in terms of age, comorbidities, severity of illness, or other factors; standard of care may be compromised and unable to evolve quickly based on emerging research for new diseases; errors may be made in randomization and medication delivery; and investigators may have hidden agendas or vested interests influencing design, operation, analysis, reporting, and the potential for fraud. All of these biases have been observed with COVID-19 RCTs. There is no guarantee that a specific RCT provides a higher level of evidence.

Conflicts of interest for COVID-19 RCTs

RCTs are expensive and many RCTs are funded by pharmaceutical companies or other organizations with conflicts of interest, for example governments that previously denied treatment with the study drug. For COVID-19, this creates an incentive to show efficacy for patented commercial products, and an incentive to show a lack of efficacy for inexpensive treatments. The bias is expected to be

significant, for example *Als-Nielsen et al.* analyzed 370 RCTs from Cochrane reviews, showing that trials funded by for-profit organizations were 5 times more likely to recommend the experimental drug compared with those funded by nonprofit organizations. *Bekelman et al.* and *Lundh et al.* show that industry-sponsored studies are more likely to be favorable. For COVID-19, some major philanthropic organizations are largely funded by investments with extreme conflicts of interest for and against specific COVID-19 interventions.

RCTs for novel acute diseases requiring rapid treatment

High quality RCTs for novel acute diseases are more challenging, with increased ethical issues due to the urgency of treatment, increased risk due to enrollment delays, and more difficult design with a rapidly evolving evidence base. For COVID-19, the most common site of initial infection is the upper respiratory tract. Immediate treatment is likely to be most successful and may prevent or slow progression to other parts of the body. For a non-prophylaxis RCT, it makes sense to provide treatment in advance and instruct patients to use it immediately on symptoms, just as some governments have done by providing medication kits in advance. Unfortunately, no RCTs have been done in this way. Every treatment RCT to date involves delayed treatment. Among the 226 treatments we have analyzed, 67% of RCTs involve very late treatment 5+ days after onset. No non-prophylaxis COVID-19 RCTs match the potential real-world use of early treatments. They may more accurately represent results for treatments that require visiting a medical facility, e.g., those requiring intravenous administration.

RCT bias for widely available treatments

RCTs have a bias against finding an effect for interventions that are widely available—patients that believe they need the intervention are more likely to decline

COVID-19 RCT vs. observational results from 6,000+ studies

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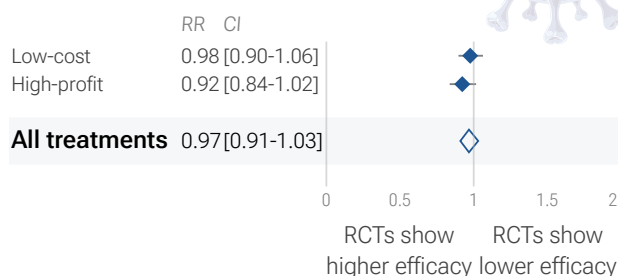


Fig. 10. For COVID-19, observational study results do not systematically differ from RCTs, RR 0.97 [0.91-1.03] across 226 treatments¹³.

participation and take the intervention. RCTs for sunlight are more likely to enroll low-risk participants that do not need treatment to recover, making the results less applicable to clinical practice. This bias is likely to be greater for widely known treatments, and may be greater when the risk of a serious outcome is overstated. This bias does not apply to the typical pharmaceutical trial of a new drug that is otherwise unavailable.

Observational studies have been shown to be reliable

Evidence shows that observational studies can also provide reliable results. *Concato et al.* found that well-designed observational studies do not systematically overestimate the magnitude of the effects of treatment compared to RCTs. *Anglemyer et al.* analyzed reviews comparing RCTs to observational studies and found little evidence for significant differences in effect estimates.

We performed a similar analysis across the 226 treatments we cover, showing no significant difference in the results of RCTs compared to observational studies, RR 0.97 [0.91-1.03]¹⁶. Similar results are found for all low-cost treatments, RR 0.98 [0.90-1.06]. High-cost treatments show a non-significant trend towards RCTs showing greater efficacy, RR 0.92 [0.84-1.02]. Details can be found in the supplementary data.

Lee et al. showed that only 14% of the guidelines of the Infectious Diseases Society of America were based on RCTs. Evaluation of studies relies on an understanding of the study and potential biases. Limitations in an RCT can outweigh the benefits, for example excessive dosages, excessive treatment delays, or re-

mote survey bias may have a greater effect on results. Ethical issues may also prevent running RCTs for known effective treatments. For more on issues with RCTs see^{18,19}.

RCTs may be less reliable

Concato et al. report a paradoxical finding—RCT results had higher variability, and only RCTs were found to sometimes report significant results the opposite of the overall result. The same trend is seen for the most popular (most politicized) COVID-19 treatments—considering all statistically significant results reported in studies, RCTs are slightly more likely to report a result in the opposite direction. In other words, for these COVID-19 treatments and for the topics covered by *Concato et al.*, assuming causality from a single study is more likely to result in an incorrect conclusion for RCTs.

Increased risk of inconsistent results for RCTs suggests higher prevalence of bias, which may arise due to many issues including design bias, conflicts of interest, treatment differences by physicians aware of allocation, attrition bias, ascertainment bias, randomization failures, errors, or fraud.

Using all studies identifies efficacy 8+ months faster (9+ months for low-cost treatments)

Currently, 59 of the treatments we analyze show statistically significant efficacy or harm, defined as $\geq 10\%$ decreased risk or $> 0\%$ increased risk from ≥ 3 studies. Of these, 54% have been confirmed in RCTs, with a mean delay of 7.8 months (62% with 8.7 months delay for low-cost treatments). The remaining treatments either have no RCTs, or the point estimate is consistent.

All studies must be carefully analyzed

Neither observational studies nor RCTs prove causation—any study can be flawed or fraudulent. We need much more, for example a combination of results from many independent teams, detailed understanding of each study, knowledge of conflicts/team reliability, dose-response relationships, delay-response relationships, logical results across outcomes, or details consistent with pre-clinical expectations.

All studies must be evaluated individually. RCTs for a given medication and disease may be more reliable, however they may also be less reliable. For off-patent medications, very high conflict of interest trials may be more likely to be RCTs, and more likely to be large trials that dominate meta-analyses.

1 sunlight COVID-19 Randomized Controlled Trial

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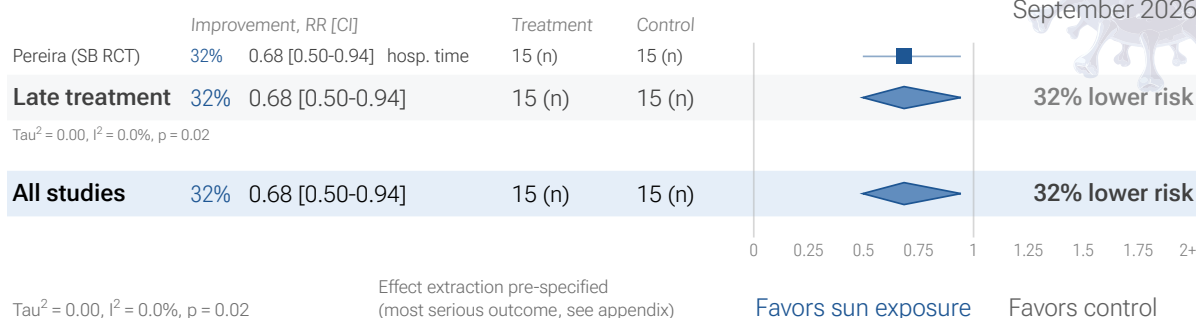


Fig. 9. Random-effects meta-analysis for all Randomized Controlled Trials. This plot shows pooled effects, see the specific outcome analyses for individual outcomes. Analysis validating pooled outcomes for COVID-19 can be found below. Effect extraction is pre-specified, using the most serious outcome reported. For details see the appendix.

