# COVID-19 therapeutics update

- Ivermectin

# October 12th, 2021

# Ivermectin

- What: anti-parasitic (strongyloides, scabies)

- *In vitro:* antiviral (dengue, SARS-CoV2)
  - at concentrations >50-fold the anti-parasitic effect

- Pros: Older drug, available, $

https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab591/6310839

| Guidelines | Ivermectin Recommendation | Website |
|---|---|---|
| National Institutes of Health | There is **insufficient evidence** for the COVID-19 Treatment Guidelines Panel (the Panel) to recommend either for or against the use of ivermectin for the treatment of COVID-19. | https://www.covid19treatmentguidelines.nih.gov/therapies/antiviral-therapy/ivermectin/ |
| Infectious Diseases Society of America | Suggest **against use** except in a clinical trial | https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/ |
| World Health Organization | We **recommend not** to use ivermectin in patients with COVID-19 except in the context of a clinical trial. | https://www.bmj.com/content/370/bmj.m3379 |
| FDA and CDC | Recommend against | https://emergency.cdc.gov/han/2021/han00449.asp |

# The ivermectin story

in-vitro data indicating some activity

**Mar. 2020**

Promising study out of Egypt

**Nov. 2020**

Multiple reports of poisoning

**Aug. 2021**

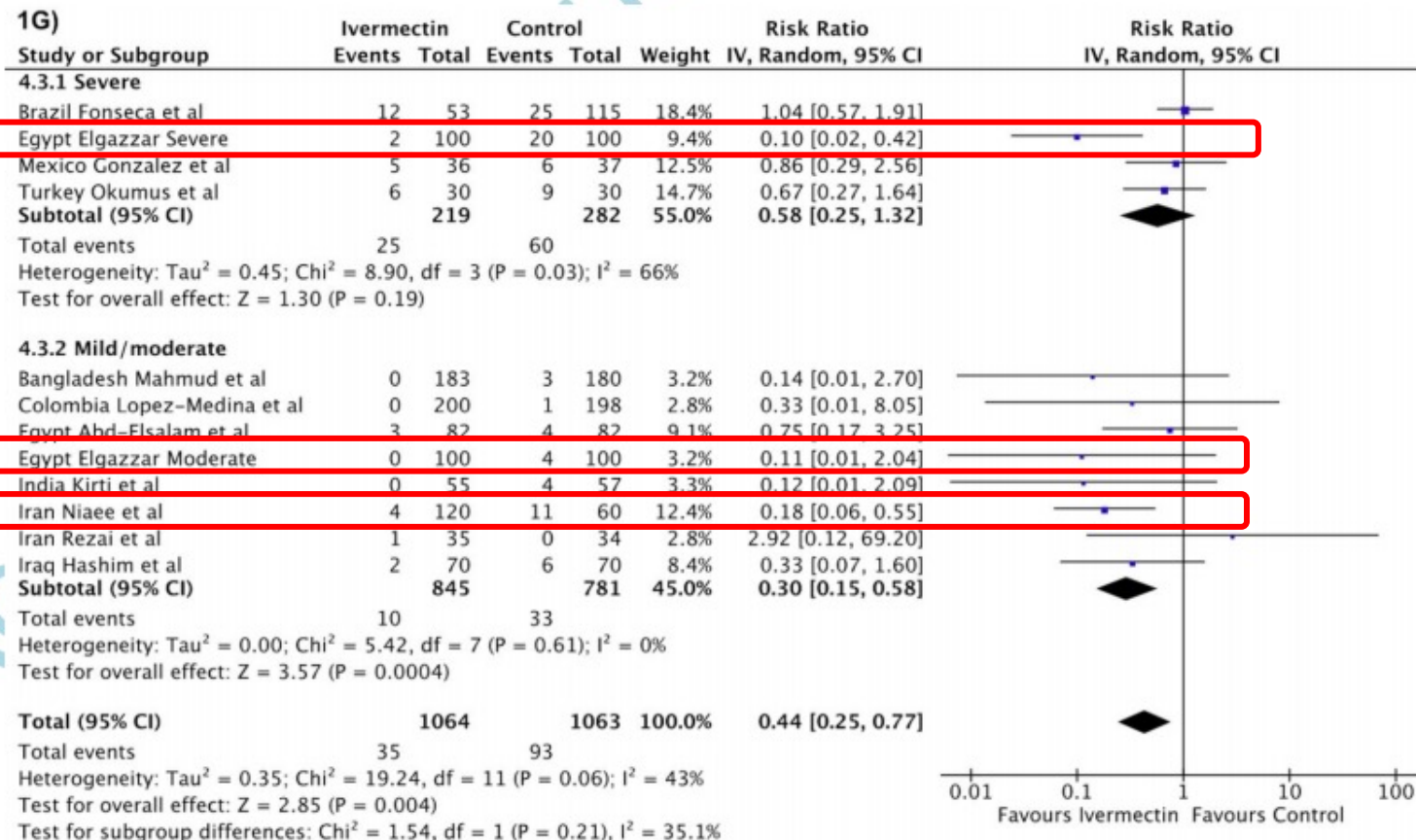**Dec. 2020**

Senate hearing

**July 2021**

Study from Egypt retracted

# Egypt study retraction

**Mortality: 35/1064 (3%) vs. 93/1063 (8.7%)**



Figure 1G

https://www.theguardian.com/science/2021/jul/16/huge-study-supporting-ivermectin-as-covid-treatment-withdrawn-over-ethical-concerns

Lawrence, J.M., Meyerowitz-Katz, G., Heathers, J.A.J. *et al.* The lesson of ivermectin: meta-analyses based on summary data alone are inherently unreliable. *Nat Med* (2021). https://doi.org/10.1038/s41591-021-01535-y

# New (old) data on Ivermectin



RETRACTED and will re-analyze data without fraudulent
studies

# What is the harm?

Jan 2021, calls to US poison control up three-fold for human exposures to ivermectin

July 2021, ivermectin calls continued to sharply increase, to a five-fold increase from baseline

These reports are also associated with increased frequency of adverse effects and emergency department/hospital visits.

**Estimated number of outpatient ivermectin prescriptions dispensed from retail pharmacies — United States, March 16, 2019–August 13, 2021\***
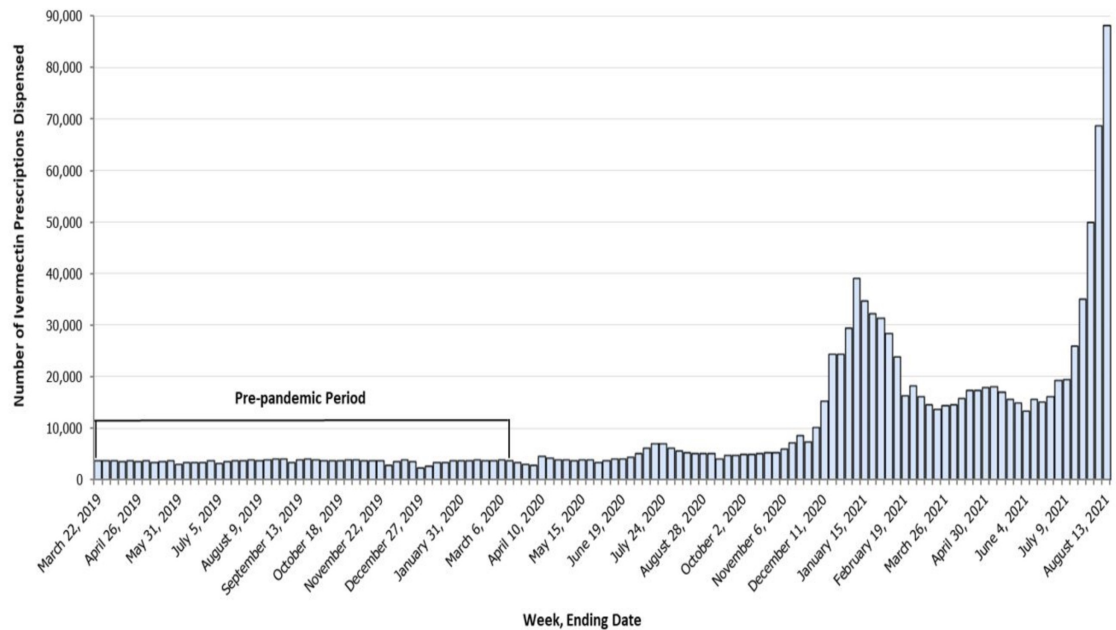
# Ongoing Clinical trials

