



## Opening a can of helminths: Ivermectin for COVID-19

### CLINICAL QUESTION

**Does ivermectin improve clinical outcomes in COVID-19?**

### BOTTOM LINE

**The best available evidence does not show that ivermectin improves clinically important outcomes in COVID-19. Use in COVID-19 is discouraged.**

### EVIDENCE

- Focusing on quality randomized controlled trials (RCTs) and systematic reviews reporting patient-oriented outcomes and published in peer reviewed journals.
- Two large, well designed, double-blind, RCTs:
  - 400 patients with mild COVID-19 (at home or hospitalized without oxygen support) randomized to ivermectin or placebo for 5 days:<sup>1</sup>
    - Time to symptom resolution:
      - Not statistically different: 10 days ivermectin, 12 days placebo.
  - 501 out-patients randomized to ivermectin or placebo for 2 days:<sup>2</sup>
    - COVID-19 related hospitalization:
      - Not statistically different: Ivermectin 5.6% versus 8.4% placebo.
- High-quality living meta-analysis found no statistically significant impact of ivermectin on any clinical outcome.<sup>3</sup>

- 19 RCTs with 2740 patients (outpatients and inpatients); primarily reported on surrogate outcomes (example viral load).
- Clinical outcomes in outpatients at day 28:
  - Clinical improvement: 2 trials (526 patients): No difference.
  - All-cause mortality: 4 trials (1255 patients): No difference.
- Formally published systematic review found similar.<sup>4</sup>

## CONTEXT

- Most ivermectin trials are not published in peer reviewed journals, have small numbers of participants, are at high risk of bias, or only report on surrogate markers.<sup>3</sup>
  - One oft-cited “meta-analysis” which reported a benefit had no authors listed, included cohort studies, and had questionable conclusions regarding study quality.<sup>5</sup>
  - The study with the largest reported mortality effect (only available in pre-print), was retracted due to data integrity issues.<sup>6,7</sup>
- Of >14,000 COVID-19 pre-prints:
  - Only ~30% are published in peer reviewed journals one year later.<sup>8</sup>
  - Pre-print results and conclusions can change substantially when published as peer reviewed publication:
    - Example COLCORONA trial: Same results, different conclusions.
      - Preprint: “colchicine reduces the composite rate of death or hospitalization”.<sup>9</sup>
      - Publication: “effect of colchicine on COVID-19-related clinical events was not statistically significant”.<sup>10</sup>
- Despite the evidence, animal feed stores inundated with requests for ivermectin.<sup>11</sup>
- Poison control centers report increased calls for ivermectin toxicity.<sup>12</sup>
  - Toxicity symptoms may include nausea/vomiting, abdominal pain, diarrhea, headache, blurred vision, dizziness, and seizures.<sup>12</sup>

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## REFERENCES

1. López-Medina E, López P, Hurtado IC, *et al.* JAMA 2021; 325(14):1426-35. doi:10.1001/jama.2021.3071
2. Vallejos J, Zoni R, Aguirre MG, *et al.* BMC Inf Dis. 2021: 635(21).
3. COVID-NMA Consortium. (2020). RCT studies on preventive measures and treatments for COVID-19: ivermectin. Available at: <https://covid-nma.com>. Accessed August 9, 2021.
4. Popp M, Stegemann M, Metzendorf M-I, *et al.* Cochrane Database of Systematic Reviews 2021, Issue 7. Art. No.: CD015017. DOI: 10.1002/14651858.CD015017.pub2.
5. No authors. Ivermectin for COVID-19: real-time meta-analysis of 61 studies. Available at: <http://ivmmeta.com>. Accessed August 9, 2021.

## AUTHORS

**Tony Nickonchuk**, BSc  
Pharm, **Michael R Kolber**,  
MD CCFP MSc

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6. Elgazzar A, Eltaweel A, Abo Youssef S, *et al.* [Retracted] Research Square. doi: <https://doi.org/10.21203/rs.3.rs-100956/v3>.
7. Reardon S. Nature. 2021 Aug 2. Available at: <https://www.nature.com/articles/d41586-021-02081-w>. Accessed August 9, 2021.
8. Authors' calculations using medrxivr R package. Available at: <https://cran.r-project.org/web/packages/medrxivr/index.html>. Accessed August 12, 2021.
9. Tardif JC, Bouabdallaoui N, L'Allier PL, *et al.* MedRxiv 2021. 01.26.21250494; doi: <https://doi.org/10.1101/2021.01.26.21250494>.
10. Tardif JC, Bouabdallaoui N, L'Allier PL, *et al.* Lancet Respir Med. 2021; 9:924-32.
11. CBC news Aug 30, 2021. Available at: <https://www.cbc.ca/news/canada/calgary/ivermectin-alberta-covid-1.6157200>
12. Centers for Disease Control (CDC) Advisory. Available at: <https://emergency.cdc.gov/han/2021/han00449.asp>. Accessed Aug 30, 2021.