Media Censorship

Low-cost treatments were subject to bias and censorship during the pandemic. Scientific bias is seen in the design, analysis, presentation, and selective reporting of studies, which often favored negative results. A similar bias is seen in the media coverage for low-cost treatments. While broadly seen, bias was particularly notable for ivermectin and hydroxychloroquine, e.g., Scott Alexander noted that *"if you say anything in favor of ivermectin you will be cast out of civilization and thrown into the circle of social hell reserved for Klan members and 1/6 insurrectionists. All the health officials in the world will shout 'horse dewormer!' at you and compare you to Josef Mengele."*²⁰.

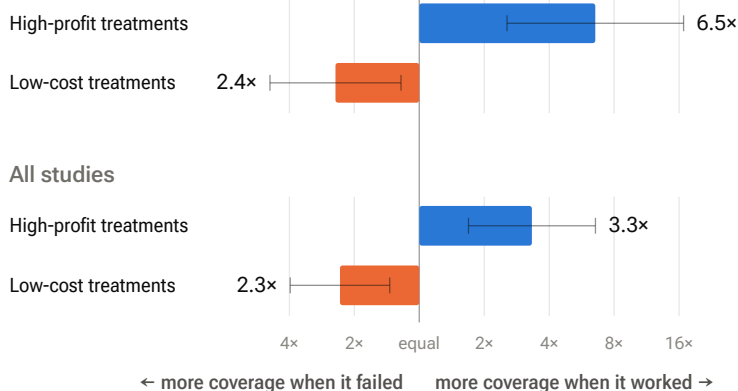
We analyze media coverage for the 226 treatments we cover using Altmetric²¹, which reports the number of ~12,000 tracked news outlets that covered each study²². Studies are considered to have received significant media coverage if they were covered by at least 0.5% of the tracked news outlets. Fig. 11, 12, and 13 show the bias toward negative results for low-cost treatments, in contrast to the opposite bias for high-profit treatments. This may result in widespread incorrect perceptions on the relative efficacy of high-profit and low-cost treatments. The impact is significant—increased cost limits the use of high-profit treatments and treatment equity, and high-profit treatments were also more difficult to access, especially for earlier treatment which improves efficacy and minimizes community transmission.

The mainstream media did not cover any of the positive studies for sunlight.

Media coverage was highly biased High-profit: preferred positive results Low-cost: preferred negative results

Media preferred to cover positive results for high-profit treatments. And negative/inconclusive results for low-cost treatments.

Randomized trials only



Many studies show lower risk with low-cost treatments 98% of these were not covered by the media

Coverage of positive vs. negative/inconclusive results; whiskers are 95% confidence intervals. Data from Altmetric. Log scale. See: c19early.org/msm.html

Fig. 11. Media was more likely to cover negative or inconclusive results for low-cost treatments, and positive results for high-profit treatments.

Media censorship for COVID-19 low-cost treatments

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Media selectively covered negative studies for low-cost treatments

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Only 18 positive studies were covered:

fluvoxamine (3), HCQ (2), antiandrogens (2), budesonide (2), vitamin D, melatonin, probiotics, ivermectin, cannabidiol, famotidine, curcumin, resveratrol, UDCA

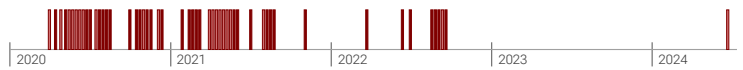


98% of studies showing significantly lower risk were censored:



53 negative studies were covered:

HCQ (15), ivermectin (7), lopinavir/r. (5), vitamin D (5), azithromycin (4), zinc (2), vitamin C (2), metformin (2), fluvoxamine (2), indomethacin, colchicine, selenium, probiotics, vitamin A, ibuprofen, antiandrogens, vitamin B9, cannabidiol



Data from Altmetric: studies receiving significant mainstream media coverage from 6,000+ studies for 226 treatments

Fig. 12. Mainstream media was biased against positive results for low-cost treatments.

Media coverage for COVID-19 high-profit treatments

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Media selectively covered positive studies for high-profit treatments

September 2026

28 positive studies were covered:

tocilizumab (5), paxlovid (5), conv. plasma (4), casirivimab/c. (3), molnupiravir (3), remdesivir (2), peg. lambda (2), sargramostim (2), sarilumab, tixagevimab/c.



11 negative studies were covered:

remdesivir (4), conv. plasma (2), molnupiravir, bebtelovimab, sotrovimab, bamlan./e., paxlovid



97% of negative studies were not covered:



Data from Altmetric: studies receiving significant mainstream media coverage from 6,000+ studies for 226 treatments

Fig. 13. In contrast to the results for low-cost treatments, mainstream media was biased towards positive results for high-cost treatments.

A combination of factors may have led to the media's suppression of low-cost treatments:

- Politicization led to a media environment where coverage was often framed to support a political narrative rather than to provide objective scientific information. As Scott Alexander said: *"if you say anything in favor of ivermectin you will be cast out of civilization and thrown into the circle of social hell reserved for Klan members and 1/6 insurrectionists. All the health officials in the world will shout 'horse dewormer!' at you and compare you to Josef Mengele."* There was strong social pressure to discredit low-cost treatments.
- Censorship of information conflicting with selected authorities. For example, individuals and organizations presenting conflicting science were often banned on Twitter and YouTube.
- FDA requires *"no adequate, approved, and available alternatives"* in order to grant an EUA for novel high-profit interventions, creating a strong incentive for authorities to ignore or downplay existing low-cost treatments.
- Regulatory capture biases authorities towards high-profit interventions.
- Authorities ignored most evidence for low-cost treatments, for example the NIH references only 2% of studies in delayed, rarely-updated, biased commentaries with no quantitative analysis.
- Media coverage of science is often not very accurate, e.g., misunderstanding confounding issues. For example the media widely considered the RECOVERY HCQ RCT to be conclusive on efficacy, but very late treatment of

late stage patients (mostly on oxygen already) with an excessive toxic dose (shown dangerous in a dose comparison RCT) provides no information on the recommended early/prophylactic treatment. With difficulting in understanding basic confounders like treatment delay and dose, the media may favor deferring to authorities. Many studies for low-cost treatments require greater expertise to analyze. Relatively few journalists have a strong ability to analyze clinical trials and are outnumbered by the rest.

- Substantial funding from pharmaceutical advertising biases editorial decisions towards high-profit interventions.
- PR power - companies/teams with strong PR presence are favored in the media, which correlates with high-profit and high conflict of interest studies.
- The media was very negative in general, inflating risk, fear, and anxieties. A negative bias may improve ratings and revenue, increasing motivation to continue watching coverage. A combination of low-cost treatments greatly reducing risk conflicts with the negative narrative.

Authority Delay

25 low-cost treatments were approved in one or more countries, yet many countries approved no low-cost treatments. The countries that did adopt low-cost treatments analyzed the evidence early and made timely approvals. With few exceptions, authorities did not change their initial views, regardless of how much evidence accumulated showing either efficacy or harm. Why?

The harms of smoking here hidden for 25 years^A. Authorities did not analyze the data in real-time, failing to act when harm was known. Widespread acknowledgement of harm came only after attempts by two new surgeon generals, along with pressure from health advocates and a new president, and a review of 7,000 studies.

