# A timeline of ivermectin-related events in the COVID-19 pandemic

Mika Turkia

M.Sc., mika.turkia@alumni.helsinki.fi, March 24, 2021

**Abstract**

Ivermectin is an antiparasitic medication invented in Japan in 1975 by Kitasato University professor emeritus Satoshi Ōmura, for which he won the 2015 Nobel Prize in physiology or medicine. The drug proved effective in eradicating parasitic infections, with several billion doses administered since 1981. The patent for the product was owned by Merck & Co/MSD. In most countries the patent expired in 1996. Currently, ivermectin preparations are available internationally from many sources, with the production cost of a single dose estimated to be less than 0.1 US dollars.

The interest in ivermectin with regard to COVID-19 was initiated by an Australian in vitro study published on April 3, 2020, indicating that a a single treatment with ivermectin effected an approximately 5000-fold reduction in SARS-CoV-2 virus at 48 h in cell culture. A few days later, two doctors in Peru begun treating a COVID-19 outbreak in a prison with ivermectin, later also treating the local police.

In the second and third quarter of 2020 the use of ivermectin spread to or emerged independently in other South and Central American countries, Egypt and India. The first country to adopt it nationwide appears to have been Honduras, followed by Peru and Bangladesh. Eventually in the fourth quarter of 2020 and the first quarter of 2021 it spread to Lebanon and selected countries of Southern Africa and Southeastern Europe, with Slovakia being the first European Union country to adopt ivermectin for COVID-19, followed by Bulgaria and the Czech Republic.

Ivermectin treatments raised controversy within most wealthy industrialized countries including other European Union countries and the United States ignoring ivermectin referring to lack of evidence of its efficacy and safety. There was a difference in attitudes: many developing countries acted early based on clinical experimentation or their own clinical trials initiated early in 2020, whereas the industrialized countries predominantly did not initiate ivermectin trials and appeared to rely solely on recommendations of the World Health Organization (WHO), the US National Institutes of Health (NIH), the US Food and Drug Administration (FDA), and the European Medicine Agency (EMA), which held predominantly negative views on ivermectin. Many developing countries adopted ivermectin before the existence of any trial results, whereas the industrialized countries did not adopt it even after results of twenty randomized controlled clinical trials were available in February 2021. The WHO initiated its first ivermectin trial in late February 2021.

In the United States, allocation of government funding between novel and existing pharmaceuticals appeared inefficient at times, with significant government funding allocated for example to the development of a novel pharmaceutical estimated to possess an efficacy comparable to ivermectin but priced several magnitudes higher.

Major social media companies censored ivermectin researchers and research, with for example YouTube censoring results of a meta-analysis commissioned by the WHO. Traditional media in the USA and the European Union appeared to either ignore ivermectin or publish negative commentaries only.

This article aims at giving a brief overview of ivermectin-related events, presenting them on a timeline from April 2020 to the second half of March 2021. There was a widespread disagreement on the fundamentals: which methods were appropriate as a basis for decision making, what counted as evidence, and what was ethical.

***Keywords:*** *COVID-19, SARS-CoV-2, ivermectin*

***ORCID iD:*** 0000-0002-8575-9838

## Introduction

This article aims at giving an overview of the ivermectin controversy, including current practices of research, publishing and governmental policy formation, by presenting a timeline of relevant events, compiled from peer-reviewed academic journals indexed in PubMed, preprint servers such as medRxiv, chemRxiv, SSRN, Research Square and ResearchGate, international clinical trials registers, international newspapers and medical news service providers as well as websites. As there have been a lot of sparsely documented events internationally, the search has not been systematic, the timeline is unavoidably incomplete, and there may naturally be some personal bias with regard to what has been selected. Also, the main focus of the article is on the last quarter of the 2020s and the first quarter of 2021. Despite these limitations the timeline may serve as a template for more detailed inquiries.

Due to the large number of studies and limited space, each study is mentioned only briefly, without a possibility to analyze methodologies or results in depth. Statistically significant endpoints are reported, with nonsignificant endpoints mostly left out. For consistency, results are in most cases formatted as they appear in a meta-analysis by the CovidAnalysis research group, possibly reformulated in comparison to the original sources (e.g. odds ratios converted to relative risk or methodological errors corrected).[1,2,3]

Ivermectin is best known as an antiparasitic agent. For prophylaxis of onchocerciasis (river blindness) and strongyloidiasis it is administered as a single oral yearly dose of 0.15-0.20 mg/kg.[4,5] For lymphatic filariasis, a once-yearly dose of 0.3-0.4 mg/kg or bi-yearly dose of 0.15–0.2 mg/kg is administered.[4] For classic scabies, two doses of 0.2 mg/kg approximately one week apart are recommended, and for crusted scabies three to seven doses of 0.2 mg/kg depending on the infection severity.[6,7] With regard to malaria, repurposing ivermectin as a complement to current malaria vector control tools is currently being investigated, with a proposed dosing regime of 0.4 mg/kg repeated three times during the malaria season, and another proposed dosing regime of 0.3 mg/kg on three consecutive days in combination with two other pharmaceuticals also repeated three times during the season.[8]

With regard to its in vitro antiviral action, ivermectin has shown robust antiviral action towards a range of RNA and DNA viruses, including HIV-1, dengue, Zika and West Nile Virus, Venezuelan equine encephalitis virus, Chikungunya, pseudorabies virus, adenovirus, and SARS-CoV-2 (COVID-19).[9] For dengue virus, a combined phase II/III patient randomized controlled trial (RCT) has been completed.[10]

Another recent line of research has been an investigation into ivermectin's efficacy in cancer. A study found out that ivermectin at a very low dose drastically reversed the resistance of the tumor cells to the chemotherapeutic drugs both in vitro and in vivo.[11] Ivermectin could thus be used in combination with chemotherapeutic agents to treat drug-resistant cancers.

With regard to the mechanism of action of ivermectin as an antiparasitic medication, Chung et al. describe that ivermectin interacts with vertebrate and invertebrate γ-aminobutyric acid (GABA) receptor and invertebrate glutamate-gated chloride channels, increasing chloride ion influx with subsequent paralysis and death in the target organism.[12] Ivermectin is effective in killing nematodes and arthropods with a single dose of 0.1-0.3 mg/kg but has has a very wide margin of safety in mammals because in mammals GABA-mediated nerves occur only in the central nervous system and ivermectin does not readily cross the blood-brain barrier.[12]

With regard to safety of overdosing, in chickens and most dogs subcutaneous doses of approximately 5 mg/kg have been shown to cause mild symptoms and doses of approximately 15 mg/kg severe symptoms up to coma and death. In two described cases on humans, a 16-month-old child ingesting 6.7 to 8.7 mg/kg ivermectin resulted in frequent vomiting, somnolence, mild tachycardia, and hypotension, and a 61-year old woman became comatose three hours after ingesting 15.4 mg/kg agricultural ivermectin, requiring supportive intensive care but was discharged uneventfully on day 9.[12]

The FDA-approved dosing for treatment of parasitic diseases is 0.2 mg/kg. The doses used in COVID-19 related clinical trials described in this article varied between 0.2-0.6 mg/kg. With regard to safety of ivermectin in general, a current World Health Organization (WHO) document on the treatment of onchocerciasis states that "ivermectin is safe and can be used on a wide scale".[13] With regard to safety for children, a recent systematic review and and an individual patient data meta-analysis of ivermectin use in children weighing less than 15 kg concluded that existing limited data between January 1980 and October 2019 suggest that oral ivermectin in children weighing less than 15 kilograms is safe.[14] Overall a total of 1.4% (15/1,088) of children experienced 18 adverse events all of which were mild and self-limiting. No serious adverse events were reported.

With regard to safety of ivermectin during pregnancy, a document from 2004 published by the WHO titled "Mass treatment with ivermectin: an underutilized public health strategy" describes safety during pregnancy, noting that "a number of follow-up studies have found that inadvertent filariasis mass campaign use of ivermectin during pregnancy has not been associated with adverse pregnancy outcomes or negative effects on pregnant women or their offspring", referring to a study by Gyapong et al. who concluded "there is no evidence of a higher risk of congenital malformation or abortions in those who are inadvertently exposed".[15,16]

## April 2020

On April 3, a Monash University of Australia in vitro ivermectin study by Caly et al. reported that ivermectin is an inhibitor of SARS-CoV-2 virus in vitro, that a single treatment effected approximately 5000-fold reduction in virus at 48 h in cell culture, and that ivermectin is FDA-approved for parasitic infections and included on the WHO model list of essential medicines, thus being widely available.[17,18,19]

On April 6, a French biotechnology company MedinCell which had been studying ivermectin for malaria announced an initiative to develop an injectable form of ivermectin for prophylaxis of COVID-19.[20,21,22]

On April 10, mentioning increased interest in ivermectin after the Australian in vitro study, US FDA issued a warning against using veterinary ivermectin as treatment for COVID-19 in humans, citing safety concerns.[23] It noted additional testing is needed to determine whether ivermectin might be safe or effective in COVID-19 in humans.

On April 13, two Florida, US pulmonologists Rajter and Cepelowicz-Rajter were said to be pioneering early treatments with ivermectin, reporting a nearly 100% response rate with early administration, adding that they were initiating clinical studies.[24]

On April 13, a preprint by Patel et al. described an observational registry-based study from 169 hospitals claiming that a single dose of 0.15 mg/kg of ivermectin produced a significant mortality reduction (7.7% vs. 18.6%) in 1,970 patients requiring mechanical ventilation.[25,26]

On April 14, two medical doctors, Gustavo Elera Arévalo and Fernando Polanco Hinostroza in La Merced (Chanchamayo) in Peru, begun treating a COVID-19 outbreak in a prison with ivermectin, later also treating the local police.[27]

On April 19, a second preprint by Patel et al. described an observational propensity-matched case-controlled study in 1,408 patients (of which 704 received ivermectin) which claimed to demonstrate an association of ivermectin use with lower in-hospital mortality 1.4% vs 8.5%, concluding that ivermectin was associated with a potential survival benefit in COVID-19 and should be investigated urgently in randomized controlled trials.[28,29] The data was said to originate from an international multi-institutional deidentified healthcare outcomes database compiled by Surgisphere Corporation, Chicago, IL, using data from hospitals located throughout the world. The registry was said to ensure compliance with the FDA's guidance on real-world evidence. Data was said to have been collected through "automated data transfers that capture 100% of the data from each healthcare entity at regular, predetermined intervals, thus reducing the impact of selection bias".

On April 19, Chaccour criticized the methods and the analysis of the Patel et al. study on Twitter, subsequently contacting the authors about inconsistencies in the data.[30]

On April 21, Antiviral Research journal published letters to the editors commenting the Caly et al. study, with Rayner et al. commenting that "a small window exists for the current data to have relevance for humans", and Noël commenting that the higher than usual doses that would be necessary could be toxic and thus a phase I study is absolutely needed. Jans and Wagstaff commented that a vitally important reason to be very cautious is that ivermectin's key direct target in mammalian cells is a not a viral component but a host protein important in intracellular transport. They also commented that the basis of ivermectin's broad-spectrum activity against a number of different RNA viruses in vitro is the fact that it is a host-directed agent (HDA), and the way a HDA can reduce viral load is by inhibiting a key cellular process that the virus hijacks to enhance infection by suppressing the host antiviral response. Reducing viral load by even a modest amount by using a HDA at low dose early in infection can be the key to enabling the body's immune system to begin to mount the full antiviral response before the infection takes control. However, it cannot be assumed that even low doses are safe in the context of a burgeoning viral infection, where a measured immune response is key to recovery.[31]

On April 23, Honduras adopted ivermectin country-wide.[3]

On April 26, a preprint by Schmith et al. described pharmacokinetic model simulations to predict plasma concentration-time profiles after a single and repeat fasted administration of the approved dose of ivermectin (200 μg/kg), noting that plasma or lung ivermectin concentrations do not reach the IC50 indicated by the Caly et al. in vitro study, even for a dose level ten times higher than the approved dose, thus concluding that a "likelihood of a successful clinical trial using the approved dose of ivermectin is low. Combination therapy should be evaluated in vitro. Re-purposing drugs [...] is an ideal strategy but is only feasible when product safety has been established and experiments of re-purposed drugs are conducted at clinically relevant concentrations".[32]

## May 2020

On May 2, Aguirre Chang published a preprint of an observational case study of seven patients, showing improvement and resolution of fever within 48 hours and a 100% recovery.[33]

On May 6, a randomized clinical trial of ivermectin for treatment and prophylaxis of COVID-19 (ECIT-PRO19) was started Spain (EudraCT 2020-001994-66).[34]

On May 7, a peer-reviewed version of the Schmith et al. pharmacokinetic model simulations study was published.[32] On the same day, a pilot study to evaluate the potential of ivermectin to reduce COVID-19 transmission (SAINT) by Chaccour et al. was started by University of Navarra in Pamplona, Spain (EudraCT 2020-001474-29).[35]

On May 8, Peru adopted ivermectin country-wide.[3]

On May 11, in an editorially independent blog from the publishers of Science Translational Medicine, Lowe discussed organic chemistry aspects of ivermectin.[36]

On May 15, a multi-center, randomized, double-blind, placebo-controlled study investigating efficacy, safety and tolerability of ivermectin in patients with a proven SARS-CoV-2 infection (HUVE-19-CT-001) by Huvepharma EOOD (Petkov) was started in Sofia, Bulgaria (EudraCT 2020-002091-12).[37]

On May 19, an Indian newspaper wrote about an observational trial by Alam et al. in Bangladesh, with 60 patients treated with a combination of ivermectin and doxycycline recovering within four days.[38] Alam, who was referred to as "a reputed clinician in Bangladesh", said the combination "yielded virtually the near-miraculous result in curing the patients" with no side effects. He mentioned being "a hundred per cent hopeful about the effectiveness" and that they had contacted government regulators to prepare for national and international adoption of the treatment.

On May 20, an observational early treatment outpatient study in Peru by Mogrovejo Ramos et al. with 63 symptomatic patients diagnosed through teleconsultations and prescribed 0.2 mg/kg ivermectin reported that symptoms such as fever had significantly decreased at 24 hours, with sense of smell recovered and discomfort overcome at 48 hours, while the cough and muscle aches remained on day 5.[39] The authors concluded that "a massive distribution of this drug with a prescription should be considered as a public health strategy to be applied by the first-line establishments, in order to avoid overcrowding and collapse of the national health system".

On May 27, Rizzo suggested that ivermectin may have an ionophore role, thus introducing a possible new mechanism of action.[40]

On May 31, another Indian newspaper referred to the results of the study by Alam et al. in Bangladesh, saying that the Indian Council of Medical Research (ICMR), the country's apex medical research body, is reviewing the benefits of the combination. A senior ICMR researcher said the agency had reviewed ivermectin multiple times and continued to study it, adding that "however, to conclude anything we would need solid evidence or a published study, backed by statistically significant data on a bigger sample size". The article mentioned ivermectin being a part of at least five ongoing trials in India.[41]

## June 2020

On June 1, to prevent outpatient deterioration and hospital congestion, the government of Peru launched a 'Territorial Aid Operation for Treatment and Isolation in Response to COVID-19' (Tayta), consisting of

early outpatient treatment with individually prescribed combinations of paracetamol, azithromycin, hydroxychloroquine and ivermectin.[42]

On June 2, a study about ivermectin as an antiviral treatment for patients infected by SARS-COV2 (CORIVER) was started by Hospital Universitario Virgen de las Nieves (Sergio Sequera) in Granada, Spain (EudraCT 2020-001971-33).[43]

On June 2, Science wrote about Expressions of Concern (EOCs) posted by the Lancet and the New England Journal of Medicine about two non-ivermectin studies based on the Surgisphere database.[44] The two EOCs led to temporary halting of many hydroxychloroquine studies unrelated to Surgisphere database. A researcher involved in one of the halted studies commented that "the problem is, we are left with all the damage that has been done ... the whole world thinks now that these drugs are poisonous".

On June 3, The Guardian (UK) wrote about "flawed data" from Surgisphere Corporation having prompted the Peruvian government to add ivermectin to its national COVID-19 therapeutic guidelines.[45,46] The story described Surgisphere employees having little or no scientific background, saying a science editor appeared to be a science fiction author and fantasy artist, and a marketing executive being an adult model and events hostess. The article referred to a peer-reviewed hydroxychloroquine study published in The Lancet, based on the same database, stating that seven hospitals "whose cooperation would have been essential for the Australian patient numbers in the database to be reached ... denied any role in such a database, and said they had never heard of Surgisphere". The ivermectin preprint based on the database was available on June 2 but no longer on June 3.[29]

On June 4, Science wrote about retractions of two peer-reviewed articles by Patel et al. published by The Lancet and The New England Journal of Medicine that were not about ivermectin but based on the same database compiled by Surgisphere Corporation.[47] The Science article noted that the ivermectin study was only posted online as a preprint and was no longer available but it was said to have prompted increased use and government authorization of the drug in several Latin American countries. On June 8, Science wrote about the backgrounds of the researchers involved in the Surgisphere scandal.[48]

On June 4, a Brazilian clinician Lucy Kerr described her ivermectin treatments, stating that "I decided to use it on patients because the side effects are almost nonexistent and if it worked I would save a lot of lives. Now I have more than 30 cases that I treated and cured. Many more were cured by doctors in the group of 570 doctors that I administer in WhatsApp and Telegram".[49,50]

On June 7, a news report from Peru wrote that Arévalo and Hinostroza had treated 1,200 patients with ivermectin "with excellent results" since April 14.[27] Arévalo had initially treated prisoners, then the police and later the residents in the community. The report said that the government had announced a plan to acquire 490 000 doses. About the role of the WHO, Arévalo commented that "the WHO has made serious mistakes that resulted in thousands of human deaths at the beginning of the pandemic, such as not replying to the October 2020 letter from South Korea reporting atypical pneumonia in that region, the advice against masks, the banning of ivermectin after promising results from two Australian researchers, as well as ten more mistakes. After this pandemic we have to look back and restructure that organization". About the lack of evidence from large trials he said that "in this disease the only evidence we had was about the mechanisms by which the patients died and trials of drugs that had little or no effect in the late phase of the disease ... the great discoveries in medicine have been based on observations, accidents and coincidences". The report also mentioned ivermectin treatments having been carried out in neighboring countries including Bolivia commencing several weeks earlier, with good results.

On June 10, initial results of an observational controlled 280-patient ICON ivermectin trial were made available as a preprint on medRxiv.[51] The trial used propensity matching. Mortality was significantly lower among ivermectin-treated patients with severe pulmonary involvement (38.8% vs 80.7%, OR 0.15, 95% CI 0.05-0.47, p=0.001). Among all ivermectin-treated patients, mortality was also lower in the ivermectin group (13.3% vs 24.5%, OR 0.47, 95% CI 0.22-0.99, $p<0.05$).[52]

On June 12, Heidary et al. published a systematic peer-reviewed review of the antimicrobial, antiviral, and anti-cancer properties of ivermectin.[53] On the same day, TrialSite News wrote about early grassroots experimentation with ivermectin in Peru.[54]

On June 12, a peer-reviewed article about case series of 100 patients treated with a combination of ivermectin and doxycycline in Bangladesh by Alam et al. found the combination very effective in viral clearance in mild and moderately sick patients, with all of them testing negative and symptoms improving within 72 hours.[55]

On June 12, a randomized double-blind multi-centre phase II proof of concept dose finding clinical trial on ivermectin for the early treatment of COVID-19 (COVER) was started in Negrar di Valpolicella, Italy (EudraCT 2020-002283-32).[56,57,58]

On June 13, a news article described "an avalanche of cases" in May 2020 in Iquitos, Peru, a lack of response from the officials, and a successful containment of the initial epidemic by local doctors utilizing ivermectin for early outpatient treatments.[59] One of the doctors, Sergio Bardon, a neurosurgeon, occupational physician and specialist in community and rural health trained at the University of Buenos Aires and the University of Sheffield in the United Kingdom, described that ivermectin reduced viral loads, causing a drastic improvement in the clinical representation of the patients. Bardon mentioned chaotic changes in the WHO and national regulations, saying a ministerial resolution prohibiting the use of antibiotics and corticosteroids but allowing ivermectin had just been issued. Bardon stressed the need for early treatment to prevent the patient going into an inflammationary phase in which the viral load was not relevant any longer and in which "ivermectin no longer makes much sense". Bardon described the phase-specificity of COVID-19, including the stopping of viral replication in a few days after the beginning of the symptoms, and the lack of efficacy of antivirals in the inflammatory phase. Bardon said he had only needed to hospitalize his first COVID-19 patient, after which he had been able to treat all the others as outpatients. He said he had also treated patients in Loreto, Amazonas where there were no hospitals but all patients had been successfully treated as outpatients with a combination of ivermectin and azithromycin. With regard to the hospital in Iquitos, Bardon added that the internationally publicized immediate crisis with people dying outside the hospital had been solved a few days later by administering single-dose injectable ivermectin, with Bardon participating in the process. The problem was that pharmacies were becoming out of stock and the prices had multiplied by approximately seven, from USD 4 to USD 30. Bardon stressed the importance of ensuring the supply. Many patients had been unable to obtain the drug even though Brazil produced it nationally and it had initially been relatively affordable. Even if the production had been sufficient the drug had not been properly distributed in the areas in need. Also, the situation was worsening, with too many infected patients leading to a chaos in the underresourced health care system.

On June 14, Sparavigna published an initial version of an ongoing review of the history of ivermectin in COVID-19, describing, among other issues, the case of Iquitos, Peru. The review was continuously updated up to July 29, then again updated on September 8 and September 20.[60] On the same day, German weekly magazine Der Spiegel wrote about the Surgisphere scandal.[61]

On June 15, a preprint discussed the role of CD147 transmembrane receptor in the binding of SARS-CoV-2 and mentioned treatments of 71 patients by Rajter in Florida had yielded a statistically significant reduction in mortality, with fast reversals of rapidly deteriorating oxygen status.[62,63,64]

On June 17, a Japanese treatment manual listed ivermectin as one of the treatment options.[65]

On June 19, an in-silico analysis indicated ivermectin may interfere with SARS-CoV-2 spike attachment to cell membrane.[66]

On June 21, an in vitro study by Zhang et al. concluded that ivermectin produces genotoxicity and cytotoxicity by inducing DNA damage and AMPK/mTOR-mediated autophagy, thereby posing a potential risk to human health.[67] The authors also warned that accumulation of ivermectin in animal tissues and the excretion of urine and feces in the environment is a major source of potential toxicity.

On June 23, the Ministry of Health of Peru published instructions for making 6 mg/ml oral solution of ivermectin.[68]

On June 24, Molento et al. published "a word of caution" against self-medication.[69]

On June 30, a peer-reviewed version of Caly et al's in vitro study was published.[19] On the same day, the president of a company operating three hospitals and several outpatient clinics and other facilities in the Dominican Republic, José Natalio Redondo, described their experience with off-label treatment of 1,300 patients with 0.1-0.4 mg/kg of ivermectin in conjunction with azithromycin, stating that 99% of them had been cured within 8-10 days, the average duration of the full infection was reduced from 21 days to 10 days, and the only side effects had been mild heart burn and diarrhea.[70] Doctors from Mexico, Ecuador, Peru, Bolivia, Brazil and a few other countries had formed a network for sharing protocols. Redondo mentioned that the public healthcare has less flexibility and followed WHO, the US and other guidance based on funding. He mentioned companies cannot profit off of a generic drug, adding that the priorities are wrong: early treatment should have been prioritized. Redondo mentioned that Merck &Co/MSD had been in touch with them at one point but the medicine used in the Dominican Republic had been produced by a local

company. Redondo stressed the importance of harm reduction by saying that "the health, economic and social benefit of cutting 10 days out of the sickness and reducing the amount of time a person is contagious ... [it has had] a huge impact. A huge value to society. Look at what this pandemic has done to the global economy! Look at New York City – the greatest city with per capital perhaps the greatest doctors and health systems yet look at the amount of death and the impact. It is horrific; a tragedy". With regard to trials, Redondo commented that "it is very expensive to conduct clinical trials. In developed nations in the Caribbean, Central and South America, countries in Africa and some in Asia we must act now to stop the disease from progressing and spreading. We have an investigation we are in fact undertaking and there are other good studies in the works from Johns Hopkins University to Sheba Medical Center in Israel. But those will take some time. The network in Latin America and the Caribbean has acted on observational, off-label data, and it is working. After all, over a trillion doses of ivermectin are given annually for fighting parasites. It is an incredibly safe drug ... The results speak for themselves".

In June, country-wide ivermectin use begun in Bangladesh.[3]

## July2020

On July 1, a preprint by Scheim hypothesized about alleviation of CD147 transmembrane receptor mediated vascular occlusion with ivermectin.[71]

On July 2, Syed discussed studies by Caly et al. and Rajter et al. and the Dominican Republic experiences, commenting that ivermectin appears useful in all stages of COVID-19 but should not be used in individuals with a compromised blood-brain barrier.[19,51,72]

On July 7, the deputy director of the Bulgarian Center for Parasitic and Infectious Diseases described ivermectin as "the most promising", citing the long experience (1975 onwards) about it as a benefit, however noting that there is a need to wait for results of its possible clinical efficacy in COVID-19.[73] She also expressed satisfaction that there was a company in Bulgaria that was ready to produce it.

On July 8, a small open-label pilot trial by Gorial et al. with 87 inpatients of which 16 treated with ivermectin indicated a 42% lower mean hospital stay with a 0.2mg/kg single dose of ivermectin added to a standard regime of hydroxychloroquine and azithromycin (7.62 vs 13.22 days, p=0.00005) (NCT04343092).[74]

On July 9, an in-silico docking and simulation study indicated that a combination of ivermectin and doxycycline might inhibit viral entry and enhance viral load clearance by targeting various viral functional proteins.[75]

On July 11, Aguirre-Chang et al. reported a high rate of clinical improvement in 33 patients with persistent or post-acute symptoms treated with ivermectin.[76] A complete remission of symptoms was observed in 87.9% of the patients after two daily doses of ivermectin. An additional dose of ivermectin for the rest of the patients resulted in a compete remission in 94% of cases.

On July 12, the BBC wrote about fake cures in Latin America, citing Pan American Health Organization (PAHO), a regional office for the Americas under the World Health Organization (WHO).[77] PAHO stated ivermectin was being used "incorrectly ... without any scientific evidence of its efficacy and safety".

On July 14, a randomized controlled trial by Chowdhury et al. about early treatment of 116 patients compared ivermectin-doxycycline and hydroxychloroquine-azithromycin. Times to symptomatic recovery were 5.93 days vs 6.99 days, respectively, not indicating a significant difference.[78]

On July 15, Rajter and Cepelowicz-Rajter discuss their ivermectin experiences in Florida.[79,80]

On July 17, a letter to the editor by Peña-Silva et al. stated that there was no evidence that the 5 μM concentration used in the Caly et al. in vitro study could be achieved in vivo.[81] The authors stated that even with the highest reported dose of approximately 1.7 mg/kg (8.5 times the FDA-approved dose of 0.2 mg/kg) the maximum plasma concentration was only 0.28 μM. They also stated that 93% of ivermectin is bound to plasma proteins which limits its cellular uptake by endothelial cells, thus the free plasma concentration of ivermectin would be 250 times lower than the required concentration. In addition, it was suggested to be unlikely that lung accumulation would be sufficient to achieve the antiviral effect with conventional doses. Also the clinical effects of ivermectin at a concentration of 5 μM range were said to be unknown and possibly associated with toxicity. In summary the authors suggested that ivermectin has in vitro activity against SARS-CoV-2 but the effect is unlikely to be observed in vivo using current dosing. On the

same day, Arpornsuwan et al. presented a proposal for early diagnosis and management of COVID-19 with ivermectin.[82]

On July 18 in India, a panel of senior doctors including Behera evaluated ivermectin and concluded it can be a potential agent for prophylaxis and treatment of COVID-19, due to its antiviral properties, affordability, availability and safety.[83] The suggested dose was 12 mg BD. The panel recommended randomized controlled trials.

On July 30, Aguirre-Chang et al. published a proposal on post-exposure prophylaxis with ivermectin.[84]

On July 30, Stauffer et al. presented a potential strategy to avoid potentially fatal steroid-related strongyloides hyperinfection.[85] They reported that 10% to 40% of populations in tropical and subtropical regions may be infected with a nematode causing strongyloidiasis. The estimated prevalences among immigrants varied between 11% and 50%. The authors suggested either screening or presumptive treatment with ivermectin.

On July 31, a comparative study by Rahman et al. of 400 patients in Bangladesh compared ivermectin-doxycycline and hydroxychloroquine-azithromycin, concluding that ivermectin-doxycycline was a safe and effective combination for obtaining early viral clearance in mild to moderate COVID-19 patients.[86]

In July, the city of Cali in Colombia adopted ivermectin, with an initial distribution of 10,000 doses.[87] The decision was based on good results achieved in Guayaquil, Ecuador. Ivermectin was used in the early phase to prevent progression of disease and subsequent hospitalization. It was distributed to all COVID-19 positive patients and people suspected of exposure to the SARS-CoV-2 virus. The mayor of Cali stated that "we are going to do it even if there is no consensus in the scientific community".

