Editorial

Journal of INDEPENDENT MEDICINE

Treat the Patient, Not Just the Virus: Rethinking Influenza Treatment

Paul E. Marik[1]

Every winter, millions get the flu. Most recover. Some don't. The difference isn't fully explained by the virus alone — it depends on the terrain it meets: the immune system, the mitochondria, the oxidative balance, the inflammatory response. For decades, we've treated influenza as if it were a single-target disease. It isn't.

The Virus, Briefly

Influenza is a small, enveloped RNA virus that hijacks the host cell nucleus to replicate — an unusual trick among RNA viruses. Its two surface proteins, hemagglutinin (HA) and neuraminidase (NA), let it enter cells and then escape them to spread further. Its genome is split into eight segments, which lets small mutations accumulate each year (antigenic drift, the reason vaccines need updating) and occasionally lets two strains swap segments entirely (antigenic shift, the mechanism behind pandemics). Clinically, much of the damage comes not from the virus directly but from the intense inflammatory response it triggers — which also explains why influenza opens the door to secondary bacterial pneumonia, the leading cause of death in severe cases.

Where the Standard Model Falls Short

The conventional approach — identify the virus, prescribe a neuraminidase inhibitor (usually oseltamivir/Tamiflu), and treat symptoms — has three problems. First, the new REMAP-CAP randomized trial reported a signal of increased 90-day mortality with oseltamivir compared with no antiviral in critically ill influenza patients, regardless of whether treatment lasted 5 or 10 days; the trial was stopped early after crossing a pre-specified monitoring threshold, though this preliminary, preprint finding still awaits full peer review and confirmation. (1) Second, outside the ICU, evidence that neuraminidase inhibitors meaningfully reduce hospitalization or pneumonia remains inconsistent. Third, and most fundamentally, this model ignores host biology: the immune response, not viral load alone, drives severity — which is why two patients with the same virus can have completely different outcomes.

A Multi-Axis Alternative

If influenza is really a collision between virus and host across four fronts — nasopharyngeal viral replication, immune dysregulation, oxidative/mitochondrial injury, and inflammatory lung damage — then no single drug should be expected to fix it. A more rational approach applies pressure across all four simultaneously:

Reduce viral load at the entry site. The nose is where infection starts, so early, repeated nasal irrigation or spray (saline, iota-carrageenan, xylitol, povidone-iodine, or similar) two to three times daily, paired with an antiseptic mouthwash, is a simple, underused, and biologically sound intervention (2,3) — for the whole household, not just the sick patient.

Apply direct antiviral pressure beyond Tamiflu. Nitazoxanide (600 mg twice daily), a broad-spectrum, host-directed antiviral, (4) and elderberry extract — which appears to interfere with viral entry and may modestly shorten symptom duration when started early (5,6) — are reasonable adjuncts, though elderberry supports rather than replaces antiviral therapy in severe cases.

Support, don't just fight, the host response. Vitamin C (500 mg two to three times daily), zinc (20–50

[1] Independent Medical Alliance, Washington, D.C., USA

Corresponding author:
Paul E. Marik, MD, FCCM, FCCP
Chief Scientific Officer
Independent Medical Alliance, Washington, D.C., USA
Email: pmarik@imahealth.org

mg/day), and melatonin all target inflammatory and immune pathways implicated in why some patients deteriorate even without runaway viral replication.

Address oxidative and mitochondrial injury, an often-overlooked axis. NAC restores glutathione, vitamin C adds antioxidant synergy, and even sunlight exposure may help — notably, open-air treatment was associated with lower mortality during the 1918 pandemic. (7) Repurposed drugs like minocycline or ivermectin are sometimes proposed as adjuncts here, but the evidence for both remains limited or indirect, and neither should be considered a foundational therapy. (8,9)

Put together, a practical framework might look like: nasal spray, mouthwash, vitamin C, zinc, and NAC in the first 1–3 days; adding nitazoxanide for confirmed or worsening disease; melatonin and light exposure as a supportive layer; minocycline or ivermectin only in select cases; and antibiotics reserved strictly for proven bacterial complications, never given prophylactically.

