Rapid recovery of peripheral oxygen saturation in hypoxic COVID-19 patients with ivermectin-based multidrug therapy

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Ivermectin–Testimonials from Physicians Worldwide

https://ivermectinbook.com/index.htm

- The use of ivermectin in the treatment of COVID-19 has generated extensive scientific debate and controversy
- A collection of doctor testimonials was published in 2025 in a book published by Nantosha Co (Tokyo, Japan)
- Clinical observations were reported from: United States, Canada, Argentina, Australia, Brazil, India, Japan, Netherlands, Nigeria, Philippines, South Africa, St Lucia, Zimbabwe.
- All doctors reported successful treatment of COVID-19 patients using ivermectin-based multidrug treatment protocols.
- All doctors also reported persecution by government authorities and/or medical boards.

Ivermectin-based COVID-19 therapy for severely ill patients was announced by Borody and colleagues in 2021

using a 10-day ivermectin, doxycycline, zinc triple-drug combination baseline protocol

Ivermectin: a multifaceted drug of Nobel prize-honoured distinction with indicated efficacy against a new global scourge, COVID-19

A. D. Santin[1], D. E. Scheim[2], P. A. McCullough[3], M. Yagisawa[4] and T. J. Borody[5]

1) *Department of Obstetrics & Gynecology, Yale University School of Medicine, New Haven, CT,* 2) *US Public Health Service, Inactive Reserve, Blacksburg, VA,* 3) *Texas A & M College of Medicine, Dallas, TX, USA,* 4) *Ōmura Satoshi Memorial Institute, Infection Control Research Center, Kitasato University, Tokyo, Japan and* 5) *Centre for Digestive Diseases, New South Wales, Australia*

New Microbe and New Infect 2021; **43:** 100924

- **Quote:** *"Results using IVM, doxycycline and zinc to treat serious and critical cases having $SpO_2 \leq 90\%$ prior to treatment, with SpO_2 changes tracked 24 hours after treatment, will be reported by TJB with Sabine Hazan, MD. Pronounced improvements of serious COVID-19 symptoms within 1-2 days after IVM administration have been observed in several patients treated by the lead author (ADS), and studies to objectively track such short-term clinical benefits of IVM for COVID-19 are underway."*

Goals of our study: Ivermectin-based treatment of hypoxemic patients

⟨Review Article⟩

Critical appraisal of multidrug therapy in the ambulatory management of patients with COVID-19 and hypoxemia Part I. Evidence supporting the strength of association

Eleftherios Gkioulekas, Ph.D.[1,*], Peter A. McCullough, M.D., M.P.H.[2] and Colleen Aldous, Ph.D.[3]

⟨Review Article⟩

Critical appraisal of multidrug therapy in the ambulatory management of patients with COVID-19 and hypoxemia Part II: Causal inference using the Bradford Hill criteria

Eleftherios Gkioulekas, Ph.D.[1,*], Peter A. McCullough, M.D., M.P.H.[2] and Colleen Aldous, Ph.D.[3]

- Independent reanalysis: 3 patient case series of 119 patients combined.
- 61 severely hypoxic patients ($SpO_2 \leq 90\%$) treated with 10-day ivermectin protocol
- *Locations:* United States (Hazan case series), Zimbabwe (Stone case series), Nigeria (Babalola case series).
- **Part 1:** Established reduction in mortality and hospitalizations.
- **Part 2:** Established the Bradford Hill criteria of: temporality, biological plausibility, consistency, biological gradient, and coherence

Descriptive characteristics of the three case series

Case series	Patients with baseline SpO2 $\leq 100\%$	$\leq 93\%$	$\leq 90\%$ (p_1)	Deaths	Deterioration	Period
Hazan	24	23	23 (95.8%)	0	0	2020-08 to 2021-02
Stone	34	34	28 (82.3%)	0	1	2020-08 to 2021-05
Babalola	61	21	10 (16.4%)	0	5	2021-04 to 2021-06

Demographic characteristics for the severely hypoxic patients with $SpO_2 \leq 90\%$