## August 2020

On August 1, state of Chiapas in Mexico adopted ivermectin.[88]

On August 6, an expert panel in Uttar Pradesh, India gave a recommendation for ivermectin prophylaxis of health-care workers and COVID-19 contacts, and for ivermectin treatment of symptomatic patients, with the exception of pregnant and lactating women, and children below 12 years.[89]

On August 11, interestingly, Pan American Health Organization's (PAHO) update of potential therapeutics still included two retracted preprints by Patel et al., in addition to Caly et al. in vitro study, and studies by Rajter et al. and Gorial et al., concluding that the evidence is unconvincing.[90]

On August 13, The Guardian wrote that "world-leading parasite researcher Dr Carlos Chaccour says using the drug in fight against the virus could be 'very, very harmful'", warning against Australia adopting the drug without proper evidence.[91]

On August 14, a peer-reviewed observational retrospective late treatment study by Battacharya et al. in Kolkata, India indicated that a triple therapy with ivermectin, N-acetylcysteine and atorvastatin for 148 patients resulted in an in-hospital mortality rate of 1.35% which was well below the national average.[92]

On August 14, Lier et al. reported a complicated case of disseminated strongyloidiasis in a patient with severe COVID-19 requiring ventilation.[93]

On August 15, a peer-reviewed early treatment study by Espitia-Hernandez et al. in Mexico with 28 treated patients and 7 controls indicated that ivermectin, azithromycin and cholecalciferol reduced viral positivity by 97% at day 10 and the mean duration of symptoms from ten days to three days.[94]

On August 15, an Australian new article described a triple therapy with ivermectin, doxycycline and zinc by Borody as effective, adding that "other than Borody, almost nobody in Australia is treating patients with ivermectin ... at first glance, it seems inexplicable ... the safety profile is so well-known that there is virtually no risk. There are already 33 clinical trials running around the world. The results so far are uniformly positive".[95,96] The article concluded that "medical litigation has created an ultra-cautious culture even when there is virtually no risk, and second, doctors are mostly imprisoned in the prevailing paradigm which holds that there is no effective treatment to cure Covid-19 and that the only way out of Australia's pandemic penitentiary is a vaccine ... a vaccine for a coronavirus should never have been Plan A for anyone as a way out of a pandemic ... it is extraordinary how little thought has been given to an effective cure ... in part that's because the only drug, other than ivermectin, that has shown promise as a prophylactic, an anti-viral and in dampening down Covid's fearful cytokine storm is hydroxychloroquine, which has been

demonized both by Big Pharma and by US Democrats. It is now an article of faith on the Left that it doesn't work, despite remarkable results at some of America's leading hospitals and support from Ivy League academics".[95]

On August 21, a second preprint of the observational ICON study by Rajter et al. in Florida, USA indicated mortality rates of 12.4% vs 25.8% (OR 0.41, CI 0.19-0.87, p=0.02) with and without ivermectin, respectively, in a propensity-matched cohort of 194 patients.[97] As stated earlier, mortality was significantly lower among ivermectin-treated patients with severe pulmonary involvement (38.8% vs 80.7%), although this result had been observed before corticosteroid use became more widespread.

On August 22, capital city of Lucknow in Uttar Pradesh, India, adopted ivermectin.[88]

On August 27, the National Institute for Health (NIH) of the United States gave a recommendation on ivermectin, advising against using it except in clinical trials.[98] The FLCCC group noted the recommendation was rated A III, i.e. a strong recommendation based on expert opinion only.[88] The rating implied that there was no available evidence at the time to make an "evidence-based" grading (in quality of evidence for recommendation classes I, IIa and IIb). However, the results of the ICON trial were available, indicating a possibility for a class IIa or IIb recommendation.[51]

On August 27, Shouman et al. posted results of a randomized clinical trial in Egypt about prophylactic ivermectin treatment of family members of COVID-19 outpatients, indicating that 7% of treated were infected vs 58% in the control group (NCT04422561).[99,100]

On August 27, MedPage Today mentioned the Australian study, use of ivermectin in Peru and Bolivia, commenting that "although the drug is relatively safe, some scientists are worried that clinicians are putting the cart before the horse", and quoted Chaccour emphasizing the need for scientific rigor and the possibility of side effects.[101] The article mentioned the FDA warning cautioning against the use of veterinary formulation of ivermectin, mentioning it was presumably intended "to protect the public against misinformation, after a man died in March from consuming chloroquine phosphate, an aquarium cleaner, when hydroxychloroquine (HCQ) was making headlines", adding that "however, in doses used off-label for scabies, for example, ivermectin has a low side-effect profile". The article then mentioned "positive signal in Florida" interviewing Rajter about his early experience in April 2020, who mentioned that "the success story we had in early April has been duplicated in other smaller studies across the world". Two other researchers commented that the studies were difficult to interpret and saw parallels to hydroxychloroquine studies. The article also referred to the Surgisphere scandal, positive findings from India, and a triple therapy with ivermectin, doxycycline and zinc by Borody, ending with comments by Chaccour that "the drug should not be written off, but neither is it ready for widespread clinical use" and by Rajter that he is "frustrated by an intentionally slow review process ... certain drugs are expedited by the FDA, while other treatments which have been shown to be quite effective – like ivermectin – have not seen the light of day", and an Italian researcher commenting that "it's a shame that so few randomized controlled trials have been performed in the U.S. on potential treatments such as this one".

On August 27, a news story described mass ivermectin distribution of 1.5 million pills in the city of Itajaí in Brazil organized by the city's mayor (who was also a medical doctor) as a "pseudo-health", "a magic potion to circumvent what scientific evidence is showing", "irrational and reckless" and a "national joke".[102] An infectious diseases consultant commented that ivermectin had "sparked an ideological war ... no one speaks the same language anymore".

## September 2020

On September 3, an open-label randomized controlled study by Podder et al. in Bangladesh with 62 mild to moderate patients did not produce statistically significant results.[103]

On September 6, state of Alto Parana in Paraguay adopted ivermectin.[88]

On September 10, Marchese et al. in Italy reported a case of strongyloidiasis after eleven-day treatment with high-dose corticosteroids and tocilizumab for severe COVID-19, with a 4-day course of ivermectin leading to full recovery.[104]

On September 11, Elkholy et al. proposed that inhaled ivermectin could attain the desired lung concentration rendering it effective against SARS-CoV-2.[105]

On September 14, Manikappa suggested a quadruple therapy involving ivermectin, doxycycline, zinc and vitamin $D_3$ for both prophylaxis and treatment.[106]

On September 15, an article by Jans et al. reviewed the existing data on broad-spectrum antiviral effects of ivermectin, writing that "an instinctive response in developing antiviral agents is to strive for high specificity since ideally they don't impact host function. However, viral genomes of RNA viruses have a high propensity to mutate. Host-directed agents that impact host cellular pathways utilized by many viruses may largely circumvent the problem of development of viral resistance and have true potential to be broad-spectrum antivirals".[4]

On September 15, a preprint by Carvallo et al. described an early treatment prospective trial of ivermectin, dexamethasone, enoxaparin and aspirin in Argentina with 167 patients, indicating a mortality rate of 3% in hospitalized cases in study vs 25% cases in the same hospital not in the study (RR 0.12, p=0.05) (NCT04425863).[107,108,109]

On September 20, Sparavigna's review was updated.[60] Among other issues it mentioned that the reason for continuing high mortality in Peru was self-medication with corticosteroids in the early phase, with these patients being hospitalized in worse condition than patients who had not self-medicated.[110] The review also suggested that it was not possible to separate the effect of ivermectin among widespread self-medication with ivermectin, chloroquine, hydroxychloroquine, azithromycin and a "famous triple" consisting of piperacillin-tazobactum, metamizole and intramuscular dexamethasone.

On September 22, a study by Li et al. was the first to provide ivermectin-regulated virus-related pathways by SILAC quantitative proteomics analysis, which revealed a broad-spectrum antiviral property of ivermectin.[111] The 52 identified ivermectin-regulated proteins included some reported SARS-CoV-2 related proteins, which the authors suggested could assist in exploiting potential ivermectin-related biomarkers and the novel mechanisms in the treatment of SARS-CoV-2 infection.

On September 24, a retrospective late treatment study by Khan et al. with 115 ivermectin-treated patients and 133 controls indicated a mortality rate of 0.9% vs 6.8% (RR 0.13, $p<0.05$) and 73.3% lower time to viral clearance (relative time 0.27, $p<0.001$).[112]

On September 24, Tilli et al. warned that even low-dose corticosteroids may induce a strongyloidiasis hyperinfection and dissemination with very high fatality rate, suggesting that immigrants and elderly patients should be either screened for strongyloidiasis or presumptively treated with ivermectin when treatment with steroids is imminent.[113]

On September 30, a peer-reviewed randomized controlled late treatment study by Chachar et al. with 25 ivermectin-treated patients and 25 controls did not produce a statistically significant result.[114] On the same day, the Dominican Republic adopted ivermectin country-wide.[3]

## October 2020

In the beginning of October, Chamie published a preprint reviewing the epidemiological "real-world" evidence of the effect of ivermectin mass distribution in Peru on COVID-19 excess deaths in the population older than 60 years.[115]

The data was presented also on TrialSite News on October 5.[116] The article commented that "the Peruvian government approved the use of ivermectin by decree on May 8. Despite having received several requests to suspend it in September ... the new Minister of Health ratified it. These measures have aroused much criticism among the scientific community. They do not understand why [Peru] continues to distribute the antiparasitic drug without having a randomized blind study to prove its effectiveness and overlook that the total death toll from COVID-19 in Peru is one of the world's highest".

On October 8, an in silico study by Frances-Monerris et al. indicated that a wide spectrum of actions of ivermectin involving interference with cell infection, inhibition of viral replication and elusion of the host immune system could point to an unprecedented synergy between host- and virus-directed effects explaining the observed high anti-SARS-CoV-2 activity.[117]

On October 8, a retrospective database study about late treatment by Soto-Becerra et al. in Peru indicated no beneficial effect from ivermectin.[118,119] The CovidAnalysis group and others criticized the methodology of the study.[120,121]

On October 9, a preprint of a randomized controlled late treatment study by Mahmud et al. (NCT04523831) with 183 patients in the treatment group and 183 controls indicated 49% lower risk of no recovery (23% vs 37.2%, RR 0.51, p<0.004), 55% lower risk of disease progression (8.7% vs 17.8%, RR 0.45, p<0.01) and 42.0% lower risk of no virological cure (7.7% vs 20.0%, RR 0.58, p<0.001).[122,123]

On October 10, states of Uttar Pradesh in Northern India with a population 210 million people and the state of Goa on the Southwestern coast of India with a population of 1.5 million people adopted early home treatment kits which include ivermectin.[88,124]

On October 11, Kant et al. from Uttar Pradesh published a review of ivermectin describing the Uttar Pradesh treatment model of prophylaxis for contacts: 0.2 mg/kg on days 1 and 7, and prophylaxis for healthcare workers: 0.2 mg/kg on days 1, 7 and 30, followed by monthly for six months. The total cost of ivermectin treatment of COVID-19 patients was USD 15 for 12 mg BID for 3-7 days; it was used in combination with doxycycline.[125] Earlier on September 20, Medtalks had published an interview of the researchers.[126]

On October 12, Scheim hypothesized that ivermectin may limit virulence of SARS-CoV-2 by steric interference with multivalent spike protein attachments to sialic acid binding sites, blocking hemagglutination, an effect likely to target mutant viral strains.[127]

On October 12, the Ministry of Health of Peru retracted the ivermectin recommendation for hospitalized patients.[128] Distribution in many outpatient clinics continued.

On October 13, final results of the 280-patient retrospective late-treatment ICON study by Rajter et al. were published in the journal Chest, indicating 13.3% vs 24.5% total mortality (OR 0.47, 95% CI 0.22-0.99, p=0.045) and 32% vs 81.8% mortality in severe disease (OR 0.27, 95% CI 0.08-0.92, p=0.002).[51,52]

On October 15, a Peruvian newspaper reported on a controversy about the Ministry of Health first allowing treatment of hospitalized patients with hydroxychloroquine, azithromycin and ivermectin in May, then disallowing them in October.[129] The news report pointed to a local study indicating no benefit from ivermectin and harm from hydroxychloroquine-azithromycin combination in hospitalized patients. Apparently, the change only concerned inpatients, not outpatients, for which self-treatment kits had been distributed since May.

On October 18, a trial in Sofia, Bulgaria was completed (EudraCT 2020-002091-12).[37]

On October 19, a study about prophylaxis of healthcare workers with ivermectin and carrageenan by Carvallo et al. (IVERCAR, NCT04425850) with 131 treated and 98 controls indicated a 96.3% reduction in infections (0% vs 11.2%, RR 0.04, p<0.001).[130,131] Carvallo later reported that carrageenan is not necessary.[132]

On October 22, a review of ivermectin use in Africa by Guerrero et al. estimated a 28% lower COVID-19 mortality in African countries using ivermectin for control of onchocerciasis vs African countries not using it (RR 0.72, 95% CI 0.67-0.78).[133,134]

On October 26, a randomized controlled late treatment study by Hashim et al. in Iraq (NCT04591600) with 70 patients treated with ivermectin and doxycycline and 70 controls indicated mean times to recovery of 6.3 vs 13.7 days in patients with mild or moderate disease (p<0.0001) and 10.6 vs 17.9 days for all patients (p<0.0001).[135,136]

On October 28, Gupta et al. published a study about the binding mechanism of ivermectin, identifying RNA-dependent RNA polymerase (RdRp), an enzyme that catalyzes the replication of RNA from an RNA template, as the most probable target for ivermectin.[137]

On October 30, the Front Line COVID-19 Critical Care Alliance (FLCCC) published an ivermectin-based I-MASK+ protocol for prophylaxis and early outpatient treatment of COVID-19.[138,139] According to the authors, ivermectin was considered the first agent effective for both prophylaxis (prevention) of COVID-19 and for treatment of all phases of COVID-19 including outpatient treatment of the early symptomatic phase. Ivermectin was also upgraded from an optional component to an essential component of the group's MATH+ inpatient protocol which was later renamed to I-MATH+ protocol.

On October 31, a preprint by Chang et al. described ivermectin pre-exposure prophylaxis of 129 persons, indicating a dose and dosing interval dependent prophylactic responses between 90% and 100%.[140]

Off-label use of ivermectin for COVID-19 begun in some regions of the US by the end of October, with the total prescription count of ivermectin multiplying approximately six-fold.[3] A Reddit channel /r/covidlonghaulinfo was founded.[141]

## November 2020

On November 3, a matched case-control study by Behera et al. in India with 41 cases and 76 controls about ivermectin prophylaxis of healthcare workers using two doses of 0.3 mg/kg on days 1 and 4 indicated a 73% reduction in infections in the following month ($p<0.001$).[142,143]

On November 3, a peer-reviewed article by Morgenstern et al. in the Dominican Republic described a retrospective observational study about early treatment with ivermectin and azithromycin.[144] 2,706 outpatients with mild infection were treated with a single dose of 0.4 mg/kg ivermectin and 500 mg of azithromycin for five days. The average delay between the onset of symptoms and the initiation of treatment was 3.6 days. Sixteen (0.59%) later required hospitalization without ICU care. Two (0.08%) required hospitalization with ICU care, of which one (0.04% of total) died.

On November 4, a preprint describing an open-label observational prospective study by Cadegiani et al. about early outpatient treatment of 110 patients and 137 controls (a group of paired untreated patients randomly obtained retrospectively from the COVID-19 patient population of the same community) with 0.2 mg/kg/day of ivermectin for three consecutive days indicated 98.0% lower risk of hospitalization (0% vs 19.7%, RR 0.02, $p<0.001$) and 94.2% lower risk of ventilation (0% vs 6.6%, RR 0.06, $p=0.005$).[145,146,147]

On November 6, Carvallo said in an interview that after publication of the results (IVERCAR, NCT04425850) in Argentina, the group met resistance from many doctors working in the pharmaceutical industry, likely due to the too low cost of treatment, approximately USD 2 per day.[132] He also stated that at that time, half of Argentina's states had adopted ivermectin protocols by decisions by local governments, with the rest of the states working on adoption. According to Carvallo, the protocols were also used in Chile, Paraguay, Bolivia, Southern Brazil, Peru, Venezuela, Colombia, Equador, Costa Rica, the Dominican Republic and Honduras. He also commented that "for those who follow the WHO, it's like blind person following another blind person, because WHO has committed so many mistakes that we sometimes wonder whether WHO has doctors in its staff, because the mistakes they have made are really blunders, and it's impossible to believe that experienced people working in an international organization like WHO could commit so many mistakes".

On November 6, in France, a criminal lawyer representing the Association of COVID-19 Coronavirus Victims in France pleaded in favor of ivermectin before an administrative tribunal, asking for temporary permit. Neither a representative of the Ministry of Health nor the national drug agency was present at the hearing. The request was rejected by the judge.[148]

On November 10, a preprint by Turkia briefly reviewed the early history of the FLCCC Alliance protocols, suggesting that ivermectin should be used based on existing data suggesting significant benefits, and that waiting for additional data may result in significant harm.[149,150]

On November 11, a preprint indicated that 0.6 mg/kg/day for five days was well tolerated (NCT004381884).[151] A significant difference in reduction in viral load was found in patients with higher median plasma ivermectin levels (72% IQR 59–77) versus untreated controls (42% IQR 31–3) ($p=0.004$). The mean ivermectin plasma concentration levels also showed a positive correlation with viral decay rate ($r=0.47$, $p=0.02$).

On November 11, a peer-reviewed retrospective study by Camprubi et al. with 13 treated patients and 13 controls about late treatment of severe disease with 0.2 mg/kg ivermectin plus hydroxychloroquine initiated a median of 12 days after symptoms did not indicate a statistically significant result, leading the authors to suggest a trial with a larger dose.[152,153] On the same day, a podcast described Brazilian distribution of ivermectin.[154]

On November 13, a preprint by Elgazzar et al. of a randomized controlled prophylaxis trial with a group including healthcare workers (pre-exposure) and outpatients' family members (post-exposure) with 100 members in total, compared to 100 healthcare workers and family members using only standard personal protective measures (hand hygiene, social distancing measures, avoiding touching the eyes or nose, and face masks, gloves, respiratory etiquette and self-isolation). The prophylaxis group received a single dose of 0.4 mg/kg ivermectin at days 1 and 8. The results indicated infection rates of 2% vs 10%, i.e. 80% lower risk of infection (RR 0.20, $p=0.03$).[155,156] The same preprint included results of a late treatment randomized controlled trial comparing ivermectin and relatively low dose of hydroxychloroquine indicated a 50% reduction in time to viral clearance and a substantially lower risk of death, although the effect of hydroxychloroquine in late treatment is inconsistent and it may increase mortality.

On November 13, an initial version of a preprint by the FLCCC group was posted on osf.io.[157] The preprint included a brief meta-analysis of mortality data from three observational studies (Rajter et al, Khan et al, Gorial et al; OR 0.48, 95% CI 0.27-0.84, p=0.011) and two randomized controlled studies (Mahmud et al, Hashim et al; OR 0.26, 95% CI 0.06-1.09, p=0.065), indicating a statistically significant overall mortality benefit (OR 0.44, 95% CI 0.26-0.75, p=0.002). The report also cited a study by Chamie that compared one state in Paraguay with mass distribution of ivermectin to three states without distribution, showing a reduction in case counts and deaths, and Chamie's similar study about reduction of excess deaths of over 60 year olds in Peru.

On November 14, a peer-reviewed late-treatment prospective trial in India by Spoorthi et al. with 50 treated patients and 50 controls using ivermectin (a single dose of 0.2 mg/kg) and doxycycline combination indicated a 15.5% lower hospitalization time (relative time 0.84, p=0.01) and 21.1% lower recovery time (relative time 0.79, p=0.03).[158,159]

On November 17, a peer-reviewed report of a prophylaxis study (IVERCAR, NCT04425850) in Argentina by Carvallo et al. with 788 healthcare workers and 407 controls indicated 0 (0%) vs 237 (58.2%) cases of COVID-19, respectively (99.9% lower risk of infection, RR 0.001, p<0.001).[160,161] The reported dosing regime was one drop of ivermectin-containing liquid orally five times a day (every four hours) for 14 days, with food and liquids avoided for one hour before and after treatment. The dosing regime amounted to 12 mg per week. Hirsch and Carvallo also published an updated prophylaxis protocol.[162]

On November 17, Facebook begun removing ivermectin-related posts by the FLCCC Alliance, stating that they did not follow Facebook's community standards.[163]

On November 18, an updated version of a preprint by the FLCCC group added a randomized controlled trial by Elgazzar et al. to the meta-analysis, with three randomized controlled studies indicating a statistically significant overall mortality benefit (OR 0.14, 95% CI 0.05-0.39, p<0.001), larger than the observational studies or the overall result (OR 0.36, 95% CI 0.21-0.59, p<0.001).[157]

On November 18, a retrospective late treatment study in India by Budhiraja et al. of 34 ivermectin-treated patients and 942 controls indicated a 99.1% lower risk of death (0% vs 10.9%, RR 0.009, p=0.04).[164,165]

On November 19, in an US Senate hearing, George C. Fareed, a Harvard professor with a background in virology research at NIH, witnessed about usefulness of an early outpatient treatment with hydroxychloroquine, zinc and ivermectin.[166,167] A group called CovidAnalysis had earlier published a meta-analysis of nine randomized controlled trials about early, pre-exposure prophylaxis, or post-exposure prophylaxis treatment with hydroxychloroquine, stating that all trials reported positive effects with an average of 30% risk reduction (RR 0.70, 95% CI 0.53-0.93, p=0.002).[168]

On November 24, the New York Times published an opinion by Brown University dean Jha, another witness at the November 19 US Senate hearing. In the opinion, Jha called other witnesses including Fareed "snake oil salesmen" and the hearing a "misinformation super-spreader event".[169]

On November 24, a preprint about a late treatment randomized controlled trial by Niaee et al. with 180 hospitalized patients with ivermectin but all patients receiving also a low dose of hydroxychloroquine indicated dosing-dependent reductions in risk of death between 45.5% and 94.3%.[170,171]

On November 25, the Wall Street Journal published an article about too much caution killing COVID-19 patients, saying doctors should follow the evidence for promising therapies but "instead they demand certainty".[172] The article stated that "fear and panic are central impediments to competent decision-making during a crisis ... [creating] an air of inevitability, as if politicians have no choice but again to restrict civil liberties, limit social gatherings, and cripple businesses that survived the initial lockdowns. But there's a better way: following the evidence for early treatment of Covid-19 ... The health system would be less burdened if more patients were treated before they require hospitalization, and there are promising therapeutic options that patients can administer themselves at home. This was the subject of a Nov. 19 hearing before the Senate Homeland Security and Governmental Affairs Committee. Testimony from the hearing underscored an important issue: Too many doctors have interpreted the term 'evidence-based medicine' to mean that the evidence for a treatment must be certain and definitive before it can be given to patients. Because accusing a physician of not being 'evidence based' can be a career-damaging allegation, fear of straying from the pack has prevailed, favoring inertia and inaction amid uncertainty about Covid-19 treatments ... when options are limited and there are safe treatments with evidence for effectiveness, holding out for certainty can be catastrophic".

On November 26, the CovidAnalysis group published a random-effects meta-analysis of 21 existing ivermectin studies at the website ivmmeta.com, indicating an overall 75% reduction in the effect measured (death, hospitalization, etc.) (RR 0.25, 95% CI 0.16-0.40, p=0.00000048),[173] and 60% reduction in twelve late treatment studies (RR 0.40, 95% CI 0.24-0.66, p=0.00024). Eight randomized controlled trials indicated a 72% risk reduction (RR 0.28, 95% CI 0.13-0.59, p=0.0039). All 21 studies reported positive effects, indicating a consistent effect in all stages of COVID-19.

On November 26, Syed discussed the mechanisms behind ivermectin's action against SARS-CoV-2, also introducing the I-MASK+ protocol.[174,175,176,177,178,179]

On November 28, a peer-reviewed statistical analysis of ivermectin prophylaxis by Hellwig et al. compared African states with ivermectin mass distribution to African states without distribution, concluding that mass distribution is associated with lower COVID-19 incidence and that prophylaxis could help bridge the time until a vaccine becomes widely available.[180]

On November 28, a peer-reviewed retrospective study in France by Bernigaud et al. described a case of 69 residents of a care home with a median age of 90, treated with ivermectin for scabies outbreak, with seven (10.1%) later diagnosed with probable or certain COVID-19, with no serious cases and no deaths.[181,182] In residents in comparable care homes there were 22.6% infections and 5% deaths. The CovidAnalysis group calculated 99.4% lower risk of death (0% vs 4.9%, RR 0.006, p=0.08) and 55.1% lower risk of infection (10.1% vs 22.6%, RR 0.45, p=0.01).

On November 30, Egypt adopted ivermectin country-wide.[3]

## December 2020

On December 1, preliminary results of an early treatment observational study in Argentina by Alonso et al. with 311 patients treated with ivermectin and 128 controls indicated 91.8% lower risk of death with one (0.3%) deaths in the treatment group vs five (3.9%) in the controls (RR 0.08, p=0.009).[183]

On December 2, a peer-reviewed randomized controlled trial by Ahmed et al. with 72 patients treated with 5-day course of ivermectin indicated a 42.5% lower risk of no virological cure at day 7 (50% vs 87%, RR 0.58, p=0.01) and a 62.7% lower risk at day 14 (22.7% vs 60.9%, RR 0.37, p=0.02).[184,185]

On December 3, Chamie posted a diagram of an analysis on Twitter, suggesting that distribution of ivermectin home treatment kits since July 2020 in the state of Chiapas had resulted in lower mortality in that state, compared to states without home treatment kits.[186,187,188]

On December 4, the FLCCC Alliance organized a press conference, urging the NIH and CDC to immediately review the research evidence that had appeared after the NIH's September guideline, to allow early outpatient treatment. The alliance suggested that widespread, immediate use of ivermectin "would allow for a rapid and safe reopening of businesses and schools across the nation and quickly reduce the strain on overwhelmed hospitals and ICUs".[189]

On December 7, a preprint of an early treatment double-blind randomized controlled trial (SAINT) in Spain by Chaccour et al. with 12 patients treated with a single dose of 0.4 mg/kg ivermectin and 12 controls indicated 52.9% lower risk of unresolved symptoms at day 28 (RR 0.47, p<0.05) but no difference in the primary outcome (the proportion of PCR positives), for which the trial was labeled negative by many commentators.[190,191]

On December 7, the New York Times wrote that an upcoming December 8 US Senate panel had been transformed into "a forum amplifying dubious theories and questionable treatments pushed by President Trump", adding that two witnesses "promote the use of ivermectin, a drug often used to fight lice and pinworms, to treat coronavirus patients, despite the National Institutes of Health's recommendation against its use outside clinical trials".[192] A democrat senator feared that the witnesses would "amplify theories that are at odds with the broader scientific community and, according to experts, could cause harm" and that "these fringe views run counter to what the Senate should be doing — working on a bipartisan basis to protect the American people and tackle this deadly pandemic".

On December 8, the Front Line COVID-19 Critical Care Alliance (FLCCC) president Pierre Kory gave a testimony to US Senate Committee on Homeland Security and Governmental Affairs about the state of ivermectin research.[193]

On December 9, a post on FLCCC Alliance Facebook page commented that "we are thrilled to be back with you after a three-day stint in Facebook jail for writing the name of a component of our I-Mask+ Prophylaxis and Early Outpatient Treatment Protocol on our Sunday post". The post also gave a link to YouTube video of Pierre Kory's testimony on December 8. Facebook issued a warning that further mentions of 'ivermectin' would result in a permanent deletion of the FLCCC page. Later posts on the page referred to the 'i-word' and referred readers to the group's website and Twitter for further information.

On December 11, a peer-reviewed early treatment case series study in Bangladesh by Hussain et al. with 8 patients resulted in all patients testing negative by day six.[194,195]

On December 11, an article by Associated Press, "a part of The Associated Press' ongoing effort to fact-check misinformation that is shared widely online, including work with Facebook to identify and reduce the circulation of false stories on the platform", discussed Kory's Senate Committee testimony mentioning it had received one million views on YouTube, and referring to comments by two infectious disease experts it concluded that "there's no evidence ivermectin has been proven a safe or effective treatment against COVID-19".[196]

On December 12, a post on FLCCC Alliance Facebook page noted that YouTube had taken down the video of Kory's US Senate Committee testimony. On December 14, another post commented that the group's repeated attempts to reach out to US health authorities including NIH, CDC and FDA in order to discuss the information given in the Senate Committee testimony had failed.

On December 15, a preprint of an 95-patient early treatment study in Pakistan by Afsar et al. with all patients receiving a low dose of hydroxychloroquine an azithromycin and the treatment group also receiving ivermectin indicated 92.2% lower risk of fever at day 14 (0% vs 13.2%, RR 0.08. p=0.04).[197,198]

On December 15, a peer-reviewed observational prophylaxis study in Bangladesh by Alam et al. with 118 healthcare workers, of which 58 received 12 mg ivermectin monthly, indicated 90.6% lower risk of infection (6.9% vs 73.3%, RR 0.09, p<0.001).[199,200]

On December 17, the National Institutes of Health published an update to their guideline on prevention and prophylaxis of SARS-CoV-2 infection.[201] The panel gave a strong recommendation based on expert opinion only (class A III), recommending against the use of any agents in either pre-exposure or post-exposure prophylaxis, except in clinical trials. Ivermectin was not mentioned in the recommendation.

