Principles of Economic Evaluation in a Pandemic Setting: An Expert Panel Discussion on Value Assessment During the Coronavirus Disease 2019 Pandemic

Yumi Asukai1 · Andrew Briggs2 · Louis P. Garrison3 · Benjamin P. Geisler4,5 · Peter J. Neumann6 · Daniel A. Ollendorf6

Accepted: 2 September 2021 / Published online: 24 September 2021 © The Author(s) 2021

Abstract
As the coronavirus disease 2019 (COVID-19) pandemic continues to generate significant morbidity and mortality as well as economic and societal impacts, the landscape of potential treatments has slowly begun to broaden. In the case of a novel disease with widespread consequences, society is more likely to place significant value on interventions that reduce the outsized economic burden of COVID-19. Treatments for severe disease will have a different value profile to that of large-scale vaccines because of their application in targeted and potentially small subsets of those with symptomatic disease vs broad deployment as a preventative measure. Where vaccines reduce transmissibility of COVID-19, use of therapeutics will target symptoms, up to and including death for infected individuals. This paper describes discussions from a virtual expert panel that met to attempt a consensus on how existing principles of economic evaluation should be applied to therapeutics that emerge in a pandemic setting, with specific focus on severe hospitalised cases of COVID-19. The panel concluded that the core principles of economic evaluation do not need to be drastically overhauled to meet the challenges of a pandemic, but that there are several additional elements of value such as equity, disease severity, insurance value, and scientific and family spillover effects that should be considered when presenting results to decision makers. The panel also highlighted the persistent challenges on how society should value novel therapies, such as the appropriate cost-effectiveness threshold to apply, which are particularly salient during a pandemic.

Key Points for Decision Makers

Although usual economic evaluation principles remain unchanged within the context of the coronavirus disease 2019 pandemic, treatment evaluation should consider the broader benefits of restoring economic and social activity.

Several additional elements of value should be considered, including the disproportionate impact on certain patient groups, long-term effects of the disease, insurance value and impact on families, and the evaluation should adapt as the relative importance of these elements change as the pandemic evolves.

Finally, careful consideration should be given to the most appropriate cost-effectiveness threshold to apply in a pandemic setting.
1 Introduction

The coronavirus disease 2019 (COVID-19) pandemic has, as of July 2021, infected over 180 million individuals and caused almost four million deaths worldwide, with over 30 million cases in the USA and India, with 600,000 deaths in the USA and 400,000 in India [1]. Alongside significant health impacts, countries around the world have endured heavy and wide socioeconomic consequences of the virus—in the USA alone, the economic toll of COVID-19 is estimated at over $16 trillion, which is considered a conservative estimate [2].

The majority of patients with COVID-19 have no or mild symptoms and recover from the disease. Up to 22% of patients experience severe infection and require hospitalisation [3]. These patients may experience severe consequences such as acute respiratory distress syndrome, necessitating intubation/mechanical ventilation or extracorporeal membrane oxygenation in intensive care units, and COVID-19, sometimes independent of an intensive care unit stay, can lead to long-lasting symptoms post-discharge. Through improvements in clinical management, mortality rates have dropped since the start of the pandemic; however, 8–20% of patients hospitalised with COVID-19 in the USA still die [4, 5]. Mortality rates adjusted for population size have been particularly high in South American countries such as Brazil, Peru and Argentina, as well as European countries such as the UK and Italy [6]. Patients at increased risk of severe COVID-19 include those of an older age and/or with underlying medical conditions including obesity [7].

A key issue from a health economics perspective is whether and in what situations standard utilitarian approaches and frameworks in a conventional cost-effectiveness analysis—incremental benefits as measured by quality-adjusted life-years (QALYs)—should be expanded to incorporate other elements of value that are specifically relevant to a pandemic situation. These may include additional value based on impact to non-health sectors, equity impact, or interventions that are life saving or drastically improve lives in the face of imminent death. Methods currently exist to incorporate these impacts by, for example, weighting of QALYs [8, 9]. There is, however, no indication that these methods should be specifically invoked in times of a pandemic. Indeed, if cost-effectiveness frameworks are modified for pandemics, results cannot be directly compared to pre-pandemic therapies. None of the issues raised below is exclusively relevant for a pandemic, but some issues were brought into sharp relief during the COVID-19 pandemic. In addition to the methodological considerations pertinent to economic evaluations during a pandemic, how we interpret the results and assign appropriate value to interventions during a pandemic is another key issue.

