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EDITORIAL

Are health care policies for COVID-19 evidence-based?

The SARS CoV-2 infection has represented the most dramatic global outbreak of modern history, calling worldwide institutions and governments to take health care countermeasures that have significantly affected the life of citizens. Are these measures based on scientific evidence? And if so, why did some common questions and challenges to fight the pandemic (Table I) result in different and often changing approaches in different countries?

Table I. Health policy questions and challenges of COVID-19

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• Should COVID-19 vaccines be mandatory?

• What kind of non-pharmacological preventive measures (masks, social distancing, smart work) must be adopted?

• Schools should be kept open during the pandemic?

• Are antigenic tests reliable to diagnose infection?

• Is quarantine necessary for vaccinated people after contacts at-risk and how long it should last?

• Should a “green-pass” be mandatory (to travel, at workplaces or to enter restaurants and other

social venues such as cinemas, theatres, gyms, stadiums….) and which requirements should be satisfied to issue it (negative swab? one, two or three vaccine doses?)

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There is no doubt that the fight against a new virus and its incoming variants is a learning process and that heath care measures should be adapted to the changing epidemiology of the infection in specific contexts.

However, the common citizen often felt confused by the contrasting opinions of "experts" and by the changing policies adopted by regulatory and political bodies. This has often been responsible for a dangerous distrust toward science and institutions. Therefore, it may be useful to reflect on what scientific evidence is of validity and on the complex relationships between scientific evidence and strength of recommendations.

During the COVID-19 pandemics, available scientific evidence for regulatory and political decisions has been provided by health care institutions and ad hoc consulting bodies nominated by governments. A prerequisite for making the public confident of this scientific advice, is a full transparency about the multidisciplinary competence and the absence of conflict of interests of the experts to whom this difficult task is assigned.

The next step for providing a sound scientific advice must be a correct methodology to review all studies available and to carefully evaluate their quality. This is not an easy task, since PubMed lists 233,262 articles on COVID-19. Interestingly, the only 1,131 randomized controlled clinical trials (CTs) produced 25,472 reviews, 4,551 systematic reviews, 1,901meta-analysis and 460 Practice Guidelines. (https://pubmed.ncbi.nlm.nih.gov/, accessed March 1, 2022). Therefore, distilling high quality data from this massive body of literature is essential to reach scientific evidence. Articles addressing evidence-based medicine in COVID-19, major databases and the list of some of the most recent meta-analysis from PubMed addressing the health policy questions mentioned in Table I are provided as a supplementary file.

A very simple grading of scientific evidence, also easily understandable by the public and media, is provided
by the classification of Shekelle[1] (Table II).

Table II. Grading of evidence according to Shekelle

Level of evidence	*To be supported by*
Evidence A	Meta-analysis of high quality controlled CTs
Evidence B	At least one large, controlled CT
Evidence C	Observational studies and case reports
Evidence D	Opinion of experts

Interestingly, opinion of experts not based on a systematic review and a careful reading of all high-quality studies available, represents the lowest level of evidence. This should be kept in mind when considering the
high number "experts" giving their recommendations at TV talk shows or at lay press interviews. These recommendations for turning evidence into action often follow the "GOBSAT method (Gold Old Boys Sitting Around a Table, pontificating about their own -usually biased- opinions)"[2].

According to the Shekelle classification, recommendations of regulatory bodies should relate to the level of evidence: Evidence A and B should support strong recommendations about preventing or therapeutic interventions, while Evidence C and D might only support suggestions, waiting for more experimental evidence.

An important step forward for understanding the complex relationships between scientific evidence and recommendations is represented by the GRADE method (Grading of Recommendations, Assessment, Development and Evaluation) [3], a tool for rating the quality of evidence and the strength of recommendations, endorsed by over 100 well-known organizations around the world[4].
GRADE highlights the importance of the quality of studies for rating evidence, indicating criteria that may downgrade (inconsistency of results across studies, risk of bias, indirectness of evidence, imprecision and

publication bias) or upgrade evidence (large magnitude of the effect, a dose-response gradient between the intervention and the outcome, no other plausible confounding factors affecting conclusions on the effect of the intervention)[4].

Accordingly, not all evidence emerging from clinical trials should allow binding recommendations if the quality of the trials is poor, while even observational studies or single case reports may support strong recommendations if one or more criteria for upgrading evidence are answered.

The article of Smith and Pell[5] may represent an example of the latter eventuality. The question of this provocative paper is whether the use of parachute should be recommended to avoid death and injuries caused by free gravitational falls. Since no randomized controlled trial in volunteers was found in a systematic review of the literature but only case reports, according to the Shekelle classification the use of parachute should only be suggested. However, the magnitude and consistency of the effect (death or survival) should upgrade in this case the level of evidence, and strongly recommend using the parachute without waiting ~~for waiting~~ for large interventional controlled trials.

Based on this accurate review of the quality of studies GRADE provides a reproducible and transparent framework for grading certainty in evidence that, as in the Shekelle classification, can be rated
in four levels : high, moderate, low and very low. High and moderate evidence should imply strong recommendations in favor or against an intervention, while weak recommendations imply an important variation in the decision that informed persons are likely to make.

However, GRADE introduces an important difference in the complex relationships between the level of evidence and the strength of recommendations. In fact, given an accurate estimate of scientific evidence, the strength of recommendations may also depend on its implications for the different categories who make the recommendations and targets (scientists, physicians, citizens, policy makers) as well as on other factors such as benefits, risks, burden and costs~~5~~[6]. For instance, policy makers in making recommendations
on preventive and therapeutic interventions during the COVID-19 pandemic, beside scientific evidence, should also consider the changing epidemiology of the infection in the specific context, the availability of other effective interventions, the economic impact, values and preferences of the population, the cost for

individuals vs the cost for society (with special reference to personnel and resources available for providing
adequate health care services in front of an increasing demand)[7].

In conclusion, whether appropriate methodological tools are applied, scientists may come to an objective evaluation of evidence on the most appropriate preventive and therapeutic interventions to fight the COVID-19 pandemic. However, these should be continuously reviewed and adapted to the changing epidemiology of SARS CoV-2 infection and acquisition of new data from a necessary global data sharing approach. On the other hand, recommendations by policy makers are more subjective, depending on the weight assigned to other additional parameters underlying difficult decisions. These should be necessarily accompanied by a detailed and transparent communication, an essential tool to guarantee trustiness and compliance of citizens.

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