On December 18, a preprint by Kory et al. presented a meta-analysis of one observational prophylaxis studies (OR 0.06, 95% CI 0.03-0.11) and three randomized controlled prophylaxis studies (OR 0.13, 95% CI 0.07-0.22).[202]

On December 18, Belize adopted ivermectin country-wide for serious cases.[203,3,88]

On December 18, MedinCell announced that a continuous administration over a one-month period to healthy volunteers confirmed ivermectin's safety up to a daily dose of 75 µg/kg (NCT04632706).[204,205] A news report commented that "as the vaccines won't solve all of the short -term potential problems with COVID-19 the challenge is that at least thus far government agencies in wealthy GPD nations show little to no interest in such repurposed, generic drug responses".[206]

On December 20, a preprint of a prophylaxis study in Argentina by Vallejos et al. with 389 treated patients and 486 controls indicated 73.4% lower risk of COVID-19 case (3.3% vs 12.6%, RR 0.27, p<0.001).[207,208]

On December 21, a news report described a late stage treatment experiment just initiated by professor Cacopardo in Sicily, Italy, with results not yet available.[209]

On December 23, Macedonia adopted ivermectin country-wide.[3]

On December 23, Merck & Co/MSD announced it had entered into agreement with the United States Government to develop, manufacture and distribute a biological therapeutic MK-7110 upon approval or emergency use authorization from the FDA.[210] The company was to receive USD 356 million for supply of 60,000-100,000 doses of MK-7110 for US Government through June 30, 2021 (apparently indicating a price of USD 3,560.00-5,933.00 per dose). An interim analysis of 203 participants (75% of planned enrollment) of a phase 3 study evaluating MK-7110 for severe and critical COVID-19 indicated that a single dose showed a 60% higher probability of improvement and a more than 50% reduction in risk of death or respiratory failure.

On December 24, a Macedonian newspaper wrote that the drug agency MALMED is going to approve ivermectin for COVID-19 in Macedonia.[211] The price was said to be 12 euros (USD 14) per 12 mg. Ivermectin was said to be an integral part of hospital protocols in Bulgaria already, utilized by for example professor Ivo Petrov at Acibadem City Clinic in Sofia, Bulgaria. Petrov commented when ivermectin is applied in the first few days after the onset of symptoms they resolve significantly faster and oxygenation is required less often. Petrov was also taking ivermectin for personal prophylaxis.

On December 24, a Facebook post by the FLCCC group commented that "the Associated Press refuses to retract its article saying there is no evidence that the medicine we cannot name on FB can prevent or treat COVID-19. To suppress this information is to bless a massacre that can be stopped."

On December 24, a South African newspaper wrote that import ivermectin into South Africa had been declared illegal by the South African Health Products Regulatory Authority (SAHPRA). Its chief executive stated that "our stance is unambiguous. This drug is not approved by SAHPRA and any attempt to import it into the country will be dealt with by SAHPRA's regulatory compliance unit in conjunction with law enforcement agencies ... SAHPRA is focused on quality, safety and efficacy and its ultimate goal is to protect the health and well-being of all those who live in South Africa".[212]

On December 25, a Facebook post by the FLCCC group commenting NIH's December 17 guideline update stated that "the refusal of the NIH to cite or even acknowledge the irrefutable evidence in our scientific manuscript means that tens of thousands of Americans will now go to their early graves. This is an unconscionable and murderous declaration not based in science or the medical facts ... When history is written about how the NIH inexplicably placed the citizens it was impaneled to protect in harm's way, we will weep bitter tears at the words on the page".

On December 27, Hill et al. published a YouTube video "Ivermectin meta-analysis by Dr. Andrew Hill" giving out initial results of a WHO-funded meta-analysis.[213] The presented conclusions were as follows: "In this meta-analysis of 11 randomized trials in 1452 patients, ivermectin treatment was associated with: faster time to viral clearance, shorter duration of hospitalization, 43% higher rates of clinical recovery (95% C.I. 21-67%), 83% improvement in survival rates (95% C.I. 65-92%)". The video was branded with University of Liverpool, Access to COVID Tools Accelerator and Unitaid logos. Unitaid is a global health agency hosted by the World Health Organization.[214] The Access to COVID Tools Accelerator is a partnership of the Bill & Melinda Gates Foundation, CEPI, FIND, Gavi, The Global Fund, Unitaid, Wellcome, WHO and the World Bank.[215] On February 26, 2021, the link lead to a notice "This video has been removed for violating YouTube's Terms of Service".

On December 27, without warning or explanation, Twitter deleted the account of the CovidAnalysis group which had provided meta-analyses of randomized controlled trials on various proposed treatment agents for COVID-19, including ivermectin, vitamin D, hydroxychloroquine and zinc.[216] However, the FLCCC Alliance was allowed to tweet about ivermectin, and in December 2020 it routinely referred people from its Facebook page to its Covid19Critical Twitter account for news and updates about its ivermectin protocols.

On December 28, in France, a preliminary filing was forwarded to the minister of health and to the national medicines agency, requesting a temporary recommendation.[148]

On December 30, a review by McCullough et al. stressing the need for early outpatient treatment with a sequential multi-drug treatment algorithm mentioned home-based treatment kits with ivermectin having been distributed in Argentina, Bangladesh, Colombia, India, Mexico and Peru.[217]

On December 31, a peer-reviewed version of the brief review of the early history of the FLCCC Alliance was published.[138]

On December 31, a peer-reviewed study by Madrid et al. investigating safety of ivermectin in a fish model stated that high doses of 0.22 and 0.86 mg/kg were not harmful to the intestinal tissues of the animal model neither affected the blood cells counting in general.[218] An overdose of 170 mg/kg (10.2 g for a 60 kg person) in increased expression of the Myosin-Vb which may have implications in the intestinal epidermal integrity.[219]

On December 31, a report of three late-stage cases by Wijaya et al. reported significant clinical and radiological improvement after a single dose of ivermectin.[220]

## January 2021

On January 3, Lawrie et al. published a preprint of a rapid review and meta-analysis of seven ivermectin trials, indicating a mortality relative risk RR 0.17 (0.18-0.35) and prophylaxis cases RR 0.12 (0.08-0.18).[221,222] Also on January 3, Kaur et al. published a review including results of molecular dynamics simulations.[223]

On January 4, Lawrie submitted an initial report to the UK government, including results of RCT trial and basic quality observational controlled trials, showing 83% reduction in mortality.[224] On March 6, she mentioned not getting any response from the government.

On January 4, Arab News published in Saudi Arabia with a target audience of businessmen, executives and diplomats wrote about the meta-analysis by Hill et al., describing it as possibly transformative, with a cost of USD 1-2 for a treatment course.[225,226]

On January 6, an uncontrolled retrospective study about ivermectin prophylaxis (0.2mg/kg weekly for eight weeks, followed by 4 months rest) for healthcare workers in in Argentina by Hirsch and Carvallo reported no infections among the 162 participants.[227]

On January 6, a randomized controlled clinical trial in Nigeria by Babalola et al. indicated a 58% lower risk of no virological cure with 12 mg of ivermectin (n=40, p=0.01).[228]

On January 6, Marik and Kory from the FLCCC Alliance appeared before the NIH's COVID-19 Treatment Guidelines Panel to urge review of current data and an updated NIH guidance.[229]

On January 6, MedPage Today wrote about "maverick physicians spurning randomized trials", reviewing the views of the FLCCC and its critics, writing that "[FLCCC members] don't see a need for more data and argue it would be unethical to give placebo to patients given the established safety of ivermectin. But that's raising more than a few eyebrows among others in the field".[230] The article reviewed Marik's invention of the hydrocortisone, ascorbic acid and thiamine protocol for sepsis, the FLCCC's early adoption of corticosteroids and the resulting 75% reduction in mortality in comparison to average hospital mortality, and the introduction of the FLCCC's I-MASK+ ivermectin protocol in October 2020. The article then continued on to "what the science says", mentioning four RCTs and South American experiences about prophylaxis, five RCTs about early treatment, and four RCTs for late treatment, plus "a host of observational studies and case series". The article notes that only one of the studies, a retrospective study, was done in the US.

FLCCC's Kory was quoted commenting that "if someone wants to discount those studies ... and says they want to do an RCT with placebo, that's problematic for me ... I could not have a patient admitted to my care and give placebo knowing what I know about ivermectin ... [FLCCC members] are firm believers in evidence-based medicine. But we disagree with how most practice evidence-based medicine. We think they are way too biased toward randomized controlled trials and completely dismiss evidence from anything but RCTs. We think that's harmful and loses a lot of valuable data". In contrast, an US medical ethicist was quoted saying that he "doesn't believe clinicians should be lowering our standards of evidence because we're in a pandemic ... this group should be advocating strongly for a large, generalizable randomized trial if they believe so strongly in the efficacy of ivermectin ... If in fact it is effective, the only way to convince the clinical and scientific community and allow patients all over the world to benefit is to prove the case in such a trial ... with good data and safety monitoring, if the benefits are as overwhelming as they claim, the trial could be stopped early on the basis of interim data and the treatment rapidly instituted".

MedPage Today mentioned the meta-analysis by Hill et al. supporting the conclusions of the FLCCC, said MedPage Today had been unable to confirm whether Hill had been contracted by the WHO, then quoted an infectious diseases physician who called Hill et al's overall evidence "very low grade", adding that "this whole thing feels like déjà vu of the first two months of the pandemic when we weren't decided about hydroxychloroquine ... we don't want to come around a year later saying it didn't help and it may have hurt". The rest of the article surveyed whether the FLCCC might have financial connections to pharmaceutical companies with an interest in ivermectin, the politicization of the issue in the US, whether the intention of the FLCCC was to undermine vaccinations, and ended with a demand for "proper studies".

On January 8, a social media post about an epidemiological analysis by data analyst Juan Chamie compared the state of Chiapas, Mexico which had adopted ivermectin, to other states which had not adopted it, indicating a stabilization of cumulative case count in Chiapas but increasing case counts in other states.[231]

On January 8, the Ministry of Health of Peru reinstated ivermectin-containing home-treatment kits after retracting them in late 2020.[232]

On January 8, South African Health Products Regulatory Authority (SAHPRA) raided a hospital in search of ivermectin, not finding any.[233,234]

On January 9, a preprint about a double blind randomized placebo-controlled trial (n=112) about ivermectin for mild to moderate disease in India by Kirti et al. did not achieve a statistically significant result but suggested a trend to benefits with regard to mortality, ventilation and ICU admission, for example a 79% lower risk of ventilation (p=0.09) and 89% lower risk of death (p=0.12) (CTRI/2020/08/027225).[235,236]

On January 9, Lawrie posted an open video letter to Prime Minister of the United Kingdom Boris Johnson, stating her company's biggest clients are the National Health Service of the United Kingdom (NHS) and the WHO, for whom the company produces industry-independent medical evidence synthesis to support international clinical practice guidelines.[237,238,239,240,241,242] Lawrie urged Johnson to look at the evidence of ivermectin's effectiveness, stating her analysis solidly substantiated the FLCCC's recommendation to adopt ivermectin globally and systematically for COVID-19.

On January 11, a preprint about an animal dosing study by Mousquet-Melou et al. suggested that ivermectin maintenance doses should be based on lean body weight instead of the total body weight in obese subjects, while the loading dose should be based on the total body weight.[243]

On January 11, a randomized controlled trial (Ivercar-Tuc) about ivermectin and iota-carrageenan prophylaxis of 234 healthcare workers in Tucumán, Argentina by Chahla et al. indicated 0% vs 8% severe cases (p=0.003) and 3.4% vs 21.4% of all cases (p<0.001) (NCT04701710).[244]

On January 11, a Macedonian journal wrote the drug agency MALMED had confirmed ivermectin was going to be available in pharmacies across the country in a few days.[245]

On January 11, a German magazine for pharmacists introduced the Monash University in vitro study, FLCCC protocols and their meta-analysis, experiences of Peru, Brazil and Paraguay, the ICON study in the US, the NIH hearing on January 6 with a mention of Hill et al's meta-analysis, and listed 18 observational or randomized controlled trials that were completed by December 2020.[246]

On January 12, a preprint about a randomized controlled trial (n=60) about late treatment (severe illness) in Turkey by Okumuş et al. compared low dose hydroxychloroquine, azithromycin and favipiravir with and without ivermectin, indicating 80% lower risk of no virological cure (12% vs 63%, p=0.02) on day 10 (NCT04646109).[247]

On January 12, a post on the FLCCC group's Facebook page commented that a post by a group member "had been taken down for using the full name of the the medicine—and then restored one day later upon appeal" which was interpreted as Facebook "beginning to recognize the growing body of irrefutable scientific medical evidence".

On January 13, a review by Kory et al. (the FLCCC group) was provisionally accepted by Frontiers of Pharmacology.[248]

On January 14, the US NIH updated its guideline on ivermectin, stating that there are insufficient data to recommend either for or against the use of ivermectin.[249] The NIH COVID-19 Treatment Guidelines Panel Financial Disclosure for Companies Related to COVID-19 Treatment or Diagnostics (updated on February 11, 2021 but covering a period from October 1, 2019 to September 30, 2020, thus not indicating up-to-date situation), indicated that the panel had 59 members, of which 35 (59%) reported no disclosures.[250] Eight (14%) reported a connection to Merck & Co/MSD, of which one advisory board/consultant role, three advisory board roles, two research support roles, one consultant/research support role and one honoraria role. The updated guideline opened up the possibility of treating COVID-19 patients with ivermectin.

On January 15, the Association of American Physicians and Surgeons (AAPS) applauded the NIH guideline change.[251] AAPS executive director Jane M. Orient referred to 49 ivermectin studies summarized on c19study.com, 100 percent of which showing favorable results. Orient noted that many medical facilities and many physicians refuse to prescribe it for COVID-19, citing NIH guidance, adding that "Perhaps with this change, patients won't need a court order to get a lifesaving drug ... To have a doctor withdraw a drug that appears to be saving a patient's life, because a federal bureaucracy thinks it hasn't been studied enough for that use, is shocking to those who believe in the traditional ethic of Hippocrates".

On January 15, a news report described a case in the US, in which family members of a 80-year ventilated patient in a severe condition had asked the ICU doctors to administer her ivermectin.[252] A doctor had administered one dose, with the patient then taken off the ventilator and transferred out of the ICU in less than 48 hours. Her condition had then deteriorated but the hospital had refused to administer further doses. The family members had subsequently acquired a court order for the hospital to immediately administer the patient more ivermectin, which the judge had agreed to.

On January 15, a newspaper reported that El Salvador had classified ivermectin as an over-the-counter product to boost self-medication in order to combat a second wave of COVID-19.[253] A television channel in Honduras was said to have promoted ivermectin as a prophylaxis against COVID-19 "for months". The government of Honduras, Guatemala, El Salvador and others in South America were said to have begun distributing home kits with vitamins, acetaminophen, antibiotics and ivermectin in mid-2020 for patients with mild symptoms. By the end of 2020, 18,000 kits had been distributed in El Salvador. In Honduras, packages with azithromycin, ivermectin and zinc were distributed. A Honduran scientist commented that "developed countries make adequate studies to make decisions and our countries are based on anecdotal information and, practically, anything they hear they set it in motion". The government was accused of overpaying and corruption after having purchased 6 mg tables for 1.08 dollars instead of 0.19 cents per tablet.

On January 15, Bulgarian Drug Agency issued a marketing authorization for 3 mg ivermectin tablets by prescription.[254]

On January 16, a preprint about a randomized controlled trial (n=103) in Pakistan by Asghar et al. indicated a 90% viral clearance with 0.2mg/kg ivermectin vs 44% in controls ($p<0.001$) on day 7 (NCT04392713).[255,256]

On January 16, a preprint about a randomized controlled trial (n=100) about early treatment in Beirut, Lebanon by Raad et al. indicated a 59% lower risk of viral load ($p=0.01$) at day 3 (ChiCTR2000033627).[257]

On January 16, a research letter by Bernigaud et al. described a case of oral ivermectin administration for controlling a concomitant COVID-19 and ivermectin-treated scabies outbreak in a French long-term care facility.[258]

On January 17, the FLCCC Alliance commented the updated NIH guideline, stating that it "considers the Panel's unwillingness to provide more specific guidance in support of the use of ivermectin in COVID-19 to be severely out of alignment with the known clinical, epidemiological, and observational data".[259]

On February 17, Africa CDC issued a statement on using ivermectin for COVID-19, citing "no scientific evidence", "no safety data", limitations of the existing studies, that "the doses used in the in laboratory to produce those results are 100-fold higher than those approved for use in humans", concluding that "data from well-designed, randomized, controlled clinical trials are needed to provide evidence for decision".[260]

On January 18, a preprint asked whether a part of the mortality assigned to COVID-19 may be due to an undiagnosed concomitant strongyloidiasis hyperinflammation.[261]

On January 19, a WHO-funded meta-analysis with 40 authors including Andrew Hill analyzed 18 randomized controlled trials with a total of 2,282 patients. The results indicated improved clinical recovery, and lower hospitalization and mortality. Six RCTs of moderate or severe infection indicated a 75% reduction in mortality (RR 0.25, CI 0.12-0.52, $p=0.0002$).[262] The report stated that "this meta-analysis investigated ivermectin in 18 randomized clinical trials (2,282 patients) identified through systematic searches of PUBMED, EMBASE, MedRxiv and trial registries. Ivermectin was associated with reduced inflammatory markers (C-Reactive Protein, d-dimer and ferritin) and faster viral clearance by PCR. Viral clearance was treatment dose- and duration-dependent. In six randomized trials of moderate or severe infection, there was a 75% reduction in mortality (Relative Risk=0.25 [95% CI 0.12-0.52]; $p=0.0002$); 14/650 (2.1%) deaths on ivermectin; 57/597 (9.5%) deaths in controls) with favorable clinical recovery and reduced hospitalization. Many studies included were not peer reviewed and meta-analyses are prone to confounding issues. Ivermectin should be validated in larger, appropriately controlled randomized trials before the results are sufficient for review by regulatory authorities."

On January 19, a randomized controlled trial on hospitalized patients (n=103) in Iran by Rezai et al. indicated a 21% lower recovery time ($p=0.02$) and 18% lower hospitalization time ($p=0.01$).[263,262] On the same day, Tehran Times wrote that Iran was starting its own production of ivermectin.[264]

On January 20, MedPage Today interviewed an US chief of hospital medicine who warned against parasitic "hyperinfection" in foreign patients, saying they "will need to be treated prophylactically for strongyloides,

a parasitic infection that can emerge after corticosteroids are administered. The regimen is two doses of ivermectin, one day apart, with the first dose preferably given before steroids are administered".[265]

On January 20, a peer-reviewed in vitro study by Mody et al. indicated that ivermectin blocked more than 85% of $3CL^{pro}$ activity of SARS-CoV-2, thus suggesting an additional antiviral mechanism via inhibitory effects on $3CL^{pro}$, in addition to the previously identified blocking of $\alpha/\beta 1$ importin.[266]

On January 20, the Financial Times wrote that a cheap antiparasitic could cut chance of Covid-19 deaths by up to 75%, citing the WHO-funded meta-analysis carried out by Hill et al.[267] Hill stated that the drug costs USD 3 in India and USD 960 in the US. Hill also noted that the purpose of his group's meta-analysis was "to forewarn people that this is coming: get prepared, get supplies, get ready to approve it ... we need to be ready".

On January 21, a second, more polished preprint by Chamie-Quintero et al. analyzed the effects of distribution of ivermectin in Peru, spanning an area equivalent to that from Denmark to Italy and Greece in Europe or from north to south along the US, with a total population of 33 million.[268] In 24 Peruvian states vs one state without distribution, excess deaths for ages >=60 dropped by 59% vs 25% at 30 days, and by 75% vs 25% at 45 days after the day of peak deaths, even though indices of community mobility rose over the same period. For nine states that carried out mass distributions of IVM in a short timeframe through a national program, excess deaths at 30 days dropped by a population-weighted mean of 74%, each drop beginning within 11 days after the program start.

On January 23, the Times (UK) wrote that researchers at Oxford University are planning "the first, large high-quality trial of a cheap drug that has been credited with dramatically reducing Covid-19 deaths in the developing world".[269] The trial was named 'Principle', aimed at identifying an early treatment method that would prevent severe illness.

On January 24, the FLCCC Alliance posted an open letter to the investigators of the Principle trial, urging the investigators to properly inform enrolling patients about the efficacy of ivermectin, stating that "inadequately communicating this information to potential participants would be a violation of the primary responsibilities of clinical researchers as directed by the Belmont report to protect human subjects of biomedical research".[270]

On January 25, a third attempt to allow emergency use of ivermectin in France was addressed to the Council of State. Among the plaintiffs were 18 doctors and three associations: Syndicat des Médecins d'Aix et Région, International Association for Scientific, Independent and Benevolent Medicine, and Bon Sens.[148,271]

On January 25, Merck & Co/MSD announced that it discontinues development of COVID-19 vaccine candidates but continues development of two investigational therapeutic candidates, MK-4482 (molnupiravir) and MK-7110.[272] Molnupiravir was described as an oral novel antiviral agent for both in- and outpatients, with initial efficacy data expected to be available in the first quarter of 2021.

On January 25, a news report described professor Cacopardo's experiment in treating patients with severe disease in Sicily, Italy a success, with Cacopardo commenting that "the patients who were given ivermectin did very well ... I have the impression that ivermectin combined with traditional therapies is able to effect a dramatic improvement in clinical picture ... we have used it in four serious cases of bilateral pneumonia ... after the administration of ivermectin, an impressive improvement of the clinical picture was observed in the next 48 hours".[273] The medicine was said to cost 12 cents per dose to produce.

On January 26, a news report about the trial in Sofia, Bulgaria (EudraCT 2020-002091-12) said the double-blinded, placebo-controlled ivermectin study had been conducted with 100 patients in 12 centers, with 0.4 mg/kg of ivermectin on three consecutive days.[274,275,276] The results were said to be positive, with a mention about reporting them to the WHO in order to include ivermectin in the COVID-19 treatment options.

On January 27, the CovidAnalysis group claimed that the retrospective database analysis of 5,683 patients in Peru by Soto-Becerra exhibited "clear evidence of extreme bias".[118,121]

On January 27, in a parliament session, an UK member of parliament David Davis asked Prime Minister Boris Johnson about enhancing primary care to reduce the need for hospitalization, mentioning ivermectin has been observed to reduce mortality by 75%. Johnson replied that he is aware of the results and that therapeutics task-forces are currently reviewing ivermectin.[277]

On January 27, a preprint of a meta-analysis by Castañeda-Sabogal et al. including twelve studies (five retrospective cohort studies, six RCTs and one case series) with a total of 7,412 participants stated that

all studies had a high risk of bias and showed a very low certainty of the evidence. Ivermectin was not associated with reduced mortality (logRR 0.89, 95% CI 0.09-1.70, p=0.04, $I^2$=84.7%), or reduced patient recovery (logRR 5.52, 95% CI -24.36-35.4, p=0.51, $I^2$=92.6%). The meta-analysis concluded that there was insufficient certainty and quality of evidence to recommend the use of ivermectin to neither outpatients, inpatients nor prophylaxis.[278] The CovidAnalysis group described the meta-analysis as "student-written meta analysis of a very small subset of studies exhibiting very high bias and significant flaws ... [having] no logic in the exclusion reasons ... we checked the reported results for the mortality outcome and found they do not appear to match the actual papers".[279]

On January 27, a news report stated that the South African Health Products Regulatory Authority (SAHPRA) will consider ivermectin on a case-by-case basis, requiring practitioners to apply for approval before use.[280]

On January 29, a final peer-reviewed version of an article by Jans and Wagstaff was published.[9]

On January 29, the French national institute of health and medical research (Institut national de la santé et de la recherche médicale) issued a press release warning against the use of ivermectin outside clinical trials, criticizing the first in vitro study and studies by Rajter et al. and Bernigaud et al.[281,282]

On January 30, Tokyo metropolitan government announced plans to conduct clinical trials for patients with mild symptoms at hospitals. The plan was to eventually apply the method for outpatient treatment.[283] The article also mentioned that a 240-patient clinical ivermectin trial had begun at Kitasato University Hospital in September 2020 for 240 patients.

Slovakia adopted ivermectin country-wide in January, with reports indicating limited availability and late treatment only.[3] It had been used since early January by professor Pavol Török who later convinced the Ministry of Health to adopt it.[284]

Country-wide adoptions of ivermectin happened in Guatemala on January 23, in Nicaragua on January 25, in Lebanon on January 27, and in Zimbabwe on January 28.[3,285]

## February 2021

On February 1, a news report was published by an UK and Australia based medical news site describing itself as "one of the world's leading open-access medical and life science hubs ... with 374,000 members, 12,000 Twitter followers and 268,000 likes on Facebook ... [and] a trusted source of all your medical and life science needs", compliant with a Switzerland-based Health on the Net Foundation's HONCODE certificate of compliance. The news report reviewed the meta-analysis by Castañeda-Sabogal et al., concluding that there was no evidence that ivermectin changed the clinical outcome of inpatients or outpatients.[286]

On February 2, the Wall Street Journal published an opinion piece by US senate representative Ron Johnson, stating that YouTube had censored Dr. Pierre Kory's testimony to US Senate Committee in which he asked the National Institutes of Health to review the current data on ivermectin.[287]

On February 2, a preprint about a randomized controlled trial about early ivermectin treatment in mild and moderate COVID-19 (RIVET-COV) in India by Mohan et al. comparing 24 mg (n=40), 12 mg (n=40) and placebo (n=45) did not indicate a statistically significant result.[288]

On February 3, Al Jazeera briefly covered India's experiences of ivermectin, interviewed Wasif Ali Khan from Bangladesh and Kory of the FLCCC, and mentioned Slovakia.[289] On the same day, a news report from Peru described some details of the conflicts in the country, saying attempts to talk about ivermectin "lead to stoning ... it's like trying to discuss abortion with ultraconservatives".[290]

On February 4, Ramírez et al. published a commentary in the Lancet, stating that "in the face of a virus with a high mutation rate that could lead to loss of effectiveness of vaccines, worldwide research of therapies for COVID-19 such as ivermectin should not be idled".[291]

On February 4, Merck & Co/MSD gave a statement on the use of ivermectin on COVID19.[292] They noted that their analysis identified "no scientific basis for a potential therapeutic effect against COVID-19 from pre-clinical studies; no meaningful evidence for clinical activity or clinical efficacy in patients with COVID-19 disease, and; a concerning lack of safety data in the majority of studies", concluding that they "do not believe that the data available support the safety and efficacy of ivermectin beyond the doses and populations indicated in the regulatory agency-approved prescribing information".

On February 4, a Belgian virologist Wathelet proposes a plan to eradicate SARS-CoV-2 in Belgium in six weeks using ivermectin, calling for prophylaxis with two doses of 0.3 mg/kg 72 hours apart every month, early treatment of outpatients, and treatment of hospitalized patients.[293] The author of the news report concludes that "a failure to act swiftly on [the existing research] evidence might begin to look like dereliction of moral responsibility".

On February 5, a Brazilian manufacturer of ivermectin issued a declaration, stating that in Brazil, ivermectin has been an option for early treatment since the beginning of the pandemic but especially after publication of the Monash University study.[294] It mentioned that due to existing widespread use in other diseases and low impact in terms of side effects, a large part of the medical community had adhered to treatment protocols based on ivermectin, among other options. The statement mentioned proven safety due to previous use, and dozens of international studies. It also stated that "the growth of market for ivermectin, a low-cost and therapeutically low-risk product, naturally bothers especially companies that are interested in launching high-cost patented products for the same disease, and this can motivate campaigns against it in the media".

On February 5, a preprint of a randomized controlled trial of relatively low risk hospitalized patients (n=100) by Bukhari et al. indicated a significantly lower risk of no virological cure (10% vs 56%, $p<0.001$) at day 7 (NCT04392713).[295]

On February 5, the FLCCC Alliance responded to YouTube's removal of the video of Kory's senate hearing, stating that "YouTube unilaterally decided that [Kory] citing extensive scientific evidence, was giving 'dangerous and misleading' information ... while he was attempting to inform the government that there was a safe, proven and inexpensive way to immediately begin to save lives, dramatically lower case counts and significantly slow the pandemic itself ... [it is] dangerous for social media giants like YouTube to indiscriminately discredit and summarily remove official government information given under oath".[296]

On February 7, the FLCCC Alliance published a response to Merck & Co/MSD's statement, citing FLCCC's provisionally accepted review, the CovidAnalysis group's meta-analysis and other published studies and preprints on ivermectin's efficacy and safety.[297]

On February 9, a new 'Together' trial led by McMaster University and partly funded by the Bill and Melinda Gates Foundation was announced (NCT04727424).[298,299,300,301] The ivermectin arm was apparently planned to be carried out in Brazil, with a single dose of 18 mg for participants weighing 40-60 kg and 24 mg for participants over 60 kg. The number of participants was expected to be up to 3,200, with results available within three to six months. On the same day, the chairman of Tokyo Medical Association in Japan stated that family doctors should administer ivermectin to infected outpatients.[302,65]

On February 10, a peer-reviewed report of a prospective trial of outpatients (n=768) by Lima-Morales et al. indicated that 481 patients treated with ivermectin, azithromycin, montelukast and aspirin showed significantly lower mortality (3% vs 18%, $p<0.001$) and hospitalization (9% vs 31%, $p<0.001$), and lower risk of no recovery at 14 days (16% vs 41%, $p<0.001$) in comparison to 287 controls.[303]

On February 11, the NIH declined a Freedom of Information Act request about details on the process that lead to its most recent ivermectin recommendation.[304]

On February 11, ivermectin had become available without prescription in Bulgaria, with people later queueing to buy it at pharmacies across the country.[305,306,307]

On February 12, preliminary results of a double blind randomized controlled trial about early ivermectin treatment of mild-moderate outpatients by Schwartz et al. in Israel indicated a significantly faster reduction in viral load (NCT04429711).[308,309]

On February 15, a Japanese magazine noted that ivermectin was a Japanese invention by Satoshi Ōmura and referred to a FLCCC Alliance report and promising studies from Egypt, Iraq, India and Bangladesh.[310]

On February 15, a preprint of a second, larger study on prophylactic role of ivermectin in SARS-CoV-2 infection among healthcare workers (n=3,532) by Behera et al. indicated a 83% lower risk of infection ($p<0.001$) in 2,199 workers who had received a two-dose ivermectin prophylaxis.[311]

On February 16, a peer-reviewed version of Behera et al. study about ivermectin prophylaxis of healthcare workers (n=117) indicated a 73% lower risk of in infection ($p<0.001$).[142,143]

On February 16, a peer-reviewed non-randomized controlled trial (n=113) on the effect of a combination of nitazoxanide, ribavirin and ivermectin plus zinc supplement (MANS.NRIZ) on the clearance of mild COVID-

19 by Elalfy et al. indicated a significantly faster viral clearance: 58% vs 0% on day seven, and 89% vs 7% on day 15 (p<=0.001).[312]

On February 16, the Guardian wrote that a member of parliament of Australia had been banned from Facebook for a week for posting three pieces of misinformation, one of which was claiming ivermectin's usefulness for COVID-19.[313]

On February 18, version 34 of the CovidAnalysis group's meta-analysis covered 41 studies including 14,833 patients, 100% of which reported positive effects.[314] 20 of the studies were randomized controlled trials with a total of 2,796 patients, indicating an estimated risk reduction of 72% (RR 0.28, CI 0.17-0.47, n=2,796, p<0.000001). Of these, improvement in early treatment was 70% (RR 0.30, CI 0.17-0.51, n=611), in late treatment 57% (RR 0.43, CI 0.25-0.72, n=1,447), and in prophylaxis 91% (RR 0.09, CI 0.06-0.15, n=738). Six RCTs investigating mortality indicated a 75% reduction (RR 0.25, CI 0.12-0.52, n=1,258, p=0.00012). Considering all 41 studies, prospective studies indicated a slightly larger improvement than retrospective studies.