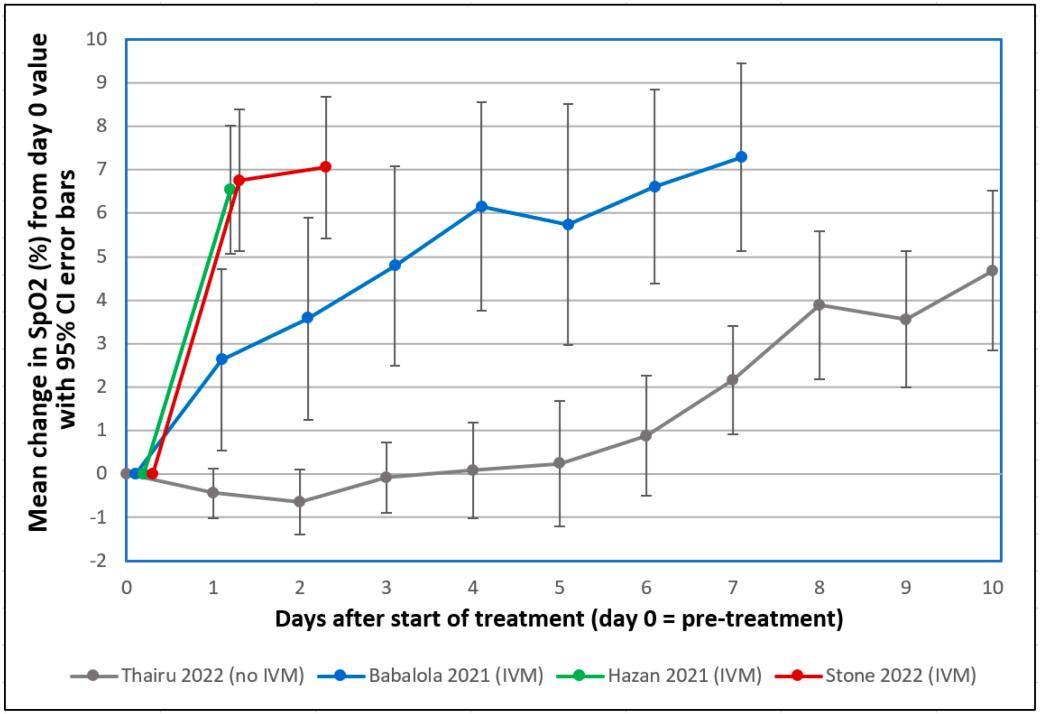
	Hazan		Stone		Babalola		H+B		S+B		H+S		H+S+B	
Characteristic	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Sex														
Male	14	60.9	16	57.1	6	60	20	60.6	22	57.9	30	58.8	36	59
Female	9	39.1	12	42.9	4	40	13	39.4	16	42.1	21	41.2	25	41
Age brackets														
21 to 30 years	0	0.0	1	3.6	2	20	2	6.1	3	7.9	1	2	3	4.9
31 to 40 years	0	0.0	3	10.7	4	40	4	12.1	7	18.4	3	5.9	7	11.5
41 to 50 years	4	17.4	6	21.4	1	10	5	15.2	7	18.4	10	19.6	11	18
51 to 60 years	4	17.4	8	28.6	1	10	5	15.2	9	23.7	12	23.5	13	21.3
61 to 70 years	9	39.1	6	21.4	1	10	10	30.3	7	18.4	15	29.4	16	26.2
71 to 80 years	2	8.7	3	10.7	0	0.0	2	6.1	3	7.9	5	9.8	5	8.2
81 to 90 years	2	8.7	1	3.6	0	0.0	2	6.1	1	2.6	3	5.9	3	4.9
91 years or older	2	8.7	0	0.0	0	0.0	2	6.1	0	0.0	2	3.9	2	3.3
Baseline SpO2 at room air														
$85\% < SpO2 \leq 90\%$	19	82.6	16	57.1	7	70	26	78.8	23	60.5	35	68.6	42	68.9
$80\% < SpO2 \leq 85\%$	2	8.7	7	25	0	0.0	2	6.1	7	18.4	9	17.6	9	14.8
$75\% < SpO2 \leq 80\%$	1	4.3	4	14.3	3	30	4	12.1	7	18.4	5	9.8	8	13.1
$70\% < SpO2 \leq 75\%$	1	4.3	0	0.0	0	0.0	1	3	0	0.0	1	2	1	1.6
$65\% < SpO2 \leq 70\%$	0	0.0	1	3.6	0	0.0	0	0.0	1	2.6	1	2	1	1.6

