



Benefit of OTC Formula Against COVID-19—Statistical Analysis Explained

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We certainly agree with the author(s) of the letter that randomized controlled trials are advocated and necessary. Review of our article shows that this issue was clearly and repeatedly addressed:

“Our adoption of conservative exposure-and-symptom-presentation values in data analysis may compensate for lacunae in study design and execution. The study emerged from our efforts to protect our patients and staff members from COVID-19 [in the time-frame March-July 2020, when no or very limited effective guidelines or treatments were available]...it is our hope that the study will serve as a basis for future larger-scale studies of enhanced design...While we believe that the stark difference in clinical outcomes between the test and control groups demonstrates the utility of the study formulations, we certainly welcome future extensive prospective studies.”

The letter’s core issue was self-selection by subjects of their inclusion in the control group or the test group. Indeed, we were acutely aware of the issue and directly addressed it in the article: “[F]actor[s] other than implementation of supplementation may be contributing to the outcomes. For instance, subjects interested and motivated to implement and maintain compliance with a multi-component supplement regimen, apparently being more health conscious than control group subjects, may indeed actually be healthier, with more robust immune systems more resistant to viral infection. Perhaps also or alternatively, health conscious subjects are more careful about minimizing their exposure to virus-carrying sources and/or about post-exposure disinfection.” In light of such potentially confounding but not readily quantifiable factors, our article presented a series of analyses in which statistical significance of the results was increasingly ‘handicapped’ away from relevance to supplementation. (See our multiple Binomial Analyses.) However, while we well recognized that non-supplementation-related factors may contribute portions of the raw 530% better outcomes relative to presentation of flu-like symptoms of the test group (2 out of 53) over the control group (12 out of 60), it is difficult to conceive of confounding factors that erode all the stark difference between the groups’ outcomes away from a conclusion of

efficacy of the OTC study formulations. In particular with regard to the letter’s discussion of possible ‘systematic life-style and other differences between people who chose and those who do not chose [sic] to participate in interventional trials,’ we note both that (a) the patient population of our Comprehensive Pain Management Institute is comprised of people who have chosen intervention in management of their pain; and (b) our control and test groups’ essentially identical sets of inclusion criteria included such life-style-related factors as hypertension, coronary artery disease and type 2 diabetes mellitus. Yet another factor constraining and shaping our work was that randomization, alternative allocation or denial of potentially effective treatment under the emergency circumstances of our March-July 2020 time-frame may not have been feasible, or even ethical or compliant with state and federal regulations.

We were very open and direct about potential limitations:

“Several other caveats regarding study design and execution are to be noted:

- (a) The study was obviously conducted neither double-blinded nor even blinded.
- (b) Some of the test group subjects were consistent with their implementation of only part of the core formulation and only selected methods. Possible weaknesses in study-findings’ significance stemming from that deficiency may be balanced against experience of the high-exposure sub-group, who were diligent in taking at least quercetin as zinc ionophore with their zinc, as well as most if not all of the rest of the core formulations. Despite their repeated exposures to clinically- and/or

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test-confirmed COVID-19 carriers, this sub-group presented no cases of COVID-19.

- (c) Self-reporting, both of compliance and of off-site exposures, can be suspected of introducing biasing of data (stemming from subjects' desire to please the physician, researcher and/or employer). Here, one should note—perhaps a tribute to our practice's amicable and accepting atmosphere—that subjects had had no difficulty or hesitation declining the study regimen; opting out from groups and sub-groups during the study; and reporting only partial compliance with the core formulations and methods—all of which bolster a strong presumption of truth-telling in the self-reporting.”

These limitations of our moderately sized study do not render the conclusions invalid or even biased. Rather, the strong raw statistical significance demonstrated, likely at least partly offsetting potential influences of the limitations, is to be treated as a serious indicator both of the need for large scale gold-standard studies and of the potential utility of a low-side-effect OTC tool in the healthcare toolkit for managing COVID-19. There are multiple examples in the literature of similarly gathered data that later contributed to and were confirmed by large randomized studies. It seems that the value of

our study, within its known and stated limitations, is already being seriously considered by other researchers (e.g., *IJID* 110 (2021) 155–159 doi: 10.1016/j.ijid.2021.07.051).

In conclusion, analysis of the clinical outcome data from our sample of 113 subjects—comprised of roughly equal sized regimen-compliant (test) and non-compliant (control) groups meeting equivalent inclusion criteria of age and overall health, including prevalence of COVID-19 comorbidities—demonstrates a strong statistical significance in favor of use of the core formulations of zinc, zinc ionophores and the other presented components.


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