On February 20, Lawrie and a British company, Evidence-based Medicine Consultancy Limited (E-BMC Ltd) organized a meeting under the name of British Ivermectin Recommendation Development (BIRD), a recording of which was put available on YouTube.[315] The recording was apparently censored from YouTube but later reinstated there and advertised on Twitter. The meeting panel of 75 participants issued issued a recommendation for immediate global use of ivermectin. The summary described desirable effects as large, undesirable effects as trivial, the certainty of evidence as high, and indicated large savings of resources and a favorable cost-effectiveness, acceptability and feasibility.

On February 20, a Czech Republic newspaper reported that the head of the department of anesthesiology and intensive care at the Bratislava National Oncology Institute had administered ivermectin to her patients for two weeks, since they became aware of the possibility.[284] She stated its safety had been demonstrated and when started early it appeared to eliminate the virus. The article also noted there had been resistance towards its use in the country, however there had been a promising trial by Schwartz et al. in Israel, and the Slovakian experience had been good. The article referred to a statement by the mayor of Bratislava, the capital of Slovakia, stating that local real-life results suggest a benefit especially in the outpatient setting, preventing deterioration and hospitalization. The mayor stressed the need to obtain ivermectin in large quantities.

On February 22, the Brazilian manufacturer of ivermectin, Vitamedic, reportedly commented further on Merck/MSD's statement on February 4, saying Merck's stance on effectiveness of ivermectin "reflects its isolated opinion on the matter", adding that "contrary to what Merck says, there is medical and scientific evidence around the world demonstrating the antiviral action of the drug. Dozens of studies carried out in several countries demonstrate the benefits of the drug, especially in the early stages of the disease and, for this reason, the international medical community and also in Brazil started to include it in the treatment protocols of COVID-19. It is a low-cost drug with low impact in terms of adverse effects".[316]

.On February 23, a small study (n=106) by Beltran-Gonzalez et al. about hydroxychloroquine (n=33), ivermectin (n=36) and placebo (n=37) did not produce statistically significant results (NCT04391127).[317]

On February 23, a report on TrialSite News accused Soto-Becerra et al. study about unreported protocol violations causing it to show a negative result which was later quoted in the NIH recommendation and was claimed to have negatively influenced it.[120]

On February 23, a hospital in the Czech Republic was reported to have tested ivermectin in 30 severe patients with COVID-19 since November 2020, with all patients recovering. Doctors intended to continue ivermectin treatments, commenting its affordability and the good results, despite comments by the director of the State Institute for Drug Control saying studies were incomplete and the Prime Minister saying ivermectin was not suitable or effective.[318]

On February 24, CovidAnalysis group wrote that WHO approved ivermectin for scabies after six studies with a total of 613 patients indicating that ivermectin provided 35% improvement, yet WHO had not approved ivermectin for COVID-19 after 21 randomized controlled trials with 2,869 patients indicating 70% improvement and a total of 42 studies with 14,906 patients indicating 75% improvement.[314]

On February 25, UK newspapers reported ivermectin could cut deaths by 75%, referring to Paul E. Marik and Pierre Kory of the FLCCC group, and to Lawrie's and E-BMC Ltd's 97-page report that was said to

have been sent to the WHO.[319,320] On the same day, the Medical Association of Jamaica requested adoption of ivermectin.[321]

On February 25, the Scottish government responded to a January 14 information request about adoption of ivermectin, stating it is aware of the ongoing trials, that prescribers should pay particular attention to the risks associated with using a licensed medicine off-label, and that granting a license for use in COVID-19 would require an application for a marketing authorization be made to the Medicines and Healthcare products Regulatory Agency (MHRA), which has not received such an application but would have processes in place to expedite such an application, as required.[322] It further explained that compassionate access authorization for unlicensed medicines in individual extreme medical cases is initiated by the patient's doctor "who will have decided that the medicine is the best and the only available treatment option" but that "it is for a pharmaceutical company to determine whether they will offer a medicine though a compassionate use process ... the decision to grant an individual patient compassionate access is one that the pharmaceutical company makes".

On February 25, a mayor in Slovakia denounced obedience to the government and provided ivermectin for the inhabitants of his village, stating that "waiting for the government does not make sense. We start not only with treatment, but also with prevention. All under the strict supervision of a doctor".[323] The article reported that Ministry of Health had granted an exception for ivermectin and it was available at hospitals but not yet available at pharmacies. The mayor said he was convinced it should be used also at outpatient clinics for early intervention, and after weeks of searching he had been able to acquire 500 doses, to be delivered by the local doctor. The mayor had discontinued COVID-19 testing in favor of ivermectin prophylaxis, saying "testing is not a cure".

On February 25, a South African civil rights organization claimed that due to a failure by the regulatory authority SAHPRA to properly register ivermectin as a medicine, and due to unregistered medicines not automatically being illegal, ivermectin for COVID-19 had been legal all along.[324]

On February 26, Syed and Kory discussed prevailing basic misunderstandings about COVID-19, such as it still being characterized as viral pneumonia instead of organizing pneumonia, and varying clinical practices with regard to timing of corticosteroid administration.[325] Kory also described Aguirre-Chang's "therapeutic test" for post-COVID-19 syndrome, consisting of 0.2-0.3 mg/kg ivermectin twice daily for five days, with aspirin 600 mg divided into 2-3 doses daily. If the patient responds to the treatment after five days, both medicines were continued until symptoms had completely resolved. According to Aguirre-Chang, 75%-85% of approximately 300 patients had responded.

On February 27, version 37 of the CovidAnalysis group's meta-analysis added an analysis including only peer-reviewed studies, of which there were 18.[314] In these studies, improvement in early treatment was 84% (RR 0.16, CI 0.06-0.44, n=268), in late treatment 39% (RR 0.61, CI 0.39-0.94, n=1,275), and in prophylaxis 92% (RR 0.08, CI 0.02-0.25, n=2,127). All in all the 18 studies indicated a 75% improvement (RR 0.25, CI 0.16-0.41, n=3,670, $p<0.0001$).

On February 28, a preprint by Bartoszko et al. presented a meta-analysis in which only three ivermectin trials fulfilled the eligibility criteria (Shouman et al. (NCT04422561),[99] Chahla et al. (NCT04701710),[244] and Elgazzar et al.[155]), concluding that there was a "very low certainty evidence" of the efficacy of ivermectin.[326]

On February 28, an Irish newspaper reported that critical patients would start receiving ivermectin as part of an international REMAP-CAP clinical trial (NCT02735707).[327,328] Some hospitals had reportedly already begun using ivermectin off-label.

## March 2021

On March 1, the abstract of the already peer-reviewed and provisionally accepted ivermectin review by Kory et al. with over 86,000 views was removed from Frontiers of Pharmacology.[248] A media statement published the next day by the chief executive editor stated that the article made "a series of strong, unsupported claims based on studies with insufficient statistical significance, and at times, without the use of control groups. Further, the authors promoted their own specific ivermectin-based treatment which is inappropriate for a review article and against our editorial policies ... this paper does not offer an objective nor balanced scientific contribution".[329] A news article noted that there was no explanation as to why such concerns were not taken into account earlier in the process.[330]

On March 1, a preprint of an in-silico analysis predicted that ivermectin has a large binding affinity for the SARS-CoV-2 spike protein.[331]

On March 2, a Canadian broadcast station posted a video interview of Ondrej Halgas at the University of Toronto.[332] The interview host referred to the unsatisfactory results of lockdowns and delays with vaccinations. The interview reviewed the cost, availability and status of the research on ivermectin.

On March 3, ivermectin was provisionally authorized by the Ministry of Health of the Czech Republic.[333] The decision cited FLCCC protocols and the CovidAnalysis group's meta-analysis.[334] A Czech Republic newspaper reported the head of a university hospital in Brno saying a large scale distribution to hospitals and outpatients was beginning, with an initial inventory of 20,000 packages.[335] The prime minister was quoted saying that "we cannot wait for results of clinical trials, let's just try this".[336] On the same day, a German MD criticized German health politicians for ignoring ivermectin, demanding that every possibility for the pharmaceutical industry to influence political decisions to be abolished.[337]

On March 3, a double-blind randomized trial to assess the safety and efficacy of ivermectin in asymptomatic and mild severity COVID-19 patients started in Budapest, Hungary (EudraCT 2021-000166-15).[338]

On March 3, Yang et al. published an article showing that ivermectin's broad spectrum antiviral activity relates to its ability to target the host importin (IMP) $\alpha/\beta 1$ nuclear transport proteins responsible for nuclear entry of cargoes, and that ivermectin can limit infection by the West Nile virus at low ($\mu$M) concentrations.[339]

On March 3, Syed discussed whether ivermectin interferes with efficacy of the vaccines, concluding that it does not.[340] On the same day, an US clinic announced they are offering telemedicine-based early outpatient treatment for patients with active infection and for patients experiencing post-COVID long-hauler symptoms.[341]

On March 4, a randomized clinical trial of low risk patients (n=398) in Colombia by López-Medina et al. did not reach statistical significance (NCT04405843).[342] The CovidAnalysis group claimed that endpoints had been changed mid-study, the authors had received grants and personal fees from five pharmaceutical companies including Merck/MSD also during the study period, a large part of the control group was excluded due to receiving ivermectin, and it was suspected that even more controls had received ivermectin instead of placebo.[343,224]

On March 4, the New York Times wrote that "a controversial anti-parasitic drug that has been touted as a potential Covid-19 treatment, does not speed recovery in people with mild cases of the disease, according to a randomized controlled trial published on Thursday in the journal JAMA ... scientific evidence for its efficacy against the coronavirus is thin ... the trial was relatively small and did not answer the most pressing clinical question, whether ivermectin can prevent severe disease or death ... bigger trials, which are currently underway, could provide more definitive answers ... there's such chaos in the field".[344]

On March 4, MedPage Today wrote about "a Colombian trial flop", mentioning a change of the primary outcome and a labeling error resulting in all patients receiving ivermectin for two weeks, these patients being excluded from the primary analysis and additional patients being recruited", adding that the authors had described the study as possibly underpowered.[345]

On March 4, the Kory et al. preprint previously provisionally accepted to Frontiers of Pharmacology was posted at ResearchGate with explanations stating that the the manuscript had passed through three rounds of peer-review by four different peer reviewers, two of them being career FDA scientists.[346] After these reviews it was accepted for publication on January 13. After a long delay without online publication of the full paper, the abstract was suddenly taken down on March 1, with the authors receiving a rejection letter based on an anonymous external reviewer's opinion that conflicted with the previous four peer reviewers and found the manuscript to contain "unsupported conclusions". The authors noted that the rejection occurred despite the journal's documented knowledge of identical conclusions by the 75-member international consortium on February 20, the British Ivermectin Recommendation Guideline (BIRD) panel.

On March 4, a news article reported Portuguese MDs using ivermectin prophylaxis for themselves for a cost of EUR 5 per month, and one doctor using it to contain an outbreak at a senior home with 63 residents.[347] The ivermectin was produced by a Portuguese pharmaceutical company.

On March 4, Syed discussed whether ivermectin can fight all SARS-CoV-2 variants.[348] According to him, the only area in which ivermectin's efficacy may be compromised is in preventing the spike protein binding to receptors. Ivermectin binds to the spike protein, and if the spike protein changes significantly, ivermectin might not bind to it. However, this has not happened. The second phase is viral fusion with the cell

membrane and release of RNA. Ivermectin does not have a function in this phase. The third phase is viral replication. Ivermectin affects RNA-dependent RNA polymerase (RdRp) and $3CL^{pro}$ which are common for all variants.[349,137,266] Fourth phase is cellular defense reduction, during which the virus enters the nucleus through the host importin (IMP) $\alpha/\beta 1$ nuclear transport proteins.[339] Ivermectin disrupts this process common for all variants. Another function of ivermectin is NF-kB (nuclear factor kappa-light-chain-enhancer of activated B cells) blocking to prevent inflammation.[4] This is also common for all variants. In summary, ivermectin is effective against all variants in preventing replication, entrance of viral cargo to cell nucleus, and inflammation, but in theory, efficacy against binding may vary.

On March 5, FDA issued a consumer update warning against use of ivermectin to treat or prevent COVID-19, yet simultaneously stated that it had not reviewed data to support use of ivermectin in COVID-19.[350]

On March 5, German medical magazine wrote about the Colombian trial, starting from the Caly et al. in vitro study, moving on to the Surgisphere scandal, and finally the Colombian trial, ending by mentioning that the authors of the trial "assumed that the treatment will probably not be of any (great) benefit".[351] Readers' comments referring to the meta-analysis by Lawrie et al. objected with the conclusion.

On March 5, MedinCell published a preprint of an expert review on the safety of ivermectin by Descotes who held shares to MedinCell but had no other relevant affiliations or financial involvement.[352,353,354] MedinCell noted the review will be submitted for peer review to an acknowledged journal. The report stated that "it is of note that neither deaths nor severe adverse events attributable to ivermectin have been reported ... the safety profile of ivermectin has so far been excellent in the majority of treated human patients so that ivermectin human toxicity cannot be claimed to be a serious cause for concern".

On March 6, according to a news report, professor Cacopardo in Sicily, Italy had successfully healed all of his 13 ivermectin-treated patients in just 3-5 days.[355] Also, a Milan pharmacy announced it had begun shipping ivermectin throughout Italy.

On March 6, a news article described outpatient treatment practices in Uttarakhand, India, consisting of a home-delivered kit with a thermometer, an oximeter, azithromycin, paracetamol, three tablets of ivermectin, vitamin C, ten masks, a bag for biohazardous waste and precise instructions, follow-up calls by a doctor every two days, an in-person visit by two doctors on day 9 to check for a need of medication or oxygen, and a test on day 14, all free of charge.[356]

On March 6, Lawrie stated that a two-week randomized controlled trial for the post-COVID-19 syndrome ("long Covid") would be appropriate and interesting.[357] She mentioned the production cost of ivermectin was USD 168 per kilogram, with a WHO document on treatment of scabies mentioning 100 tablets of 12 mg each being available for a total cost of USD 2.90, thus indicating that the cost of a single treatment with 12-24 mg would be USD 0.03-0.06.[358]

On March 6, Merck & Co/MSD announced positive results of a 182-patient phase 2a RCT with MK-4482 (molnupiravir).[359,360,361]

On March 7, the FLCCC group issued a statement calling the FDA statement misleading, saying the guidance may lead to avoidance of off-label prescribing and that the patients cannot wait for phase III trial results.[362] On March 7, in a CBS News interview, the director of the NIH mentioned a need for an oral broad-spectrum medication for early treatment to be given immediately after a positive test result, that would also be effective against viral variants. The director added that the NIH is working "right now" on producing evidence on repurposed medicines including "colcichine, fluvoxamine and potentially ivermectin".[363,364] The text of the story, however, only mentioned fluvoxamine. The director also mentioned that the hydroxychloroquine controversy had had "a detrimental impact on looking for existing drugs ... maybe it got in the way of trying other kinds of repurposed drugs ... we had to get over that. I think we're over it now".

On March 8, a preprint by Chamie-Quintero et al. suggested that mass treatments with ivermectin most likely caused a 14-fold reduction in excess deaths in Peru, and a later reversal of ivermectin policy caused a 13-fold increase.[365,366] The preprint was reviewed by TrialSite News on March 3.

On March 8, an article in MedPage Today criticized Facebook third-party fact-checkers in a case of an op-ed about epidemiology, stating that the fact-checkers appeared to be "disproportionately academics on Twitter who have mega-follower counts. They mostly have similar worldviews, and advertise those views on Twitter. In a different case, a reviewer already tweeted criticism of the article before being selected as a 'fact-checker' ... it is cherry picking criticism from Twitter celebrities in order to extinguish dissenting

opinions ... it feels like a high school clique ... it is antithetical to the spirit of the academy ... this process is not acceptable or fair".[367]

On March 9, a preprint by Scheim et al. accused the recent trial by López-Medina et al. (NCT04405843) of several protocol violations, including a labeling error substituting ivermectin for placebo doses of 38 patients, in addition to a blinding failure and patients in the control group possibly self-medicating with over-the-counter ivermectin.[342,368]

On March 9, a peer-reviewed report of a small late treatment trial with 32 patients by Pott-Junior et al. did not produce statistically significant results (NCT04431466).[369]

On March 9, referring to FDA consumer update on March 5, a MedPage Today article titled "FDA pooh-poohs ivermectin" mentioned that "FDA detailed a laundry list of reasons on why not to use ivermectin for COVID-19, including that it's 'not an anti-viral' and that overdose could cause 'seizures, coma and even death' ".[370]

On March 10, a commentary by Kory stated that "doctors fighting COVID-19 should be supported by their profession and their government, not suppressed. Yet today physicians are smothered under a wave of censorship ... many in positions of authority [are] stubbornly refusing to allow any repurposed treatments. This departure from traditional medical practice risks catastrophe ... when doctors on the front lines try to bring awareness of and use such medicines, they get silenced ... actually 'following the science' means listening to practitioners and considering the entirety and diversity of clinical studies".[371]

On March 11, a preprint by Bryant et al. (with Lawrie) presented a systematic review and meta-analysis done using rigorous Cochrane methods.[372] The review included 21 RCTs with 2,741 patients. Meta-analysis of 13 trials indicated 68% reduction in mortality (RR 0.32, 95% CI 0.14-0.72, n=1,892, low to moderate-certainty evidence). Low-certainty evidence found ivermectin prophylaxis reduced infections by 86% (95% CI 79-91). Low-certainty evidence also indicated reduction in deterioration to severe disease, and 'improvement' measured with various indicators, but no reduction in need for mechanical ventilation. As implications of all the available evidence the authors stated that the apparent safety and low cost suggested that "ivermectin could have an impact on the SARS-CoV-2 pandemic globally. Ivermectin is not a new and experimental drug with safety concerns; it is a WHO 'essential medicine' usually used in different indications. It may be useful for more health professionals to get access to this medicine for use against covid-19 during the ongoing pandemic".

On March 11, the discoverer of ivermectin Satoshi Ōmura stated that ivermectin should be used for COVID-19 immediately without requiring any specific approval.[373,374] According to Ōmura, ivermectin suppresses both replication of the virus and the inflammation, in addition to activating the immune system.

On March 12, a preprint about an early treatment retrospective database analysis by Roy et al. with 56 patients with mild disease, all treated with zinc and vitamins C and D, compared placebo, ivermectin plus doxycycline, azithromycin, and hydroxychloroquine, without finding statistically significant differences.[375,376]

On March 12, the CovidAnalysis group presented a comparison of the mortality results across the five existing meta-analyses, with Kory et al. indicating 72% reduction (RR 0.28, 95% CI 0.19-0.45), Hill et al. indicating 75% reduction (RR 0.25, 95% CI 0.12-0.52), Bryant et al. indicating 68% reduction (RR 0.32, 95% CI 0.14-0.72), Lawrie et al. indicating 83% reduction (RR 0.17, 95% CI 0.08-0.35), and the CovidAnalysis group's analysis indicating 75% reduction (RR 0.25, 95% CI 0.15-0.44).

On March 12, an editorial by Nardelli et al. presented a yet another meta-analysis of randomized clinical trials on the impact of ivermectin on mortality.[377] The meta-analysis utilized Mantel-Haenszel test and a fixed-effects model, and included 1,323 hospitalized patients in seven RCTs performed in six countries. The included studies were the early treatment trial by Ahmed et al. in Bangladesh and the late treatment trials by Elgazzar et al. in Egypt, Hashim et al. in Iraq, Mahmud et al. in Bangladesh, Niaee et al. in Iran, Okumus et al. in Turkey, and Kirti et al. in India.[184,155,135,170,247,235,122] Mortality in patients treated with 12-24 mg ivermectin for 1-5 days was 2% vs 9% in the controls (OR 0.19, 95% CI 0.10-0.34, p<0.01). The authors wrote that "ivermectin followed the opposite pathway of hydroxychloroquine: use of hydroxychloroquine was supported at first by medical agencies worldwide, and later proven ineffective by several RCTs including the RECOVERY Trial. On the contrary, ivermectin was mostly neglected so far and only used in a few countries; nevertheless, scientific community is progressively building a body of randomized evidence which points in favor of its use. After the ruinous experience during the first wave, however, physicians became more 'skeptical' and less prone to use repurposed drugs in COVID-19 patients. Having cried wolf for too long may be preventing the spread of ivermectin use all over the world. While modern medicine cannot

do without ironclad evidence, in an emergency situation the use of a cheap medication without major side effects may be reasonable even if strong verification of its efficacy is still lacking. While there is an urge of large high quality RCTs, results from the reported trials all point in the same direction, and cannot be overlooked".

On March 15, in a TrialSite News interview, Lawrie said that in the meta-analysis by Hill et al. she had noticed a mismatch between the analysis and the conclusion. When she had contacted Hill asking him to explain the mismatch, Hill had, according to Lawrie, replied that the conclusion of the meta-analysis had not been his own: it had been changed by the sponsor of the study Unitaid.[378,262] Lawrie also explained difficulties in her attempts to get her group's meta-analysis published by the Cochrane or journals. TrialSite News commented that "there doesn't seem to be any urgency here" with regard to adoption of treatments.

On March 16, the FLCCC announced on its Twitter account that their article rejected by Frontiers of Pharmacology had been accepted by American Journal of Therapeutics.[379]

On March 16, an online television channel Reform TV in the United Kingdom, launched by a prominent Eurosceptic Nigel Farage's Reform UK, stated it had been exactly a year since the enactment of "the most draconian legislation" that had "decimated peoples' lives", asking whether this progression could have been prevented.[380,381] Reform UK Deputy Leader, MD David Bull compared ivermectin to penicillin and aspirin, explaining recent research and data from Peru by Chamie-Quintero et al. suggesting a decrease in excess deaths after mass distribution and increase in excess deaths after restriction of distribution by the new president in December 2020,[365] with the interviewer describing it as 'an extraordinary coincidence', asking why there had been very little discussion about ivermectin in the UK. Journalist David Rose described international experiences (e.g. India, French care homes) and two "striking" meta-analyses by British scientists Hill and Lawrie. Commenting on Merck & Co/MSD's negative view of ivermectin Rose referred to economic incentives related to Merck's new drug in development, adding that with regard to ivermectin, "the Big Pharma is going to have to take a back seat on this one". Lawrie mentioned 14 RCTs consistently showing benefits in prophylaxis and treatment. She added she believed the government had been informed about ivermectin by their foreign colleagues in 2020, but "for some reason it has not been prioritized ... the developed countries seem to be very highly influenced by the pharmaceutical industry", with most studies conducted in low-to-middle income countries familiar with ivermectin. She suspected more interest in smaller European countries was due to being "last in line for vaccines" or unable to afford them. She mentioned developing countries relying not only on RCTs but also on case studies and clinical experience accumulated since May 2020. Lawrie said it was already unethical to randomize people to a placebo group in an ivermectin trial, but that there were no obstacles to an immediate rollout of ivermectin without further studies. According to her, an earlier rollout would have saved hundreds, potentially thousands of lives of UK citizens.

On March 16, Orient wrote that the US pandemic response has failed at every level, likely causing 100,000 or more preventable US deaths. Orient concluded that "the disastrous global response to COVID-19 has been plagued by lack of preparedness, conflicts of interest, highly politicized 'science', suppression of open discussion, disregard of the bedrock principle of informed consent, and willful neglect of what is likely the most important pillar of response: early treatment. Risk/benefit assessment is fatally compromised by inaccurate, distorted, or absent data concerning the incidence and mortality of disease and the safety and efficacy of countermeasures".[382,383]

On March 17, a systematic review and and an individual patient data meta-analysis of ivermectin use in children weighing less than 15 kg by Jittamala et al. concluded that existing limited data between January 1980 and October 2019 suggest that oral ivermectin in children weighing less than 15 kilograms is safe.[14,384] Overall a total of 1.4% (15/1,088) of children experienced 18 adverse events all of which were mild and self-limiting. No serious adverse events were reported.

On March 17, an interview of a Brazilian MD Adler Menezes described an ivermectin prophylaxis experiment in a factory with 12,000 employees.[385] Ivermectin was administered weekly to workers of one of two work shifts, with infections disappearing in the prophylaxis group. Ivermectin was then administered also to workers in the other shift, with the same result.

On March 18, the Infectious Diseases Society of America (IDSA), citing very low certainty of evidence, gave a conditional recommendation against the use of ivermectin in hospitalized patients with severe COVID-19 and in outpatients with COVID-19, outside of the context of a clinical trial, adding that "adding that well-designed, adequately powered, and well-executed clinical trials are needed to inform decisions on treating COVID-19 with ivermectin".[386]

On March 18, a Yale professor Santin, referring to Kory and CovidAnalysis group, stated he initially did not believe such efficacy was possible but witnessed firsthand very rapid responses in both post-COVID-19 syndrome patients with months of breathing issues, and in extremely severe patients close to intubation.[387,388,389]

On March 18, Haroldo et al. published a retrospective follow-up of 856 patients.[390]

On March 19, a French magazine wrote about the French care home experience, the Hill et al. meta-analysis and several other developments, and interviewed a French ivermectin proponent Maudrux who stated "we are witnessing a drift in the analysis of scientific studies: we look at the methodology but we do not look at the result".[391,392]

On March 19, a news report claimed that the participants of the study by López-Medina et al. had not been informed that they were receiving ivermectin and that they had only been informed that they were receiving "D11AX22 molecule".[393]

On March 21, The Manila Times in Indonesia wrote about the ivermectin controversy.[394]

On March 22, the CovidAnalysis group's listing of all studies about ivermectin on COVID-19 included 72 studies, of which 35 were peer-reviewed and 46 with results comparing treatment and control groups.[395] A March 17, 2021 version 47 of their meta-analysis of the 46 studies included eight randomized controlled trials (of which six double-blind RCTs, one single-blind RCT, and one open-label RCT) on COVID-19 mortality in early treatment (two RCTs) or late treatment (six RCTs) indicated a 69% lower risk of death (RR 0.31, 95% CI 0.16-0.61, p=0.00032, n=1,729).[396]

24 randomized controlled trials (of which 12 double-blind RCTs, two single-blind RCTs, and 10 open-label RCTs) with 3,414 patients indicated a 70% improvement on the various measured indicators including death, viral clearance, hospitalization, ICU admission, recovery, resolution of symptoms and infection (RR 0.30, 95% CI 0.19-0.47, p<0.0001, n=3,414). Improvement in early treatment was 71% (RR 0.29, 95% CI 0.17-0.50, n=1,125), in late treatment 55% (RR 0.45, CI 0.28-0.72, n=1,551), and in prophylaxis 91% (RR 0.09, CI 0.06-0.15, n=738).

21 peer reviewed trials (of which 11 observational trials, five double-blind RCTs, and five open-label RCTs) with 4,215 patients indicated a 75% improvement on the same indicators (RR 0.25, 95% CI 0.16-0.40, p<0.0001, n=4,215). Improvement in early treatment was 83% (RR 0.17, 95% CI 0.07-0.40, n=782), in late treatment 41% (RR 0.59, CI 0.38-0.90, n=1,306), and in prophylaxis 92% (RR 0.08, CI 0.02-0.25, n=2,127).

The probability that an ineffective treatment generated results as positive as the 46 studies was estimated to be one in 70 trillion (p=0.000000000000014). A remarkable feature was the unusual consistency of the results, with all studies indicating positive effects, regardless of the phase of the disease.