Summary of treatment protocols for each case series

- **Hazan treatment protocol:** 24 patients, treated via telemedicine, United States
  - *Baseline protocol:* doxycycline (100 mg twice a day for 10 days), ivermectin (12 mg on day 1, day 4, and day 8), zinc (25 mg elemental zinc twice a day for 10 days), vitamin D3 (1,500 IU twice a day for 10 days), and vitamin C (1,500 mg twice a day for 10 days).
  - Ivermectin dosage escalated daily in 12 mg increments when SpO_2 plateaued or exhibited decreasing trend
  - Ivermectin dosage was further escalated during the first 24 hours, ro accelerate the rate of recovery with the goal of stabilizing patients at $SpO_2 \geq 90\%$ on room air.
  - 36 mg stat dose was given to patients immediately if serious concern about prognosis for the next 24 hours. ($SpO_2 \leq 75\%$ on room air)
- **Stone protocol:** 34 patients, treated in person or via traveling nurses at home, Zimbabwe
  - Three multidrug protocols for *mild disease*, *severe disease*, *salvage protocol*, that combined ivermectin, nanosilver nebulizations, doxycycline, zinc, vitamin C, vitamin D.
  - Similar ivermectin dose escalation depending on patient severity and response.
  - Optional use of prednisone, enoxaparin, rivaroxaban, ceftriaxone, azithromycin, aspirin.
  - Rule of thumb: Duration of ivermectin treatment and nanosilver nebulizations was continued for 48 hours after the resolution of symptoms, with dosage adjusted to severity
- **Babalola protocol:** 61 patients; clinical trial, Nigeria
  - *Baseline protocol:* ivermectin 0.2 mg/kg daily for 5 days, zinc sulfate (50-100 mg daily for 7 days), vitamin C (1000 mg daily for 7 days)
  - *Additional medications:* hydroxychloroquine 200 mg per day for 3 days and azithromycin 500 mg per day for 3 days (given to 31 of 61 patients).
- **Patients were treated on room air with no supplemental oxygen!**

Rapid recovery of oxygen saturations. Part 1

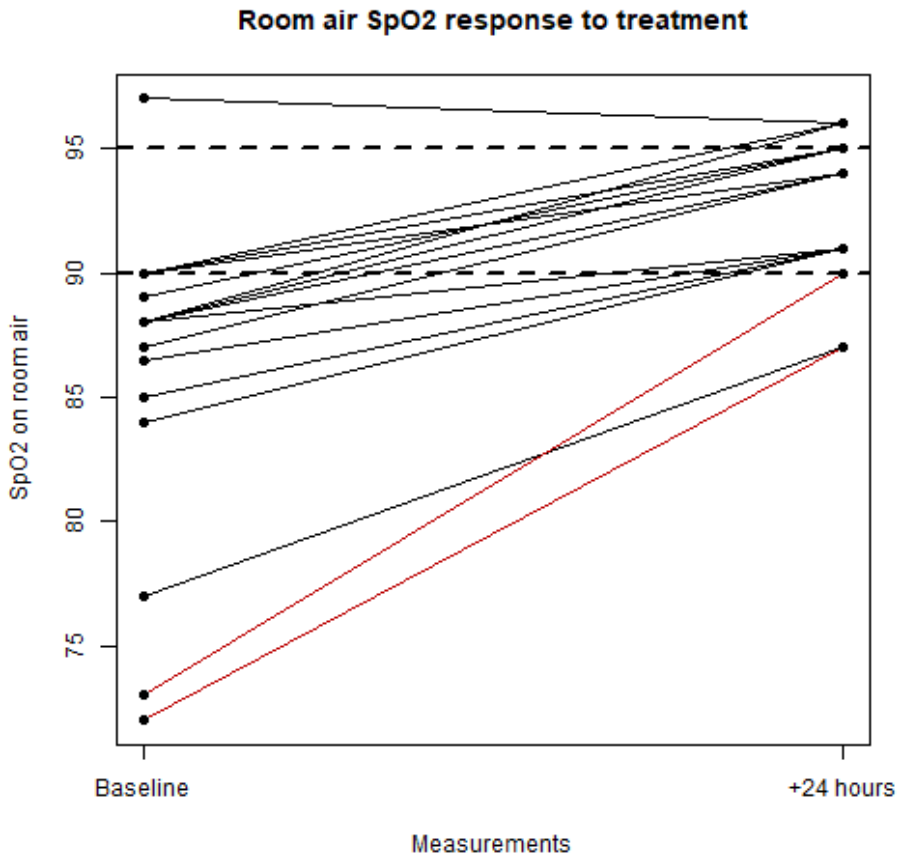
Bradford Hill criteria: Temporality, Consistency, Biological gradient, Biological plausibility