1.1 Therapeutics for COVID-19 in the Context of Vaccines

There are 20 COVID-19 vaccines that have gained regulatory approval in at least one country as of July 2021 [10], and government-sponsored vaccination campaigns are now underway. Uncertainty surrounding the rate of uptake, a full picture of the vaccine safety profile, and the length of conferred immunity and effectiveness against emerging variant strains of the virus in real-world settings are still to be clarified. While vaccines will reduce population-level infection spread, any of these factors may mean a continued reliance on therapeutics to reduce mortality, symptom severity, duration, or complications among infected patients. We therefore limit the scope of this paper to the therapeutics class in patients with COVID-19 requiring treatment, where decision problems around resource allocation are more likely to arise. We define the therapeutics class as any active treatment for symptomatic infection. Discussions on this topic took place in a 1-week virtually convened panel in October 2020, using an interactive platform that allowed the six authors to answer questions and post replies directly to each other.

Over 460 trials of COVID-19 therapeutics have been evaluated by the US Food and Drug Administration with 11 Emergency Use Authorizations being issued [11]. Three Emergency Use Authorizations cover therapy options for patients requiring hospitalisation, two of which include remdesivir [12–14]. Another Food and Drug Administration-approved drug, dexamethasone, was repurposed for patients with COVID-19 on supplemental oxygen or those who are intubated [15]. The Institute for Clinical and Economic Review’s assessment of remdesivir monotherapy [16] was met with praise for its rapidity and transparency, but also with some criticism over its lack of consideration of non-health effects and a societal perspective, lack of an open-source model, as well as the use of a more stringent cost-effectiveness threshold than the organisation typically considers [17, 18]. The remdesivir evaluation underscores debates at the heart of valuing therapeutics during the COVID-19 pandemic: compared with vaccines, there is less clarity on the degree of impact for therapeutics on broader social and economic consequences of the pandemic. There was also consideration of the appropriate willingness-to-pay threshold to be used, in the face of potentially a large number of patients requiring therapy. As financing for therapeutics research and development is concentrated in the USA, this paper uses the US healthcare system for most examples. However, the larger context of pandemic-based value assessment may be applied globally keeping in mind that countries will generally vary in their assessment given differences in epidemiology, healthcare delivery and economic conditions. This paper starts with a presentation of different elements of
value currently identified in existing frameworks and how they relate to economic evaluations for pandemic interventions, followed by a discussion on how these considerations impact on a willingness-to-pay threshold for value assessments and price setting.

2 Existing Value Frameworks and Elements Relevant to a Pandemic

The existing value frameworks [9, 19, 20] and methods are, by and large, generalisable—with rewards driven by health gain and medical cost offsets—but some different emphases are warranted as a result of a pandemic, with specific implications for including or excluding them from a value assessment. Alternative or additional elements of value have been discussed in a number of different forums, with the International Society for Pharmacoeconomics and Outcomes Research Special Task Force on Value Assessment Frameworks’ “value flower” [9] having summarised many elements not incorporated in traditional value assessments. In the following sections, we discuss a selection of value elements of particular importance to novel therapeutics in the pandemic context.

2.1 Equity

COVID-19 disproportionately affects racial and ethnic minorities and low-income patients in terms of case rates, severity of disease and mortality [21, 22]. Existing inequalities in the US healthcare system persist in the face of a pandemic and may be exacerbated. “Essential workers”, disproportionately low income and minority, are more likely to be unable to work from home, more often in service occupations, childcare, factory, farm work, or custodial work, and have borne the brunt of infection risk since the spread of COVID-19 in the USA [23]. Even in countries with a homogenous ethnic population, such as Japan, disparities in outcomes were found among those with differing socioeconomic status [24], suggesting that equity considerations will have widespread application globally. In low-income and middle-income countries (LMICs), equity may need to be considered slightly differently. It may not only be accounting for differing outcomes among sub-populations, but which outcomes are being considered. For example, the emphasis on mortality as the most readily available metric may ignore the morbidity impact on the younger generations who have a lower risk of dying from COVID-19, but who make up a larger proportion of the population in LMICs and who may form the essential core of the country’s economy [25].

When valuing therapeutics for a pandemic that has a disproportionate impact on particular subsets of the population, it is advisable to consider methods that can account for any differential impacts. The distributional form of cost-effectiveness analysis (DCEA) evaluates interventions with differential impacts on socioeconomic subgroups and compares the magnitude in each group [26, 27]. In lieu of a full DCEA, which would require trial data or a decision-analytic model to empirically inform the distribution of effects, Love-Koh et al. describe an aggregate DCEA for health technologies that rolls up existing data alongside a measure of inequality [28]. Use of the DCEA model can help value therapies based on reductions in health inequities among specified at-risk subgroups. As an alternative, the Generalized Risk-Adjusted Cost-Effectiveness (GRACE) approach [29] could also provide a means of conducting economic evaluations that allow incorporation of variables such as severity of illness for those who experience a disproportionate burden of the same disease. Both methods challenge the implicit assumption that a gain in health utility is equally valued by everyone.