As mentioned above, Bryant et al. had reviewed 21 RCTs with 2,741 patients, of which a selection of thirteen RCTs in the Cochrane-standard meta-analysis had indicated 68% reduction in mortality (RR 0.32, 95% CI 0.14-0.72, n=1,892, low to moderate-certainty evidence).[372]

On March 22, "after reviewing the latest evidence", the European Medicine Agency (EMA) advised against use of ivermectin for the prevention or treatment of COVID-19 outside randomized clinical trials.[397] EMA stated that ivermectin medicines were not authorized for use in COVID-19 in the EU, and EMA had not received any application for such use, however it noted that the Czech Republic and Slovakia had allowed temporary use within the remit of their national legislation. EMA stated that "although ivermectin is generally well tolerated at doses authorized for other indications, side effects could increase with the much higher doses that would be needed to obtain concentrations of ivermectin in the lungs that are effective against the virus. Toxicity when ivermectin is used at higher than approved doses therefore cannot be excluded". EMA added that "further well-designed, randomized studies are needed to draw conclusions".

On March 24, a review by Yagisawa et al., a group including the discoverer of ivermectin Satoshi Ōmura, was published in the Japanese Journal of Antibiotics.[398]

## Discussion

A central question in the communications was whether more studies were needed. In November 2020, when the FLCCC Alliance recommendation on ivermectin was formed, the decision to recommend it was assumedly largely based on the perceived consistent positivity of the effects: "seeing a 'signal' in the data". This method could also be called reliance on "clinical experience" or even "intuition".

Comparing five CovidAnalysis group's meta-analyses from October 26 (n=21), December 29 (n=28), January 26 (n=35), February 27 (n=42), and March 17 (n=46),[399] calculated improvements in clinical indicators, with probabilities of an equal or greater percentage of positive results from an ineffective treatment, were as follows: improvements in prophylaxis (pre-exposure/post-exposure or total) were 98%/87% (p=0.063/0.25), 91%/90% (p=0.0078/0.25), 90% (p=0.00098), 89% (p=0.00049), and 89% (p=0.00049), respectively. In early treatment, the improvements were 91% (p=0.13), 87% (p=0.016), 84% (p=0.00098), 83% (p=0.00012), and 79% (p=0.000015). In late treatment, the improvements were 60% (p=0.00024), 48% (p=0.00012), 39% (p=0.000031), 51% (p=0.0000038), and 52% (p=0.0000019). All together, the improvements were 75% (p=0.00000048), 78% (p=0.0000000037), 74% (p=0.000000000029), 75% (p=0.00000000000023), and 72% (p=0.000000000000014). It appears that in 2021 the variation in estimated efficacy due to addition of more studies to the meta-analysis was too small to be clinically meaningful. Therefore, more studies provided little additional clinically relevant information, and the argument against the treatment was solely based on the assumed unreliability of all the existing data.

One of the main obstacles for reception of the idea of repurposed medicines may have been the Surgisphere scandal and the widespread controversy regarding hydroxychloroquine in early 2020, leading to a generalized distrust of research among the politicians, governmental administrative personnel and the public, especially in the more developed countries which appeared to put more importance on the research. This distrust, in turn, possibly opened new avenues for various kinds of societal manipulation.

The distrust appreared to have also lead to, for example, social media and video streaming platforms actively but inconsistently and indiscriminately censoring many subjects and groups, including ivermectin research groups and their results, regardless of their level of academic merit. These practices often appeared similar to censorship practices in authoritarian countries. Mainstream media appeared to maintain an inverted understanding on the process of science in which scientific knowledge was apparently assumed to flow down from the NIH and WHO to the researchers, not the other way around. Financial newspapers (Wall Street Journal, Financial Times) may have possessed a more realistic view on medical research and ivermectin than generalist press conventionally considered high quality (e.g. The New York Times, Associated Press, The Guardian), with some practically accusing researchers of not adhering to the guidelines given by the NIH, for example. The open encyclopedia Wikipedia took pains to only mention negative studies about ivermectin, listing it among the COVID-19 misinformation, even citing a commentator saying that "the narrative of ivermectin as a 'miracle cure' for COVID-19 is a 'metastasized' version of a similar conspiracy theory around the drug hydroxychloroquine, in which unspecified powers are thought to be suppressing news of the drug's effectiveness for their own malign purposes".[400,401,402]

As noted by Wall Street Journal quite early on in the ivermectin saga, the majority of the medical establishment appeared to require almost absolute certainty, resulting in "too much caution killing patients", both health-wise and financially.[172] This approach seemed to only take into account quite theoretical health risks, disregarding not only the very probable societal harms of not taking any action but also the possible health benefits of taking an action under uncertainty. Thus, the process appeared largely a failure of a relatively simple risk-benefit analysis.

The more medically oriented arguments against the adoption of ivermectin were usually based on the hypothesis that the required (as indicated by the Caly et al. in vitro study[19]) plasma and lung tissue concentrations for an antiviral effect would likely not be achievable. Another argument was based on the host-directedness and the assumed toxicity of larger doses.

During the period there appeared to be somewhat scarce interest in treatments research, with the wealthy societies' focus on vaccinations and lockdowns, despite vaccinations being largely unavailable and lockdowns harmful for the economy. These countries appeared to pursue expensive, narrow-spectrum vaccination and new pharmaceuticals based strategies, ignoring cheaper options, whereas developing countries put more emphasis on affordable, broad-spectrum antivirals. One factor may have been the developing nations' clinicians' familiarity with ivermectin and its easy availability, whereas it has been a rarely prescribed medicine in most industrialized countries. In addition, prejudices and a bias against ideas originating outside of familiar or-

ganizations or one's own country may have played a part in the industrialized countries ignoring ivermectin research carried out in the developing countries.[403]

Cost-effectiveness of government funding for development of new medications and vaccines is an important issue. The US government invested USD 356 million in 60,000-100,000 doses of MK-7110, indicating a unit price between USD 5,933.00 and USD 3,560.00, with the initial results of efficacy indicating the same or slightly smaller efficacy as that of ivermectin. A 2015 article about mass treatment of onchocerciasis in Africa stated that Merck & Co/MSD had offered ivermectin at USD 1.51 per treatment, indicating a 2300 to 3900-fold difference between the prices of ivermectin and MK-7110.[404,210] In this example, allocation of US government funding appeared inefficient with respect to investment in an experimental product with the unit costs in thousands of dollars, versus the option to use an existing medication with similar efficacy proven at least on a similar level of evidence and the unit costs in single digits.

There was a widespread disagreement on the fundamentals: which methods were appropriate as a basis for decision making, what counted as evidence, and what was ethical. In a broader view, the appropriateness and usefulness of the evidence based medicine paradigm as it was understood and applied during the period appeared questionable. US and European governmental bodies appeared to reject or ignore most of the ivermectin-related data, referring to insufficient evidence. In the US, the paradigm appeared inconsistently applied; more specifically, not applied to US Food and Drug Administration Emergency Use Authorization of remdesivir, whereas strictly applied to other medications including ivermectin. In addition, a strict requirement to compare a significantly more effective treatment to placebo may be considered unethical with regard to high mortality of patients in control groups. These indicate a clear need for a new methodology better than the current understanding and application of evidence-based medicine.

With regard to conflicts of interest, the US Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for the use of remdesivir in patients with severe disease on May 1, even before the initial results of an ongoing trial were published and despite remdesivir being an investigational drug not approved for any indication. The 1,063-patient randomized controlled trial of remdesivir published on May 22 only indicated that remdesivir shortened the time to recovery (11 days vs 15 days, $p<0.001$).[405] There wasn't an obvious difference in mortality rates (8% vs. 11.6%, $p=0.059$) and the endpoints were changed mid-study which was deemed a questionable practice.[406] The final results were published on October 8. On August 28 the EUA was extended to "no longer require a severe disease".

The adoption of corticosteroids as a consequence of the WHO-initiated 2,000-patient RECOVERY trial results was relatively swift. Also the emergency use authorization of remdesivir in the US was swift, based on initial and conflicting evidence. Twenty randomized clinical trial results on ivermectin's efficacy for COVID-19 were available in February 2021. These trials were predominantly carried out outside the US and the EU, and did not lead to emergency use authorizations in the US or the EU.

US FDA document "Emergency Use Authorization of Medical Products and Related Authorities – Guidance for Industry and Other Stakeholders" section "1. Criteria for Issuance" subsection "d. No Alternatives" states that "For FDA to issue an EUA, there must be no adequate, approved, and available alternative to the candidate product for diagnosing, preventing, or treating the disease or condition. A potential alternative product may be considered 'unavailable' if there are insufficient supplies of the approved alternative to fully meet the emergency need. A potential alternative product may be considered 'inadequate' if, for example, there are contraindicating data for special circumstances or populations (e.g., children, immunocompromised individuals, or individuals with a drug allergy), if a dosage form of an approved product is inappropriate for use in a special population (e.g., a tablet for individuals who cannot swallow pills), or if the agent is or may be resistant to approved and available alternative products".[407]

It may thus be derived that licensing of repurposed medicines such as ivermectin for outpatient treatment and prophylaxis of COVID-19 would have prevented emergency use authorizations of new pharmaceuticals in development. In the case of prophylaxis, such licensing might even have affected vaccines. Thus, there appeared to exist substantial financial conflicts of interest against licensing of repurposed medicines.

Considering the total net utility of a society it is unlikely that unilateral support to only the investments of the pharmaceutical industry could ever offset the harms to other industries and the population. The society thus has a strong incentive to abolish the financial incentive structures of the pharmaceutical industry and the government that led to the current situation, in order to prevent a similar outcome in the future.

Considering the estimated efficacy of ivermectin around 90% in prophylaxis and the option of an early outpatient treatment with an estimated efficacy around 80%, an early introduction of ivermectin might have

prevented a large part of COVID-19 infections post first wave in many European Union countries and in the United States.

Administrative issues, inconsistent requirements of evidence related to the evidence-based medicine paradigm, and possibly conflicts of interest with patentable, commercial products in development prevented introduction of early outpatient ivermectin treatments in the last quarter of 2020 and the first quarter of 2021. This lack of response is likely to have caused unnecessary deaths and difficult-to-repair financial and health consequences in the affected societies.

The culture of medical litigation prevalent in the United States may have created patterns of behavior that have also spread to countries with less actual litigation, yet leading to mental paradigms favoring extreme caution and non-action, in turn leading to stagnation. One of the features of a paradigm is an inability of the involved people to transcend it or even see that it is just one possible paradigm out of many options, some of which may be more optimal in a given situation.

## Conclusion

The period appeared conflicted, with researchers, clinicians, governmental agencies and commercial entities holding deeply conflicting views on fundamental issues, including which methods were considered appropriate as a basis for decision making, what could be considered as sufficient evidence, and what was ethical. In a broader historical perspective, the timeline of events depicts rather dysfunctional societies unable to properly communicate and organize themselves, leading to misallocation of resources and decisions that may have conflicted with elementary ethical considerations, with this behavior rationalized by claiming adherence to mental paradigms that may have poorly matched the situation. In summary, the pandemic response especially in the United States and the European union appeared severely lacking. Further research on the details of these processes is warranted.

*Acknowledgments: the author wishes to thank Simon Barber for a grammar check.*

*Funding: None.*

*Conflict of Interest: None.*

*Ethical Approval: Not applicable.*

## References


1. CovidAnalysis. Ivermectin is effective for COVID-19: real-time meta analysis. 2021. https://ivmmeta.com/

2. CovidAnalysis. Ivermectin for COVID-19: real-time analysis of all studies. 2021. https://c19ivermectin.com/

3. CovidAnalysis. Global ivermectin adoption for COVID-19. 2021. https://ivmstatus.com/

4. Jans DA, Wagstaff KM. Ivermectin as a broad-spectrum host-directed antiviral: the real deal?. *Cells*. 2020;9(9):2100. https://doi.org/10.3390/cells9092100

5. Higazi T, Geary T, MacKenzie C. Chemotherapy in the treatment control, and elimination of human onchocerciasis. *Research and Reports in Tropical Medicine*. October 2014:77. https://doi.org/10.2147/rrtm.s36642

6. Centers for Disease Control and Prevention. Scabies - resources for health professionals - medications. *US Department of Health & Human Services*. 2021. https://web.archive.org/web/20210319125545/https://www.cdc.gov/parasites/scabies/health_professionals/meds.html

7. Engelman D, Steer A. Control strategies for scabies. *Tropical Medicine and Infectious Disease*. 2018;3(3):98. https://doi.org/10.3390/tropicalmed3030098

8. A roadmap for the development of ivermectin as a complementary malaria vector control tool. *The American Journal of Tropical Medicine and Hygiene*. 2020;102(2s):3–24. https://doi.org/10.4269/ajtmh.19-0620

9. Jans DA, Wagstaff KM. The broad spectrum host-directed agent ivermectin as an antiviral for SARS-CoV-2?. *Biochemical and Biophysical Research Communications*. 2021;538:163–172. https://doi.org/10.1016/j.bbrc.2020.10.042

10. Suputtamongkol Y, Avirutnan P, Mairiang D, et al. Ivermectin accelerates circulating nonstructural protein 1 (NS1) clearance in adult dengue patients: a combined phase 2/3 randomized double-blinded placebo controlled trial. *Clinical Infectious Diseases*. January 2021. https://doi.org/10.1093/cid/ciaa1332

11. Jiang L, Wang P, Sun Y-J, Wu Y-J. Ivermectin reverses the drug resistance in cancer cells through EGFR/ERK/Akt/NF-$k$B pathway. *Journal of Experimental & Clinical Cancer Research*. 2019;38(1). https://doi.org/10.1186/s13046-019-1251-7

12. Chung K, Yang C-C, Wu M-L, Deng J-F, Tsai W-J. Agricultural avermectins: an uncommon but potentially fatal cause of pesticide poisoning. *Annals of Emergency Medicine*. 1999;34(1):51–57. https://doi.org/10.1016/s0196-0644(99)70271-4

13. WHO African Programme for Onchocerciasis Control. Ivermectin. 2021. https://web.archive.org/web/20210311193155/https://www.who.int/apoc/cdti/ivermectin/en/

14. Jittamala P, Monteiro W, Smit MR, et al. A systematic review and an individual patient data meta-analysis of ivermectin use in children weighing less than fifteen kilograms: Is it time to reconsider the current contraindication?. Downs JA, ed. *PLOS Neglected Tropical Diseases*. 2021;15(3):e0009144. https://doi.org/10.1371/journal.pntd.0009144

15. Gyapong JO, Chinbuah MA, Gyapong M. Inadvertent exposure of pregnant women to ivermectin and albendazole during mass drug administration for lymphatic filariasis. *Tropical Medicine & International Health*. 2003;8(12):1093–1101. https://doi.org/10.1046/j.1360-2276.2003.01142.x

16. Speare R, Durrheim D. Mass treatment with ivermectin: an underutilized public health strategy. *Bulletin of the World Health Organization*. 2004;82(8). https://web.archive.org/web/20210104194334/https://www.who.int/bulletin/volumes/82/8/editorial30804html/en/

17. Monash University. Possible coronavirus drug identified: Ivermectin stops SARS-CoV-2 virus growing in cell culture. 2020. https://web.archive.org/web/20200404174008/https://www.sciencedaily.com/releases/2020/04/200403115115.htm

18. Monash University. Lab experiments show anti-parasitic drug, Ivermectin, eliminates SARS-CoV-2 in cells in 48 hours. December 2020. https://web.archive.org/web/20200406210318/https://www.monash.edu/discovery-institute/news-and-events/news/2020-articles/Lab-experiments-show-anti-parasitic-drug,-Ivermectin,-eliminates-SARS-CoV-2-in-cells-in-48-hours

19. Caly L, Druce JD, Catton MG, Jans DA, Wagstaff KM. The FDA-approved drug ivermectin inhibits the replication of SARS-CoV-2 in vitro. *Antiviral Research*. 2020;178:104787. https://doi.org/10.1016/j.antiviral.2020.104787

20. MedinCell. MedinCell has launched a COVID-19 research initiative based on its experience to formulate long-acting injectable ivermectin. 2020. https://web.archive.org/web/20210314203705/https://invest.medincell.com/wp-content/uploads/2020/04/PR_MedinCell-Covid19-EN.pdf

21. MedinCell continues its investigational pursuit of ivermectin targeting COVID-19 patients. *TrialSite News*. 2020. https://web.archive.org/web/20200511102723/https://trialsitenews.com/medincell-continues-its-investigational-pursuit-of-ivermectin-targeting-covid-19-patients/

22. MedinCell Announces Great Success with Capital Raise of 15.6M€ & Use of Proceeds Includes Ivermectin Prophylactic for COVID-19. *TrialSite News*. 2020. https://web.archive.org/web/20200715183357/https://www.trialsitenews.com/medincell-announces-great-success-with-capital-raise-of-15-6me-use-of-proceeds-includes-ivermectin-prophylactic-for-covid-19/

23. FDA's Center for Veterinary Medicine. Do not use ivermectin for animals as treatment for COVID-19 in humans. 2020. https://web.archive.org/web/20200411022909/https://www.fda.gov/animal-veterinary/product-safety-information/fda-letter-stakeholders-do-not-use-ivermectin-intended-animals-treatment-covid-19-humans

24. NBC Miami. Local doctor tries new coronavirus drug treatment. 2020. https://web.archive.org/web/20200414024411/https://www.nbcmiami.com/news/local/local-doctor-tries-new-coronavirus-drug-treatment/2219465/

25. Patel A, Desai S. Ivermectin in COVID-19 related critical illness. *SSRN Electronic Journal*. 2020. https://web.archive.org/web/20210315083615/https://www.isglobal.org/documents/10179/6022921/Patel+et+al.%20+2020+version+1.pdf/fab19388-dc3e-4593-a075-db96f4536e9d

26. Patel A, Desai S. Ivermectin in COVID-19 Related Critical Illness by Amit Patel, Sapan Desai :: SSRN. *SSRN Electronic Journal*. 2020. https://web.archive.org/web/20200414142415/https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3570270

27. "La Ivermectina fue creada para el tratamiento de humanos". *La Industria*. 2020. https://web.archive.org/web/20200608055559/http://laindustria.pe/nota/16073-la-ivermectina-fue-creada-para-el-tratamiento-de-humanos

28. Patel AN, Desai SS, Grainger DW, Mehra MR. Usefulness of ivermectin in COVID-19 illness. *SSRN Electronic Journal*. 2020. https://web.archive.org/web/20210315083837/https://www.isglobal.org/documents/10179/6022921/Patel+et+al.+2020+version+2.pdf/

29. Patel A. Usefulness of ivermectin in COVID-19 illness. *SSRN Electronic Journal*. 2020. https://web.archive.org/web/20200602150544/https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3580524

30. Oropeza V. La sospecha del doctor Chaccour. *Pulitzer Center*. 2020. https://web.archive.org/web/20200716234039/http://factor.prodavinci.com/lasospechadeldoctorchaccour/

31. Bray M, Rayner C, Noël F, Jans D, Wagstaff K. Ivermectin and COVID-19: a report in Antiviral Research widespread interest, an FDA warning, two letters to the editor and the authors' responses. *Antiviral Research*. 2020;178:104805. https://doi.org/10.1016/j.antiviral.2020.104805

32. Schmith VD, Zhou J(J, Lohmer LRL. The approved dose of ivermectin alone is not the ideal dose for the treatment of COVID-19. *Clinical Pharmacology & Therapeutics*. 2020;108(4):762–765. https://doi.org/10.1002/cpt.1889

33. Aguirre-Chang G. Inclusión de la ivermectina en la primeira línea de acción terapéutica para COVID-19. Se reporta una muy significativa disminución de la Tasa de Letalidad con su uso. *ResearchGate*. 2020. https://www.researchgate.net/publication/342466502_INCLUSION_DE_LA_IVERMECTINA_EN_LA_PRIMERA_LINEA_DE_ACCION_TERAPEUTICA_PARA_COVID-19_Se_reporta_una_muy_significativa_disminucion_de_la_Tasa_de_Letalidad_con_su_uso

34. A randomised clinical trial of ivermectin for treatment and prophylaxis of COVID-19 (ECIT-PRO19). *European Medicine Agency Clinical Trials Register*. 2020. https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001994-66/ES

35. A pilot study to evaluate the potential of ivermectin to reduce COVID-19 transmission (SAINT). *European Medicine Agency Clinical Trials Register*. 2020. https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001474-29/ES

36. Lowe D. What's up with ivermectin?. *Science Translational Medicine In the Pipeline Blog*. 2020. https://web.archive.org/web/20200518021117/https://blogs.sciencemag.org/pipeline/archives/2020/05/11/whats-up-with-ivermectin

37. Huvepharma EOOD. Multicenter, randomized, double-blind, placebo-controlled study investigating efficacy, safety and tolerability of ivermectin HUVE-19 in patients with proven SARS-CoV-2 infection (COVID-19) and manifested clinical symptoms (EudraCT 2020-002091-12). *European Medicine Agency Clinical Trials Register*. 2020. https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-002091-12/BG

38. Press Trust of India. Bangladesh medical team says ivermectin with antibiotic doxycycline works to treat COVID-19 patients. *Firstpost*. 2020. https://web.archive.org/web/20200724160329/https://www.firstpost.com/health/bangladesh-medical-team-says-ivermectin-with-antibiotic-doxycycline-works-to-treat-covid-19-patients-8381321.html

39. Ramos WM, Pérez MAGM, Acosta AC, et al. Intervención de la ivermectina pre-hospitalaria para la modificación de la evolución del Covid-19. Estudio realizado en Perú. *Caretas*. 2020. https://web.archive.org/web/20200616111752/https://caretas.pe/wp-content/uploads/2020/05/ESTUDIO-PERU-DEFINITIVO-corregido-en-Word-y-pasado-a-PDF.pdf

40. Rizzo E. Ivermectin antiviral properties and COVID-19: a possible new mechanism of action. *Naunyn-Schmiedeberg's Archives of Pharmacology*. 2020;393(7):1153–1156. https://doi.org/10.1007/s00210-020-01902-5

41. Chandna H. ICMR to review 'wonder' drug combo used to treat Covid patients in Bangladesh. *The Print*. 2020. https://web.archive.org/web/20200917183516/https://theprint.in/health/icmr-to-review-wonder-drug-combo-used-to-treat-covid-patients-in-bangladesh/432987/

42. Peru: Minsa steps up efforts to deliver medicines home and prevent hospital congestion. *Editora Perú/Peru News Agency*. 2020. https://web.archive.org/web/20210311151457/https://andina.pe/ingles/noticia-peru-minsa-steps-up-efforts-to-deliver-medicines-home-and-prevent-hospital-congestion-799759.aspx

43. Ivermectin as an antiviral treatment for patients infected by SARS-COV2 (CORIVER). *European Medicine Agency Clinical Trials Register*. 2020. https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001971-33/ES

44. Servick K. A mysterious company's coronavirus papers in top medical journals may be unraveling. *Science*. June 2020. https://doi.org/10.1126/science.abd1337

45. Davey M, Kirchgaessner S, Boseley S. Surgisphere: governments and WHO changed Covid-19 policy based on suspect data from tiny US company. *The Guardian*. 2020. http://www.theguardian.com/world/2020/jun/03/covid-19-surgisphere-who-world-health-organization-hydroxychloroquine

46. Ministerio de Salud. Resolución Ministerial N° 270-2020-MINSA. 2020. https://web.archive.org/web/20210308110555/https://www.gob.pe/institucion/minsa/normas-legales/563764-270-2020-minsa

47. Piller C, Servick K. Two elite medical journals retract coronavirus papers over data integrity questions. *Science*. June 2020. https://doi.org/10.1126/science.abd1697

48. Piller C. Who's to blame? These three scientists are at the heart of the Surgisphere COVID-19 scandal. *Science*. June 2020. https://doi.org/10.1126/science.abd2252

49. Kerr L. Alguns esclarecimentos sobre a ivermectina. *Portal Lucy Kerr*. 2020. https://web.archive.org/web/20200617021627/https://portallucykerr.com/alguns-esclarecimentos-sobre-a-ivermectina/

50. An old drug tackles new tricks: ivermectin treatment in three Brazilian towns. *TrialSite News*. 2020. https://web.archive.org/web/20201002172248/https://trialsitenews.com/an-old-drug-tackles-new-tricks-ivermectin-treatment-in-three-brazilian-towns/

51. Rajter JC, Sherman MS, Fatteh N, Vogel F, Sacks J, Rajter J-J. ICON (Ivermectin in COvid Nineteen) study: Use of Ivermectin is Associated with Lower Mortality in Hospitalized Patients with COVID19. *medRxiv*. June 2020. https://doi.org/10.1101/2020.06.06.20124461

52. Rajter JC, Sherman MS, Fatteh N, Vogel F, Sacks J, Rajter J-J. Use of ivermectin is associated with lower mortality in hospitalized patients with coronavirus disease 2019. *Chest*. 2021;159(1):85–92. https://doi.org/10.1016/j.chest.2020.10.009

53. Heidary F, Gharebaghi R. Ivermectin: a systematic review from antiviral effects to COVID-19 complementary regimen. *The Journal of Antibiotics*. 2020;73(9):593–602. https://doi.org/10.1038/s41429-020-0336-z

54. How a grass roots health movement led to acceptance of ivermectin as a COVID-19 therapy in Peru. *TrialSite News*. 2020. https://web.archive.org/web/20201222145639/https://trialsitenews.com/how-a-grass-roots-health-movement-led-to-acceptance-of-ivermectin-as-a-covid-19-therapy-in-peru/

55. Alam MT, Murshed R, Bhiuyan E, Saber S, Alam RF, Robin RC. A case series of 100 COVID-19 positive patients treated with combination of ivermectin and doxycycline. *Journal of Bangladesh College of Physicians and Surgeons*. 2020;38:10–15. https://doi.org/10.3329/jbcps.v38i0.47512

56. A randomized, double-blind, multi centre phase II, proof of concept, dose finding clinical trial on ivermectin for the early treatment of COVID-19 (COVER). *European Medicine Agency Clinical Trials Register*. 2020. https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-002283-32/IT

57. Vigneri M. L'ivermectina è un farmaco straordinario ma poco noto, ha buone chance anche contro il Coronavirus. *The Post Internazionale (TPI)*. 2020. https://web.archive.org/web/20210313210733/https://www.tpi.it/cronaca/coronavirus-ivermectina-farmaco-straordinario-intervista-20200405579792/

58. Angheben A. Covid 19: facciamo il punto sui farmaci oggi efficaci - IRCCS Ospedale Sacro Cuore Don Calabria. *IRCCS Ospedale Sacro Cuore Don Calabria*. 2020. https://web.archive.org/web/20210313211658/https://www.sacrocuore.it/covid-19-facciamo-il-punto-sui-farmaci-oggi-efficaci/

59. El verdadero Comando COVID-19 de Iquitos: médicos independientes lograron contener el azote del coronavirus, no el Minsa ni Essalud. *Con Nuestro Perú*. 2020. https://web.archive.org/web/20200615181035/https://www.connuestroperu.com/actualidad/entrevistas/65760-el-verdadero-comando-covid-19-de-iquitos-medicos-independientes-lograron-contener-el-azote-del-coronavirus-no-el-minsa-ni-essalud

60. Sparavigna AC. Ivermectin for Covid-19. *ResearchGate*. September 2020. https://doi.org/10.5281/zenodo.3893750

61. Köppe J. Zurückgezogene Covid-19-Studien - das steckt hinter der Datenbank von Surgisphere. *Der Spiegel*. June 2020. https://www.spiegel.de/wissenschaft/medizin/corona-zurueckgezogene-covid-19-studien-das-steckt-hinter-der-datenbank-von-surgisphere-a-3f5986b8-d9d6-492f-a562-81d3bccbe4fa

62. Scheim D. Antimalarials for COVID-19 treatment: rapid reversal of oxygen status decline with the Nobel prize-honored macrocyclic lactone ivermectin. *SSRN Electronic Journal*. 2020. https://doi.org/10.2139/ssrn.3617911

63. Wang K, Chen W, Zhou Y-S, et al. SARS-CoV-2 invades host cells via a novel route: CD147-spike protein. *medRxiv*. March 2020. https://doi.org/10.1101/2020.03.14.988345

64. Wang K, Chen W, Zhang Z, et al. CD147-spike protein is a novel route for SARS-CoV-2 infection to host cells. *Signal Transduction and Targeted Therapy*. 2020;5(1). https://doi.org/10.1038/s41392-020-00426-x

65. Clinical management of patients with COVID-19 – a guide for front-line healthcare workers. Version 2.1, June 17, 2020. 2020. http://web.archive.org/web/20200708033632/https://www.mhlw.go.jp/content/000646531.pdf

66. Lehrer S, Rheinstein PH. Ivermectin docks to the SARS-CoV-2 spike receptor-binding domain attached to ACE2. *In Vivo*. 2020;34(5):3023–3026. https://doi.org/10.21873/invivo.12134

67. Zhang P, Ni H, Zhang Y, et al. Ivermectin confers its cytotoxic effects by inducing AMPK/mTOR-mediated autophagy and DNA damage. *Chemosphere*. 2020;259:127448. https://doi.org/10.1016/j.chemosphere.2020.127448

68. Resolución Ministerial 426-2020 MINSA. *Ministerio De Salud (Peru)*. 2020. https://web.archive.org/web/20210315081458/https://cdn.www.gob.pe/uploads/document/file/874053/RM_426-2020-MINSA.pdf

69. Molento MB. COVID-19 and the rush for self-medication and self-dosing with ivermectin: A word of caution. *One Health*. 2020;10:100148. https://doi.org/10.1016/j.onehlt.2020.100148

70. President of Dominican Republic's largest private health group discusses the success of ivermectin as a treatment for early stage COVID-19. *TrialSite News*. 2020. https://web.archive.org/web/20210319114033/https://trialsitenews.com/president-of-dominican-republics-largest-private-health-group-discusses-the-success-of-ivermectin-as-a-treatment-for-early-stage-covid-19/