Similarly for COVID-19, most authorities and experts did not proactively analyze data in real-time. This guarantees delayed recognition of efficacy or harm, by which time moral, legal, career, and reputational liabilities strongly disincentivize any admission of error. Claims of no efficacy (for effective treatments) or safety (for harmful treatments) were often made prior to strong data being available. Correction would require admitting to errors that increased mortality, which is unlikely with the same generation of officials.

Analysis of potential treatments was rarely done, and when done these were typically minimal efforts. For example, NIH reviews were highly delayed, cover only a tiny fraction of treatments, reference only 2% of studies for the treatments covered, and include no quantitative analysis. They appear as rarely updated side projects from external panels implicitly tasked with justifying prior failures. As with smoking, the thousands of studies could (and should) have been analyzed and acted on in real-time.

A key structural improvement, applicable to all current and future diseases, is for authorities to implement real-time proactive analysis of clinical evidence. This does not remove all bias, but does make it possible to act on evidence, whereas delayed action may be unlikely due to moral, legal, career, and reputational liabilities.

Heterogeneity

Heterogeneity in COVID-19 studies arises from many factors including:

Patient demographics

Details of the patient population including age and comorbidities may critically affect how well a treatment works. For example, many COVID-19 studies with relatively young low-comorbidity patients show all patients recovering quickly

with or without treatment. In such cases, there is little room for an effective treatment to improve results, for example as in *López-Medina et al.*

SARS-CoV-2 variants

Efficacy may depend critically on the distribution of SARS-CoV-2 variants encountered by patients. Risk varies significantly across variants²⁴, for example the Gamma variant shows significantly different characteristics²⁵⁻²⁸. Different mechanisms of action may be more or less effective depending on variants, for example the degree to which TMPRSS2 contributes to viral entry can differ across variants^{29,30}.

Other treatments

The use of other treatments may significantly affect outcomes, including supplements, other medications, or other interventions such as prone positioning. Treatments may be synergistic³¹⁻⁵⁵, therefore efficacy may depend strongly on combined treatments.

Effect measured

Across all studies there is a strong association between different outcomes, for example improved recovery is strongly associated with lower mortality. However, efficacy may differ depending on the effect measured, for example a treatment may be more effective against secondary complications and have minimal effect on viral clearance.

Meta-analysis

The distribution of studies will alter the outcome of a meta-analysis. Consider a simplified example where everything is equal except for the treatment delay, and effectiveness decreases to zero or below with increasing delay. If there are many studies using very late treatment, the outcome may be negative, even though early treatment is very effective. All meta-analyses combine heterogeneous studies, varying in population, variants, and potentially all factors above, and therefore may obscure efficacy by including studies where treatment is less effective. Generally, we expect the estimated effect size from meta-analysis to be less than that for the optimal case. Looking at all studies is valuable for providing an overview of all research, important to avoid cherry-picking, and informative when a positive result is found despite combining less-optimal situations. However, the resulting estimate does not apply to specific cases such as early treatment in high-risk populations. While we present results for all studies, we also present treatment time and individual outcome analyses, which may be more informative for specific use cases.

Pooled Effects

Pooled effects are no longer required to show efficacy as of April 2022

This section validates the use of pooled effects for COVID-19, which enables earlier detection of efficacy, however pooled effects are no longer required for sunlight as of April 2022. Efficacy is now known based on specific outcomes. Efficacy based on specific outcomes was delayed by 3.8 months compared to using pooled outcomes.

Combining studies is required

For COVID-19, delay in clinical results translates into additional death and morbidity, as well as additional economic and societal damage. Combining the results of studies reporting different outcomes is required. There may be no mortality in a trial with low-risk patients, however a reduction in severity or improved viral clearance may translate into lower mortality in a high-risk population. Different studies may report lower severity, improved recovery, and lower mortality, and the significance may be very high when combining the results. "The studies reported different outcomes" is not a good reason for disregarding results. Pooling the results of studies reporting different outcomes allows us

Delayed public health acknowledgments

Official acknowledgment of efficacy or harm is often delayed—legal, career, and status risks disincentivize admission of error.

	EVIDENCE	OFFICIAL ACKNOWLEDGMENT	APPROX. DELAY
Citrus Fruit (vitamin C) for Scurvy (effectiveness)	1747: James Lind conducted one of the first-ever controlled clinical trials, proving that oranges and lemons cured scurvy in sailors.	1795: The British Royal Navy finally made a daily ration of lemon juice a standard issue for all its sailors, effectively eliminating the disease.	48 years
Handwashing (lower mortality)	1847: Dr. Ignaz Semmelweis provided conclusive proof that having doctors wash their hands with a chlorine solution before delivering babies reduced maternal mortality rates from over 18% to around 1%.	~1870s: Semmelweis's findings were rejected and he was ridiculed. His work was only validated decades later (after his death).	~20+ years
Helicobacter pylori (bacteria causes ulcers)	1982-1984: Marshall and Warren discovered that Helicobacter pylori bacteria causes ulcers, confirmed via direct exposure. Officials maintained that ulcers were caused by stress and spicy food.	1994: The US NIH released a consensus statement officially recommending antibiotics as the standard treatment for peptic ulcers, overturning decades of acid-suppression therapy.	~12 years
Asbestos (causes asbestosis & cancer)	1924: The <i>British Medical Journal</i> published the first case study of a death from "asbestosis." By 1918, U.S. insurance companies had stopped selling life insurance to asbestos workers.	1971 (US): The Occupational Safety and Health Administration (OSHA) was formed and began regulating asbestos as a carcinogen, setting the first federal workplace safety standards for it.	~47 years
Leaded Gasoline (neurotoxicity)	~1924: Dangers of low-level lead exposure were known. Experts like Alice Hamilton warned the U.S. Surgeon General that adding lead to gasoline would cause widespread public poisoning.	1973 (US): The Environmental Protection Agency (EPA) ordered the first phasedown of lead in gasoline, following the Clean Air Act of 1970. A full ban for on-road vehicles took effect in 1996.	~49 years
Harms of Smoking (causes lung cancer)	1939: Franz Müller (Germany) published the first case-control epidemiological study strongly linking tobacco smoking to lung cancer. This was followed by major U.S. & U.K. studies in the 1950s.	1964 (US): The U.S. Surgeon General's report, "Smoking and Health," was released. It was the first U.S. government report to definitively link smoking to lung cancer and heart disease.	25 years

to use more of the available information. Logically we should, and do, use additional information when evaluating treatments—for example dose-response and treatment delay-response relationships provide additional evidence of efficacy that is considered when reviewing the evidence for a treatment.

Specific outcome and pooled analyses

We present both specific outcome and pooled analyses. In order to combine the results of studies reporting different outcomes we use the most serious outcome reported in each study, based on the thesis that improvement in the most serious outcome provides comparable measures of efficacy for a treatment. A critical advantage of this approach is simplicity and transparency. There are many other ways to combine evidence for different outcomes, along with additional evidence such as dose-response relationships, however these increase complexity.

Ethical and practical issues limit high-risk trials

Trials with high-risk patients may be restricted due to ethics for treatments that are known or expected to be effective, and they increase difficulty for recruiting. Using less severe outcomes as a proxy for more serious outcomes allows faster and safer collection of evidence.

Validating pooled outcome analysis for COVID-19

For many COVID-19 treatments, a reduction in mortality logically follows from a reduction in hospitalization, which follows from a reduction in symptomatic cases, which follows from a reduction in PCR positivity. We can directly test this for COVID-19.