2.2 Severity of Disease

Hospitalised patients with COVID-19 may experience complications, including bacterial infections, acute kidney injury, respirator-induced lung injury, malnutrition and generalised weakness [21]. Moreover, patients with COVID-19 of any severity may experience ongoing fatigue, the inability to concentrate and/or other symptoms, collectively dubbed post-acute sequelae of SARS-CoV-2 infection [30]. Willingness to pay for therapies may be increased from both the patient and societal perspective in reducing potential long-term hospitalisation and post-hospitalisation outcomes even if average QALY gains across the entire population are similar to those for a non-severe condition. In theory, therapeutics that prevent severe COVID-19 cases would be rewarded for clinical improvement among patients with the most burdensome symptoms. Given that only a minority of COVID-19 cases require hospitalisation, as well as the dearth of long-term clinical data post-discharge to compare against other severe conditions, the additional value for therapeutics in preventing severe COVID-19 outcomes remains an issue of debate. However, some sub-populations are at high risk of severe complications of COVID-19 including prolonged hospital stay or death [31], potentially even after vaccination, either due to breakthrough infection or waning immunity [32, 33]. Adjusting for life expectancy and the impact of existing co-morbidities, a recent study has shown that the burden of QALYs lost due to such deaths can be substantial in many countries [34]: international variation in this burden is driven by age distribution at the time of death, which implicitly accounts for differing levels of co-morbidities, as well as total number of deaths within each country.

What further confounds these evaluations is the uncertainty of results in current studies. Uncertainty around the
long-term impacts of COVID-19 is especially large and to be expected; however, evaluations of acute outcomes are also subject to uncertainty because of several factors. Trials are being designed in a rapid adaptive manner, in a disease area that continues to evolve, with therapy guidelines that are constantly being updated. These are all leading, at times, to contradictory results on acute outcomes. An example of this was the extent to which remdesivir could prevent mortality, estimates of which initially relied on the ACTT-1 trial [35] and were later contradicted by the SOLIDARITY trial [36]. This highlights the difficulty of quantifying reductions in severity, morbidity and mortality from treatment when evidence is emerging at a rapid pace, as well as the importance of conducting thorough sensitivity analyses to account for all plausible outcomes.

2.3 Fear of Contagion/Insurance Value

Reducing the “fear of contagion” has been suggested as an externality that is often overlooked in economic evaluations [9]. Though a single therapeutic may not have a significant or oversized effect on fear of contagion reduction, its benefits may be accrued as one component of a complementary successful intervention landscape (including vaccines and other nonpharmaceutical interventions). The economic consequences of fear of contagion have been called “fearonomic effects” and may include business health impact and social life losses [37]. According to one study, “fearonomic effects” in China totalled $275 billion, or 1.9% of GDP, during the Lunar New Year week alone. Ma et al. have published a checklist for measuring the economic impact due to fear of contagion, quantifying both near and long-term deficits during a pandemic [37].

Insurance value places an additional value on the personal health risk reduction from being infected as well as the financial risk protection of insuring the population [9]. As with fear of contagion, any single therapeutic is unlikely to have significant benefit in illness or financial risk reduction, but rather, incorporates some share of benefit from the landscape of COVID-19 treatment options. In diseases with severe or long-term sequelae, as with COVID-19, therapeutics that address and/or add certainty in the reduction of ill-desired health consequences have an associated value benefit. Lakdawalla et al. describe the methodology for reflecting insurance value through consumer utility maximisation in an economic value assessment [9]. Consideration of either of these value elements is unlikely to have a significant impact on economic evaluations of current therapeutics; these elements would be considered more important when evaluating a therapeutic with significant effectiveness, for example, one that lowers viral load and therefore leads to decreased transmission along with symptom alleviation, or when evaluating the entire therapeutic class as a strategy.

2.4 Scientific and Family Spillover Effects

Scientific spillovers, a type of economic externality, can add value to a therapy that creates a significant advancement in the scientific knowledge base for a novel or unknown disease. Therapies with novel mechanisms of action, or therapies that treat previously untreatable diseases, “light the path” for additional innovation and can be rewarded to encourage additional knowledge production in the therapy area [9, 38]. Therapies developed for COVID-19 have the potential to provide this spillover effect, or indeed to benefit from prior spillovers (e.g. remdesivir and dexamethasone were originally developed for other diseases).

The impact of severe disease and its associated therapies on family members, particularly those fulfilling an informal caregiving role, has been well documented, especially in neurological diseases such as Alzheimer’s disease and Parkinson’s disease [39], though systematic incorporation of such an impact into economic evaluations remains low [40]. This may be particularly true for LMICs, where data to quantify the impact on non-patients are difficult to generate. Imposed self-isolation for patients with severe COVID-19 whether within a home or hospital will undoubtedly affect the entire household (i.e. “family spillover” effects), including those who must give informal care to the patient from a distance. Matters are further complicated by the potential economic impact on the family, if the patient is also the main source of income. There is some measure of value associated with improved treatment outcomes at the family/household level.