71. Scheim D. Ivermectin for COVID-19 treatment: clinical response at quasi-threshold doses via hypothesized alleviation of CD147-mediated vascular occlusion. *SSRN Electronic Journal*. 2020. https://doi.org/10.2139/ssrn.3636557

72. Syed M. Ivermectin remdesivir leronlimab. *Drbeen Medical Lectures*. 2020. https://youtu.be/wR6CuBu_mA8

73. Проф. Христова: Ивермектин е обещаващ препарат срещу Covid-19. *Economic*. 2020. https://web.archive.org/web/20210312075642/https://www.economic.bg/bg/a/view/prof-hristova-ivermektin-e-obeshtavasht-preparat-sreshtu-covid-19-119076

74. Gorial FI, Mashhadani S, Sayaly HM, et al. Effectiveness of ivermectin as add-on therapy in COVID-19 management (pilot trial). *medRxiv*. July 2020. https://doi.org/10.1101/2020.07.07.20145979

75. Maurya DK. A combination of ivermectin and doxycycline possibly blocks the viral entry and modulate the innate immune response in COVID-19 patients. *chemRxiv*. July 2020. https://doi.org/10.26434/chemrxiv.12630539.v1

76. Aguirre-Chang G, Castillo-Saavedra E, Yui-Cerna M, Trujillo-Figueredo A, Córdova-Masías J. Post-acute or prolonged COVID-19: ivermectin treatment for patients with persistent or post-acute symptoms. *ResearchGate*. 2020. https://www.researchgate.net/publication/344318845_POST-ACUTE_OR_PROLONGED_COVID-19_IVERMECTIN_TREATMENT_FOR_PATIENTS_WITH_PERSISTENT_SYMPTOMS_OR_POST-ACUTE

77. Goodman J, Carmichael F. Coronavirus: fake cures in Latin America's deadly outbreak. *BBC*. 2020. https://web.archive.org/web/20200712002646/https://www.bbc.com/news/53361876

78. Chowdhury A, Mohiuddin TM, Shahbaz M, et al. A randomized trial of ivermectin-doxycycline and hydroxychloroquine-azithromycin therapy on COVID19 patients. *Research Square*. 2020. https://www.researchsquare.com/article/rs-38896/v1

79. Dr. Jean-Jacques Rajter and Dr. Juliana Cepelowicz Rajter discuss ivermectin In Broward County. *TrialSite News*. 2020. https://youtu.be/nzqnAIfEbv4

80. Dr. Jean-Jacques Rajter and Dr. Juliana Cepelowicz Rajter discuss ivermectin In Broward county – podcast S2 E 27. *TrialSite News*. 2020. https://trialsitenews.com/dr-jean-jacque-rajter-and-dr-juliana-cepelowicz-rajter-discuss-ivermectin-in-broward-county-podcast-s2-e-27/

81. Peña-Silva R, Duffull SB, Steer AC, Jaramillo-Rincon SX, Gwee A, Zhu X. Pharmacokinetic considerations on the repurposing of ivermectin for treatment of COVID-19. *British Journal of Clinical Pharmacology*. 2020;87(3):1589–1590. https://doi.org/10.1111/bcp.14476

82. Arpornsuwan M, Arpornsuwan M. Early diagnosis and early management proposal in dengue infection: new normal to applied strategy for COVID-19 infection. *SSRN Electronic Journal*. 2020. https://doi.org/10.2139/ssrn.3649412

83. Vora A, Arora VK, Behera D, Tripathy SK. White paper on Ivermectin as a potential therapy for COVID-19. *Indian Journal of Tuberculosis*. 2020;67(3):448–451. https://doi.org/10.1016/j.ijtb.2020.07.031

84. Aguirre- Chang G, Trujillo Figueredo A. COVID-19: post-exposure prophylaxis with ivermectin in contacts. At homes, places of work, nursing homes, prisons, and others. *ResearchGate*. July 2020. https://doi.org/10.13140/RG.2.2.34561.48483/2

85. Stauffer WM, Alpern JD, Walker PF. COVID-19 and dexamethasone. *JAMA*. 2020;324(7):623. https://doi.org/10.1001/jama.2020.13170

86. Rahman A, Iqbal SA, Islam A, Niaz K, Hussain T, Siddiquee TH. Comparison of viral clearance between ivermectin with doxycycline and hydroxychloroquine with azithromycin in COVID-19 patients. *J Bangladesh Coll Phys Surg*. 2020;38:5–9. https://web.archive.org/web/20210129105721/http://bcpsjournal.org/mhcms-admin/media/pdf/article761.pdf

87. Empezarán a usar Ivermectina en tratamiento de pacientes covid en Cali, dice Ospina. *El País*. 2020. https://web.archive.org/web/20200717042008/https://www.elpais.com.co/ultimo-minuto/empezaran-a-usar-ivermectina-en-tratamiento-de-pacientes-covid-en-dice-ospina.html

88. Front Line COVID-19 Critical Care Alliance. FAQ on ivermectin. 2021. https://web.archive.org/web/20210301170808/https://covid19criticalcare.com/i-mask-prophylaxis-treatment-protocol/faq-on-ivermectin/

89. Prasad A. A meeting regarding the role of ivermectin. 2020. https://web.archive.org/web/20201004145236/dgmhup.gov.in/DocumentsCovid19/1621.pdf

90. Ongoing living update of potential COVID-19 therapeutics: summary of rapid systematic reviews - 11 August 2020. https://web.archive.org/web/20210323105539/https://docs.bvsalud.org/biblioref/2020/08/1094870/pahoimseihcovid-19200016_eng.pdf

91. Davey M. What is ivermectin, and should we be using it to treat Covid-19?. *Guardian*. 2020. https://web.archive.org/web/20200813032207/http://www.theguardian.com/australia-news/2020/aug/13/what-is-ivermectin-and-should-we-be-using-it-to-treat-covid-19

92. Bhattacharya R, Ray I, Mukherjee R, Chowdhury S, Kulasreshtha M, Ghosh R. Observational study on clinical features, treatment and outcome of COVID 19 in a tertiary care centre in India – a retrospective case series. *Int J Scientific Research*. 2020;9(10):69–71. https://doi.org/10.36106/ijsr/7232245

93. Lier AJ, Tuan JJ, Davis MW, et al. Case report: disseminated strongyloidiasis in a patient with COVID-19. *The American Journal of Tropical Medicine and Hygiene*. 2020;103(4):1590–1592. https://doi.org/10.4269/ajtmh.20-0699

94. Espitia-Hernandez G, Munguia L, Diaz-Chiguer D, Lopez-Elizalde R, Jimenez-Ponce F. Effects of ivermectin-azithromycin-cholecalciferol combined therapy on COVID-19 infected patients: a proof of concept study. *Biomedical Research*. 2020;31(5). https://www.biomedres.info/biomedical-research/effects-of-ivermectinazithromycincholecalciferol-combined-therapy-on-covid19-infected-patients-a-proof-of-concept-study-14435.html

95. Weisser R. No guts, no glory. *The Spectator Australia*. 2020. https://web.archive.org/web/20200817155704/https://www.spectator.com.au/2020/08/no-guts-no-glory/

96. Well-respected Australian researcher: consider triple therapy (ivermectin, zinc, doxycycline) for COVID-19. *TrialSite News*. 2020. https://web.archive.org/web/20200820141526/https://trialsitenews.com/well-respected-australian-researcher-consider-triple-therapy-ivermectin-zinc-doxycycline-for-covid-19/

97. Rajter JC, Sherman MS, Fatteh N, Vogel F, Sacks J, Rajter J-J. ICON (Ivermectin in COvid Nineteen) study: use of ivermectin is associated with lower mortality in hospitalized patients with COVID-19. *SSRN Electronic Journal*. 2020. https://doi.org/10.2139/ssrn.3631261

98. US National Institutes of Health. COVID-19 treatment guidelines: ivermectin (August 27, 2020). 2020. https://web.archive.org/web/20200920093445/https://www.covid19treatmentguidelines.nih.gov/antiviral-therapy/ivermectin/

99. Shouman W. Prophylactic ivermectin in COVID-19 contacts (NCT04422561). *ClinicalTrialsgov*. 2020. https://clinicaltrials.gov/ct2/show/results/NCT04422561

100. Zagazig University randomized controlled ivermectin study results confirms PI hypothesis: drug effective against COVID-19. *TrialSite News*. 2020. https://web.archive.org/web/20200830164247/https://trialsitenews.com/zagazig-university-randomized-controlled-ivermectin-study-results-confirms-pi-hypothesis-drug-effective-against-covid-19/

101. Hlavinka E. Ivermectin for COVID-19: worth a shot?. *MedPage Today*. August 2020. https://web.archive.org/web/20200828000211/https://www.medpagetoday.com/special-reports/exclusives/88310

102. Dias I. The Brazilian city being turned into a coronavirus lab experiment. *Coda*. 2020. https://web.archive.org/web/20200902222937/https://www.codastory.com/waronscience/brazil-covid19-ivermectin/

103. Podder CS, Chowdhury N, Sina MI, Haque WMMU. Outcome of ivermectin treated mild to moderate COVID-19 cases: a single-centre, open-label, randomised controlled study. *IMC J Med Sci*. 2020;14(2):002. http://imcjms.com/registration/journal_full_text/353

104. Marchese V, Crosato V, Gulletta M, et al. Strongyloides infection manifested during immunosuppressive therapy for SARS-CoV-2 pneumonia. *Infection*. September 2020. https://doi.org/10.1007/s15010-020-01522-4

105. Elkholy KO, Hegazy O, Erdinc B, Abowali H. Ivermectin: a closer look at a potential remedy. *Cureus*. 2020;12(9):e10378. https://doi.org/10.7759/cureus.10378

106. Quadruple therapy with ivermectin is effective in treating COVID-19. *The Hindu*. 2020. https://web.archive.org/web/20200917040005/https://www.thehindu.com/news/national/karnataka/quadruple-therapy-with-ivermectinis-effective-in-treating-covid-19/article32601262.ece

107. Carvallo H, Hirsch R, Farinella ME. Safety and efficacy of the combined use of ivermectin dexamethasone, enoxaparin and aspirin against COVID 19. *medRxiv*. September 2020. https://doi.org/10.1101/2020.09.10.20191619

108. CovidAnalysis. Analysis of: Safety and efficacy of the combined use of ivermectin, dexamethasone, enoxaparin and aspirin against COVID-19. 2020. https://web.archive.org/web/20210211203641/https://c19ivermectin.com/carvallo.html

109. Carvallo H. Ivermectin, aspirin, dexamethasone and enoxaparin as treatment of Covid 19. *ClinicalTrialsgov*. 2020. https://clinicaltrials.gov/ct2/show/NCT04425863

110. Coronavirus: las lecciones no aprendidas de Loreto. *Caretas*. 2020. https://web.archive.org/web/20210224151105/https://caretas.pe/nacional/coronavirus-las-lecciones-no-aprendidas-de-loreto/

111. Li N, Zhao L, Zhan X. Quantitative proteomics reveals a broad-spectrum antiviral property of ivermectin benefiting for COVID-19 treatment. *Journal of Cellular Physiology*. 2020;236(4):2959–2975. https://doi.org/10.1002/jcp.30055

112. Khan MSI, Khan MSI, Debnath CR, et al. Ivermectin treatment may improve the prognosis of patients with COVID-19. *Archivos de Bronconeumología*. 2020;56(12):828–830. https://doi.org/10.1016/j.arbres.2020.08.007

113. Tilli M, Olliaro P, Gobbi F, Bisoffi Z, Bartoloni A, Zammarchi L. Neglected tropical diseases in non-endemic countries in the era of COVID-19 pandemic: the great forgotten. *Journal of Travel Medicine*.

2020;28(1). https://doi.org/10.1093/jtm/taaa179

114. Chachar AZK, Khan KA, Asif M, Tanveer K, Khaqan A, Basri R. Effectiveness of ivermectin in SARS-CoV-2/COVID-19 patients. *International Journal of Sciences*. 2020;9(09):31–35. https://doi.org/10.18483/ijsci.2378

115. Chamie J. Real-world evidence: the case of Peru. Causality between ivermectin and COVID-19 infection fatality rate. *ResearchGate*. 2020. https://www.researchgate.net/publication/344469305_Real-World_Evidence_The_Case_of_Peru_Causality_between_Ivermectin_and_COVID-19_Infection_Fatality_Rate

116. Chamie J. Real-world evidence: the case of Peru. *TrialSite News*. 2020. https://web.archive.org/web/20201021075542/https://trialsitenews.com/real-world-evidence-the-case-of-peru/

117. Francés-Monerris A, Garcia-Iriepa C, Iriepa I, et al. Has ivermectin virus-directed effects against SARS-CoV-2? Rationalizing the action of a potential multitarget antiviral agent. *chemRxiv*. August 2020. https://doi.org/10.26434/chemrxiv.12782258.v1

118. Soto-Becerra P, Culquichicón C, Hurtado-Roca Y, Araujo-Castillo RV. Real-world effectiveness of hydroxychloroquine azithromycin, and ivermectin among hospitalized COVID-19 patients: results of a target trial emulation using observational data from a nationwide healthcare system in Peru. *medRxiv*. October 2020. https://doi.org/10.1101/2020.10.06.20208066

119. Soto-Becerra P, Culquichicón C, Hurtado-Roca Y, Araujo-Castillo RV. Real-world effectiveness of hydroxychloroquine, azithromycin and ivermectin among hospitalized COVID-19 patients: results of a target trial emulation using observational data from a nationwide healthcare system in Peru. *SSRN Electronic Journal*. 2020. https://doi.org/10.2139/ssrn.3710623

120. Yim PJ. Systemic unreported protocol violations in key ivermectin study. *TrialSite News*. 2021. https://trialsitenews.com/systemic-unreported-protocol-violations-in-key-ivermectin-study/

121. CovidAnalysis. Analysis of: Real-world effectiveness of hydroxychloroquine, azithromycin, and ivermectin among hospitalized COVID-19 patients: results of a target trial emulation using observational data from a nationwide healthcare system in Peru. 2020. https://c19ivermectin.com/sotobecerrai.html

122. Mahmud R. Clinical trial of ivermectin plus doxycycline for the treatment of confirmed Covid-19 infection. *ClinicalTrialsgov*. 2020. https://clinicaltrials.gov/ct2/show/results/NCT04523831

123. CovidAnalysis. An analysis of: Clinical trial of ivermectin plus doxycycline for the treatment of confirmed Covid-19 infection. 2020. https://c19ivermectin.com/mahmud.html

124. COVID-19: Goa CM Pramod Sawant launches 'home isolation kit'. *2LT News*. 2020. https://web.archive.org/web/20201013035055/https://www.2lt.com.au/covid-19-goa-cm-pramod-sawant-launches-home-isolation-kit/

125. Kant S, Rastogi H, Bajpai J, Aggarwal KK. Ivermectin – a potent weapon in the anti-COVID-19 armamentarium. *Indian Journal of Clinical Practice*. 2020;31(5). https://ijcp.in/Admin/CMS/PDF/6.%20ReviewArticle2_IJCP_OCT2020.pdf

126. Medtalks. Ivermectin: a potent weapon in the anti-COVID armamentarium. 2020. https://youtu.be/HN06xiTmdZc

127. Scheim D. From cold to killer: how SARS-CoV-2 evolved without hemagglutinin esterase to agglutinate then clot blood cells in pulmonary and systemic microvasculature. *SSRN Electronic Journal*. 2020. https://doi.org/10.2139/ssrn.3706347

128. Resolución Ministerial N° 839-2020-MINSA. 2020. https://www.gob.pe/institucion/minsa/normas-legales/1264399-839-2020-minsa

129. Controversia sobre el uso de la hidroxicloroquina, azitromicina e ivermectina en tratamiento hospitalario. *Caretas*. 2020. https://caretas.pe/nacional/controversia-sobre-el-uso-de-la-hidroxicloroquina-azitromicina-e-ivermectina-en-tratamiento-hospitalario/

130. Carvallo HE. Usefulness of topic ivermectin and carrageenan to prevent contagion of Covid 19 (IVERCAR) (NCT04425850) – Study Results. *ClinicalTrialsgov*. 2020. https://clinicaltrials.gov/ct2/show/results/NCT04425850

131. CovidAnalysis. Analysis of: Usefulness of topic ivermectin and carrageenan to prevent contagion of Covid 19 (IVERCAR). 2020. https://c19ivermectin.com/carvalloprep2.html

132. Interview with Dr. Hector Carvallo: pioneer in ivermectin, iota carrageenan, bromhexine and COVID-19. *Whiteboard Doctor*. 2020. https://youtu.be/CB6Bvi_g-w8

133. Guerrero R, Bravo LE, Muñoz E, Ardila EKG, Guerrero E. COVID-19: The ivermectin African enigma. *Colombia Médica*. 2020;51(4):e-2014613. https://doi.org/10.25100/cm.v51i4.4613

134. CovidAnalysis. Analysis of: COVID-19: the ivermectin African enigma. 2020. https://c19ivermectin.com/guerrero.html

135. Hashim HA, Maulood MF, Rasheed AM, Fatak DF, Kabah KK, Abdulamir AS. Controlled randomized clinical trial on using Ivermectin with Doxycycline for treating COVID-19 patients in Baghdad Iraq. *medRxiv*. October 2020. https://doi.org/10.1101/2020.10.26.20219345

136. CovidAnalysis. Analysis of: Controlled randomized clinical trial on using ivermectin with doxycycline for treating COVID-19 patients in Baghdad, Iraq. 2020. https://c19ivermectin.com/hashim.html

137. Gupta PSS, Biswal S, Panda SK, Ray AK, Rana MK. Binding mechanism and structural insights into the identified protein target of COVID-19 and importin-α with in-vitro effective drug ivermectin. *Journal of Biomolecular Structure and Dynamics*. October 2020:1–10. https://doi.org/10.1080/07391102.2020.1839564

138. Turkia M. The History of Methylprednisolone, Ascorbic Acid, Thiamine, and Heparin Protocol and I-MASK+ Ivermectin Protocol for COVID-19. *Cureus*. December 2020. https://doi.org/10.7759/cureus.12403

139. FLCCC Alliance. I-MASK+ Protocol. 2020. https://covid19criticalcare.com/covid-19-protocols/i-mask-plus-protocol/

140. Aguirre-Chang G, Trujillo Figueredo A. COVID-19: efficacy of pre-exposure prophylaxis with ivermectin in exposed persons. *ResearchGate*. October 2020. https://www.researchgate.net/publication/347890660_COVID-19_EFFICACY_OF_PRE-EXPOSURE_PROPHYLAXIS_WITH_IVERMECTIN_IN_EXPOSED_PERSONS

141. r/covidlonghaulinfo. *Reddit*. 2020. https://www.reddit.com/r/covidlonghaulinfo/

142. Behera P, Patro BK, Singh AK, et al. Role of ivermectin in the prevention of COVID-19 infection among healthcare workers in India: a matched case-control study. *medRxiv*. November 2020. https://doi.org/10.1101/2020.10.29.20222661

143. Behera P, Patro BK, Singh AK, et al. Role of ivermectin in the prevention of SARS-CoV-2 infection among healthcare workers in India: a matched case-control study. Adrish M, ed. *PLOS ONE*. 2021;16(2):e0247163. https://doi.org/10.1371/journal.pone.0247163

144. Morgenstern J, Redondo JN, León AD, et al. The use of compassionate ivermectin in the management of symptomatic outpatients and hospitalized patients with clinical diagnosis of Covid-19 at the Centro Medico Bournigal and at the Centro Medico Punta Cana, Grupo Rescue, Dominican Republic, from May 1 to August 10, 2020. *J Clin Trials*. 2020;11(59). https://www.longdom.org/open-access/the-use-of-compassionate-ivermectin-in-the-management-of-symptomatic-outpatients-and-hospitalized-patients-with-clinical.pdf

145. Cadegiani FA, Goren A, Wambier CG, McCoy J. Early COVID-19 therapy with azithromycin plus nitazoxanide ivermectin or hydroxychloroquine in outpatient settings significantly reduced symptoms compared to known outcomes in untreated patients. *medRxiv*. November 2020. https://doi.org/10.1101/2020.10.31.20223883

146. Cadegiani FA, Goren A, McCoy J, Wambier CG. Hydroxychloroquine nitazoxanide and ivermectin have similar effects in early COVID-19: a head-to-head comparison of the Pre-AndroCoV trial. *Research Square*. October 2020. https://doi.org/10.21203/rs.3.rs-98106/v1

147. CovidAnalysis. Analysis of: Early COVID-19 therapy with azithromycin plus nitazoxanide, ivermectin or hydroxychloroquine in outpatient settings significantly reduced symptoms compared to known outcomes in untreated patients. 2020. https://c19ivermectin.com/cadegianii.html

148. France: the ivermectin dossier before the council of state. *Covexit*. 2021. https://web.archive.org/web/20210120110202/https://covexit.com/france-the-ivermectin-dossier-before-the-council-of-state/

149. Turkia M. FLCCC Alliance MATH+ ascorbic acid and I-MASK+ ivermectin protocols for COVID-19 – a brief review. *SSRN Electronic Journal*. 2020. https://doi.org/10.2139/ssrn.3723854

150. CovidAnalysis. Analysis of: FLCCC Alliance MATH+ ascorbic acid and I-MASK+ ivermectin protocols for COVID-19 — a brief review. 2020. https://c19ivermectin.com/turkia.html

151. Krolewiecki A, Lifschitz A, Moragas M, et al. Antiviral effect of high-dose ivermectin in adults with COVID-19: a pilot randomised controlled, open label, multicentre trial. *SSRN Electronic Journal*. 2020. https://doi.org/10.2139/ssrn.3714649

152. Camprubí D, Almuedo-Riera A, Martí-Soler H, et al. Lack of efficacy of standard doses of ivermectin in severe COVID-19 patients. Dorlo TPC, ed. *PLOS ONE*. 2020;15(11):e0242184. https://doi.org/10.1371/journal.pone.0242184

153. CovidAnalysis. Analysis of: Lack of efficacy of standard doses of ivermectin in severe COVID-19 patients. 2020. https://c19ivermectin.com/camprubi.html

154. Alan Cannell talks COVID-19: nobody likes cheap solutions – podcast S2 E41. *TrialSite News*. 2020. https://trialsitenews.com/alan-cannell-talks-covid-19-nobody-likes-cheap-solutions-podcast-s2-e41/

155. Elgazzar A, Hany B, Youssef SA, Hany B, Hafez M, Moussa H. Efficacy and safety of ivermectin for treatment and prophylaxis of COVID-19 pandemic. *Research Square*. November 2020. https://doi.org/10.21203/rs.3.rs-100956/v1

156. CovidAnalysis. Analysis of: Efficacy and safety of ivermectin for treatment and prophylaxis of COVID-19 pandemic. 2020. https://c19ivermectin.com/elgazzarpep.html

157. Kory P, Meduri GU, Iglesias J, et al. Review of the emerging evidence demonstrating the efficacy of ivermectin in the prophylaxis and treatment of COVID-19. *OSF Preprints*. November 2020. https://doi.org/10.31219/osf.io/wx3zn

158. CovidAnalysis. Utility of ivermectin and doxycycline combination for the treatment of SARS-CoV-2. 2020. https://c19ivermectin.com/spoorthi.html

159. Spoorthi V, Sasank S. Utility of ivermectin and doxycycline combination for the treatment of SARS-CoV-2. *IAIM*. 2020;7(10):177–182. http://iaimjournal.com/wp-content/uploads/2020/10/iaim_2020_0710_23.pdf

160. Carvallo H, Hirsch R, Alkis P, Contreras V. Study of the efficacy and safety of topical ivermectin + iota-carrageenan in the prophylaxis against COVID-19 in health personnel. *Journal of Biomedical Research and Clinical Investigation*. 2020;2(1). https://doi.org/10.31546/2633-8653.1007

161. CovidAnalysis. Analysis of: Study of the efficacy and safety of topical ivermectin + iota-carrageenan in the prophylaxis against COVID-19 in health personnel. 2020. https://c19ivermectin.com/carvalloprep.html

162. Hirsch RR, Carvallo HE. Covid 19 and ivermectin prevention and treatment update. *Journal of Infectious Diseases & Travel Medicine*. 2020;4(S1). https://doi.org/10.23880/jidtm-16000s1-007

163. Kamen J. Facebook censored our posts. And that just might cost many people their lives. *Medium*. 2020. https://web.archive.org/web/20210305164645/https://joyce-kamen.medium.com/facebook-censored-our-posts-and-that-just-might-cause-many-people-their-lives-be3c9e09acbd

164. Budhiraja S, Soni A, Jha V, et al. Clinical profile of first 1000 COVID-19 cases admitted at tertiary care hospitals and the correlates of their mortality: an Indian experience. *medRxiv*. November 2020. https://doi.org/10.1101/2020.11.16.20232223

165. CovidAnalysis. Analysis of: Clinical profile of first 1000 COVID-19 cases admitted at tertiary care hospitals and the correlates of their mortality: an Indian experience. 2020.
https://c19ivermectin.com/budhirajai.html

166. Early outpatient treatment: an essential part of a COVID-19 solution. Full committee hearing. *US Senate Committee on Homeland Security & Governmental Affairs*. 2020.
https://www.hsgac.senate.gov/hearings/early-outpatient-treatment-an-essential-part-of-a-covid-19-solution

167. Fareed G. My reflections on the suppression of early C19 treatment. *Twitter*. 2021.
https://web.archive.org/web/20210323122411/https://twitter.com/GeorgeFareed2/status/1360717827359997952?s=20

168. CovidAnalysis. HCQ is effective for COVID-19 when used early: analysis of 143 studies. 2020.
https://web.archive.org/web/20201119043548/https://hcqmeta.com/

169. Jha A. Opinion: the snake-oil salesmen of the Senate. *New York Times*. 2020.
https://web.archive.org/web/20201204013806/https://www.nytimes.com/2020/11/24/opinion/hydroxychloroquine-covid.html

170. Niaee MS, Gheibi N, Namdar P, et al. Ivermectin as an adjunct treatment for hospitalized adult COVID-19 patients: a randomized multi-center clinical trial. *Research Square*. November 2020.
https://doi.org/10.21203/rs.3.rs-109670/v1

171. CovidAnalysis. Analysis of: Ivermectin as an adjunct treatment for hospitalized adult COVID-19 patients: a randomized multi-center clinical trial. 2020. https://c19ivermectin.com/niaee.html

172. Ladapo JA. Opinion: too much caution is killing Covid patients. *Wall Street Journal*. 2020.
https://web.archive.org/web/20210310063317/https://www.wsj.com/articles/too-much-caution-is-killing-covid-patients-11606238928

173. CovidAnalysis. Ivermectin is effective for COVID-19: analysis of 20 studies. 2020.
https://web.archive.org/web/20201126092305/https://ivmmeta.com/

174. Syed M. How ivermectin helps against SARS-COV-2?. 2020. https://youtu.be/JEO7Adv3tVI

175. Zhang X, Song Y, Ci X, et al. Ivermectin inhibits LPS-induced production of inflammatory cytokines and improves LPS-induced survival in mice. *Inflammation Research*. 2008;57(11):524–529.
https://doi.org/10.1007/s00011-008-8007-8

176. Ci X, Li H, Yu Q, et al. Avermectin exerts anti-inflammatory effect by downregulating the nuclear transcription factor kappa-B and mitogen-activated protein kinase activation pathway. *Fundamental & Clinical Pharmacology*. 2009;23(4):449–455. https://doi.org/10.1111/j.1472-8206.2009.00684.x

177. Zhang X, Song Y, Xiong H, et al. Inhibitory effects of ivermectin on nitric oxide and prostaglandin E2 production in LPS-stimulated RAW 264.7 macrophages. *International Immunopharmacology*. 2009;9(3):354–359. https://doi.org/10.1016/j.intimp.2008.12.016

178. Mittal N, Mittal R. Inhaled route and anti-inflammatory action of ivermectin: Do they hold promise in fighting against COVID-19?. *Medical Hypotheses*. 2021;146:110364.
https://doi.org/10.1016/j.mehy.2020.110364

179. Andersson U, Ottestad W, Tracey KJ. Extracellular HMGB1: a therapeutic target in severe pulmonary inflammation including COVID-19?. *Molecular Medicine*. 2020;26(1).
https://doi.org/10.1186/s10020-020-00172-4

180. Hellwig MD, Maia A. A COVID-19 prophylaxis? Lower incidence associated with prophylactic administration of ivermectin. *International Journal of Antimicrobial Agents*. 2021;57(1):106248.
https://doi.org/10.1016/j.ijantimicag.2020.106248

181. Bernigaud C, Guillemot D, Ahmed-Belkacem A, et al. Bénéfice de l'ivermectine : de la gale à la COVID-19 un exemple de sérendipité. *Annales de Dermatologie et de Vénéréologie*. 2020;147(12):A194.
https://doi.org/10.1016/j.annder.2020.09.231

182. CovidAnalysis. Ivermectin benefit: from scabies to COVID-19, an example of serendipity. 2020.
https://c19ivermectin.com/bernigaud.html

183. CovidAnalysis. Analysis of: COVID-19: uso de ivermectina. 2020. https://c19ivermectin.com/alonso.html

184. Ahmed S, Karim MM, Ross AG, et al. A five-day course of ivermectin for the treatment of COVID-19 may reduce the duration of illness. *International Journal of Infectious Diseases*. 2021;103:214–216. https://doi.org/10.1016/j.ijid.2020.11.191