Analysis of the the association between different outcomes across studies from all 226 treatments we cover confirms the validity of pooled outcome analysis for COVID-19. Fig. 14 shows that lower hospitalization is very strongly associated with lower mortality ($p < 0.000000001$). Similarly, Fig. 15 shows that improved recovery is very strongly associated with lower mortality ($p < 0.000000001$). Considering the extremes, *Singh et al.* show an association between viral clearance and hospitalization or death, with $p = 0.003$ after excluding one large outlier from a mutagenic treatment, and based on 44 RCTs including 52,384 patients. Fig. 16 shows that improved viral clearance is strongly associated with fewer serious outcomes. The association is very similar to *Singh et al.*, with higher confidence due to the larger number of studies. As with *Singh et al.*, the confidence increases when excluding the outlier treatment, from $p = 0.0000000074$ to $p = 0.0000000015$.

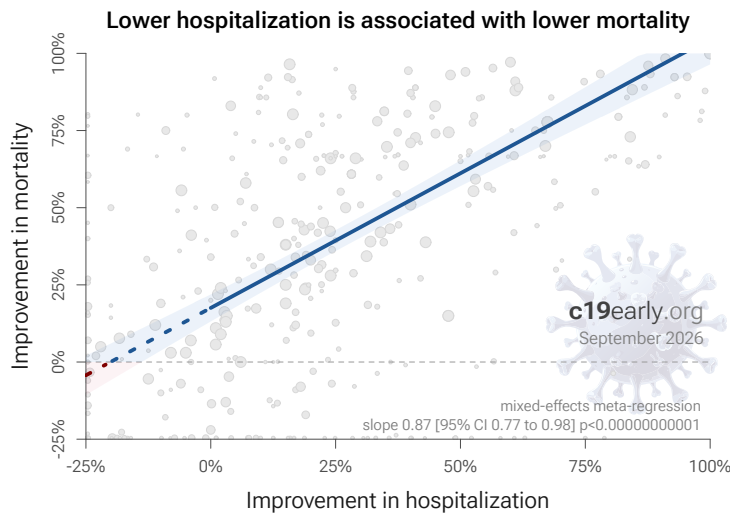


Fig. 14. Lower hospitalization is associated with lower mortality, supporting pooled outcome analysis.

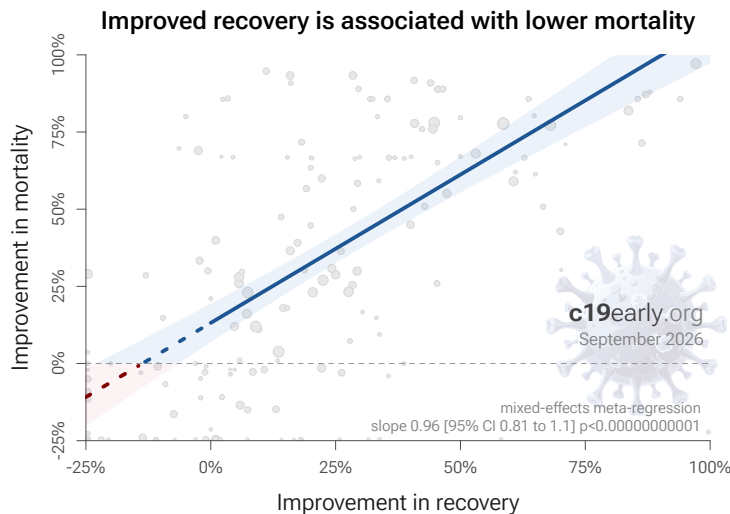


Fig. 15. Improved recovery is associated with lower mortality, supporting pooled outcome analysis.

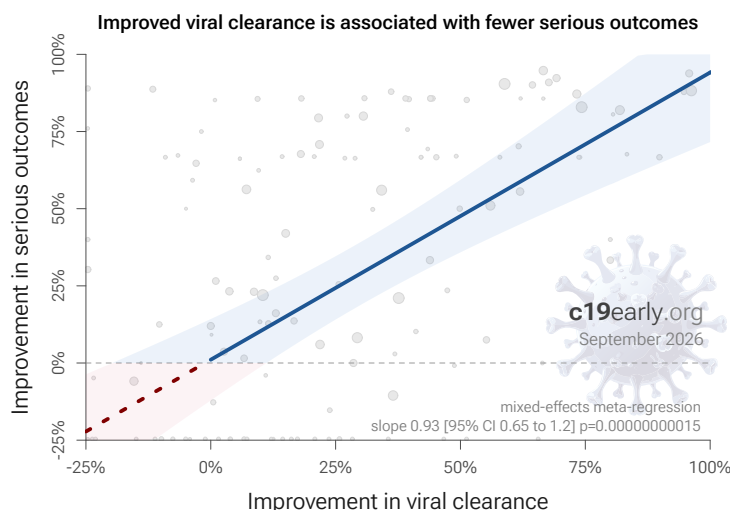


Fig. 14. Improved viral clearance is associated with fewer serious outcomes, supporting pooled outcome analysis.

Pooled outcomes identify efficacy 5 months faster (7 months for RCTs)

Currently, 59 of the treatments we analyze show statistically significant efficacy or harm, defined as $\geq 10\%$ decreased risk or $>0\%$ increased risk from ≥ 3 studies. 85% of these have been confirmed with one or more specific outcomes, with a mean delay of 4.6 months. When restricting to RCTs only, 53% of treatments showing statistically significant efficacy/harm with pooled effects have been confirmed with one or more specific outcomes, with a mean delay of 7.5 months. Fig. 17 shows when treatments were found effective during the pandemic. Pooled outcomes often resulted in earlier detection of efficacy.

Time when COVID-19 studies showed efficacy

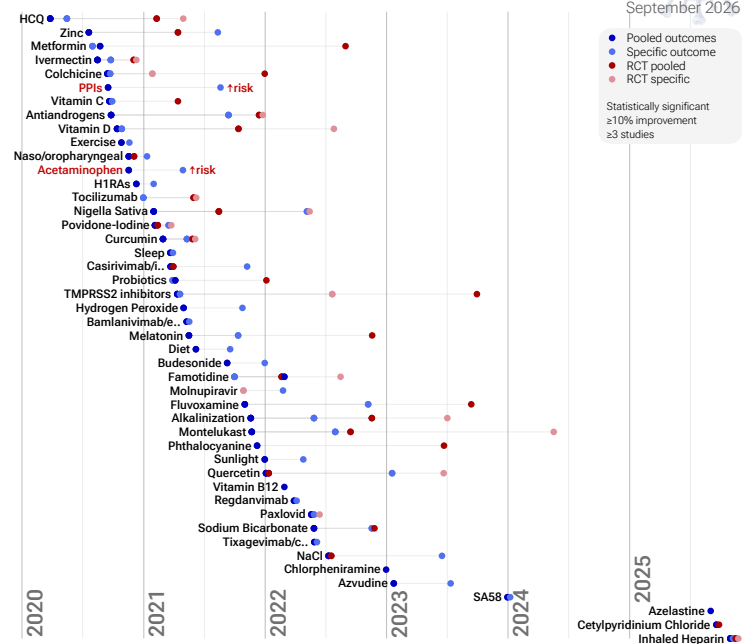


Fig. 17. The time when studies showed that treatments were effective, defined as statistically significant improvement of $\geq 10\%$ from ≥ 3 studies. Pooled results typically show efficacy earlier than specific outcome results. Results from all studies often shows efficacy much earlier than when restricting to RCTs. Results reflect conditions as used in trials to date, these depend on the population treated, treatment delay, and treatment regimen.