2.5 Incorporation of Additional Perspectives

For the purposes of an economic evaluation, including setting the price of a single therapeutic, the healthcare sector tends to be the main focus as payers do not generally consider non-health effects when underwriting premiums or setting reimbursement levels [41]. However, the Second Panel on Cost-Effectiveness in Health and Medicine recommended that economic evaluations consider both healthcare sector and societal perspectives [9, 42] as the reference case for all appraisals. The case for presenting both perspectives is especially relevant in a pandemic setting, where the value of a vaccine or therapeutic that addresses social, economic and health system upheaval necessitates consideration of societal benefits relevant to health systems and policymakers. Rewards for improvement in constrained hospital system capacity and return to work/school are not appreciated by a traditional value assessment [43]. Non-health impacts are essential components of a therapeutic’s value assessment from a societal perspective, for example, given significant unemployment during COVID-19. The Second Panel recommends including productivity effects in added costs.
in the numerator rather than as a utility adjustment in the
denominator along with the “Impact Inventory” that lists
the affected non-health sectors, including lost productivity,
consumption and social services [19]. However, a lack of
systematically produced non-health estimates hampers
the synthesis of evidence from a valuation and price-setting
perspective. Variation in the methods employed to incorporate
these non-healthcare perspectives can also be a challenge
[44], with results that lead to different conclusions. As bet-
ter data become available, estimation of non-health effects
will improve. The challenge is especially compounded in
LMICs, where reliance on informal family care is high but data to quantify it are low [45]. In the meantime, societal
and non-societal costs can be included in evaluations to be
presented as scenario analyses alongside a base case as is
already permissible in many countries’ pharmacoeconomic
guidance, such as Spain, Italy and Australia [46–48].

Opportunity costs, however, could be more readily incor-
porated into an economic evaluation of COVID-19 therapies. Opportunity costs for COVID-19 vaccines/therapeutics vs
other interventions can be explicitly measured to support
decisions from a public health and healthcare system capacity
perspective. Burdens on the healthcare system in general
and intensive care beds in particular have meant that patients
with other acute illnesses and preventative health services
have in some settings been de-prioritised [49]. Hospital
capacity has also been used as an explicit metric by which to trigger other non-pharmaceutical interventions that have
large effects on society and the economy. Sandmann and
colleagues have explored several techniques for estimating
the value of foregone bed-days in a scarcity setting [50],
which could be incorporated into an economic evaluation
of COVID-19 therapies that affect time in critical care or
the hospital generally. The inclusion of both health sector
and societal perspectives is recommended in evaluations of
any pandemic treatments, whether vaccine or therapeutic.

3 Willingness-To-Pay/Cost-Effectiveness
Thresholds

In addition to the consideration of expanding the scope
of economic evaluations for COVID-19 therapeutics with
these elements of value, the appropriate cost-effectiveness
threshold to apply has also been called into question. In the
Institute for Clinical and Economic Review’s remdesivir
assessment in 2020, the cost-effectiveness threshold was set
at $50,000 per QALY in a departure from the organisation’s
standard $100,000–$150,000 per QALY range, with the rea-
soning that thresholds should be reduced during pandemics
with a sizable patient population uptake [16]. It is also pos-
sible to argue that inclusion of added value elements when
valuing therapeutics should reduce the cost-effectiveness
threshold further, at least from the healthcare sector per-
pective, as the additional elements of value take into con-
sideration non-health benefits. It could be argued that part of
the payment for a fuller capture of value should be borne by
sectors other than healthcare, and the threshold used to set
a price for the healthcare sector should therefore be lower.

However, a higher threshold may be justified given the
urgent need to restore functioning economies. Effective ther-
apies may not only have direct health benefits for the patient,
but also have non-health effects around productivity and
the opening of society by relieving pressure on the health-
care system. There may even be a case for the suspension,
or abbreviation, of formal health technology assessment
approaches during the pandemic in lieu of implicit judgement,
and to conduct value assessments at a later point. Therapeutics that treat human immunodeficiency virus, for
example, have only in the past year been selected for a full
technology appraisal by the National Institute for Health
and Care Excellence in the UK, resulting from the 2019
Voluntary Pricing and Access Scheme [51]. The National
Institute for Health and Care Excellence has also issued
rapid guidelines over the course of the pandemic specifici-
cally recommending the use of such therapeutics as tocili-
zumab without a formal technology appraisal [52, 53]. Sev-
eral other countries are also conducting abbreviated forms
of their standard appraisals, sometimes foregoing economic
analyses altogether. This can be seen in such examples as
the modified approach used to develop COVID-19 therapy
evidence reviews in Canada [54], or in Australia through the
formation of a new taskforce dedicated to evaluating evi-
dence for COVID-19 clinical care. In countries where health
technology assessments and economic evaluations are not as
well established, such as India and other LMICs, it is even
more likely that there has not been any explicit considera-
tion of a cost-effectiveness threshold or willingness to pay
specifically for COVID-19.

