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## A Critique of Recent Medical Research on COVID-19

#### Michael McAleer1-5\*

- <sup>1</sup>Department of Finance, Asia University, Taichung City, Taiwan
- <sup>2</sup>Discipline of Business Analytics, University of Sydney Business School, Sydney, Australia
- <sup>3</sup>Econometric Institute, Erasmus School of Economics, Erasmus University Rotterdam, Rotterdam, Netherlands
- <sup>4</sup>Department of Economic Analysis and ICAE, Complutense University of Madrid, Madrid, Spain
- <sup>5</sup>Institute of Advanced Sciences, Yokohama National University, Kanagawa, Japan

#### **Abstract**

The world community has been changed irrevocably by the highly infectious and mutating SARS-CoV-2 virus that causes the COVID-19 disease. The necessary research output on COVID-19 has been revolutionary, especially in the medical and biomedical sciences, where the search for a vaccine is essential for the world to have a semblance of normality in the era of COVID-19. Much of the advanced research has been distributed in the leading medical journals, including the Journal of the American Medical Association (JAMA), where the latest medical research is distributed on a daily basis, and where comments can also be published. The purpose of this paper is to provide a critique of 26 interesting and highly topical research papers that have been published in JAMA, mostly within the past two months. The diverse topics include treating infuenza and COVID-19 simultaneously, dealing with a second wave of COVID-19 in Beijing, honesty is best for known and unknown GAWI and WIST, unreliability of asymptomatic COVID-19 testing outcomes for children, the effectiveness of fu vaccines, acute anxiety during COVID-19, MAID as an end of life option, longer-term effects of corticosteroids on the mortality of critically ill COVID-19 patients, isolation, loneliness and psychological distress during COVID-19, the selection of volunteers for COVID-19 vaccine trials, the mental health of children and adolescents during COVID-19, fertility preservation through hormonal intervention for transgender adolescents, safe, effective and affordable COVID-19 vaccines, essential requirements for acceptance of a COVID-19 vaccine, ischemic stroke rates from COVID-19 and infuenza, mandatory COVID-19 vaccination of children, COVID-19 asymptomatic children and adults, and Who Dares Wins (Qui Audet Adipiscitur), even against

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\*Corresponding author: Dr. Michael McAleer, Department of Finance, Asia University, Taichung City, Taiwan, Tel: (+886) 3 571 5131; E-mail: michael. mcaleer@gmail.com

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of the coronavirus pandemic and help care for those a ected." e list currently has around 730,000 entries [12].

e purpose of this paper is to supplement the previous reviews and perspectives discussed above by providing a critique of 26 interesting, informative, and highly topical research papers that have been published in JAMA, mostly within the past two months. e diverse topics include public health, general medicine, internal medicine, oncology, pediatrics, geriatrics, and biostatistics.

Each of the papers evaluated here is worth highlighting as they cover several highly topical medical issues in the COVID-19 era, including treating in uenza and COVID-19 simultaneously, dealing with a second wave of COVID-19 in Beijing, honesty is best for known and unknown GAWI and WIST, unreliability of asymptomatic COVID-19 testing

information, advice and a warning to every country that is experiencing a wave of whatever order a er purported abatement, to prepare and plan public health policy in anticipation of a shock that is likely to occur [14].

For purposes of interpretation, a preliminary case study involving 33 asymptomatic positive infections were not recorded as part of the 335 con rmed cases until 5 July 2020, with no informed consent, but with immediate and aggressive contact tracing, self-isolation, and quarantining.

In a stark warning to act quickly with a prepared plan of attack, the public health intervention led to a duration of 7 days from early symptom onset to con rmed case and outbreak alert, with rapid community containment imposed within 24 hours.

Further studies in dealing with second and subsequent waves would make the results of the present study more robust and widely applicable.

As the second wave was attened quickly, a rapid response with strict isolation measures should be a cornerstone of public healthcare policy for any COVID-19 wave that might be churning.

## Honesty is Best for Known and Unknown GAWI and WIST

e honest and sensitive declaration by a caring pediatrician [15] on known and unknown "Got Away With It" (GAWI) and "Will I Sleep Tonight" (WIST) outcomes re ect on the issue that honesty is always the best policy for the physician and their patient.

In many countries, physicians will not always inform their patients of serious diagnoses that a ect morbidity and mortality in order to "spare the patient unnecessary stress and anxiety", which is a denial of informed consent.

GAWI might, in fact, be "Got Away with It Somehow" (GAWIS), but maybe only this time?

If only all physicians could be so humble and compassionate.

# **Unreliability of Asymptomatic COVID-19 Testing Outcomes for Children**

- e analysis by a team of medical researchers [16] investigating the reliability of asymptomatic COVID-19 testing outcomes for children bears careful scrutiny because of the indicative prevalence of infection in children without symptoms that can have a signi cant e ect on infection control policy.
- e data and statistical analysis suggest that there is a strong correlation between disease prevalence in asymptomatic children and the weekly general incidence of COVID-19 in the population.
- e estimated linear regression models in Figures 2A and 2B seem, at rst glance, to support the inferences that are drawn, though the lack of statistical diagnostic checks raises serious questions relating to the robustness of the empirical analysis.
- e estimated model in Figure 2A shows the linear relationship between prevalence and general incidence.

Two obvious outliers in the top and centre right in Figure 2A lead to a downward bias in the estimated linear model, with a concomitant atter relationship between prevalence and general incidence.