Limitations

Pooled analysis could hide efficacy, for example a treatment that is beneficial for late stage patients but has no effect on viral clearance may show no efficacy if most studies only examine viral clearance. In practice, it is rare for a non-antiviral treatment to report viral clearance and to not report clinical outcomes; and in practice other sources of heterogeneity such as differences in treatment delay are more likely to hide efficacy.

Summary

Analysis validates the use of pooled effects and shows significantly faster detection of efficacy on average. However, as with all meta-analyses, it is important to review the different studies included. We also present individual outcome analyses, which may be more informative for specific use cases.

Discussion

Results for other infections

Efficacy with sunlight has also been shown for influenza³⁻⁵.

Reviews

Many reviews cover sunlight for COVID-19, presenting additional background on mechanisms and related results, including⁵⁷⁻⁶².

Perspective

Results compared with other treatments

SARS-CoV-2 infection and replication involves a complex interplay of 500+ host and viral proteins and other factors⁶³⁻⁷⁰, providing many therapeutic targets. Over 12,000 compounds have been predicted to reduce COVID-19 risk⁷¹, either by directly minimizing infection or replication, by supporting immune system function, or by minimizing secondary complications. Fig. 18 shows an overview of the results for sunlight in the context of multiple COVID-19 treatments, and Fig. 19 shows a plot of efficacy vs. cost for COVID-19 treatments.

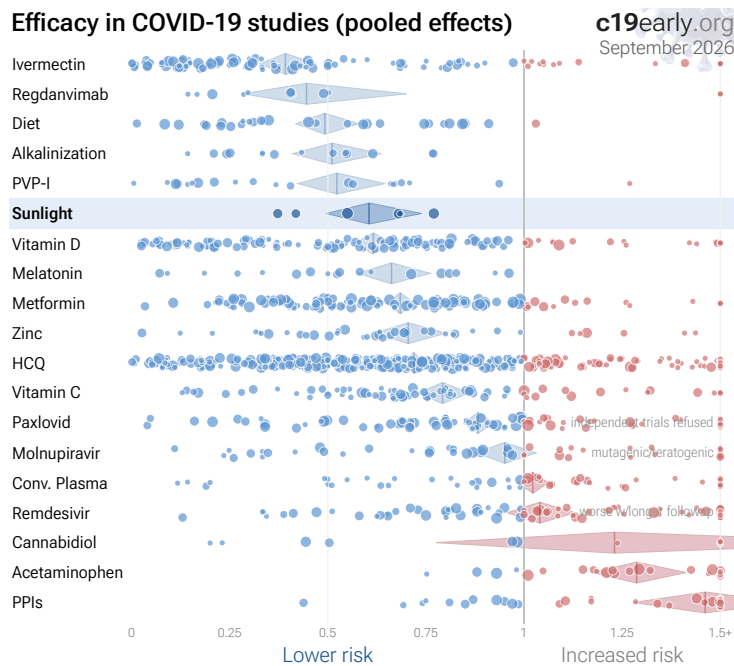


Fig. 18. Scatter plot showing results within the context of multiple COVID-19 treatments. Diamonds show the results of random-effects meta-analysis. 0.5% of 12,000+ proposed treatments show efficacy⁷².

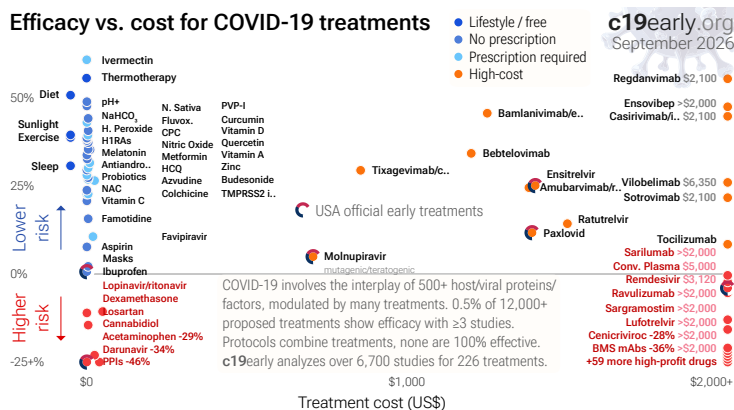


Fig. 19. Efficacy vs. cost for COVID-19 treatments.

Conclusion

Increased sun exposure reduces risk for COVID-19. Significantly lower risk is seen for mortality, hospitalization, recovery, and cases. 6 studies from 6 independent teams in 4 countries show significant benefit. Meta-analysis using the most serious outcome reported shows 39% [26-50%] lower risk. Results are similar for Randomized Controlled Trials.

Efficacy with sunlight has also been shown for influenza³⁻⁵.

Contact. Contact us on X at @CovidAnalysis.

Funding. We have received no funding or compensation in any form, and do not accept donations. This is entirely volunteer work.

Conflicts of interest. We have no conflicts of interest. We have no affiliation with any pharmaceutical companies, supplement companies, governments, political parties, or advocacy organizations.

Disclaimer. We do not provide medical advice. No treatment is 100% effective, and all may have side effects. Protocols combine multiple treatments. Consult a qualified physician for personalized risk/benefit analysis.

AI. We use AI models (Gemini, Grok, Claude, and ChatGPT) tasked with functioning as additional peer-reviewers to check for errors, suggest improvements, and review spelling and grammar. Any corrections are manually verified. Our preference for em dashes is independent of AI.

Updates. Our COVID-19 meta-analyses involve the extraction of over 227,000 datapoints from thousands of papers for 226 treatments. We thank the thousands of scientists, physicians, and other contributors that have provided updates, suggestions, feedback, and corrections. These are all welcome and can be submitted at <https://c19early.org/sunmeta.html>.

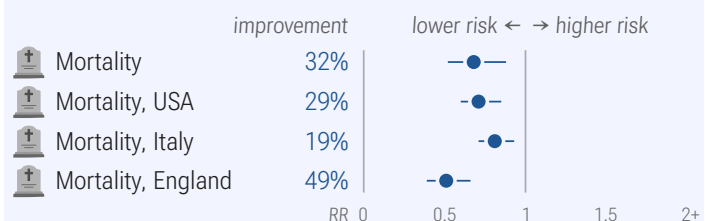
Dedication. This work is dedicated to top evidence-based physicians that worked tirelessly to analyze evidence and greatly reduce mortality and morbidity during the pandemic. In alphabetical order: Dr. Thomas J. Borody, Dr. Mary Talley Bowden, Dr. Flavio Cadegiani, Dr. Shankara Chetty, Dr. Ryan Cole, Dr. George Fareed, Dr. Sabine Hazan, Dr. Pierre Kory, Dr. Tess Lawrie, Dr. Robert Malone, Dr. Paul Marik, Dr. Peter McCullough, Dr. Didier Raoult, Dr. Harvey Risch, Dr. Jackie Stone, Dr. Brian Tyson, Dr. Joseph Varon, and Dr. Vladimir Zelenko.

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Study Notes

Cherrie

Sunlight for COVID-19 Cherrie et al. PROPHYLAXIS



Is sunlight beneficial for COVID-19?

Retrospective study in multiple countries (January - April 2020)

Lower mortality with increased sunlight exposure (p=0.0041)

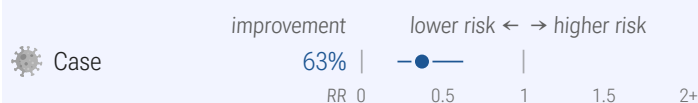
Cherrie et al., British J. Dermatology, Apr 2021

c19early.org

Analysis of UVA exposure and COVID-19 mortality in the USA, England, and Italy, showing increased UVA exposure associated with lower mortality.