It is important to remember, however, that even during,
or perhaps especially during pandemic times, healthcare
budgets are finite. Considering a higher cost-effectiveness
threshold, or indeed suspending health technology assess-
ment altogether for a set period of time, which essentially
signals an unlimited cost-effectiveness threshold, will need
to balance the opportunity costs of such a suspension. Clax-
ton et al. have described methods for quantifying oppor-
tunity costs of investing in new technologies in the UK
National Health Service and incorporating those costs in
the National Institute for Health and Care Excellence cost-
effectiveness thresholds [55]. Incorporation of such oppor-
tunity costs would undoubtedly lead to a lower threshold
given the impact on the ability of the healthcare system to
offer services for other acute illnesses and preventive health
services by funding COVID-19-specific therapies. These
considerations may be particularly acute in LMICs, where
the trade-off between COVID-19-specific interventions and existing preventative health measures is likely to have a larger impact [56, 57]. There may also have to be consideration of other COVID-19-specific, but non-therapeutic health measures, such as vaccines and screening programs. These are complicated not only by the estimation of opportunity costs, but also by the interactions between these efforts. A public health strategy including multiple measures may have different outcomes and value associated with it compared to individual strategies considered separately.

The consequences of altering the cost-effectiveness threshold should also be considered. Depending on the reasoning behind the alteration, this can send different signals to manufacturers about what innovations are desirable. Dedicated resources to vaccines at the expense of therapeutics may disincentivize innovation for future treatments, which has implications for future pandemics where vaccines may not be developed with as much speed as has been the case for COVID-19, leading to more dependence on effective therapeutics.

When making decisions around the adoption of new technologies and the appropriate price, decision makers should be aware of these arguments, as well as the implications of altering an existing threshold specifically in response to a pandemic. In particular, there should also be awareness of the implications for post-pandemic and non-COVID19 diseases in the future to maintain a sustainable healthcare system. Indeed, such implications further complicate the policy environment and could hamper the implementation of any health strategies that are considered a good use of resources. It requires a multi-stakeholder discussion, across several sectors, of whose resources we are trying to judiciously allocate.

### 4 Conclusions

Economic evaluation principles remain unchanged within the context of COVID-19. However, given significant morbidity and mortality, in addition to the widespread economic and public health impact of the COVID-19 pandemic, any treatment developed should be evaluated with a view toward the broader benefits of restoring economic and social activity; although quantifying some of these value elements, especially as the knowledge base evolves rapidly, is difficult. From a pragmatic perspective, the traditional health sector valuation of therapeutics should remain as a reference case. Modelling strategies allow us to evaluate both the traditional and potential larger societal value of COVID-19 therapeutics. In the future, as the pandemic evolves into different stages, the elements of value discussed above may also shift in their relative importance. Where strong evidence of a therapeutic’s effect on the wider pandemic situation exists, the appropriate additional elements of value could be incorporated in a scenario analysis to highlight potential therapeutic value and to present a full picture to decision makers. As the external environment is evolving rapidly, it is important to remain reactive to the potential non-health benefits of an intervention, but also to retain a core reference case for comparison.

### Declarations

**Funding** The virtual summit on economic evaluation in a pandemic setting was supported by GlaxoSmithKline plc (GSK). Medical writing support was provided by Gina Nicholson on behalf of Fishawack Indicia Ltd UK, and was funded by GSK.

**Conflict of interest** YA is an employee and shareholder of GSK. AB has received personal fees from Roche, Pfizer, Novartis, Takeda, Eisai, Daiichi Sankyo, ALK and Merck. LPG has received personal fees from Genentech, Inc., Pfizer, Inc., Merck and Novartis. BPG has been employed by Wing Tech Inc.; has received in-kind access from Public Library of Science, Society for General Internal Medicine and Society for Hospital Medicine; has received royalties and in-kind access from UpToDate; and his organisation has received fees from Cardiovascular Systems, Ceterix Orthopaedics, Cook Medical, Intact Vascular, Limflow, Magnolia Medical, Medtronic, PneumRx, ResMed, SafeHeal, Sofinnova Partners, Springer, Vapotherm, Veracyte and W. L. Gore & Associates. PN has received a grant from Amgen, Lundbeck, Gates Foundation, NPC, Alzheimer’s Association, NIH, Arnold Ventures and PhRMA Foundation; has participated in an advisory board for Novo Nordisk, Congressional Budget Office, Sarepta, Biogen, PhRMA Foundation, AveXis, Intercept, Bayer, Amgen, Sanofi and Panalogo; has acted as a consultant for Cytokinetins and Precision Health Economics; and reports CEA Registry funding by NSF, NLM, AHRQ, CDC and various pharmaceutical/device companies who subscribe to the data. DAO has participated in advisory boards for Aspen Institute/University of Southern California, Sunovion and Neurocrine; acted as a consultant for EMD Serono, Amgen, Analysis Group and Cytokinetins; received fees for early payer coverage advice from GalbraithWight; participated in a steering committee for University of Colorado; received fees for training from Center for Global Development; and reports CEA Registry funding by NSF, NLM, AHRQ, CDC and various pharmaceutical/device companies who subscribe to the data. All authors participated in this virtual advisory board, which was organized and funded by GSK.