The Tamiflu Problem

Oseltamivir shortens uncomplicated influenza by roughly 17–25 hours — about a day. Its ability to prevent serious complications like hospitalization has long been debated, and part of that debate traces back to how its evidence base was built. A pivotal 2003 pooled analysis backing Tamiflu drew on ten trials, but only two were published; the rest stayed hidden until a 2011 freedom-of-information request led to their release. (10) When Cochrane reviewers examined the complete data in 2014, their conclusions were more cautious than the original pooled analysis: they did not find convincing evidence that Tamiflu reduced pneumonia, hospitalization, or other serious complications, and noted a higher rate of adverse events such as nausea, vomiting, and some psychiatric and renal effects in adults. (11) A later analysis of the 2009 pandemic did not find a mortality benefit either, which has led some researchers to suggest oseltamivir's main measurable effect may be symptomatic (e.g., fever reduction) rather than a reduction in complications — though this remains one interpretation among several. The REMAP-CAP trial adds a further data point worth watching closely: in 442 critically ill patients across 18 countries, oseltamivir was associated with higher odds of death at 90 days, a signal strong enough that the trial's monitoring committee halted enrollment early. (1) As a preprint, this finding requires independent replication and formal peer review before it should influence clinical practice, but taken together with the Cochrane findings, it suggests the evidence behind Tamiflu's widespread use is less settled than it is often assumed to be.

The Bigger Point

None of this is really about any single drug or vaccine. It's about a shift already underway in how we should think about infectious disease: from "one drug, one target" to multi-system modulation. The virus is only part of the story. The host response determines the trajectory. And outcomes likely depend on how many biological systems we support at once, not which single molecule we reach for first. Influenza has been underestimated for decades — not because it's rare or mild, but because we've treated it too narrowly, possibly leaning more heavily on a single class of antiviral drugs than the current evidence may support. Disease is rarely one-dimensional. Treatment shouldn't be either.

References

1. Oseltamivir for Critically Ill Patients with Influenza: A Randomised Trial (REMAP-CAP). Lancet, preprint/preliminary results released June 2026; formal peer-reviewed publication pending.
2. Stathis C, Victoria N, Loomis K, Nguyen SA, Eggers M, Septimus E, et al. Review of the use of nasal and oral antiseptics during a global pandemic. Future Microbiol. 2021;16(2):119–130.
3. Hemilä H, Chalker E. Carrageenan nasal spray may double the rate of recovery from coronavirus and influenza virus infections: re-analysis of randomized trial data. Pharmacol Res Perspect. 2021;9(4):e00810.
4. Haffizulla J, Hartman A, Hoppers M, Resnick H, Samudrala S, et al. Effect of nitazoxanide in adults and adolescents with acute uncomplicated influenza: a double-blind, randomised, placebo-controlled, phase 2b/3 trial. Lancet Infect Dis. 2014;14:609–618.
5. Zakay-Rones Z, Thom E, Wollan T, Wadstein J. Randomized study of the efficacy and safety of oral elderberry extract in the treatment of influenza A and B virus infections. J Int Med Res. 2004;32:132–140.
6. Wieland LS, Piechotta V, Feinberg T, Ludeman E, Hutton B, Kanji S, et al. Elderberry for prevention and treatment of viral respiratory illnesses: a systematic review. BMC Complement Med Ther. 2021;21:112.
7. Hobday RA, Cason JW. The open-air treatment of pandemic influenza. Am J Public Health. 2009;99(Suppl 2):S236–S242.
8. Saha P, Saha R, Datta Chaudhuri R, Sarkar R, Sarkar M, Koley H, Chawla-Sarkar M. Unveiling the antiviral potential of minocycline: modulation of nuclear export of viral ribonuclear proteins during influenza virus infection. Viruses. 2024;16(8):1317. (In vitro/in vivo evidence for an influenza-specific antiviral mechanism; clinical trial evidence in influenza patients is still lacking.)
9. Wagstaff KM, Sivakumaran H, Heaton SM, Harrich D, Jans DA. Ivermectin is a specific inhibitor of importin α/β-mediated nuclear import able to inhibit replication of HIV-1 and dengue virus. Biochem J. 2012;443(3):851–856.
10. Kaiser L, Wat C, Mills T, Mahoney P, Ward P, Hayden F. Impact of oseltamivir treatment on influenza-related lower respiratory tract complications and hospitalizations. Arch Intern Med. 2003;163(14):1667–1672.
11. Jefferson T, Jones MA, Doshi P, Del Mar CB, Hama R, Thompson MJ, et al. Neuraminidase inhibitors for preventing and treating influenza in healthy adults and children. Cochrane Database Syst Rev. 2014;(4):CD008965.

This page is intentionally left blank