- Mean change to room air SpO2 levels from initial value at Day 0 for the patients in the Hazan, Stone, and Babalola case series with baseline room air SpO2 $\leq 93\%$.
- *Temporality:* Rapid response to treatment
- *Consistency:* Same effect in patients from United States, Zimbabwe, Nigeria
- *Biological gradient:* Stronger response with the most aggressive protocols.
- *Biological plausibility:* Known mechanisms, reviewed in our paper.

Rapid recovery of oxygen saturations. Part 2

Bradford Hill criteria: Temporality, Biological gradient



- Change in SpO_2 levels on room air are shown at baseline and after 24 hours (day 2) for the Hazan case series patients.
- Red color shows the change in SpO_2 levels on room air for the two patients that received the 36 mg stat dose of ivermectin on day 1.
- Horizontal dotted lines demarcate the patient stabilization threshold of 90% and the curative threshold of 95% for room air SpO_2 levels.

Mechanism of action responsible for oxygen saturation recovery

Bradford Hill criteria: biological plausibility

International Journal of *Molecular Sciences*

MDPI

Review

Sialylated Glycan Bindings from SARS-CoV-2 Spike Protein to Blood and Endothelial Cells Govern the Severe Morbidities of COVID-19

David E. Scheim [1,*], Paola Vottero [2], Alessandro D. Santin [3] and Allen G. Hirsh [4]

- According to Scheim *et al.*, the formation of the pulmonary microemboli, responsible for oxygen desaturation, is caused by red blood cell clumping which is mediated by glycan bindings between the glycans on the SARS-CoV-2 viral spike protein and sialoglycoproteins on the surface of red blood cells.
- The reason why common cold viruses do not cause a similar formation of microemboli is because, unlike the more virulent SARS, SARS-CoV-2, and MERS viruses, common cold viruses express hemagglutinin esterase, which releases these glycan bindings.
- Scheim *et al.*also reviewed an in-vitro experiment by Boschi *et al.*in which it was observed that:
  1. Adding viral spike protein from the Wuhan, Alpha, Delta, and Omicron variants to human blood induced red blood cell clumping.
  2. Ivermectin blocks hemagglutination, if it is added before the spike protein, and reverses hemagglutination when it is added afterwards.

Case series threshold analysis method.

COVID

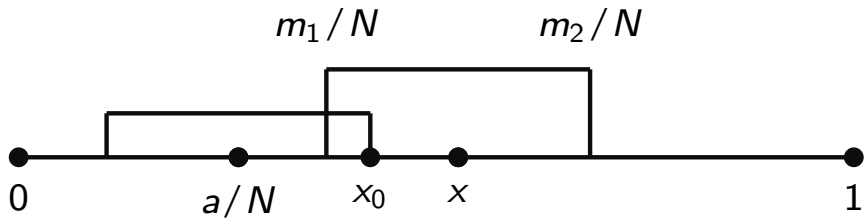
MDPI

Article

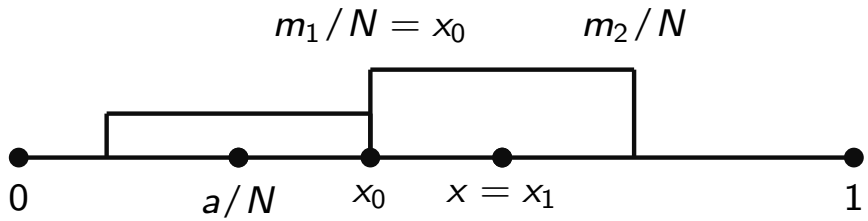
Statistical Analysis Methods Applied to Early Outpatient COVID-19 Treatment Case Series Data