185. CovidAnalysis. A five day course of ivermectin for the treatment of COVID-19 may reduce the duration of illness. 2020. https://c19ivermectin.com/ahmed.html

186. CovidAnalysis. The effect of using ivermectin to control COVID-19 in Chiapas. 2020. https://c19ivermectin.com/chamie.html

187. Luna C. Repartirán 10 mil kits con Ivermectina para combatir Covid-19 en Tuxtla. *El Sie7e*. 2020. https://web.archive.org/web/20200905213121/https://www.sie7edechiapas.com/post/repartir%C3%A1n-10-mil-kits-con-ivermectina-para-combatir-covid-19-en-tuxtla

188. Chamie J. Covid19Crusher: Ignoring the national guidelines, the Mexican State of Chiapas has decided to treat early with teams going door to door and giving a cocktail of drugs with ivermectin since July. *Twitter*. 2020. https://web.archive.org/web/20201203104414/https://twitter.com/Covid19Crusher/status/1334448128922165248

189. FLCCC Alliance. FLCCC Alliance calls on national health authorities to immediately review medical evidence showing the efficacy of ivermectin for the prevention of COVID-19 and as an early outpatient treatment. 2020. https://web.archive.org/web/20210323124932/https://covid19criticalcare.com/wp-content/uploads/2020/11/FLCCC-News-Conference-at-UMMC-Houston-Dec4.pdf

190. CovidAnalysis. Analysis of: The effect of early treatment with ivermectin on viral load, symptoms and humoral response in patients with non-severe COVID-19: a pilot, double-blind, placebo-controlled, randomized clinical trial. 2020. https://c19ivermectin.com/chaccour.html

191. Chaccour C, Casellas A, Matteo AB-D, et al. The effect of early treatment with ivermectin on viral load symptoms and humoral response in patients with non-severe COVID-19: A pilot, double-blind, placebo-controlled, randomized clinical trial. *EClinicalMedicine*. 2021;32:100720. https://doi.org/10.1016/j.eclinm.2020.100720

192. Edmondson C, Fandos N. Elevating fringe theories, Ron Johnson questions virus science. *The New York Times*. 2020. https://web.archive.org/web/20201209011103/https://www.nytimes.com/2020/12/07/us/politics/ron-johnson-coronavirus.html

193. TrialSite News. Fox News reports on the YouTube censorship of the Senate hearing testimony by Dr. Pierre Kory of the FLCCC. 2021. https://web.archive.org/web/20210214000408/https://trialsitenews.com/fox-news-reports-on-the-youtube-censorship-of-the-senate-hearing-testimony-by-dr-pierre-kory-of-the-flccc/

194. CovidAnalysis. Analysis of: Outcome of ivermectin and doxycycline in cancer patients with COVID-19: A positive experience in Bangladesh. 2020. https://c19ivermectin.com/hussain.html

195. Hussain SMA, Shuayb M, Rahman M. Outcome of ivermectin and doxycycline in cancer patients with COVID-19: a positive experience in Bangladesh. *International Journal of Molecular & Immuno Oncology*. 2021;6:27–29. https://web.archive.org/web/20210116101054/https://ijmio.com/outcome-of-ivermectin-and-doxycycline-in-cancer-patients-with-covid-19-a-positive-experience-in-bangladesh/

196. Dupuy B. No evidence ivermectin is a miracle drug against COVID-19. *The Associated Press*. 2020. https://web.archive.org/web/20210302192011/https://apnews.com/article/fact-checking-afs:Content:9768999400

197. Afsar N, Ghauri MI, Abbas M, Mukarram MS, Peracha MY, Ishaq K. Ivermectin use associated with reduced duration of COVID-19 febrile illness in a community setting. *SSRN Electronic Journal*. 2020. https://doi.org/10.2139/ssrn.3734478

198. CovidAnalysis. Analysis of: Ivermectin use associated with reduced duration of COVID-19 febrile illness in a community setting. 2021. https://c19ivermectin.com/afsar.html

199. Alam MT, Murshed R, Gomes PF, et al. Ivermectin as pre-exposure prophylaxis for COVID-19 among healthcare providers in a selected tertiary hospital in Dhaka – an observational study. *European Journal of Medical and Health Sciences*. 2020;2(6). https://doi.org/10.24018/ejmed.2020.2.6.599

200. CovidAnalysis. Analysis of: Ivermectin as pre-exposure prophylaxis for COVID-19 among healthcare providers in a selected tertiary hospital in Dhaka – an observational study. 2021. https://c19ivermectin.com/alam2.html

201. US National Institutes of Health. Prevention of SARS-CoV-2 – COVID-19 treatment guidelines. 2020. https://web.archive.org/web/20201225012308/https://www.covid19treatmentguidelines.nih.gov/overview/prevention-of-sars-cov-2/

202. CovidAnalysis. Analysis of: Review of the emerging evidence demonstrating the efficacy of ivermectin in the prophylaxis and treatment of COVID-19. 2020. https://c19ivermectin.com/kory.html

203. News BB. Ministry of Health now using ivermectin to treat COVID-19 patients. 2020. https://web.archive.org/web/20201218233647/https://www.breakingbelizenews.com/2020/12/18/ministry-of-health-now-using-ivermectin-to-treat-covid-19-patients/

204. MedinCell. Exploratory Ph I trial of the active IMP in healthy volunteers in relation to COVID-19. *ClinicalTrialsgov*. 2020. https://clinicaltrials.gov/ct2/show/NCT04632706

205. Covid-19: MedinCell presents positive first results from the clinical trial aiming at validating the safety of continuous administration of ivermectin. *Business Wire*. 2020. https://web.archive.org/web/20201217234915/https://www.businesswire.com/news/home/20201217006031/en/Covid-19-MedinCell-Presents-Positive-First-Results-From-the-Clinical-Trial-Aiming-at-Validating-the-Safety-of-Continuous-Administration-of-Ivermectin

206. MedinCell's mission for 'mass roll-out' of ivermectin for COVID-19: early study data points reveal promise. *TrialSite News*. 2020. https://web.archive.org/web/20210314204832/https://trialsitenews.com/medincells-mission-for-mass-roll-out-of-ivermectin-for-covid-19-early-study-data-points-reveal-promise/

207. Vallejos J, Zoni R, Bangher M, et al. Ivermectin to prevent hospitalizations in patients with COVID-19 (IVERCOR-COVID19): a structured summary of a study protocol for a randomized controlled trial. *Trials*. 2020;21(1). https://doi.org/10.1186/s13063-020-04813-1

208. CovidAnalysis. Analysis of: Ivermectin to prevent hospitalizations in patients with COVID-19 (IVERCOR-COVID19): a structured summary of a study protocol for a randomized controlled trial. 2020. https://c19ivermectin.com/vallejos.html

209. Bonaccorsi G. Covid, Cacopardo: «Ho avviato la profilassi con Ivermectina. Risultati fra una settimana». *La Sicilia*. 2020. https://web.archive.org/web/20201221172010/https://www.lasicilia.it/news/covid-19/380277/covid-cacopardo-ho-avviato-la-profilassi-con-ivermectina-risultati-fra-una-settimana.html

210. Merck & Co/MSD. Merck announces supply agreement with U.S. government for initial doses of investigational biological therapy for the treatment of patients with severe and critical COVID-19. 2020. https://web.archive.org/web/20201223114845/https://www.merck.com/news/merck-announces-supply-agreement-with-u-s-government-for-initial-doses-of-investigational-biological-therapy-for-the-treatment-of-patients-with-severe-and-critical-covid-19/

211. Burns M. MALMED will approve ivermectin, but then will beg the pharmaceutical companies to bring it because it is not a cure for business. *Free Press*. 2020. https://web.archive.org/web/20210224193658/https://www.slobodenpecat.mk/en/malmed-ke-go-odobri-ivermektinot-ama-posle-ke-gi-moli-farmaczevtskite-kuki-da-go-donesat-zashto-ne-e-lek-za-biznis/

212. Githahu M. SA drugs regulator bans 'miracle' Covid-19 treatment as unsafe. *Independent Online*. 2020. https://web.archive.org/web/20201224085259/https://www.iol.co.za/capeargus/news/sa-drugs-regulator-bans-miracle-covid-19-treatment-as-unsafe-4e36c339-c65c-4cc6-93d2-d7e748eefcb6

213. Hill A. Ivermectin meta-analysis by Dr. Andrew Hill. 2020. http://youtu.be/yOAh7GtvcOs

214. Unitaid. About us. 2021. https://unitaid.org/about-us/

215. WHO. What is the ACT-Accelerator. 2021.
https://www.who.int/initiatives/act-accelerator/about

216. CovidAnalysis. Twitter censors @CovidAnalysis scientific research. 2020.
https://web.archive.org/web/20210323131154/https://ivmmeta.com/twitter.html

217. McCullough PA, Alexander PE, Armstrong R, et al. Multifaceted highly targeted sequential multidrug treatment of early ambulatory high-risk SARS-CoV-2 infection (COVID-19). *Reviews in Cardiovascular Medicine*. 2020;21(4):517. https://doi.org/10.31083/j.rcm.2020.04.264

218. Madrid RRM, Mathews PD, Patta ACMF, et al. Safety of oral administration of high doses of ivermectin by means of biocompatible polyelectrolytes formulation. *Heliyon*. 2021;7(1):e05820.
https://doi.org/10.1016/j.heliyon.2020.e05820

219. Reynier M, Allart S, Goudounèche D, et al. The actin-based motor myosin Vb Is crucial to maintain epidermal barrier integrity. *Journal of Investigative Dermatology*. 2019;139(7):1430–1438.
https://doi.org/10.1016/j.jid.2018.12.021

220. Wijaya NS, Salim S. Ivermectin as a potential therapeutic agent for COVID-19 – case studies. *Cermin Dunia Kedokteran*. 2020;47(5):370–372.
https://web.archive.org/web/20210323131940/https://kalbemed.com/cdk/download/211

221. Lawrie TA. Ivermectin reduces the risk of death from COVID-19 – a rapid review and meta-analysis in support of the recommendation of the Front Line COVID-19 Critical Care Alliance. 2021.
https://www.researchgate.net/publication/348230894_Ivermectin_reduces_the_risk_of_death_from_COVID-19_-a_rapid_review_and_meta-analysis_in_support_of_the_recommendation_of_the_Front_Line_COVID-19_Critical_Care_Alliance

222. Lawrie TA. Ivermectin reduces the risk of death from COVID-19 – a rapid review and meta-analysis in support of the recommendation of the Front Line COVID-19 Critical Care Alliance (latest version v1.2 - 6 Jan 2021). 2021.
https://www.researchgate.net/publication/348297284_Ivermectin_reduces_the_risk_of_death_from_COVID-19_-a_rapid_review_and_meta-analysis_in_support_of_the_recommendation_of_the_Front_Line_COVID-19_Critical_Care_Alliance_Latest_version_v12_-_6_Jan_2021

223. Kaur H, Shekhar N, Sharma S, Sarma P, Prakash A, Medhi B. Ivermectin as a potential drug for treatment of COVID-19: an in-sync review with clinical and computational attributes. *Pharmacological Reports*. January 2021. https://doi.org/10.1007/s43440-020-00195-y

224. Campbell J. Ivermectin evidence with Dr Tess Lawrie. *YouTube*. 2021.
https://youtu.be/vYF8bnmdQfY?t=1331

225. Cheap drug could be 'transformative' COVID-19 treatment. *Arab News*. 2021.
https://web.archive.org/web/20210313054718/https://arab.news/cfaqm

226. Oxford University to test potential COVID-19 'wonder drug' ivermectin. *Arab News*. 2021.
https://web.archive.org/web/20210313055104/https://arab.news/rq46h

227. Hirsch RR, Carvallo HE. Ivermectin as prophylaxis against COVID-19 retrospective cases evaluation. *Microbiol Infect Dis*. 2020;4(4):1–8. https://scivisionpub.com/pdfs/ivermectin-as-prophylaxis-against-covid19-retrospective-cases-evaluation-1458.pdf

228. Babalola OE, Bode CO, Ajayi AA, et al. Ivermectin shows clinical benefits in mild to moderate COVID19: a randomised controlled double-blind dose-response study in Lagos. *QJM: An International Journal of Medicine*. February 2021. https://doi.org/10.1093/qjmed/hcab035

229. FLCCC Alliance. FLCCC Alliance invited to the National Institutes of Health (NIH) COVID-19 Treatment Guidelines Panel to present latest data on ivermectin. 2021.
https://web.archive.org/web/20210128043136/https://covid19criticalcare.com/wp-content/uploads/2021/01/FLCCC-PressRelease-NIH-C19-Panel-FollowUp-Jan7-2021.pdf

230. Fiore K. What's behind the ivermectin-for-COVID buzz?. *MedPage Today*. January 2021.
https://web.archive.org/web/20210312080454/https://www.medpagetoday.com/infectiousdisease/covid19/90552

231. Chamie J. Cumulative COVID-19 deaths in Mexico from July 1, 2020 to Jan 6, 2021. 2021. https://web.archive.org/web/20210225180126/https://twitter.com/Covid19Crusher/status/1347462606186029057

232. Ivermectina vuelve a ser incluida en tratamiento COVID-19. *Extra*. 2021. https://web.archive.org/web/20210311113311/https://www.extra.com.pe/actualidad/ivermectina-vuelve-a-ser-incluida-en-tratamiento-covid-19/

233. South African authorities raid hospital in search of ivermectin. *TrialSite News*. 2021. https://web.archive.org/web/20210109130425/https://trialsitenews.com/south-african-authorities-raid-hospital-in-search-of-ivermectin/

234. South African Health Products Regulatory Authority (SAHPRA) bans ivermectin with criminal liability. *TrialSite News*. 2021. https://web.archive.org/web/20210323072901/https://trialsitenews.com/south-african-health-products-regulatory-authority-sahpra-bans-ivermectin-with-criminal-liability/

235. Kirti R, Roy R, Pattadar C, et al. Ivermectin as a potential treatment for mild to moderate COVID-19 – a double blind randomized placebo-controlled trial. *medRxiv*. January 2021. https://doi.org/10.1101/2021.01.05.21249310

236. Kirti R. CTRI/2020/08/027225: Ivermectin as a potential treatment for COVID 19: a double blind randomized placebo-controlled trial. *National Institute of Medical Statistics (NIMS) Clinical Trials Registry – India*. 2020. https://web.archive.org/web/20210314153218/http://ctri.nic.in/Clinicaltrials/showallp.php?mid1=46660&EncHid=&userName=ravi+kirti

237. Lawrie T. Message to Mr Johnson from Dr Tess Lawrie. *YouTube*. 2021. https://youtu.be/M8RMBa1UfsE

238. Lawrie T. Ivermectine: message à Boris Johnson de la Dresse Tess Lawrie. *YouTube*. 2021. https://youtu.be/l41j6V4sLQs

239. Accueil - L'ivermectine comme traitement de la COVID 19. https://web.archive.org/web/20210317210655/https://ivermectine-covid.ch/

240. Lawrie T. Dr. Tess Lawrie's systematic review on the drug DWISAMAB (the Drug Which Shall not be Named). *YouTube*. 2021. https://youtu.be/IgSlOeW_N4M

241. Medical Update Online. In discussion with Dr Tess Lawrie - full interview. *YouTube*. 2021. https://youtu.be/HXY86q3XAGI

242. Clark C. Ivermectin gathers pace in Europe. *Medical Update Online*. 2021. https://web.archive.org/web/20210318105405/https://medicalupdateonline.com/2021/01/ivermectin-gathers-pace-in-europe/

243. Bousquet-Melou A, Lespine A, Sutra J-F, Bargues I, Toutain PL. Large Impact of obesity on the disposition of ivermectin, moxidectin and eprinomectin in a canine model: relevance for COVID-19 patients. *Authorea*. January 2021. https://doi.org/10.22541/au.161047848.80388481/v1

244. Chahla RE. Prophylaxis Covid-19 in healthcare agents by intensive treatment with ivermectin and iota-carrageenan. *ClinicalTrialsgov*. 2021. https://clinicaltrials.gov/ct2/show/NCT04701710

245. Burns M. MALMED confirmed for Free Press: ivermectin has arrived in Macedonia. *Free Press*. 2021. https://web.archive.org/web/20210112064906/https://www.slobodenpecat.mk/en/malmed-potvrdi-za-sloboden-pechat-ivermektinot-stigna-vo-makedonija/

246. Blasius H. Ivermectin: Glühende Verfechter und rationale Skeptiker. *Deutsche Apotheker Zeitung (DAZ)*. 2021. https://web.archive.org/web/20210112090649/https://www.deutsche-apotheker-zeitung.de/news/artikel/2021/01/11/ivermectin-gluehende-verfechter-und-rationale-skeptiker

247. Okumuş N, Demirtürk N, ÇETİNKAYA RA, et al. Evaluation of the effectiveness and safety of adding ivermectin to treatment in severe COVID-19 patients. *Research Square*. February 2021. https://doi.org/10.21203/rs.3.rs-224203/v1

248. Review of the emerging evidence demonstrating the efficacy of ivermectin in the prophylaxis and treatment of COVID-19. 2021. https://web.archive.org/web/20210227102954/https://www.frontiersin.org/articles/10.3389/fphar.2021.643369/abstract

249. US National Institutes of Health. Ivermectin – COVID-19 treatment guidelines. 2021. https://web.archive.org/web/20210323023006/https://www.covid19treatmentguidelines.nih.gov/antiviral-therapy/ivermectin/

250. US National Institutes of Health. Financial disclosure – COVID-19 treatment guidelines. 2021. https://web.archive.org/web/20210323022912/https://www.covid19treatmentguidelines.nih.gov/panel-financial-disclosure/

251. Orient JM. Association of American Physicians and Surgeons (AAPS) applauds NIH revised stance on ivermectin for COVID-19. *Association of American Physicians and Surgeons*. 2021. https://web.archive.org/web/20210115203058/http://www.globenewswire.com/news-release/2021/01/15/2159575/0/en/Association-of-American-Physicians-and-Surgeons-AAPS-Applauds-NIH-Revised-Stance-on-Ivermectin-for-COVID-19.html

252. Herbeck D. After judge orders hospital to use experimental Covid-19 treatment, woman recovers. *Buffalo News*. 2021. https://web.archive.org/web/20210127174545/https://buffalonews.com/news/local/after-judge-orders-hospital-to-use-experimental-covid-19-treatment-woman-recovers/article_a9eb315c-5694-11eb-aac5-53b541448755.html

253. Romero C. Honduras y El Salvador insisten en usar ivermectina frente a la segunda ola. *Salud con lupa*. 2021. https://web.archive.org/web/20210115162522/https://saludconlupa.com/noticias/honduras-y-el-salvador-insisten-en-usar-ivermectina-frente-la-segunda-ola/

254. Bulgarian Drug Agency. Marketing authorization. 2021. https://web.archive.org/web/20210312071419/https://www.economic.bg/web/files/richeditor/marketing-authorization-ial.pdf

255. Asghar A. Efficacy of ivermectin in COVID-19. *Clinicaltrialsgov*. 2021. https://clinicaltrials.gov/ct2/show/NCT04392713

256. Dr. Pierre Kory – 2021 update on ivermectin science – latest studies. 2021. https://youtu.be/34dIZ6O5rjQ

257. Raad H. In vivo use of ivermectin (IVR) for treatment for corona virus infected patients (COVID-19): a randomized controlled trial. *Chinese Clinical Trial Register (ChiCTR)*. 2020. https://web.archive.org/web/20210225171134/http://www.chictr.org.cn/showprojen.aspx?proj=54707

258. Bernigaud C, Guillemot D, Ahmed-Belkacem A, et al. Oral ivermectin for a scabies outbreak in a long-term care facility: potential value in preventing COVID-19 and associated mortality. *British Journal of Dermatology*. March 2021. https://doi.org/10.1111/bjd.19821

259. FLCCC Alliance. FLCCC Alliance response to the NIH guideline committee recommendation on ivermectin use in COVID-19 dated January 14th, 2021. 2021. https://web.archive.org/web/20210124061252/https://covid19criticalcare.com/wp-content/uploads/2021/01/FLCCC-Alliance-Response-to-the-NIH-Guideline-Committee-Recommendation-on-Ivermectin-use-in-COVID19-2021-01-18.pdf

260. Africa CDC. Statement on the use of ivermectin for COVID-19. 2021. https://web.archive.org/web/20210217204320/https://africacdc.org/download/statement-on-the-use-of-ivermectin-for-covid-19/

261. Turkia M. COVID-19 and strongyloidiasis. *SSRN Electronic Journal*. 2021. https://doi.org/10.2139/ssrn.3766955

262. Hill A, Abdulamir A, Ahmed S, et al. Meta-analysis of randomized trials of ivermectin to treat SARS-CoV-2 infection. *Research Square*. January 2021. https://doi.org/10.21203/rs.3.rs-148845/v1

263. Rezai M. Effectiveness of ivermectin in the treatment of coronavirus infection in patients admitted to educational hospitals of Mazandaran in 2020. *Iranian Registry of Clinical Trials*. 2020. https://web.archive.org/web/20210225163213/https://en.irct.ir/trial/49174

264. Iran begins production of new anti-corona medicine. *Tehran Times*. February 2021. https://web.archive.org/web/20210119155413/https://www.tehrantimes.com/news/457126/Iran-begins-production-of-new-anti-corona-medicine

265. Dotinga R. COVID pro tips from hospitalists. *MedPage Today*. January 2021. https://web.archive.org/web/20210121194250/https://www.medpagetoday.com/infectiousdisease/covid19/90797

266. Mody V, Ho J, Wills S, et al. Identification of 3-chymotrypsin like protease (3CLPro) inhibitors as potential anti-SARS-CoV-2 agents. *Communications Biology*. 2021;4(1). https://doi.org/10.1038/s42003-020-01577-x

267. Mancini DP. Cheap antiparasitic could cut chance of Covid-19 deaths by up to 75%. *Financial Times*. 2021. https://www.ft.com/content/e7cb76fc-da98-4a31-9c1f-926c58349c84

268. Chamie-Quintero J, Hibberd J, Scheim D. Sharp reductions in COVID-19 case fatalities and excess deaths in Peru in close time conjunction state-by-state, with ivermectin treatments. *SSRN Electronic Journal*. 2021. https://doi.org/10.2139/ssrn.3765018

269. Blakely R. Trial for Covid 'wonder drug' that could save thousands of lives. *The Times (UK)*. 2021. https://www.thetimes.co.uk/article/trial-for-covid-wonder-drug-that-could-save-thousands-of-lives-99jc07v2s

270. FLCCC Alliance. FLCCC Alliance open letter to the investigators of the Oxford PRINCIPLE trial on ivermectin in COVID-19. 2021. https://web.archive.org/web/20210128043112/https://covid19criticalcare.com/wp-content/uploads/2021/01/FLCCC-Alliance-Open-Letter-to-the-Investigators-of-the-Oxford-PRINCIPLE-Trial-on-Ivermectin-in-COVID-19.pdf

271. Association Bon Sens. 2021. https://web.archive.org/web/20210319032242/https://bonsens.info/

272. Merck & Co/MSD. Merck discontinues development of SARS-CoV-2/COVID-19 vaccine candidates; continues development of two investigational therapeutic candidates. 2021. https://web.archive.org/web/20210125143301/https://www.merck.com/news/merck-discontinues-development-of-sars-cov-2-covid-19-vaccine-candidates-continues-development-of-two-investigational-therapeutic-candidates/

273. L'infettivologo Bruno Cacopardo: «L'Ivermerctina si sta dimostrando efficace contro il Covid». *La Sicilia*. 2021. https://web.archive.org/web/20210125150425/https://www.lasicilia.it/news/covid-19/388033/l-infettivologo-bruno-cacopardo-l-ivermerctina-si-sta-dimostrando-efficace-contro-il-covid.html

274. Bulgarian randomized, double-blind, placebo-controlled ivermectin study shows positive results against COVID-19. *TrialSite News*. 2021. https://web.archive.org/web/20210202173600/https://trialsitenews.com/bulgarian-randomized-double-blind-placebo-controlled-ivermectin-study-shows-positive-results-against-covid-19/

275. Финални тестове за използване на ивермектин в България. *Economic*. 2021. https://web.archive.org/web/20210312072341/https://www.economic.bg/bg/a/view/finalni-testove-za-izpolzvane-na-ivermektin-v-bylgarija

276. Petkov S. Study of ivermectin against COVID-19 (EudraCT 2020-002091-12). *European Medicine Agency Clinical Trials Register*. 2020. https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-002091-12/BG

277. Davis D. David Davis MP asks the Prime Minister about ivermectin & colchicine during PMQs. *YouTube*. 2021. https://youtu.be/0AYDROpDOo8

278. Castañeda-Sabogal A, Chambergo-Michilot D, Toro-Huamanchumo CJ, Silva-Rengifo C, Gonzales-Zamora J, Barboza JJ. Outcomes of ivermectin in the treatment of COVID-19: a systematic review and meta-analysis. *medRxiv*. January 2021. https://doi.org/10.1101/2021.01.26.21250420

279. CovidAnalysis. Analysis of: Outcomes of ivermectin in the treatment of COVID-19: a systematic review and meta-analysis. 2021. https://c19ivermectin.com/castanedasabogal.html

280. Kew J. South Africa allows use of parasite drug to treat Covid patients. *Bloomberg*. 2021. https://web.archive.org/web/20210127222754/https://www.bloomberg.com/news/articles/2021-01-27/south-africa-allows-use-of-parasite-drug-to-treat-covid-patients

281. INSERM. L'ivermectine, nouveau traitement « miracle » contre la Covid-19, vraiment ?. *INSERM*. 2021. https://web.archive.org/web/20210306132840/https://presse.inserm.fr/livermectine-nouveau-traitement-miracle-contre-la-covid-19-vraiment/42011/

282. Major French institute blasts ivermectin, discontinues remdesivir trial. *Covexit*. 2021. https://web.archive.org/web/20210306133045/https://covexit.com/major-french-institute-blasts-ivermectin-discontinues-remdesivir-trial/

283. Tokyo considers trials of parasite drug for COVID-19. *Nikkei Asia*. January 2021. https://web.archive.org/web/20210130045752/https://asia.nikkei.com/Spotlight/Coronavirus/Tokyo-considers-trials-of-parasite-drug-for-COVID-19

284. Primářka ARO: Ivermektin je bezpečný a zbavuje tělo viru. *Novinky*. 2021. https://web.archive.org/web/20210305093204/https://www.novinky.cz/koronavirus/clanek/primarka-aro-ivermektin-je-bezpecny-a-zbavuje-telo-viru-40351618

285. Cassim J. Zimbabwe OKs use of ivermectin after officials' deaths. *Analodu Agency*. 2021. https://web.archive.org/web/20210128005137/https://www.aa.com.tr/en/africa/zimbabwe-oks-use-of-ivermectin-after-officials-deaths/2125442

286. Thomas L. Ivermectin may not be the 'silver bullet' antiviral against COVID-19. *News-Medical*. 2021. https://web.archive.org/web/20210318112256/https://www.news-medical.net/news/20210201/Ivermectin-may-not-be-the-e28098silver-bullete28099-antiviral-against-COVID-19.aspx

287. Johnson R. Opinion: YouTube cancels the U.S. Senate. *Wall Street Journal*. 2021. https://www.wsj.com/articles/youtube-cancels-the-u-s-senate-11612288061

288. Mohan A, Tiwari P, Suri T, et al. Ivermectin in mild and moderate COVID-19 (RIVET-COV): a randomized placebo-controlled trial. *Research Square*. February 2021. https://doi.org/10.21203/rs.3.rs-191648/v1

289. COVID-19 treatments: ivermectin shows promise for poorer nations. *Al Jazeera English*. 2021. https://youtu.be/z7rudChOLJY

290. La ivermectina sigue envuelta en controversia pero investigaciones internacionales apuntan a efectos favorables en casos leves. *Caretas Nacional*. 2021. https://web.archive.org/web/20210204003022/https://caretas.pe/nacional/la-ivermectina-sigue-envuelta-en-controversia-pero-investigaciones-internacionales-apuntan-a-efectos-favorables-en-casos-leves/

291. Ramírez C, Herrera-Paz EF, Peralta G, Rodríguez G, Durón RM. Is ivermectin ready to be part of a public health policy for COVID-19 prophylaxis?. *EClinicalMedicine*. February 2021:100744. https://doi.org/10.1016/j.eclinm.2021.100744

292. Merck & Co/MSD. Merck statement on ivermectin use during the COVID-19 pandemic. 2021. https://web.archive.org/web/20210204172659/https://www.merck.com/news/merck-statement-on-ivermectin-use-during-the-covid-19-pandemic/

293. Clark C. Ivermectin – time for action. *Hospital Pharmacy Europe*. 2021. https://web.archive.org/web/20210208111227/https://hospitalpharmacyeurope.com/views/ivermectin-time-for-action/

294. Vitamedic Indústria Farmacêutica LTDA. Esclarecimento público – ivermectina. 2021. https://web.archive.org/web/20210205194247/https://www.vitamedic.ind.br/2021/02/05/esclarecimento-publico-ivermectina/

295. Bukhari KHS, Asghar A, Perveen N, et al. Efficacy of ivermectin in COVID-19 patients with mild to moderate disease. *medRxiv*. February 2021. https://doi.org/10.1101/2021.02.02.21250840

296. FLCCC Alliance. FLCCC Alliance response to Dr. Kory's senate testimony removed by YouTube. 2021. https://web.archive.org/web/20210205172713/https://covid19criticalcare.com/wp-

content/uploads/2021/02/FLCCC-Alliance-Response-to-Dr.-Korys-Senate-Testimony-Removed-by-YouTube.pdf

