



# Nutrition in times of Covid-19, how to trust the deluge of scientific information

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## **Purpose of review**

The Covid-19 pandemic has daunted the world with its enormous impact on healthcare, economic recession, and psychological distress. Nutrition is an integral part of every person life care, and should also be mandatorily integrated to patient care under the Covid-19 pandemic. It is crucial to understand how the Covid-19 does develop and which risk factors are associated with negative outcomes and death. Therefore, it is of utmost importance to have studies that respect the basic tenets of the scientific method in order to be trusted. The goal of this review is to discuss the deluge of scientific data and how it might influence clinical reasoning and practice.

## **Recent findings**

A large number of scientific manuscripts are daily published worldwide, and the Covid-19 makes no exception. Up to now, data on Covid-19 have come from countries initially affected by the disease and mostly pertain either epidemiological observations or opinion papers. Many of them do not fulfil the essential principles characterizing the adequate scientific method.

## **Summary**

It is crucial to be able to critical appraise the scientific literature, in order to provide adequate nutrition therapy to patients, and in particular, to Covid-19 infected individuals.

## **Keywords**

covid-19, nutrition, quality

## **THE COVID-19 AND THE DELUGE OF PUBLICATIONS**

The Covid-19 pandemic, began in late 2019, in Wuhan, China, followed by a rapid spread worldwide. This has daunted the world with an enormous impact on healthcare, economic recession, psychological distress, and many associated adverse events. Adequate nutrition is an integral part of every person care and should be integrated to the care of patients suffering from Covid-19. It is crucial to understand how the disease develops and what risk factors are associated with negative outcomes and death. Therefore, in order to reach conclusions, it is of utmost importance to carry out studies that respect the basic tenets of the scientific method, while being able to trust their results.

In the last years, the scientific community has been exposed to a huge increase in health scientific publications. Overall, nearly 20 million manuscripts have been reported in PubMed, with about one million defined as 'clinical trials' and almost two million as 'reviews', of which about 10% are systematic reviews [1]. This has not been different for the

Covid-19 pandemic. As of today (April 13, 2020), a search in PubMed for the key word 'covid-19' provided 3810 results [2]; remarkably, none of them was classified as a clinical trial. When the word 'nutrition' was added, the results fell to 30. Considering that there are many intertwined cause/effects variables that may interfere with outcomes, which in statistics may imply collinearity, it is even more challenging for clinicians to interpret results.

## **RISK FACTORS, STATISTICS, AND ACCURATE RESULTS**

Collinearity is a condition in which some of the independent variables are highly correlated, a

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## KEY POINTS

- Under the Covid-19 pandemic many studies have not fulfilled basic tenets of scientific methodology
- The importance of nutrition therapy for Covid-19 patients has seldom been the topic of most published studies, despite its utmost relevancy in the holistic approach of any individual
- The best patient care should mingle clinical reasoning and scientific knowledge
- Massive deluge of publications may not necessarily mean good quality science

situation that will eventually inflate the variance of at least one estimated regression coefficient, thus generating potential flawed or inflated results [3]. In regard to Covid-19 patients, it is known that death rates are increased among the elderly, as shown in particular in Italy [4]. Is this observation related to age alone? Or is it because this group of individuals have increased comorbidities, with polypharmacy as a rule which, together with social isolation make them more vulnerable to nutrition deficiencies? Adding to the confusion, smoking is still highly prevalent among the Chinese, Italian, and Iranian old people. On the other hand, smoking is not so prevalent in the United States of America where the disease has currently outnumbered other countries, with a reasonable number of young patients [5]. Could the U.S. pandemic and death rates among younger Americans be explained by the high obesity prevalence in that country [6]? Obesity is a chronic inflammatory state that may interfere with the acute immunologic response to the virus. Little is known about each one of the afore mentioned potential risk factors, and what role they play on individual populations.

A few years ago, John Ioannidis in a pivotal provocative paper – ‘How to survive the medical misinformation mess’ – addressed the deluge of scientific information [7], which affects not only physicians but also those in the healthcare field who should be thriving to adopt the best evidence practices in order to improve patient care. It is interesting to highlight that Ioannidis’ concerns about the quality of the scientific publications date back to 15 years ago, when he courageously stated that conclusions of most published research findings were false [8]. According to him, the majority of studies lacked methodological quality and were biased because of the absence of statistic power. He also depicted that most study designs and settings were flawed. Therefore, many research claims were more likely to be false than true. More recently,

**Table 1.** The basic/adequate scientific method

Raise a hypothesis
Focus on the aim
Select the right population (avoid selection bias)
Randomization helps prevent it
Determine the required sample size
Key element to prevent false conclusions
Run the proper statistics
Avoid statistical collinearity
Conclude based on the correct method

Ioannidis raised awareness to crucial topics that might interfere with the analysis of data pertaining to the Covid-19 pandemic [9<sup>¶</sup>]. In his opinion, data collected on how many people have been infected are unreliable because of the limiting testing, and death rates are flawed because of this limitation.