Eleftherios Gkioulekas [1,*], Peter A. McCullough [2] and Vladimir Zelenko [3,†]

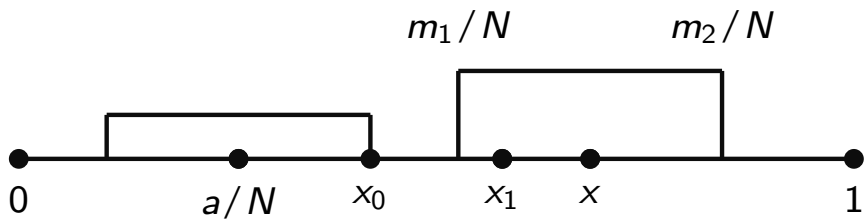
- **Preponderance of the evidence**



- **Crossover to clear and convincing**



- **Clear and convincing**



- Efficacy threshold x_0 may be increased to adjusted efficacy threshold y_0 to control a Bayesian factor. Then y_0 is used to obtain x_1.

Mortality rate reduction claim for Hazan and Stone case series

Bradford Hill criteria: strength of association

⟨Review Article⟩

Critical appraisal of multidrug therapy in the ambulatory management of patients with COVID-19 and hypoxemia Part I. Evidence supporting the strength of association

Eleftherios Gkioulekas, Ph.D.[1,*], Peter A. McCullough, M.D., M.P.H.[2] and Colleen Aldous, Ph.D.[3]

- **Method:** Risk stratified subgroups of patients with baseline $SpO_2 \leq 90\%$ were compared against historical controls of hospitalized patients in the respective locations.
- **Results:**
  - **Stone case series:** mortality rate reduction successfully established by the *preponderance of evidence*
    - Historical controls in Zimbabwe and South Africa support CFR $\geq 20\%$
    - Preponderance of the evidence finding requires CFR $\geq 12.0\%$
  - **Hazan + Stone combined case series:** existence of mortality rate reduction effect conclusively claimed by the *preponderance of evidence*
    - Any combination of the available historical controls supports CFR $\geq 12\%$
    - Preponderance of the evidence finding requires CFR $\geq 7.4\%$.
    - However, a *clear and convincing* finding cannot be claimed

Several RCTs are not generalizable

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⟨Review Article⟩

Critical appraisal of multidrug therapy in the ambulatory management of patients with COVID-19 and hypoxemia Part II: Causal inference using the Bradford Hill criteria

Eleftherios Gkioulekas, Ph.D.[1,*], Peter A. McCullough, M.D., M.P.H.[2] and Colleen Aldous, Ph.D.[3]

- Several other RCTs are not generalizable to the Hazan/Stone 10-day protocol on hypoxic high-risk patients, because of:
  1. Short duration of treatment (2 or 3 days)
     - Reis *et al.* 2022 (TOGETHER), Vallejos *et al.* 2021, Ravikirti *et al.* 2021, Bramante *et al.* 2022 (COVID-OUT), Naggie *et al.* 2022 (ACTIV-6 400)
  2. Low-risk cohorts with no deaths observed on treatment and control group
     - Buonfrate *et al.* 2022, Chaccour *et al.* 2021, Krolewiecki *et al.* 2021, Mohan *et al.* 2021, Naggie *et al.* 2023 (ACTIV-6 600)
  3. *Lopez-Medina 2021:* Low-risk patients or protocol violation with patients in control group accessing ivermectin over the counter.
- An exhaustive review of all available evidence is given in our paper.