**Ethics approval** Not applicable.

**Consent to participate** Not applicable.

**Consent for publication** Not applicable.

**Availability of data and material** Not applicable.

**Code availability** Not applicable.

**Authors’ contributions** YA was involved in the conception/design; DO, PN, LG, AB, and BG were involved in data acquisition; all authors were involved in data analysis or interpretation. All authors contributed to the development of the manuscript and approved the final version.

**Open Access** This article is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License, which permits any
non-commercial use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article’s Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article’s Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by-nc/4.0/.

References

1. Johns Hopkins University School of Medicine. Coronavirus Resource Center. 2021. https://coronavirus.jhu.edu/map.html. Accessed 3 July 2021.
2. Cutler DM, Summers LH. The COVID-19 pandemic and the $16 trillion virus. JAMA. 2020;324:1495–6.
3. Chawla D, Rizzo S, Zaloucysky K, Keebler D, Chia J, Lindsay L, et al. Descriptive epidemiology of 16,780 hospitalized COVID-19 patients in the United States. medRxiv. 2020;2020.2007.2017.20155625.
4. Horwitz LI, Jones SA, Cerfolio RJ, Francois F, Greco J, Rudy B, et al. Trends in COVID-19 risk-adjusted mortality rates. J Hosp Med. 2021;16:90–2.
5. Rosenthal N, Cao Z, Gundrum J, Sianis J, Safo S. Risk factors associated with in-hospital mortality in a US national sample of patients with COVID-19. JAMA Netw Open. 2020;3:e2029058.
6. WHO. WHO coronavirus (COVID-19) dashboard: deaths per 100,000 (2021). https://covid19.who.int/. Accessed 3 July 2021.
7. Ssentongo P, Ssentongo AE, Heilbrunn ES, Ba DM, Chinchilli VM. Association of cardiovascular disease and 10 other pre-existing comorbidities with COVID-19 mortality: a systematic review and meta-analysis. PLoS ONE. 2020;15:e0238215.
8. National Institute for Health and Care Excellence. The NICE methods of health technology evaluation: the case for change. 2020. https://www.nice.org.uk/Media/Default/About/what-we-do/our-programmes/nice-guidance/cte-methods-consultation/NICE-methods-of-health-technology-evaluation-case-for-change.docx. Accessed 19 Dec 2020.
9. Lakdawalla DN, Doshi JA, Garrison LP Jr, Phelps CE, Basu A, Danzon PM. Defining elements of value in health care: a health economics approach: an ISPOR special task force report [3]. Value Health. 2018;21:131–9.
10. Basta NE, Moodie EE, on behalf of the McGill University COVID19 Vaccine Tracker Team. COVID19 vaccine tracker. 2021. https://covid19.trackvaccines.org. Accessed 16 July 2021.
11. U.S. Food and Drug Administration. Coronavirus Treatment Acceleration Program (CTAP). 2020. https://www.fda.gov/drugs/coronavirus-covid-19-drugs/coronavirus-treatment-acceleration-program-ctapfact. Accessed 16 July 2021.
12. U.S. Food and Drug Administration. Emergency use authorization (EUA) for an unapproved product review memorandum. COVID-19 convalescent plasma. 2021. https://www.fda.gov/media/141477/download. Accessed 15 Apr 2021.
13. U.S. Food and Drug Administration. Emergency use authorization (EUA) for an unapproved product decision memorandum. Gilead Sciences/remdesivir (Veklury®). 2021. https://www.fda.gov/media/137564/download. Accessed 15 Apr 2021.
14. U.S. Food and Drug Administration. Emergency use authorization (EUA) for an unapproved product decision memorandum. Eli Lilly and Company/baricitinib (Olumiant®) in combination with remdesivir (Veklury®). 2021. https://www.fda.gov/media/143822/download. Accessed 15 Apr 2021.
15. Horby P, Lim WS, Emberson JR, Mathias M, Bell JL, Linsell L, et al. Dexamethasone in hospitalized patients with Covid-19. N Engl J Med. 2021;384:693–704.