Jabbar

Sunlight for COVID-19 Jabbar et al. PROPHYLAXIS



Is sunlight beneficial for COVID-19?

Retrospective 240 patients in Iraq

Fewer cases with increased sunlight exposure (p=0.00021)

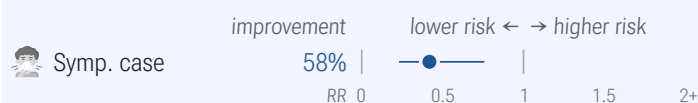
Jabbar et al., Natural Volatiles & Ess., Dec 2021

c19early.org

Analysis of 120 COVID-19 and 120 control patients in Iraq, showing lower risk of cases with regular sunlight exposure (3 times/week).

Kalichuran

Sunlight Kalichuran et al. PROPHYLAXIS



Is sunlight beneficial for COVID-19?

Prospective study of 100 patients in South Africa (Sep 2020 - Feb 2021)

Fewer symptomatic cases with increased sunlight exposure (p=0.0041)

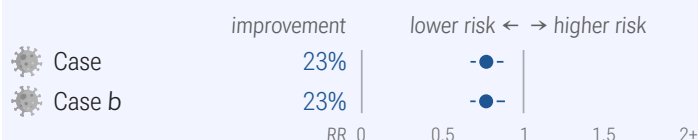
Kalichuran et al., Southern African J..., Apr 2022

c19early.org

Prospective study of 100 COVID-19 patients in South Africa, 50 with COVID-19 pneumonia and 50 asymptomatic, showing higher risk of symptomatic COVID-19 with lower exposure to sunlight, and with vitamin D deficiency. Sunlight exposure may be correlated with physical activity and may have additional benefits independent of vitamin D⁷³.

Ma

Sunlight for COVID-19 Ma et al. PROPHYLAXIS



Is sunlight beneficial for COVID-19?

Retrospective 19,535 patients in the USA (May 2020 - March 2021)

Fewer cases with increased sunlight exposure (p=0.00012)

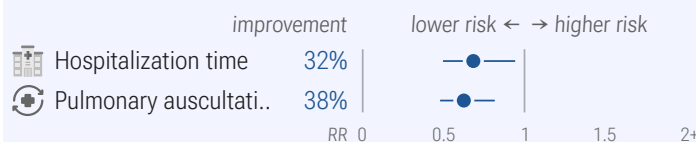
Ma et al., The American J. Clinical Nu..., Dec 2021

c19early.org

Analysis of 39,915 patients with 1,768 COVID+ cases based on surveys in the Nurses' Health Study II, showing higher UVA/UVB exposure associated with lower risk of COVID-19 cases.

Pereira

Sunlight Pereira et al. LATE TREATMENT RCT



Is late treatment with sunlight beneficial for COVID-19?

RCT 30 patients in Brazil

Shorter hospitalization (p=0.02) and faster recovery (p=0.0006)

Pereira et al., J. Photochemistry and ..., Dec 2022

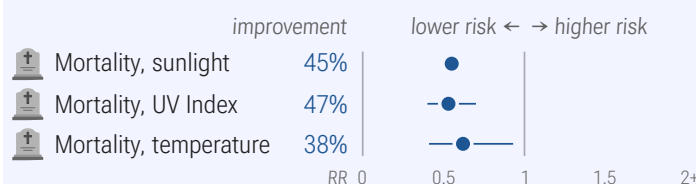
c19early.org

RCT 30 hospitalized COVID-19 patients investigating the effectiveness of photobiomodulation (PBM) using a vest with near-infrared LEDs (simulating part of the sunlight spectrum). The treatment group showed shorter hospitalization, significant improvement in cardiopulmonary function, and improvements in leukocyte, neutrophil, and lymphocyte counts post-treatment. The treatment group had higher pneumonia severity at baseline.

For more discussion see⁷⁴.

Razi

Sunlight for COVID-19 Razi et al. PROPHYLAXIS



Is sunlight beneficial for COVID-19?

Retrospective study in multiple countries (January 2020 - January 2023)

Lower mortality with increased sunlight exposure (p<0.000001)

Razi et al., COVID, March 2026

c19early.org

Ecological study of 129 geographical regions worldwide showing lower COVID-19 mortality with higher ambient Ultraviolet (UV) Index, sunlight duration, and temperature. Authors analyzed daily data from January 2020 to January 2023 utilizing panel Poisson Distributed Lag Models with 7-to-21-day exposure windows. Results demonstrated that a one-standard-deviation increase in the UV Index had the strongest negative association with mortality, followed by sunlight duration and ambient temperature. The study controlled for dynamic confounders like PM2.5 and relative humidity, which were found to be statistically insignificant, suggesting mortality reductions are driven by solar radiative intensity rather than simply clear or dry weather. However, the study relies on aggregate ecological data and deliberately excludes explicit seasonal controls to avoid over-adjustment bias, therefore the results cannot establish causality and may be confounded by human behavioral shifts, such as increased indoor crowding during colder months.

We calculate RR per standard deviation by exponentiating the sum of the 15 daily lag coefficients from the Poisson log-link model. For the confidence interval, we estimate the variance of the cumulative coefficient as $\text{Var}(\sum \beta_k) = \sum \text{SE}_k^2 + 2 \cdot \sum_{i < j} \rho \cdot \text{SE}_i \cdot \text{SE}_j$, where ρ is the assumed pairwise correlation between lag estimates. The full variance-covariance matrix is not provided in the supplementary materials, so ρ must be assumed. Given the reported VIF of ~12 for UV lags, we use $\rho \approx 0.9$ for a conservative confidence interval.

Several lines of evidence suggest the meteorological signal is not purely an artifact of behavioral confounding. First, PM2.5 and humidity - alternative proxies for winter conditions - were statistically insignificant when modeled alongside UV. Second, non-pharmaceutical interventions tightened during winter months and would have suppressed mortality during low-UV periods, biasing against the UV finding. Third, independent Bayesian estimates of COVID-19 seasonality that controlled for NPIs and mobility found a comparable seasonal effect magnitude⁷⁵. Fourth, research indicates that seasonal differences in time spent indoors are small (~10%) and that summer mass-gathering events do not trigger respiratory illness surges, suggesting behavioral crowding is not the primary seasonal driver⁷⁶. Additionally, *Gavenčiak et al.* found their seasonality estimate was robust to adjusting for country-level mobility data, further indicating the seasonal signal is not primarily behavioral.

Appendix 1. Methods and Data

Search methods

We perform ongoing searches of PubMed, medRxiv, Europe PMC, ClinicalTrials.gov, The Cochrane Library, Google Scholar, Research Square, ScienceDirect, Oxford University Press, the reference lists of other studies and meta-analyses, and submissions to the site c19early.org, which regularly receives notification of studies upon publication. Search terms are sunlight and COVID-19 or SARS-CoV-2. Automated searches are performed twice daily, with all matches reviewed for inclusion. All studies regarding the use of sunlight for COVID-19 that report a comparison with a control group are included in the main analysis. Studies with major unexplained data issues, for example major outcome data that is impossible to be correct with no response from the authors, are excluded.