Under the Covid-19 pandemic, there has not been a random sample study to correctly indicate the disease prevalence, and the same applies to most studies pertaining interventions. In fact, sample size calculation, a key methodological principle, has not been regularly addressed by many authors, and the same flaw is the rule in most of the published papers regarding the Covid-19 disease. One may understand and even accept that such important requirement may not be fulfilled under the current pandemic as most data come from observational studies. Yet, it is mandatory to either calculate it *a posteriori* (*post hoc*) or to indicate the limitations because of its absence. The methodological quality of research is mandatory, and there are no excuses not to follow it. In fact, adequate sample size has been a major drawback when assessing clinical trials, which may lead to type II statistical errors. Because of this, many authors and institutions have relied on metanalysis to draw conclusions, which is also challenging considering the appropriateness and quality of such studies [1,10<sup>¶</sup>] (Table 1). Furthermore, significant concern has recently emerged: are clinical practitioners able to adequately read and critically appraise the scientific method, and thus the results and conclusions of the studies [11–13]?

## THE COVID-19 AND NUTRITION

In the context of the Covid-19 pandemic, most patients suffering mild signs and symptoms, are treated at home, require symptomatic therapies, and a good healthy diet is recommended as it should be common practice for any individual based on the percepts of healthy living habits. Nonetheless, if the Covid-19 patients are at risk of malnutrition or

**Table 2.** Covid-19 and nutrition

Most papers do not discuss the importance of nutrition on the holistic approach of the disease

Malnutrition and obesity might be serious risk factors for worse outcomes (data not available yet)

The data that support the published papers are derived from similar health conditions, few on Covid-19 patients

malnourished, commonly among the elderly, nutrition supplements may help improve the nutritional status, similarly to at risk-patients with other diseases [14]. A minority of patients do require hospitalization, and less than 5% are admitted in the intensive care units. For these individuals, nutrition therapy should be integrated to the whole therapeutic approach, as for any critical care patient [15,16<sup>■</sup>].

Some authors have published papers addressing nutrition care for Covid-19 patients [16<sup>■</sup>,17,18,19<sup>■</sup>,20,21], but with one exception [19<sup>■</sup>], these are either editorials or based on information derived from different disease states. On the other hand and importantly, the majority of published manuscripts on Covid-19 do not mention the role of nutrition as an integral part of patient care, and the risks of associated burdens, such as obesity. The role of previous inadequate nutrition habits and behavior, two well known risk factors associated with malnutrition, which are also highly prevalent among the elderly, may cause significant impact on the outcomes of the Covid-19 patients. The latter in association with the many other risk factors, including the genetic background lead to excessive inflammation which increases morbidity and mortality (Table 2).

Rundle *et al.* [20] raise awareness to the possibility of long-term effect on children's health, because of the increased risk of obesity while schools are shut down. Luzi *et al.*, on the basis of influenza derived data, advocate that overweight and obese individuals might have an increased risk of complications, because of the permanent inflammatory status as currently seen in the United States. Also, according to these authors, the appearance of a virulent viral strain maybe associated to obesity, and they indicate mild caloric restricted diets and weight loss, and AMPK activators and PPAR $\gamma$  activators as therapeutic approaches for obese and diabetic individuals [21]. On the other hand, such interventions may increase the risk of nutrition deficiencies because many obese people are hidden malnourished individuals [22]. Caccialanza *et al.* [16<sup>■</sup>] present a pragmatic protocol for early nutrition supplementation of noncritically ill hospitalized patients; this is supported by the Italian observations that these patients, present with severe inflammation and

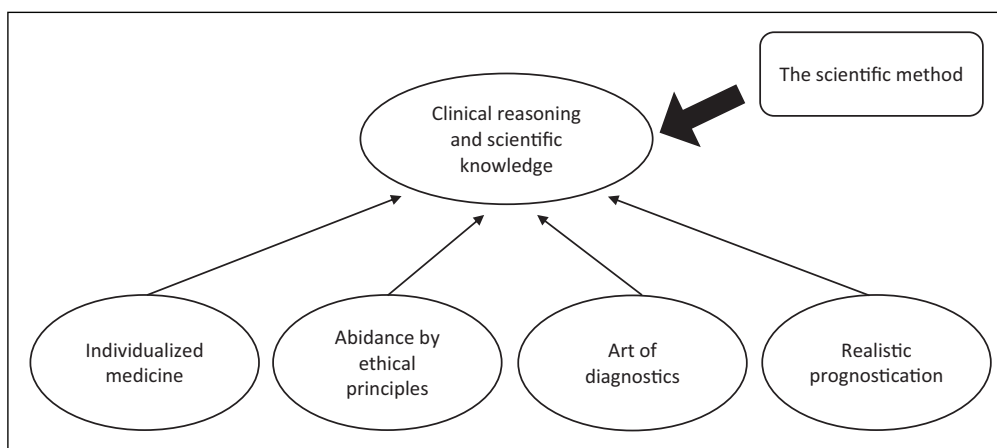
anorexia, at admission, which cause drastic decrease of food intake, further impacted by olfactory and gustatory dysfunctions. In this regard, Lechien *et al.* [19<sup>■</sup>] assessed 417 European patients with mild-to-moderate Covid-19 disease, and indicated that 85.6 and 88.0% of them reported olfactory and gustatory dysfunctions, respectively. Laviano *et al.* [18], in an editorial, raise attention to how nutrition is a determinant of health, and part of the treatment for acute and chronic diseases. They refer to the Ebola virus outbreak in 2014–2016, in Africa, for which immediate supportive care significantly reduced case fatalities. All these papers add numbers to the massive deluge of information; once again, most of them are experts' opinions based on previous observations.

