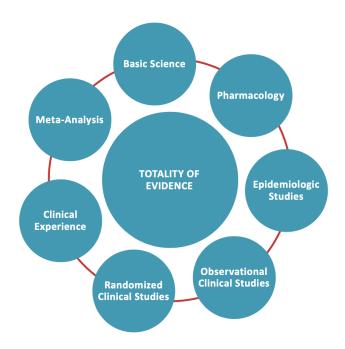


Summary of the Evidence for Ivermectin in COVID-19

Ivermectin is an anti-parasite medicine whose discovery won the Nobel Prize in 2015 for its impacts in ridding large parts of the globe of parasitic diseases via the distribution of over 3.7 billion doses within public health campaigns since 1987.

Since 2012, numerous in-vitro and in-vivo studies began to report highly potent antiviral effects of ivermectin against a diverse array of viruses including <u>SARS-CoV-2</u>. Further, increasing <u>anti-inflammatory and immuno-modulating effects</u> are being identified

Our <u>comprehensive narrative review</u> of the "totality of the evidence" supporting ivermectin was published in The American Journal of Therapeutics in April 2021, where we reviewed data on efficacy from a diverse array of scientific sources beyond just the randomized controlled trial evidence as illustrated in the diagram below.





As of September 19, 2021, the totality of the evidence is as follows.

- IN-VITRO (BASIC SCIENCE): ivermectin has been shown to inhibit the replication of many viruses, including West-Nile, Zika, Dengue, Influenza, and most recently <u>SARS-CoV-2</u> [1,2,3,4,5,6,7]
- IN-VIVO: ivermectin diminishes viral load and protects against organ damage in animal models of SARS-CoV-2 infection and has multiple, potent <u>anti-inflammatory</u> and <u>immune- modulating</u> properties [1, 2, 3]
- **IN-SILICO**: numerous <u>computer modeling studies</u> have found ivermectin to have one of the <u>highest binding affinities</u> to the SARS-CoV-2 spike protein
- PHARMACOLOGIC: unparalleled safety profile over decades, prior WHO guidelines report side effects that are "primarily minor and transient" and experts have found severe adverse events to be "unequivocally and exceedingly rare." Further, the IC-50 against SARS-CoV2 in lung and adipose tissue easily achieved with standard dosing (Caly/Wagstaff personal communication)
- CLINICAL OBSERVATIONS/EXPERIENCE: numerous cases series, most notably one
 published from the Dominican Republic in June 2020 where over 3,000 consecutive
 patients presented to the ER, were treated with ivermectin, and only 16 were
 hospitalized and only 1 died. Also, innumerable doctors from multiple countries around
 the world report observing consistent clinical responses in treated patients with few
 treatment failures.
- OBSERVATIONAL CONTROLLED TRIALS (OCT): As of August 8, 2021, the results from 31
 OCT's including over 6,800 patients find that treatment with ivermectin <u>reduces time to recovery, rates of hospitalization, and mortality</u>, the latter finding best reported in the sophisticated propensity-matched study of <u>Rajter et al</u>. published in the major medical journal *Chest*.
- META-ANALYSES OF RANDOMIZED CONTROLLED TRIALS (RCT): 27 RCT's including over 3,400 patients have been completed. Meta-analyses find that ivermectin reduces time to <u>viral clearance</u>, <u>hastens recovery</u>, and reduces <u>mortality</u>.
- OBSERVATIONAL AND RANDOMIZED TRIALS IN THE PREVENTION OF COVID-19: A
 series of 13 RCT's and OCT's consistently find that single or repeated ivermectin use
 strongly reduces the risk of contracting COVID-19, with an average level of protection of
 86% with higher levels of protection found amongst the trials with more frequent dosing
 [1,2,3,4,5,6,7 (Table 2), 8,9,10,11,12].
- EPIDEMIOLOGIC: ivermectin distribution campaigns in Peru led to <u>far lower COVID-19</u>
 <u>case- fatality rates</u> in those regions with widespread use. Further, large "test and treat"
 programs conducted by increasing numbers of Health Ministries <u>report up to 75%</u>
 <u>reductions</u> in the need for hospitalization (Mexico City) and <u>massive reductions in</u>



mortality (Misiones, Argentina and <u>La Pampas, Argentina</u>). Finally and most importantly, the Indian state of Uttar Pradesh (pop. 241 million) has <u>effectively eradicated COVID</u> via systematic and widespread use of ivermectin in both prevention and early treatment.