Mortality reduction requires rapid recovery of oxygen saturation and dynamically adjusted ivermectin dosage

infectious disease reports

MDPI

Article

Efficacy and Safety of Ivermectin and Hydroxychloroquine in Patients with Severe COVID-19: A Randomized Controlled Trial

Jose Lenin Beltran Gonzalez [1], Mario González Gámez [1,*], Emanuel Antonio Mendoza Enciso [1], Ramiro Josue Esparza Maldonado [1], Daniel Hernández Palacios [1], Samuel Dueñas Campos [1], Itzel Ovalle Robles [1], Mariana Jocelyn Macías Guzmán [1], Andrea Lucia García Díaz [1], César Mauricio Gutiérrez Peña [1], Lucila Martinez Medina [2], Victor Antonio Monroy Colin [2] and Jose Manuel Arreola Guerra [1,*]

- *Setting:* Mexico, May-August 2020, hospitalized patients
- *High risk patient cohort:* $83\% \pm 8\%$ average baseline SpO_2
- *Treatment:* 5-day ivermectin protocol at 0.15 to 0.22 mg/kg
- **Dosage and duration for ivermectin similar to Babalola case series.**
- *Mortality reduction:* 16.2% for control group; 13.8% for treatment group, not significat
- **Our interpretation:** The slower recovery rate observed in the Babalola case series is not sufficiently rapid to result in mortality rate reduction for severely ill patients with oxygen saturation near 80% or below 80%.
- **Therefore:** ivermectin dosage should be adjusted to patient severity to ensure faster patient stabilization, as per Hazan and Stone protocols.

Interesting mortality reduction signal from ITECH trial (Lim *et al.* 2022)

JAMA Internal Medicine | Original Investigation

Efficacy of Ivermectin Treatment on Disease Progression Among Adults With Mild to Moderate COVID-19 and Comorbidities

The I-TECH Randomized Clinical Trial

Steven Chee Loon Lim, MRCP; Chee Peng Hor, MSc; Kim Heng Tay, MRCP; Anilawati Mat Jelani, MMed; Wen Hao Tan, MMed; Hong Bee Ker, MRCP; Ting Soo Chow, MRCP; Masliza Zaid, MMed; Wee Kooi Cheah, MRCP; Han Hua Lim, MRCP; Khairil Erwan Khalid, MRCP; Joo Thye Cheng, MRCP; Hazfadzila Mohd Unit, MRCP; Noralfazita An, MMed; Azraai Bahari Nasruddin, MRCP; Lee Lee Low, MRCP; Song Weng Ryan Khoo, MRCP; Jia Hui Loh, MRCP; Nor Zaila Zaidan, MMed; Suhaila Ab Wahab, MMed; Li Herng Song, MD; Hui Moon Koh, MClinPharm; Teck Long King, BPharm; Nai Ming Lai, MRCPCH; Suresh Kumar Chidambaram, MRCP; Kalaiarasu M. Peariasamy, MSc; for the I-TECH Study Group

- *Setting:* Malaysia, May-October 2021, hospitalized patients + quarantine center
- *Treatment:* 5-day ivermectin at 0.4 mg/kg plus SOC vs SOC
- *High risk patient cohort:* age ≥ 50 years and at least one comorbidity, $SpO_2 \geq 95\%$ at baseline
- *Mortality reduction:* 4.0% for control group; 1.2% for treatment group, $p = 0.09$
- *Study was underpowered:* $p < 0.05$ is satisfied if CFR ≥ 3.7 for an equivalent population-level control.

Conclusion

- Rapid recovery of oxygen saturation in hypoxic patients follows from use ivermectin-based multidrug treatment protocols.
- Dose response effect has been observed.
- Viral spike protein in the bloodstream causes red blood cell clumping which causes oxygen desaturation
- Ivermectin dosage should be adjusted each day to individual patient's response to treatment due to variability of spike protein exposure per patient.
- Treatment should ideally continue until symptom resolution (typically 10 day duration)
- Day 1 ivermectin dosage can go as high as 0.6mg/kg and titrated to 1-2 mg/kg for severely ill patients with saturations below 80%, until an increase in oxygen saturation levels is observed.
- 0.2 mg/kg ivermectin for 5 days is not sufficient for the treatment of severely hypoxic patients
- 0.4 mg/kg ivermectin for 5 days provided some mortality reduction but higher dosage was clearly necessary for some patients.
- A claim of mortality rate reduction is supported by the preponderance of the evidence, based on comparison of the case series against historical controls.
- Sufficient to justify emergency adoption.