PRINCIPLE- https://www.principletrial.org/

UK study evaluating Standard of care vs Favipiravir (an antiviral drug) vs ivermectin

ACTIV-6, Trial of Repurposed drugs (NIH sponsored)

15,000 participants

- Ivermectin vs placebo

- Fluvoxamine vs placebo

- Inhaled Fluticasone vs placebo

# Resources

CDC and FDA warnings

- https://emergency.cdc.gov/han/2021/han00449.asp

Data tables:

- https://www.covid19treatmentguidelines.nih.gov/tables/table-2c/

- https://www.bmj.com/content/370/bmj.m3379

**WHO**

## Ivermectin ⌄

No suggested regimen
Trials used variable dosing strategies

### ❝ Recommendation 1

| Usual supportive care | Ivermectin |
|---|---|
| Strong | |

Patients with cov...
at any severity

When fo...
uncerta...
In addit...
there w...
small nu...

## Evidence profile ⌄

Favours usual supportive care | No important difference ⓘ | Favours ivermectin

| | Events per 1000 people | | | Evidence quality | |
|---|---|---|---|---|---|
| Mortality | 70 | No important difference | 14 | ★★★★ Very low | More ⌄ |
| Mechanical ventilation | 20 | No important difference | 10 | ★★★★ Very low | More ⌄ |
| Viral clearance at 7 days | 500 | 118 more | 618 | ★★★★ Low | More ⌄ |
| Admission to hospital | 50 | No important difference | 18 | ★★★★ Very low | More ⌄ |
| Serious adverse events | 9 | 18 fewer | 27 | ★★★★ Low | More ⌄ |
| | Mean days | | | Evidence quality | |
| Time to clinical improvement | 11.0 | No important difference | 10.5 | ★★★★ Low | More ⌄ |
| Duration of hospitalisation | 12.8 | No important difference | 11.7 | ★★★★ Very low | More ⌄ |
| Time to viral clearance | 7.3 | No important difference | 5.7 | ★★★★ Very low | More ⌄ |

▶ See all outcomes    MAGIC app

# Fluvoxamine

There is **insufficient evidence** for the COVID-19 Treatment Guidelines Panel to recommend either for or against the use of fluvoxamine for the treatment of COVID-19.

small placebo-controlled trial, none of the participants who received fluvoxamine and six (8.3%) of those who received placebo reached the primary endpoint.

Limitations:

- study's reliance on participant self-reports

- missing data

Difficult to draw definitive conclusions about the efficacy of fluvoxamine for the treatment of COVID-19.