Effect extraction

We extracted effect sizes and associated data from all studies. If studies report multiple kinds of effects then the most serious outcome is used in pooled analysis, while other outcomes are included in the outcome-specific analyses. For example, if effects for mortality and cases are reported then they are both used in specific outcome analyses, while mortality is used for pooled analysis. If symptomatic results are reported at multiple times, we use the latest time, for example if mortality results are provided at 14 days and 28 days, the results at 28 days have preference. Mortality alone is preferred over combined outcomes. Outcomes with zero events in both arms are not used, the next most serious outcome with one or more events is used. For example, in low-risk populations with no mortality, a reduction in mortality with treatment is not possible, however a reduction in hospitalization, for example, is still valuable. Clinical outcomes are considered more important than viral outcomes. When basically all patients recover in both treatment and control groups, preference for viral clearance and recovery is given to results mid-recovery where available. After most or all patients have recovered there is little or no room for an effective treatment to do better, however faster recovery is valuable. An IPD meta-analysis confirms that intermediate viral load reduction is more closely associated with hospitalization/death than later viral load reduction⁷⁷. If only individual symptom data is available, the most serious symptom has priority, for example difficulty breathing or low SpO₂ is more important than cough.

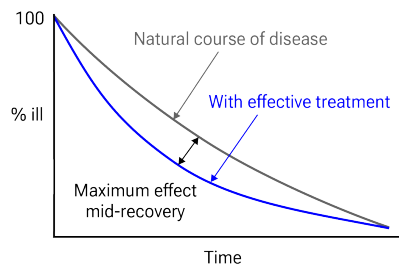


Fig. 20. Mid-recovery results can more accurately reflect efficacy when almost all patients recover. *Mateja et al.* confirm that intermediate viral load results more accurately reflect hospitalization/death.

Statistical methods

Forest plots are computed using PythonMeta⁷⁸ with the DerSimonian and Laird random-effects model (the fixed effect assumption is not plausible in this case) and inverse variance weighting. Results are presented with 95% confidence intervals. Heterogeneity among studies was assessed using the I^2 statistic. When results provide an odds ratio, we compute the relative risk when possible, or convert to a relative risk according to *Zhang et al.* Reported confidence intervals and p -values are used when available, and adjusted values are used when provided. If multiple types of adjustments are reported propensity score matching and multivariable regression has preference over propensity score matching or weighting, which has preference over multivariable regression. Adjusted results have preference over unadjusted results for a more serious outcome when the adjustments significantly alter results. When needed, conversion between reported p -values and confidence intervals followed *Altman, Altman (B)*, and Fisher's exact test was used to calculate p -values for event data. If continuity correction for zero values is required, we use the reciprocal of the opposite arm with the sum of the correction factors equal to 1⁸². Results are expressed with $RR < 1.0$ favoring treatment, and using the risk of a negative outcome when applicable (for example, the risk of death rather than the risk of survival). If studies only report relative continuous values such as relative times, the ratio of the time for the treatment group versus the time for the control group is used. Calculations are done in Python (3.14.7) with scipy (1.18.1), pythonmeta (1.26), numpy (2.5.2), statsmodels (0.15.0), and plotly (6.9.0). Mixed-effects meta-regression results are computed with R (4.4.0) using the metafor (4.6-0) and rms (6.8-0) packages, and using the most serious sufficiently powered outcome. For all statistical tests, a p -value less than 0.05 was considered statistically significant. Grobid 0.8.2 is used to parse PDF documents.

When evaluating potential effect modification across groups, we use an interaction test as described by *Altman (C) et al.* We compared the log-transformed relative risks using a z -test, deriving the standard error of the difference from the 95% confidence intervals. A two-sided interaction p -value of < 0.05 was considered a statistically significant difference in treatment effect between the groups.

Quality evaluation

Cochrane RoB 2/ROBINS-I are often used to evaluate studies, and have the advantage of providing standardized rules that can be applied with minimal understanding of the domain and study. However, the rules do not account for many real-world issues, often overemphasize or underemphasize others, and studies show low inter-rater reliability⁹⁰. Certain domains are more applicable for these tools, however the time-sensitive nature of a pandemic, with significant mortality for every day of delay in evidence assessment, and the characteristics of COVID-19 make them inappropriate for this domain. This can be demonstrated with examples where expert RoB 2/ROBINS-I ratings do not match reality for COVID-19. *Popp et al.* use RoB 2 to classify *Reis et al.* as low risk of bias, however this is the opposite of reality—the trial not only has very high risk of bias, but has very high actual known bias, refusing to release data despite pledging to, reporting multiple impossible numbers, having blinding and randomization failure, and many other issues⁹². *Axfors et al.* use RoB 2 to classify *Horby et al.* as low risk of bias, however this is the opposite of reality—the very late treatment and excessive dosage used produces results with no relevance to recommended usage. HCQ shows poor results with late treatment and excessive dosage, and the combination shows harm^B. *Hempenius et al.* use ROBINS-I to classify 33 studies for HCQ. The two rated as having the lowest risk of bias^{88,89} are far from the most informative. Both involve very late treatment, providing no information on recommended usage, and ROBINS-I does a very poor job of accounting for the impact of confounding factors^C.

Our quality evaluation focuses on known issues and bias, and the potential impact on outcomes, rather than just the risk of bias. The estimated potential impact of each confounding factor, and the direction of the impact is considered. For example, consider a study that shows significantly lower risk, the value of the study varies significantly if confounding points to an underestimate or an

overestimate of efficacy. In one case, the real effect may be null, while the other case provides stronger evidence of efficacy (which may be greater than the study shows). Analysis focusing on the risk of bias, while simpler, may penalize studies for theoretical or technical issues that have no or minimal impact on outcomes. Analysis also depends on the outcome, for example certain issues are less relevant for objective outcomes such as mortality. Inaccurate penalization, and inaccurate high-quality evaluation in the face of known major issues affecting outcomes, increases in significance during a pandemic when immediate recognition of new evidence is critical, and when considering all global studies, as required during a pandemic. Investigators in other countries may have different customs for design, analysis, and reporting, and different English language skills, however they may not be less diligent or have greater bias. Investigators in lower-pharmaceutical-profit countries may have lower bias towards profitable interventions.

Treatment time

We have classified studies as early treatment if most patients are not already at a severe stage at the time of treatment (for example based on oxygen status or lung involvement), and treatment started within 5 days of the onset of symptoms. If studies contain a mix of early treatment and late treatment patients, we consider the treatment time of patients contributing most to the events (for example, consider a study where most patients are treated early but late treatment patients are included, and all mortality events were observed with late treatment patients). We note that a shorter time may be preferable. Antivirals are typically only considered effective when used within a shorter timeframe, for example 0-36 or 0-48 hours for oseltamivir, with longer delays not being effective^{96,97}.

Living analysis

This is a living analysis and is updated regularly. We received no funding, this research is done in our spare time. We have no affiliation with any pharmaceutical companies, supplement companies, governments, political parties, or advocacy organizations.

A summary of study results is below. Please submit updates and corrections at <https://c19early.org/sunmeta.html>.

Late treatment

Effect extraction follows pre-specified rules as detailed above and gives priority to more serious outcomes. For pooled analyses, the first (most serious) outcome is used, which may differ from the effect a paper focuses on. Other outcomes are used in outcome specific analyses.

Pereira, 12/5/2022, Single Blind Randomized Controlled Trial, placebo-controlled, Brazil, peer-reviewed, 5 authors.	hospitalization time, 31.6% lower, relative time 0.68, $p = 0.02$, higher sunlight exposure 15, lower sunlight exposure 15.
	pulmonary auscultation improvement time, 37.5% lower, relative time 0.62, $p < 0.001$, higher sunlight exposure 15, lower sunlight exposure 15.

Prophylaxis

Effect extraction follows pre-specified rules as detailed above and gives priority to more serious outcomes. For pooled analyses, the first (most serious) outcome is used, which may differ from the effect a paper focuses on. Other outcomes are used in outcome specific analyses.