Further evidence of the major efficacy of ivermectin come from the rapidly increasing numbers of national and regional health ministries that employed either distribution or "test and treat" programs with ivermectin:

- Mexico City The IMSSS Health Agency compared over 50,000 patients treated early with ivermectin to over 70,000 not treated and found <u>up to a 75% reduction in need for</u> <u>hospitalization</u>.
- La Misiones, Argentina Health Ministry just analyzed the first 800 of 4,000 ivermectin treated patients and compared to the rest of the population over the same time period, they found a 75% reduction in need for hospital and an 88% reduction in death.
- Uttar Pradesh, India Used a strategy of <u>close surveillance combined with both ivermectin</u> treatment of all positive cases and preventive treatment of all family contacts. On September 10, 2021, <u>only 11 cases with no deaths were recorded in a population</u> of 241 million. As of August 31, of the previous 187,638 tests performed, only 21 were positive, an essentially zero positive rate or .01%.
- The Brazilian city of Itajai offerred ivermectin as prevention to the entire city's population with 133,051 (60%) agreeing to take ivermectin every two weeks for 6 months. The city health service collected data on the entire population prospectively and found that Ivermectin <u>users were 57% less likely to contract illness, had a 70% lower mortality rate, and a 67% lower hospitalization rate while the citywide COVID mortality fell from 6.8% to 1.8% during the program.</u>
 - In a <u>follow-up study to the above</u>, after analyzing usage of ivermectin usage data amongst the program enrollees, they compared outcomes among non-users, intermittent users, and regular users of ivermectin. They found that regular users of ivermectin had a 100% reduction in hospitalization and a 90% reduction in mortality compared to non-users.
- La Pampas, Argentina Health Ministry compared over 2,000 patients they treated early with ivermectin to over 12,000 without treatment and found that in patients over 40, rates of <u>ICU admission and death both fell by 40%</u>.
- Peru A nationwide mass-distribution program called "Mega-Operación Tayta" (MOT), initiated at various times across 25 states of Peru in May 2020, led to a 74% drop in regional excess deaths within a month, with each drop beginning 11 days after each MOT region's varied start times
- The Health Minsitry of Sultan Kudarat in the Phillipines launched an ivermectin drive and found that cases rapidly dropped by 86%.



- In Japan, the President of the Tokyo Medical Association recommended that all
 physicians start to use ivermectin as early treatment during their summer surge. They
 are now recording the lowest rate of COVID hospitalization in the pandemic.
- In Honduras, within 2 months of first detection of SARS-CoV-2 in Honduras, its government promoted nationwide implementation of multi-drug covid-19 inpatient and outpatient treatment protocols. The outpatient protocol revolved around ivermectin, azithromycin, and hydrogen peroxide mouthwashes and nasal sprays. The rapid implementation and widespread uptake of the two protocols was associated with a case fatality rate decrease from 9.33% to 2.97%. No decrease was seen in Mexico, a similar Latin American country that did not introduce multi-drug treatment protocols at that time.

Finally, in both "long-haul" COVID and post-vaccine syndromes, ivermectin is proving to be highly effective at eliminating symptoms based on the rapidly accumulating clinical experiences of the FLCCC and a number of allied experts that co-developed the <u>I-RECOVER protocol</u>, centered around the use of ivermectin in these syndromes.

CONCLUSION

Based on the totality of the existing evidence above, the FLCCC strongly recommends ivermectin be used in both the prevention and treatment of all phases of COVID-19 in both vaccinated and unvaccinated populations.

Retracted Research

The totality of evidence for ivermectin is large enough that removal of any single data set, trial or study has minimal impacts. The integrity of one study in Egypt (Elgazzar et al) out of the then 28 RCT results available, was recently called into question. While we share the concerns about this study, the removal of its data from the most comprehensive meta-analyses did not change the conclusion that ivermectin is highly effective in both prevention and treatment.