Judicious removal of the two outliers would show a steeper and stronger relationship between the two variables. e impact of outliers is even more pronounced in Figure 2B, where only one observation lies above the estimated linear regression, with 3 observations sitting on the estimated line, and 7 below, which indicates that the estimated model cannot possibly be the line of best t.

Furthermore, deletion of the two outliers on the right would make the estimated line much steeper, but without going through the origin, which is logically problematic.

As the detailed study suggests, there is undoubtedly a strong correlation between disease prevalence in asymptomatic children and the weekly incidence of COVID-19 in the general population, with greater scrutiny of the data and alternative estimated models adding greater strength, reliability, and robustness to the important investigation.

#### How E ective are Flu Vaccines?

e informative message about u vaccines by Walter bears careful attention by medical practitioners and patients alike [17].

In addition to asthma su erers, who are designated as high risk potential recipients of the u shot, and how closely monitored are they in a clinic, hospital, or at home?

What are the major causes of suppressed immune systems and chronic medical conditions?

What is the potential morbidity and mortality side e ects when a live attenuated vaccines are given to children aged 2-17 years and to adults aged 18-49 years, both with suppressed immune systems, and high does inactivated vaccines and recombinant vaccines are given to adults, presumably without suppressed immune systems?

What are the likely e ects of u vaccines on asymptomatic COVID-19 patients, and those who have purportedly recovered from the rst bout of the disease?

Potentially catastrophic?

### **Acute Anxiety during COVID-19**

Ayers et al. discussed that stress and anxiety are clear indicators of mental distress due to the possibility of infection, seeing close relatives and friends infected, the likelihood of becoming unemployed with or without medical and employment insurance, and lack of social connections and cohesion through social distancing, self-isolation, quarantining, and lockdowns [18].

e informative and helpful empirical analysis was conducted using US data from 13 March to  $9\,\mathrm{May}\ 2020.$ 

Recent research for the USA and UK through to August 2020 shows that stress, acute anxiety, mental distress, mental illness, and self-harm, all of which are keywords in any internet search, are continuing to grow across all age cohorts, especially among the young, and young women, as the COVID-19 pandemic shows little indication of abatement.

### MAID as an End of Life Option

e sensitive message from a caring neurologist [19] on medical aid in living is reminiscent of the nal words of e Last Samurai, where the Emperor Meiji asks Nathan Algren about the warrior Katsumoto: "Tell me how he died", to which the response is: "I will tell you how he lived".

e medical aid-in-dying (MAID) law enables terminally ill patients with a prognosis of six months or less to request medication to voluntarily end their lives as an end of life option.

Some terminal illnesses may provide clear indications of longevity, but others might be more opaque about the expected time to the end of life.

How accurate is the prognosis of six months for all illnesses and all patients, especially regarding the possible feedback e ect of admission to a MAID program on the prognosis?

# **Longer-Term E ects of Corticosteroids on Mortality of Critical COVID-19 Patients**

A striking nding in the important meta-analysis of clinical trials of systemic corticosteroids for critically ill COVID-19 patients, compared with usual care or placebo as the conditioning set, was associated with lower 28-day all-cause mortality.

Mortality and serious adverse e ects of the corticosteroids were mentioned, but the latter was not explained critically as the de nitions di ered across the clinical trials.

As ve of the seven randomized trials reported shorter-term mortality at 28 days, this time frame was chosen arbitrarily as the primary outcome.

ere are many questions that can be directed to the empirical ndings of meta-analyses, with the following issues of paramount importance to the health care policies, treatment and outcomes of critically ill patients infected with COVID-19:

- 1. Examining di erent age (median 60 years) and gender (29% women) cohorts;
- 2. Using surveys of random trials that are representative of socio-economic, race and ethnicity, geographic, and environmental considerations:
- 3. Analyzing longer-term mortality beyond 28 days for post-discharge patients;
- Analyzing longer-term mortality beyond 28 days for di erent age and gender cohorts;
- 5. Explaining the more serious adverse e ects, in addition to secondary infections and sepsis, across di erent intervention groups;
- 6. Evaluating the potential corticosteroid-induced complications based on consistent de nitions and methods of assessment for the clinical tria

been the most successful country in terms of dealing with COVID-19, with 509 total cases and 7 deaths (https://www.worldometers.info/coronavirus/).

It is also worth mentioning that Taiwan was not included in the Global Health Security Index.

### **Quality of Life and Dying**

Further to the interesting perspective of Tang et al., the quality of life is important and essential for every individual, regardless of their health status [32].

Anyone who is approaching the end of their life wants to be surrounded by those who will miss them the most.

Dying at home is preferred by many terminally-ill patients, but when to move from a hospital to their home or to a hospice depends on just how close they are to the end.

#### **Immunity from COVID-19?**

Vaccine or no vaccine, immunity from COVID-19 in whatever form is the end game in the battle against COVID-19, so the Viewpoint from medical specialists is encouraging in understanding and predicting the duration of protection [33].

Adaptive immunity within the  $\,$  rst 7 to 10 days of infection would seem to be useful if the precise timing and degree of severity of infection were possible.

Virus neutralizing antibodies may be a viable path to immunity, but can the duration of protection be predicted with accuracy?

Key issues to consider in existing clinical trials to strengthen the important ndings on establishing immunity from COVID-19 would be to consider the e ects of:

1. Precise timing and degree of severity of infection;