### HOW TO INTERPRET THE DELUGE OF DATA?

Machine learning techniques, for example, random forests or decision trees, might be able to approach the diversity of data and predict outcomes as it has been seen for other disease conditions [23,24<sup>■</sup>,25<sup>■</sup>,26,27]. In the current pandemic, artificial intelligence has also been used [28,29]. Nonetheless, no matter how crucial these new data analyses may help solve controversies in healthcare sciences, it is important to highlight that numbers alone should not replace medical wisdom. It is of utmost importance to understand the biology and physiology behind the data, and namely, to have substantial experience with patients, and not only with numbers. On the other hand, the single use of experts' opinions, even if supported by some evidence as those in guidelines, may be problematic [30]. However, one must acknowledge that the art of Medicine has been supported by the millennial use of aphorisms. One of Latham's aphorisms summarizes where lines cross between good science and the art of practicing medicine (or any other healthcare specialty):

'Medicine is a strange mixture of speculation and action. We have to cultivate science and exercise art. The calls of science are upon our leisure and our choice; the calls of practice are of daily emergence and necessity.' [31]

Thus, clinical experience together with methodological knowledge are key to interpret research evidence and reach conclusions to be used into practice. The excellency of patient care requires practice by the bedside and knowledge to interpret data. Unfortunately, even guidelines (which many clinicians rely on to take decisions) do not fully



**FIGURE 1.** The practice of medicine and science.

acknowledge the poor quality of the data on which they are based, not to mention that sometimes, different recommendations are given within the same guideline [7]. Furthermore, many clinicians (and also guidelines) rely on meta-analyses, considered the highest level of evidence studies, to determine recommendations. Unfortunately, as previously mentioned such studies are also at risk of poor methodological control and quality [32<sup>22</sup>,33<sup>22</sup>,34,35].

Barnard *et al.* [36] have proposed that because meta-analyses, particularly those involving nutrition, influence health policies, and are frequently used by the media, with the potential to do more harm than good, the peer-review process should go beyond the meta-analytic method and include a series of quality control techniques. It is important to highlight that nutrition science novelties, either from epidemiological, experimental or clinical studies, are commonly favorite topics used by the lay media to attract attention, in ways that may jeopardize peoples' health; this has not been different under the Covid-19 pandemic. Mostly, such news confers the benefits of miraculous treatments or discoveries, many not yet proven. The majority of medical articles in the lay media are based on inaccurate criteria, either maximizing benefits, while avoiding to mention potential harms [37].

### THE LAY MEDIA AND SCIENCE

A group of reviewers from HealthNewsReview.org, many of whom physicians, assessed news reported by organizations in the United States of America regarding new medical treatments, tests, products, and procedures. The reviewers evaluated almost 2000 documents, of which 43% were newspaper

articles, 30% wire or new services stories, 15% online material, and 12% network television stories. Most articles were rated unsatisfactory on five of 10 review criteria: costs, benefits, harms, quality of the evidence, and comparison of the new approach with alternatives. It is noteworthy that medical devices, medications, and other interventions were usually reported positively, while potential harms were minimized, and costs not indicated [37]; similar patterns are found in some of the proposed Covid-19 treatments [38]. In fact, the overwhelming number of scientific publications has created a similar awkward situation in healthcare sciences, which is further powered by the boom of scientific journals, questionable review processes, and inadequate metrics [39–41]. Has this resulted in increased wisdom? Unfortunately, not!

### THE PRACTICE OF MEDICINE AND SCIENCE

The importance of individualized medicine, the abidance by ethical principles, and the art of diagnostics, together with realistic prognostication, have their roots in the Hippocratic tradition, which seems to have been neglected in the modern era (Fig. 1). And, by the way, one of the many Hippocrates aphorisms regarded weight loss and cognitive impairment as death predictors [31,42], which are two well known risk factors for malnutrition [43,44]. Therefore, the best patient care should mingle clinical reasoning and scientific knowledge, and the latter requires adequate methods. In summary: raise an hypothesis; present its rationale; thoroughly describe the methods (as a cake recipe), include the sample size that will allow the proper interpretation of the results;



present the findings (results) with details and not as mere numbers but with logic statistical significance; and then focus on the discussion of what was found, comparing it to data from other authors, leaving room for limitations and perspectives.

## CONCLUSION

Finally, it is commonly believed that under critical situations there is a potential for the emergence of a better future. In this regard, raising awareness to the need for adequate scientific methods, and, for better-quality report and assessment might improve messages delivered by science and potentially impact patient care. Afterall, the science of 'guesswork' was long ago challenged by Descartes.

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- of special interest
- of outstanding interest

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