# Ivermectin:  no effect!



**JN JAMA** Network™

**QUESTION** What is the effect of ivermectin on duration of symptoms in adults with mild COVID-19?

**CONCLUSION** This randomized trial found t[...] a 5-day course of ivermectin compared wit[...]

**POPULATION**

231 Women
167 Men

Adult patients with mild COVID-19 and symptoms for 7 days or fewer

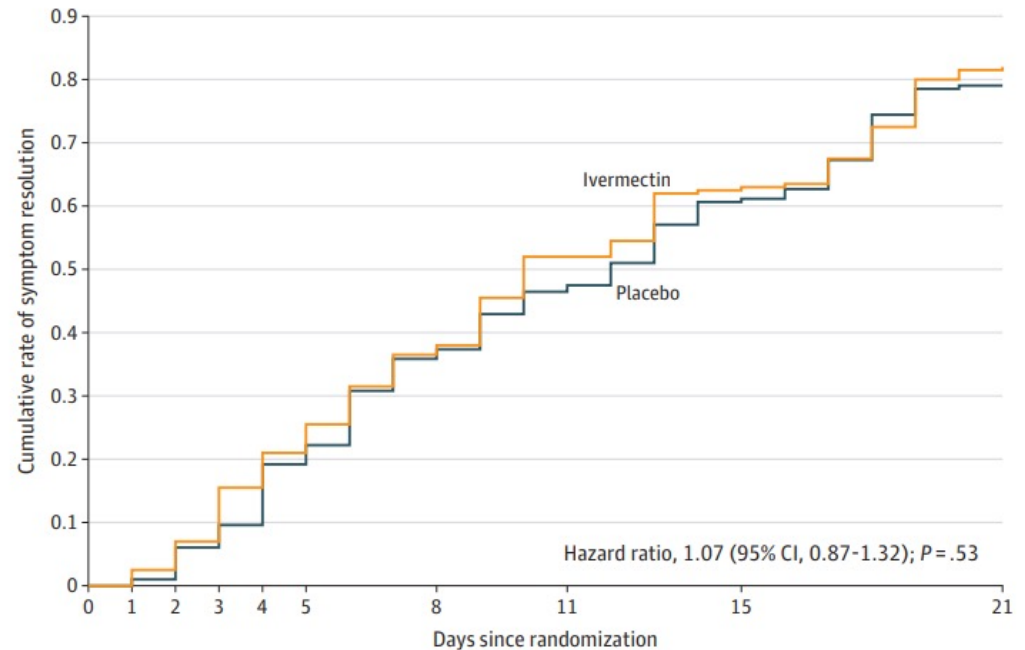Median age: **37** years

**LOCATIONS**

1
Site in Cali, Colombia

**INTERV**[...]

**Iver**[...]
Oral iv[...]
300 µg[...]
per day[...]

**PRIMAR**[...]

Figure 2. Time to Resolution of Symptoms in the Primary Analysis Population

Hazard ratio, 1.07 (95% CI, 0.87-1.32); P = .53

| | Days since randomization |
|---|---|
| No. at risk | 0  1  2  3  4  5    8    11    15    21 |
| Ivermectin | 200 195 186 169 158  127   96   75   37 |
| Placebo | 198 196 186 179 160  127  106   77   41 |

López-Medina E, López P, Hurtado IC, et al. Effect of [...]
*JAMA.* Published online March 4, 2021. doi:10.1001/[...]

# IDSA and FDA weigh in

**Overview of IDSA COVID-19 Treatment Guidelines**
*Version 4.1.0 — March 5, 2021*

| | | Setting and severity of illness | | | |
|---|---|---|---|---|---|
| | | **Ambulatory care**: *mild-to-moderate disease* | **Hospitalized**: *mild-to-moderate disease without need for suppl. oxygen* | **Hospitalized**: *severe but non-critical disease (spO₂ <94% on room air)* | **Hospitalized**: *critical disease (e.g., in ICU needing MV, or septic shock, ECMO)* |
| 17-18 | Ivermectin | Suggests against use except in a clinical trial ⊕○○○ | NA | Suggests against use except in a clinical trial ⊕○○○ | NA |

## Why You Should Not Use Ivermectin to Treat or Prevent COVID-19

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COVID-19. We've been living with it for what sometimes seems like forever. Given the number of deaths that have occurred from the disease, it's perhaps not surprising that