Cherrie, 4/8/2021, retrospective, multiple countries, peer-	risk of death, 32.0% lower, RR 0.68, $p = 0.004$, USA, England, Italy combined.
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reviewed, 7 authors, study period 22 January, 2020 - 30 April, 2020, per 100kJ m-2 increase.	risk of death, 29.0% lower, RR 0.71, $p < 0.001$, USA.
	risk of death, 19.0% lower, RR 0.81, $p = 0.002$, Italy.
	risk of death, 49.0% lower, RR 0.51, $p < 0.001$, England.
Jabbar, 12/31/2021, retrospective, Iraq, peer-reviewed, 4 authors.	risk of case, 62.8% lower, OR 0.37, $p < 0.001$, higher sunlight exposure 43 of 120 (35.8%) cases, 72 of 120 (60.0%) controls, NNT 4.1, case control OR.
Kalichuran, 4/26/2022, prospective, South Africa, peer-reviewed, survey, 4 authors, study period September 2020 - February 2021.	risk of symptomatic case, 58.2% lower, RR 0.42, $p = 0.004$, higher sunlight exposure 21, lower sunlight exposure 79, inverted to make RR<1 favor higher sunlight exposure, higher sunlight exposure vs. lower sunlight exposure.
Ma, 12/3/2021, retrospective, USA, peer-reviewed, 16 authors, study period May 2020 - March 2021.	risk of case, 23.0% lower, RR 0.77, $p < 0.001$, higher sunlight exposure 411 of 10,393 (4.0%), lower sunlight exposure 495 of 9,142 (5.4%), NNT 68, adjusted per study, odds ratio converted to relative risk, UVB, highest quartile vs. lowest quartile, model 3, table 3, multivariable.
	risk of case, 23.1% lower, RR 0.77, $p < 0.001$, higher sunlight exposure 325 of 9,325 (3.5%), lower sunlight exposure 436 of 9,079 (4.8%), NNT 76, adjusted per study, odds ratio converted to relative risk, UVA, highest quartile vs. lowest quartile, model 3, table 3, multivariable.
Razi, 3/26/2026, retrospective, multiple countries, peer-reviewed, 2 authors, study period 21 January, 2020 - 10 January, 2023, per one std. dev. increase.	risk of death, 45.0% lower, RR 0.55, $p < 0.001$, sunlight.
	risk of death, 47.0% lower, RR 0.53, $p < 0.001$, UV Index.
	risk of death, 38.0% lower, RR 0.62, $p = 0.02$, temperature.

Evaluation Notes

Analyzing the data from first principles is always important, and may be especially important for COVID-19. Bias in the design, analysis, and reporting of clinical studies has long been reported, and may be increased for COVID-19 due to politicization. For example, Scott Alexander noted that "if you say anything in favor of ivermectin you will be cast out of civilization and thrown into the circle of social hell reserved for Klan members and 1/6 insurrectionists. All the health officials in the world will shout 'horse dewormer!' at you and compare you to Josef Mengele."²⁰ Social pressure to report politically acceptable results was very strong. There may therefore be unusually strong bias in design, analysis, and reporting. For example, Prof. Greenland reports that Hayward *et al.* applied an unjustified and undisclosed extremely tight, null-centered Bayesian prior that biases towards more politically acceptable results¹⁰⁵. While the politicization focused on certain treatments, it was not limited to them. For example, media coverage was highly biased against positive results for low-cost treatments¹⁰⁶ across the 226 treatments we cover. Studies should be evaluated from first principles, incorporating the treatment delay, treatment regimen, patient population, and other confounding factors. For COVID-19, there is no significant difference in the results of RCTs compared to observational studies, RR 0.97 [0.91-1.03]¹⁶—in both cases bias varies from minimal to extreme, and all studies must be evaluated individually.

US authorities claim only three high-profit drugs from companies with strong US lobbying are beneficial for early treatment (2 repurposed drugs - remdesivir and molnupiravir, and one novel drug - nirmatrelvir)^D. COVID-19 involves the interplay of many viral and host proteins and factors, providing over 500 therapeutic targets¹⁰⁷. Given the 12,000+ proposed treatments⁷¹, existing results for many treatments with overlapping secondary complications and therapeutic targets, and the combination of known safety and pharmacokinetics for certain treatments along with strong mechanistic evidence, the probability of only 3 high-profit drugs from top lobbying companies being beneficial is extremely low. This likely reflects a bias toward evaluation of drugs with strong financial resources and efforts devoted to passing the US approval process, and very limited or non-existing evaluation of low-cost treatments. Indeed, official recommendations varied widely between countries¹⁰⁸. Some countries evaluated limited low-cost treatments early and 25 low-cost treatments were approved in one or more countries¹⁰⁸.

Contrary to claims found online, we analyze both all studies and higher-quality studies (with evaluation focusing on known issues and bias, and the potential impact on outcomes, rather than just the risk of bias), we analyze specific outcomes and pooled outcomes (with extensive analysis and validation of pooled outcomes), and we do not include preclinical studies or retracted studies in meta-analysis. Pooled outcomes can detect efficacy earlier but do not bias towards efficacy—the inclusion of less appropriate designs such as very late treatment may hide efficacy for appropriate use.

Supplementary Data

Supplementary Data

Footnotes

- a. Smoking was known to cause lung cancer since at least 1939, but this was not widely recognized in the US until 1964, 25 years later. Surgeon general Leroy Burney tried publicizing the danger starting in 1957, with limited success. Surgeon general Luther Terry, appointed in 1961, prompted by President Kennedy in 1962 amid pressure from health advocates, finally got recognition in 1964. The 1964 report reviewed 7,000+ studies, but these could (and should) have been reviewed and acted upon in real-time as they were published. Historians attribute the 25 year delay to an industry campaign to manufacture doubt and controversy, through tactics like funding biased and fraudulent research from "independent" organizations, attacking scientists, and political lobbying. The success of the industry campaign is only possible because officials did not analyze the research in detail. Fraudulent industry research supported prior failures, but would have been called out as fraudulent by officials that analyzed and understood the research in real-time.
- b. When administered late in infection, HCQ may enhance viral egress by further increasing lysosomal pH beyond the effect of ORF3a's water channel activity, thereby promoting lysosomal exocytosis, inactivating degradative enzymes, and facilitating the release of SARS-CoV-2 particles into the extracellular environment^{84,85}. Research also suggests potential cardioprotective effects at lower doses, but cardiotoxicity with excessive dosage⁸⁶. *Bobrowski et al.* also indicate negative effects if HCQ and remdesivir are combined.
- c. *Peters et al.* is subject to confounding by calendar-time (SOC evolved rapidly early in the pandemic, the linear covariate does not reflect non-linear SOC changes and hospital specific effects), hospital type (non-treatment hospitals were tertiary university centers), confounding by indication (4/7 hospitals initiated treatment on deterioration), immortal-time bias for as-treated (exposure assigned after baseline), significant differences for other experimental treatments, potential overadjustment from collider bias (steroid use and indication bias), limited baseline severity information, differences in hospice referral propensity across hospitals, unadjusted difference in time from onset to admission, difference in PCR positivity, and other

factors. *Mahévas et al.* is subject to confounding by hospital (treatment highly dependent on the hospital, different SOC/ICU transfer practices, not included in PS), immortal time (only partly addressed in sensitivity analysis), co-treatment differences, calendar-time (SOC evolved rapidly early in the pandemic), binary coding for age (age ≥ 65 despite steep age-risk gradient), residual imbalance (variables dropped from PS), a composite outcome dependent on hospital triage/capacity, and other factors.

- d. Monoclonal antibodies were previously included. Other treatments such as dexamethasone, tocilizumab, and baricitinib were recommended for late stage hospitalized patients.

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