297. FLCCC Alliance. FLCCC Alliance response to Merck's public statements on ivermectin's efficacy in COVID-19. 2021. https://web.archive.org/web/20210323142143/https://covid19criticalcare.com/wp-content/uploads/2021/02/FLCCC-Alliance-Response-to-Merck-statements-on-ivermectin-in-Covid19-Feb7-2021.pdf

298. McGuire V. New study to test drugs for early COVID-19 infection. *McMaster University, Faculty of Health Sciences, Department of Health Research Methods, Evidence and Impact*. 2021. https://web.archive.org/web/20210210155238/https://healthsci.mcmaster.ca/hei/news-events/news/2021/02/09/new-study-to-test-drugs-for-early-covid-19-infection

299. Repurposing medication for treatment of Covid-19 – Together trial. 2021. https://web.archive.org/web/20210226112023/https://www.togethertrial.com/

300. Frketich J. 'This could be a real game-changer,' says McMaster University researcher testing COVID treatments. *The Hamilton Spectator*. 2021. https://web.archive.org/web/20210210130119/https://www.thespec.com/news/hamilton-region/2021/02/10/mcmaster-university-researcher-testing-covid-treatments.html

301. Reis G, Santos E. Repurposed approved therapies for outpatient treatment of patients with early-onset COVID-19 and mild symptoms. *ClinicalTrialsgov*. 2021. https://clinicaltrials.gov/ct2/show/NCT04727424

302. Tokyo Medical Association recommends ivermectin administration to prevent aggravation of COVID-19. *Nikkei Asia*. 2021. http://web.archive.org/web/20210209102017/https://www.nikkei.com/article/DGXZQOFB25AAL0V20C21A1000000/

303. Lima-Morales R, Méndez-Hernández P, Flores YN, et al. Effectiveness of a multidrug therapy consisting of ivermectin azithromycin, montelukast and acetylsalicylic acid to prevent hospitalization and death among ambulatory COVID-19 cases in Tlaxcala, Mexico. *International Journal of Infectious Diseases*. February 2021. https://doi.org/10.1016/j.ijid.2021.02.014

304. NIH FOIA 55822 - Yim - expedited processing response. 2021. https://web.archive.org/web/20210212030503/https://drive.google.com/file/d/1W5sBfYKC-1eUsbZzTTQO7Bq4yrFTTebx/view

305. Хората масово купуват Ивермектин от аптеките. 2021. https://web.archive.org/web/20210219211719/https://www.dunavmost.com/novini/horata-masovo-kupuvat-ivermektin-ot-aptekite

306. Ивермектин е вече на българския пазар. *Economic*. 2021. https://web.archive.org/web/20210312074919/https://www.economic.bg/bg/a/view/ivermektin-e-veche-na-bylgarskija-pazar-ne-e-gotovo

307. Цели области у нас купуват „Ивермектин" и се спасяват от COVID-19. *Vesti*. 2021. https://web.archive.org/web/20210322223934/https://www.vesti.bg/temi-v-razvitie/tema-koronavirus/celi-oblasti-u-nas-kupuvat-ivermektin-i-se-spasiavat-ot-covid-19-6119252

308. Olavarria A. Prof. Eli Schwartz ivermectin Israel RCT study. 2021. https://vimeo.com/511687719

309. CovidAnalysis. Analysis of: Ivermectin vs. placebo treatment in non-hospitalized patients with COVID-19 - A double blind, randomized controlled trial. 2021. https://c19ivermectin.com/schwartz.html

310. Ivermectin discovered by Dr. Omura may end the corona pandemic – Kiyoshi Kurokawa – Ronza. 2021. https://web.archive.org/web/20210225213354/https://webronza.asahi.com/science/articles/2021020700003.html

311. Behera P, Patro BK, Padhy BM, et al. Prophylactic role of ivermectin in SARS-CoV-2 infection among healthcare workers. *Research Square*. February 2021. https://doi.org/10.21203/rs.3.rs-208785/v1

312. Elalfy H, Besheer T, El-Mesery A, et al. Effect of a combination of nitazoxanide, ribavirin and ivermectin plus zinc supplement (MANS.NRIZ study) on the clearance of mild COVID-19. *Journal of*

*Medical Virology*. February 2021. https://doi.org/10.1002/jmv.26880

313. Karp P. Craig Kelly banned from Facebook for a week for posting Covid misinformation. *The Guardian*. 2021. http://www.theguardian.com/australia-news/2021/feb/16/craig-kelly-banned-from-facebook-for-a-week-for-posting-covid-misinformation

314. CovidAnalysis. Ivermectin is effective for COVID-19: real-time meta analysis of 41 studies. February 27, 2021, version 37. 2021. https://web.archive.org/web/20210301140900/https://ivmmeta.com/ivm-meta.pdf

315. E-BMC Ltd. The BIRD Meeting 20th February 2021. 2021. https://youtu.be/7gQbi7LZvPw

316. Vitamedic contesta nota da Merck sobre o uso da ivermectina no tratamento da Covid-19. *Click Guarulhos*. 2021. https://web.archive.org/web/20210301134248/https://www.clickguarulhos.com.br/2021/02/22/vitamedic-contesta-nota-da-merck-sobre-o-uso-da-ivermectina-no-tratamento-da-covid-19/

317. Beltran-Gonzalez JL, Gonzalez-Gamez M, Mendoza-Enciso E-A, et al. Efficacy and safety of ivermectin and hydroxychloroquine in patients with severe COVID-19. A randomized controlled trial. *medRxiv*. February 2021. https://doi.org/10.1101/2021.02.18.21252037

318. Nemocnica v Brne nasadila 30 pacientom s COVID-om ivermektín: Nadšené slová primára. 2021. https://web.archive.org/web/20210223223451/https://www.cas.sk/clanok/1092596/nemocnica-v-brne-nasadila-30-pacientom-s-covid-om-ivermektin-nadsene-slova-primara/

319. Walker W. Scabies and head lice drug could be 'global solution to the pandemic' says study. *Mirror*. 2021. https://www.mirror.co.uk/news/uk-news/scabies-head-lice-drug-could-23561927

320. Rose D. Scabies drug could cut Covid deaths by up to 75%, research suggests. *Daily Mail*. 2021. https://www.dailymail.co.uk/news/article-9297449/Drug-used-treat-lice-scabies-drug-cut-Covid-deaths-75-research-suggests.html

321. Simmonds S. Medical association says gov't should include ivermectin drug in COVID-19 treatment. *Nationwide News Network*. 2021. https://nationwideradiojm.com/medical-association-says-govt-should-include-ivermectin-drug-in-covid-19-treatment/

322. Chief Medical Officer Directorate. COVID-19: Ivermectin efficacy in treating COVID-19: FOI release. *Scottish Government*. 2021. https://web.archive.org/web/20210227002612/https://www.gov.scot/publications/foi-202100137853/

323. Starosta Becík, ktorý vypovedal poslušnosť vláde, zabezpečil Ivermectín pre obyvateľov svojej obce: Čakať na vládu nemá zmysle. Začíname nielen s liečením, ale aj prevenciou. To všetko pod prísnym drobnohľadom lekárky. *Hlavné správy*. 2021. https://web.archive.org/web/20210303214218/https://www.hlavnespravy.sk/starosta-becik-ktory-vypovedal-poslusnost-vlade-zabezpecil-ivermectin-pre-obyvatelov-svojej-obce-cakat-na-vladu-nema-zmysle-zaciname-nielen-s-liecenim-ale-aj-prevenciou-to-vsetko-pod-prisnym-d/2450524

324. Dramatic turn of events in legal fight over ivermectin. *AfriForum*. 2021. https://web.archive.org/web/20210226140707/https://afriforum.co.za/en/dramatic-turn-of-events-in-legal-fight-over-ivermectin/

325. Syed M, Kory P. Dr. Pierre Kory, ivermectin, and COVID (let's help end the pandemic). *Drbeen Medical Lectures*. 2021. https://youtu.be/eeYoXGoh96w

326. Bartoszko JJ, Siemieniuk RAC, Kum E, et al. Prophylaxis for Covid-19: living systematic review and network meta-analysis. *medRxiv*. February 2021. https://doi.org/10.1101/2021.02.24.21250469

327. King A. Tropical drug to be tested on critically ill patients here. *Independent*. 2021. https://web.archive.org/web/20210228140607/https://www.independent.ie/irish-news/tropical-drug-to-be-tested-on-critically-ill-patients-here-40140143.html

328. International clinical trial 'REMAP-CAP' includes ivermectin among study drugs for COVID-19 treatment. *TrialSite News*. 2021. https://trialsitenews.com/international-clinical-trial-remap-cap-includes-ivermectin-among-study-drugs-for-covid-19-treatment/

329. Fenter F. 2 March 2021 media statement: article rejection: Review of the emerging evidence demonstrating the efficacy of ivermectin in the prophylaxis and treatment of COVID-19. *Frontiers in Pharmacology*. 2021. https://blog.frontiersin.org/2021/03/02/2-march-2021-media-statement/

330. Offord C. Frontiers removes controversial ivermectin paper pre-publication. *The Scientist*. 2021. https://web.archive.org/web/20210302212452/https://www.the-scientist.com/news-opinion/frontiers-removes-controversial-ivermectin-paper-pre-publication-68505

331. Saha JK, Raihan MJ. The binding mechanism of ivermectin and levosalbutamol with spike protein of SARS-CoV-2. *Research Square*. March 2021. https://doi.org/10.21203/rs.3.rs-160254/v1

332. The Hill update – what is ivermectin?. 2021. https://thenewsforum.ca/series/the-hill-update/

333. Ministerstvo zdravotnictví. Rozhodnutí o dočasném povolení distribuce, výdeje a používání neregistrovaného humánního léčivého přípravku HUMEVEC 3 mg, tablets s obsahem léčivé látky ivermektin. 2021. https://www.mzcr.cz/rozhodnuti-o-docasnem-povoleni-distribuce-vydeje-a-pouzivani-neregistrovaneho-humanniho-leciveho-pripravku-humevec-s-obsahem-lecive-latky-ivermektin/

334. Ministerstvo zdravotnictví. Rozhodnutí o dočasném povolení distribuce, výdeje a používání neregistrovaného humánního léčivého přípravku HUMEVEC 3 mg, tablets s obsahem léčivé látky ivermektin. 2021. https://web.archive.org/web/20210309155846/https://www.mzcr.cz/wp-content/uploads/2021/03/Rozhodnut%C3%AD-o-do%C4%8Dasn%C3%A9m-povolen%C3%AD-distribuce-v%C3%BDdeje-a-pou%C5%BE%C3%ADv%C3%A1n%C3%AD-neregistrovan%C3%A9ho-hum%C3%A1nn%C3%ADho-l%C3%A9%C4%8Div%C3%A9ho-p%C5%99%C3%ADpravku-HUMEVEC-s-obsahem-l%C3%A9%C4%8Div%C3%A9-l%C3%A1tky-ivermektin.pdf

335. Šopfová K. Primář Rezek: Zájem o ivermektin je velký. Chceme ho zpřístupnit všem. *Novinky*. 2021. https://web.archive.org/web/20210303091615/https://www.novinky.cz/domaci/clanek/primar-rezek-zajem-o-ivermektin-je-mezi-lekari-i-pacienty-40352743

336. Corona-News am Mittwoch: Die wichtigsten Entwicklungen zu Sars-CoV-2 und Covid-19. *Der Spiegel*. March 2021. https://web.archive.org/web/20210303045123/https://www.spiegel.de/wissenschaft/medizin/corona-news-am-mittwoch-die-wichtigsten-entwicklungen-zu-sars-cov-2-und-covid-19-a-140f0a16-ce5f-4524-b8d5-97f3a2e1748b

337. Schwoerer P. Corona und die Forschung: Politisches Kalkül oder Inkompetenz?. *Kontext Wochenzeitung*. 2021. https://web.archive.org/web/20210305160516/https://www.kontextwochenzeitung.de/debatte/518/politisches-kalkuel-oder-inkompetenz-7351.html

338. A randomized, double-blind, placebo-controlled study to assess the safety and efficacy of ivermectin in asymptomatic and mild severity COVID-19 patients. *European Medicine Agency Clinical Trials Register*. 2021. https://www.clinicaltrialsregister.eu/ctr-search/trial/2021-000166-15/HU

339. Yang SNY, Atkinson SC, Wang C, et al. The broad spectrum antiviral ivermectin targets the host nuclear transport importin α/β1 heterodimer. *Antiviral Research*. 2020;177:104760. https://doi.org/10.1016/j.antiviral.2020.104760

340. Syed M. Will ivermectin block a vaccine?. *Drbeen Medical Lectures*. 2021. https://youtu.be/aYo6Y71WwkU

341. Keeler B. Local doctor says older drug might successfully treat COVID. *WIBX 950*. 2021. https://web.archive.org/web/20210314110501/https://wibx950.com/local-doctor-says-older-drug-might-successfully-treat-covid/

342. López-Medina E, López P, Hurtado IC, et al. Effect of ivermectin on time to resolution of symptoms among adults with mild COVID-19. *JAMA*. March 2021. https://doi.org/10.1001/jama.2021.3071

343. CovidAnalysis. Analysis of: Effect of ivermectin on time to resolution of symptoms among adults with mild COVID-19: a randomized clinical trial. 2021. https://c19ivermectin.com/lopezmedina.html

344. Anthes E. Popular drug does not alleviate mild Covid-19 symptoms, study finds. *New York Times*. 2021. https://www.nytimes.com/2021/03/04/science/coronavirus-ivermectin-treatment.html

345. Walker M. Ivermectin disappoints in mild COVID-19. *MedPage Today*. March 2021. https://web.archive.org/web/20210312132635/https:

//www.medpagetoday.com/infectiousdisease/covid19/91479

346. Kory P, Meduri GU, Iglesias J, et al. Review of the emerging evidence demonstrating the efficacy of ivermectin in the prophylaxis and treatment of COVID-19. *ResearchGate*. 2021. https://web.archive.org/web/20210323234219/https://www.researchgate.net/publication/349732955_Review_of_the_Emerging_Evidence_Demonstrating_the_Efficacy_of_Ivermectin_in_the_Prophylaxis_and_Treatment_of_COVID-19_Manuscript_Length

347. Donn N. Portuguese doctors support Ivermectin to treat early signs of Covid-19. *Portugal Resident*. 2021. https://web.archive.org/web/20210304155756/https://www.portugalresident.com/portuguese-doctors-support-ivermectin-to-treat-early-signs-of-covid-19/

348. Syed M. Can ivermectin fight variants?. 2021. https://youtu.be/soIAcI3QhTw

349. Koulgi S, Jani V, Uppuladinne M, et al. Drug repurposing studies targeting SARS-CoV-2: an ensemble docking approach on drug target 3C-like protease (3CLpro). *Journal of Biomolecular Structure and Dynamics*. July 2020:1–21. https://doi.org/10.1080/07391102.2020.1792344

350. US Food and Drug Administration. Why you should not use ivermectin to treat or prevent COVID-19. 2021. https://web.archive.org/web/20210309024138/https://www.fda.gov/consumers/consumer-updates/why-you-should-not-use-ivermectin-treat-or-prevent-covid-19

351. Deutsches Ärzteblatt. COVID-19: Ivermectin scheitert in klinischer Studie in Lateinamerika. *Deutsches Ärzteblatt*. 2021. https://web.archive.org/web/20210318120544/https://www.aerzteblatt.de/nachrichten/121789/COVID-19-Ivermectin-scheitert-in-klinischer-Studie-in-Lateinamerika

352. MedinCell. Covid-19: MedinCell publishes an extensive ivermectin safety expert analysis. 2021. https://web.archive.org/web/20210314202230/https://invest.medincell.com/wp-content/uploads/2021/03/PR_MDCL_safety_ivermectine-50321.pdf

353. Descotes J. Expert review report: medical safety of ivermectin. *MedinCell*. 2021. https://web.archive.org/web/20210311015844/https://www.medincell.com/wp-content/uploads/2021/03/Clinical_Safety_of_Ivermectin-March_2021.pdf

354. France-based MedinCell safety study for ivermectin: three decades of safety. *TrialSite News*. 2021. https://trialsitenews.com/france-based-medincell-safety-study-for-ivermectin-three-decades-of-safety/

355. Bonaccorsi G. Forte calo dei pazienti nei reparti Covid a Catania: il virus in ritirata?. *La Sicilia*. 2021. https://www.lasicilia.it/news/covid/397628/forte-calo-dei-pazienti-nei-reparti-covid-a-catania-il-virus-in-ritirata.html

356. Sinha A. A crown of care during Covid. *Hindustan Times*. 2021. https://web.archive.org/web/20210314112820/https://www.hindustantimes.com/lifestyle/brunch/a-crown-of-care-during-covid-101615047368077.html

357. Campbell J. Ivermectin evidence with Dr Tess Lawrie: long COVID. 2021. https://youtu.be/vYF8bnmdQfY?t=1776

358. Campbell J. Ivermectin evidence with Dr Tess Lawrie: production price. 2021. https://youtu.be/vYF8bnmdQfY?t=2471

359. Merck & Co/MSD. Ridgeback Biotherapeutics and Merck announce preliminary findings from a phase 2a trial of investigational COVID-19 therapeutic molnupiravir. 2021. https://web.archive.org/web/20210306090045/https://www.merck.com/news/ridgeback-biotherapeutics-and-merck-announce-preliminary-findings-from-a-phase-2a-trial-of-investigational-covid-19-therapeutic-molnupiravir/

360. Cox RM, Wolf JD, Plemper RK. Therapeutically administered ribonucleoside analogue MK-4482/EIDD-2801 blocks SARS-CoV-2 transmission in ferrets. *Nature Microbiology*. 2020;6(1):11–18. https://doi.org/10.1038/s41564-020-00835-2

361. Haseltine WA. Molnupiravir: a new hope for prevention and treatment of Covid-19 and other dangerous viruses. *Forbes*. March 2021. https://web.archive.org/web/20210316171201/https:

//www.forbes.com/sites/williamhaseltine/2021/03/16/molnupiravir-a-new-hope-for-prevention-and-treatment-of-covid-19-and-other-dangerous-viruses/

362. FLCCC Alliance. Front Line COVID-19 Critical Care Alliance statement on misleading FDA guidance on ivermectin. 2021. https://web.archive.org/web/20210308021435/https://covid19criticalcare.com/wp-content/uploads/2021/03/FLCCC-Alliance-Statement-on-Misleading-FDA-Guidance-on-Ivermectin-March7-2021.pdf

363. Kabani M. COVID-19 research points to repurposed drugs. *CBS News*. 2021. https://web.archive.org/web/20210309084341/https://www.cbsnews.com/news/covid-19-repurposed-drugs-60-minutes-2021-03-07/

364. CBS News. NIH director on need for COVID drug. *60 Minutes*. 2021. https://twitter.com/60minutes/status/1368969843584753670?s=21

365. Chamie-Quintero J, Hibberd J, Scheim D. Ivermectin for COVID-19 in Peru: 14-fold reduction in nationwide excess deaths, p=.002 for effect by state, then 13-fold increase after ivermectin use restricted. *OSF Preprints*. 2021. https://osf.io/9egh4/

366. Chamie-Quintero JJ, Hibberd J, Scheim D. Ivermectin for COVID-19 in Peru: 14-fold reduction in nationwide excess deaths, p=.002 for effect by state, then 13-fold increase after ivermectin use restricted. *TrialSite News*. 2021. https://trialsitenews.com/ivermectin-for-covid-19-in-peru-14-fold-reduction-in-nationwide-excess-deaths-p-002-for-effect-by-state-then-13-fold-increase-after-ivermectin-use-restricted/

367. Prasad V. Facebook: a worthy judge of medical info?. *MedPage Today*. March 2021. https://web.archive.org/web/20210312105921/https://www.medpagetoday.com/blogs/vinay-prasad/91526

368. Scheim D, Hibberd JA, Chamie-Quintero J. Protocol violations in López-Medina et al.: 38 switched ivermectin (IVM) and placebo doses, failure of blinding, widespread IVM sales OTC in Cali, and nearly identical AEs for the IVM and control groups. March 2021. https://osf.io/u7ewz

369. Pott-Junior H, Paoliello MMB, Queiroz Constantino Miguel A de, et al. Use of ivermectin in the treatment of Covid-19: a pilot trial. *Toxicology Reports*. 2021;8:505–510. https://doi.org/10.1016/j.toxrep.2021.03.003

370. GOP vs herd immunity? LeBron 'private' on vax decision; FDA pooh-poohs ivermectin. *MedPage Today*. March 2021. https://web.archive.org/web/20210312110328/https://www.medpagetoday.com/infectiousdisease/covid19/91537

371. Kory P. Censorship kills: the shunning of a COVID therapeutic. *RealClearPolitics*. 2021. https://web.archive.org/web/20210311045059/https://www.realclearpolitics.com/articles/2021/03/10/censorship_kills_the_shunning_of_a_covid_therapeutic_145376.html

372. Bryant A, Lawrie TA, Dowswell T, et al. Ivermectin for prevention and treatment of COVID-19 infection: a systematic review and meta-analysis. *OSF Preprints*. 2021. https://doi.org/10.31219/osf.io/k37ft

373. Dr. Satoshi Ōmura, the discoverer of ivermectin, says a special approval should not be required. *Daily Shincho*. 2021. https://web.archive.org/web/20210314034254/https://www.dailyshincho.jp/article/2021/03141057/?all=1

374. Dr. Satoshi Ōmura, the discoverer of ivermectin, says a special approval should not be required. *Daily Shincho*. 2021. https://translate.google.com/translate?sl=ja&tl=en&u=https://www.dailyshincho.jp/article/2021/03141057/?all%3D1

375. Roy S, Samajdar SS, Tripathi SK, Mukherjee S, Bhattacharjee K. Outcome of different therapeutic interventions in mild COVID-19 patients in a single OPD clinic of West Bengal: a retrospective study. *medRxiv*. March 2021. https://doi.org/10.1101/2021.03.08.21252883

376. CovidAnalysis. Analysis of: outcome of different therapeutic interventions in mild COVID-19 patients in a single OPD clinic of West Bengal: a retrospective study. *CovidAnalysis*. 2021. https://c19ivermectin.com/roy.html

377. Nardelli P, Zangrillo A, Sanchini G, et al. Crying wolf in time of corona: the strange case of ivermectin and hydroxychloroquine. Is the fear of failure withholding potential life-saving treatment from clinical use?. *Signa Vitae*. 2021. https://doi.org/10.22514/sv.2021.043

378. News roundup: Dr. Tess Lawrie discusses her ivermectin meta-analysis, the FDA, and Dr. Andrew Hill. *TrialSite News*. 2021. https://youtu.be/y2FWPQm6sxw

379. FLCCC Alliance. Big breaking news: our scientific manuscript on emerging evidence for ivermectin has been accepted for publication in the American Journal of Therapeutics. *Twitter*. 2021. https://archive.is/6pyoM

380. Withers P. Reform TV vs Momentum: Nigel Farage's party launch channel after Labour grassroots plea. *Daily Express (UK)*. 2021. https://web.archive.org/web/20210129164202/https://www.express.co.uk/news/politics/1390893/nigel-farage-news-reform-tv-labour-party-momentum-andrew-neil-gb-news

381. Tice talk special: Ivermectin: Covid cure or coincidence? Cock up or cover up? Ep 07. *Reform TV*. 2021. https://youtu.be/w3u39moxStQ

382. Orient JM. U.S. pandemic response disastrous. *Association of American Physicians and Surgeons*. 2021. https://web.archive.org/web/20210316170839/https://aapsonline.org/u-s-pandemic-response-disastrous/

383. Orient JM. U.S. pandemic response. *Journal of American Physicians and Surgeons*. 2021;26(1). https://web.archive.org/web/20210322210908/https://jpands.org/vol26no1/orient.pdf

384. Researchers call for access to ivermectin for young children. March 2021. https://web.archive.org/web/20210319081157/https://www.eurekalert.org/pub_releases/2021-03/iddo-rcf031821.php

385. Beteti F. 12 mil funcionários sem COVID – Dr. Adler Menezes & Fernando Beteti. 2021. https://youtu.be/SocpOKEt8rE

386. Infectious Diseases Society of America. IDSA guidelines on the treatment and management of patients with COVID-19, version 4.1.1, March 18, 2021. *Infectious Diseases Society of America*. 2021. https://web.archive.org/web/20210322211747/https://www.idsociety.org/globalassets/idsa/practice-guidelines/covid-19/treatment/idsa-covid-19-gl-tx-and-mgmt-v4.1.1.pdf

387. Pedrini A. Santin (Yale): sorprendente efficacia dell'Ivermectina contro il covid. *Affaritalianiit*. 2021. https://web.archive.org/web/20210323063720/https://www.affaritaliani.it/milano/santin-sorprendente-efficacia-dell-ivermectina-contro-il-covid-729391.html

388. D'Angelo P. Covid, l'ipotesi dell'ivermectina come possibile terapia. Ecco cos'è e come funziona. *il Fatto Quotidiano*. 2021. https://web.archive.org/web/20210305071523/https://www.ilfattoquotidiano.it/2021/03/05/covid-lipotesi-dellivermectina-come-una-potenziale-terapia-santin-yale-puo-essere-il-game-changer/6122115/

389. Top Yale doctor/researcher: 'ivermectin works,' including for long-haul COVID. *TrialSite News*. 2021. https://trialsitenews.com/top-yale-doctor-researcher-ivermectin-works-including-for-long-haul-covid/

390. Haroldo DF, Roberto H, Hector C. Ivermectin in long-Covid patients: a retrospective study. *Journal of Biomedical Research and Clinical Investigation*. 2021;2(1). https://doi.org/10.31546/2633-8653.1008

391. David C. Ivermectine: la France passe-t-elle à côté d'un médicament efficace contre la Covid-19?. *Capital*. 2021. https://web.archive.org/web/20210323070142/https://www.capital.fr/economie-politique/ivermectine-la-france-passe-t-elle-a-cote-dun-medicament-efficace-contre-la-covid-19-1397573

392. Maudrux G. Blog du Dr Gérard Maudrux - L'œil d'un anti-conformiste. 2021. https://blog.gerardmaudrux.lequotidiendumedecin.fr/

393. Yim PJ. JAMA ivermectin study deceived participants on study drug. *TrialSite News*. 2021. https://web.archive.org/web/20210319173038/https://trialsitenews.com/jama-ivermectin-study-deceived-participants-on-study-drug/

394. Ivermectin: game changer vs Covid-19? What's the controversy?. *The Manila Times*. 2021. https://web.archive.org/web/20210322204958/https://www.manilatimes.net/2021/03/21/opinion/columnists/ivermectin-game-changer-vs-covid-19-whats-the-controversy/853847/

395. CovidAnalysis. Ivermectin for COVID-19: real-time analysis of all 72 studies. March 17, 2021. 2021. https://web.archive.org/web/20210324004408/https://c19ivermectin.com/

396. CovidAnalysis. Ivermectin is effective for COVID-19: real-time meta analysis of 46 studies. March 17, 2021, version 47. 2021. https://web.archive.org/web/20210317010423/https://ivmmeta.com/

397. European Medicines Agency. EMA advises against use of ivermectin for the prevention or treatment of COVID-19 outside randomised clinical trials. 22AD. https://web.archive.org/web/20210322135557/https://www.ema.europa.eu/en/news/ema-advises-against-use-ivermectin-prevention-treatment-covid-19-outside-randomised-clinical-trials

398. Yagisawa M, Foster PJ, Ōmura HHS. Global trends in clinical studies of ivermectin in COVID-19. *Japanese Journal of Antibiotics*. 2021;74(1):44–95. http://jja-contents.wdc-jp.com/pdf/JJA74/74-1-open/74-1_44-95.pdf

399. Wayback Machine: ivmmeta.com. https://web.archive.org/web/*/https://ivmmeta.com/

400. COVID-19 misinformation. *Wikipedia*. 2021. https://en.wikipedia.org/w/index.php?title=COVID-19_misinformation&oldid=1011074270

401. Ivermectin. *Wikipedia*. 2021. https://en.wikipedia.org/w/index.php?title=Ivermectin&oldid=1009079696

402. COVID-19 drug repurposing research. *Wikipedia*. 2021. https://en.wikipedia.org/w/index.php?title=COVID-19_drug_repurposing_research&oldid=1011302274

403. Piezunka H, Dahlander L. Distant search narrow attention: how crowding alters organizations' filtering of suggestions in crowdsourcing. *Academy of Management Journal*. 2015;58(3):856–880. https://doi.org/10.5465/amj.2012.0458

404. Kim YE, Sicuri E, Tediosi F. Financial and economic costs of the elimination and eradication of onchocerciasis (river blindness) in Africa. Turner HC, ed. *PLOS Neglected Tropical Diseases*. 2015;9(9):e0004056. https://doi.org/10.1371/journal.pntd.0004056

405. US National Institutes of Health. Early results show benefit of remdesivir for COVID-19. 2020. https://web.archive.org/web/20210109134342/https://www.nih.gov/news-events/nih-research-matters/early-results-show-benefit-remdesivir-covid-19

406. Desai A, Gyawali B. Endpoints used in phase III randomized controlled trials of treatment options for COVID-19. *EClinicalMedicine*. 2020;23:100403. https://doi.org/10.1016/j.eclinm.2020.100403

407. U.S. Department of Health and Human Services Food and Drug Administration. Emergency use authorization of medical products and related authorities. 2017. https://web.archive.org/web/20210311073806/https://www.fda.gov/media/97321/download