16. Institute for Clinical and Economic Review. Alternative pricing models for remdesivir and other potential treatments for COVID-19. 2020. https://icer-review.org/wp-content/uploads/2020/06/ICER-COVID_Revised_Report_20200624.pdf. Accessed 19 Nov 2020.
17. Deverka PGL, Nussbaum S. Covid-19 and remdesivir: rethinking how we measure a drug’s ‘value’. 2020. https://www.statnews.com/2020/06/15/remdesivir-covid-19-rethinking-measure-drug-value/. Accessed 19 Nov 2020.
18. Winegarden W. ICER’s cost model is not only wrong it’s dangerous. 2020. https://www.forbes.com/sites/waynewinegarden/2020/05/11/icers-cost-model-is-not-only-wrong-its-also-dangerous/?sh=7a49f32e6c26. Accessed 19 Nov 2020.
19. Sanders GD, Neumann PJ, Basu A, Brock DW, Feeny D, Krahn M, et al. Recommendations for conduct, methodological practices, and reporting of cost-effectiveness analyses: Second Panel on Cost-Effectiveness in Health and Medicine. JAMA. 2016;316:1093–103.
20. Garrison LP Jr, Neumann PJ, Willke RJ, Basu A, Danzon PM, Doshi JA, et al. A health economics approach to US value assessment frameworks: summary and recommendations of the ISPOR Special Task Force Report [7]. Value Health. 2018;21:161–5.
21. Cates J, Lucero-Obusac C, Dahl RM, Schirmer P, Garg S, Oda G, et al. Risk for in-hospital complications associated with COVID-19 and influenza: Veterans Health Administration, United States, October 1, 2018-May 31, 2020. MMWR Morb Mortal Wkly Rep. 2020;69:1528–34.
22. Adhikari S, Pantaleo NP, Feldman JM, Ogedegbe O, Thorpe L, Troxel AB. Assessment of community-level disparities in coronavirus disease 2019 (COVID-19) infections and deaths in large US metropolitan areas. JAMA Netw Open. 2020;3:e2016938.
23. Lancer T. The plight of essential workers during the COVID-19 pandemic. Lancet. 2020;395:1587.
24. Yoshikawa Y, Kawachi I. Association of socioeconomic characteristics with disparities in COVID-19 outcomes in Japan. JAMA Netw Open. 2021;4:e2111706.
25. Briggs A, Vassall A. Count the cost of disability caused by COVID-19. Nature. 2021;593:502–5.
26. Cookson R, Mirelman AJ, Griffin S, Asaria M, Dawkins B, Norheim OF, et al. Using cost-effectiveness analysis to address health equity concerns. Value Health. 2017;20:206–12.
27. Avancena ALV, Prosser LA. Examining equity effects of health interventions in cost-effectiveness analysis: a systemic review. Value Health. 2021;24:136–43.
28. Love-Koh J, Cookson R, Gutacker N, Patton T, Griffin S. Aggregate distributional cost-effectiveness analysis of health technologies. Value Health. 2019;22:518–26.
29. Lakdawalla DN, Phelps CE. Health technology assessment with diminishing returns to health: the Generalized Risk-Adjusted Cost-Effectiveness (GRACE) approach. Value Health. 2021;24:244–9.
30. Nalbandian A, Sehgal K, Gupta A, Madhavan MW, McGregor C, Stevens JS, et al. Post-acute COVID-19 syndrome. Nat Med. 2021;27:601–15.
31. D’Asciano M, Innamorato M, Pasquariello L, Pizzirusso D, Guerrieri G, Castelli S, et al. Age is not the only risk factor in COVID-19: the role of comorbidities and of long staying in residential care homes. BMC Geriatr. 2021;21:63.
admissions, and mortality in older adults in England: test negative case-control study. BMJ. 2021;373:n1088.

33. Shrotri M, Krutikov M, Palmer T, Giddings R, Azmi B, Subbarao S, et al. Vaccine effectiveness of the first dose of ChAdOx1 nCoV-19 and BNT162b2 against SARS-CoV-2 infection in residents of long-term care facilities in England (VIVALDI): a prospective cohort study. Lancet Infect Dis. 2021;S1473–3099(21):00289–99.

34. Briggs AH, Goldstein DA, Kirwin E, Meacock R, Pandya A, Vanness DJ, et al. Estimating (quality-adjusted) life-year losses associated with death; with application to COVID-19. Health Econ. 2021;30:699–707.

35. Beigel JH, Tomashek KM, Dodd LE, Mehta AK, Zingman BS, Kalil AC, et al. Remdesivir for the treatment of COVID-19: final report. N Engl J Med. 2020;383:1813–26.

36. Consortium WHOST, Pan H, Peto R, Henao-Restrepo AM, Preziosi MP, Sathiyamoorthy V, et al. Repurposed antiviral drugs for Covid-19: interim WHO solidarity trial results. N Engl J Med. 2021;384:497–511.

37. Wittenberg E, Prosser LA. Disutility of illness for caregivers and impact of informal care in cost-effectiveness studies. Pharmacoeconomics. 2015;33:123–35.

38. Brinda EM, Rajkumar AP, Enemark U, Attemann J, Jacob KS. Cost and burden of informal caregiving of dependent older people in a rural Indian community. BMC Health Serv Res. 2014;14:207.

39. Lopez-Bastida J, Oliva J, Antonanzas F, Garcia-Altes A, Gisbert R, Mar J, et al. Spanish recommendations on economic evaluation of health technologies. Eur J Health Econ. 2010;11:513–20.

40. Krol M, Papenburg J, van Exel J. Does including informal care in cost-effectiveness studies. Pharmaco- economics. 2015;33:123–35.

41. Neumann PJ, Cohen JT, Kim DD, Ollendorf DA. Measuring “fearonomic effects” in valuing therapies: an application to COVID-19 in China. Value Health. 2020;23:1405–8.

42. Duevel JA, Hasemann L, Pena-Longobardo LM, Rodriguez-Sanchez B, Aranda-Reineo I, Oliva-Moreno J, et al. Considering the societal perspective in economic evaluations: a systematic review in the case of depression. Health Econ Rev. 2020;10:32.

43. Brinda EM, Rajkumar AP, Enemark U, Attemann J, Jacob KS. Cost and burden of informal caregiving of dependent older people in a rural Indian community. BMC Health Serv Res. 2014;14:207.

44. Claxton K, Martin S, Soares M, Rice N, Spackman E, Hinde J, et al. Decreased hospital admissions through emergency departments during the COVID-19 pandemic. Am J Emerg Med. 2021;42:203–10.

45. Sandmann FG, Robotham JV, Deeny SR, Edmunds WJ, Jit M. Estimating the opportunity costs of bed-days. Health Econ. 2018;27:592–605.

46. Department of Health and Social Care. The 2019 voluntary scheme for branded medicines pricing and access: chapters and glossary. 2020. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/761834/voluntary-scheme-for-branded-medicines-pricing-and-access-chapters-and-glossary.pdf. Accessed 19 Dec 2020.

47. Australian Government. Guidelines for preparing a submission to the Pharmaceutical Benefits Advisory Committee. In: Department of Health, editor; 2016, Canberra, Australia: Australian Government Department of Health. https://pbac.pbs.gov.au/information/about-the-guidelines.html.

48. Agenzia Italiana Del Farmaco. Linee guida per la compilazione del dossier a supporto della domanda di rimborsabilità e prezzo di un medicinale; 2019, Rome, Italy: AIFA. https://www.aifa.gov.it/documents/20142/1283800/Linee_guida_dossier_doman da_rimborsabilita.pdf.

49. National Institute for Health and Care Excellence. Appendix L: interim process and methods for guidelines developed in response to health and social care emergencies. 2020. https://www.nice.org.uk/process/pmg20/resources/appendix-l-interim-process-and-methods-for-guidelines-developed-in-response-to-health-and-social-care-emergencies. Accessed 10 Aug 2021.

50. National Institute for Health and Care Excellence. 2019 rapid guideline: managing COVID-19. 2021. https://www.nice.org.uk/guidance/ng191/chapter/Recommendations. Accessed 7 Sept 2021.

51. Canadian Agency for Drugs and Technology in Health. CADTH Covid-19 pandemic. 2021. https://covid.cadth.ca/treatment/?s= &aspx_active=1&_p_asid=3&_p_asp_data=1&current_page_id=989&qtranslate_lang=0&polylang=en&filters_changed=1&filters_initial=0&asp_gen%5B%5D=title&asp_gen%5B%5D=content&asp_gen%5B%5D=excerpt&custom%5B%5D=post&termset%5Bcategory%5D%5B%5D=28. Accessed 10 Aug 2021.

52. Claxton K, Martin S, Soares M, Rice N, Stackman E, Hinde S, et al. Methods for the estimation of the National Institute for Health and Care Excellence cost-effectiveness threshold. Health Technol Assess. 2015;19(1–503):vi–vi.

53. Abbas K, Procter SR, van Zandvoort K, Clark A, Funk S, Mengistu T, et al. Routine childhood immunisation during the COVID-19 pandemic in Africa: a benefit-risk analysis of health benefits versus excess risk of SARS-CoV-2 infection. Lancet Glob Health. 2020;8:e1264–72.

54. Rehman ST, Rehman H, Abid S. Impact of coronavirus disease 2019 on prevention and elimination strategies for hepatitis B and hepatitis C. World J Hepatol. 2021;13:781–9.