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Review Paper

Economic evaluations of interventions against viral pandemics: a scoping review

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ABSTRACT

Objectives: The COVID-19 pandemic has led to suggestions that cost-effectiveness analyses should adopt a broader perspective when estimating costs. This review aims to provide an overview of economic evaluations of interventions against viral pandemics in terms of the perspective taken, types of costs included, comparators, type of economic model, data sources and methods for estimating productivity costs.

Study design: Scoping literature review.

Methods: Publications were eligible if they conducted a cost-effectiveness analysis, cost-utility analysis, cost-benefit analysis or cost-minimisation analysis and evaluated interventions aimed at viral pandemics or for patients infected with viral pandemic disease. We searched PubMed, Embase and Scopus for relevant references and charted data from the selected full-text publications into a predefined spreadsheet based on research sub-questions, summary tables and figures.

Results: From 5410 references, 36 full-text publications fulfilled the inclusion criteria. The economic evaluations were mainly model based and included direct medical costs of hospital treatment. Around half of the studies included productivity costs and the proportion of total costs attributed to productivity costs ranged from 10% to 90%, depending on estimation methods, assumptions about valuation of time, type of intervention, severity of illness and degree of transmission.

Conclusions: Economic evaluations of interventions against viral pandemics differed in terms of estimation methods and reporting of productivity costs, even for similar interventions. Hence, the literature on economic evaluations for pandemic response would benefit from having standards for conducting and reporting economic evaluations, especially for productivity costs.

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Introduction

Decision-makers involved in setting priorities for health care budgets need reliable evidence on the costs and effects of alternative interventions. This is often provided through cost-effectiveness analyses that compare the costs of two or more alternative interventions relative to their health effects.¹ To ensure that cost-effectiveness analyses are comparable and are based on the same type of information about resource use and effectiveness of health interventions, guidelines for conducting cost-effectiveness analyses have been produced.^{2,3}

Reviews on guidelines for health economic evaluations have identified consensus on key methodological principles, such as the types of economic evaluation to be used, the time horizon for analysis, relevant health outcome measures and use of sensitivity analyses.^{2,3} However, the reviews also identify aspects that lack a common understanding; for example, the study perspective, which costs are included, whether to account for indirect costs and how to do this, rates for discounting costs and effects, and methods for measuring health-related quality of life.^{2,3}

Pandemic diseases present additional challenges for cost-effectiveness analyses because of their wide consequences for society as a whole. Pandemic diseases are highly contagious compared with other diseases and the measures for controlling them (such as lockdown or immunisation programmes) also impact people who are not infected with the disease, including the ability to work and study.^{4–6} In addition, a country's limited ability

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to trade can have serious economic consequences.^{6,7} The COVID-19 pandemic resulted in a real gross domestic product (GDP) growth rate in Q2 2020 of –9.49% in the US and –11.9% in the EU.^{7–9}

In terms of the COVID-19 pandemic, some argue that a broader perspective should be adopted in economic evaluations as a new intervention against a viral pandemic is likely to impact not only the people becoming ill or receiving treatment but also the surrounding society.^{10–12} A broader perspective would ensure that all costs and benefits of an intervention are included in the health economic evaluation and that decision-makers are fully informed about the costs and consequences.^{11,12} Although the usual economic evaluation principles remain unchanged within the context of the COVID-19 pandemic, additional aspects to be considered include ‘fear of contagion, severity of illness, insurance value, and innovation and its spill over effects’¹⁴ as well as ‘the broader benefits of restoring economic and social activity’.¹⁰

One of the implications of taking a broader perspective is the inclusion of productivity costs, which can be defined as ‘the costs associated with lost or impaired ability to work or to engage in leisure activities due to morbidity and lost economic productivity due to death’.¹ The term ‘indirect costs’ has been used similarly as it ‘can include temporary absence from work due to illness, reduced working capacity due to illness and disability, or lost productivity due to early death’.¹³ There seems to be a lack of consensus in guidelines on whether productivity costs should be included and a lack of agreement in light of the pandemic on how to estimate these costs.^{10,12}

Health economic aspects of pandemics have been described in systematic reviews of pharmaceutical interventions, such as vaccination^{14,15} and antiviral treatment,¹⁶ and of non-pharmaceutical interventions, such as lockdowns, closing borders or schools, screening, isolating symptomatic individuals and near contacts, and social distancing.¹⁷ The aims of these studies were to summarise evidence and find cost-effective alternatives,¹⁷ to provide an evidence base to inform economic evaluations and health technology assessments of COVID-19 treatments,¹⁶ or to investigate the use of productivity costs in health economic evaluations of vaccine programmes and drugs.^{15,18} Although not restricted to viral pandemic disease, vaccine and immunisation programmes often target viral disease and recent reviews have reported on the inclusion of productivity costs in economic analyses.^{15,19} However, we have not been able to find reviews describing estimation of productivity costs or indirect costs in economic analyses of interventions against viral pandemics.

Therefore, the objective of this study was to provide an overview of economic evaluations of interventions against viral pandemics in terms of the perspective taken, types of costs included, comparators, type of economic model, data sources and methods for estimating productivity costs. This review provides researchers, policymakers and service providers with information about applied economic methods for evaluation of interventions against viral pandemics and suggests priorities for further research.

Methods

A scoping review was conducted to obtain an overview of existing economic evaluations of interventions against viral pandemics. A scoping review can assess a broad research question to identify and map the available evidence²⁰ and it can result in detailed descriptions of study methodologies.²¹

The specific subquestions in this scoping review were as follows:

- Which types of economic evaluations have been conducted for interventions against viral pandemics?
- Which types of interventions have been examined?
- Which perspectives have been used when measuring costs?
- Which types of study design have been used for estimation of costs?
- Which data sources have been used?
- Which types of costs have been included?
- How were productivity costs or indirect costs included?

Protocol and registration

The current review followed the updated methodological guidance for conduct of scoping reviews by Peters *et al.*²¹ and was reported in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) checklist (see Supplementary file S1).²² The scoping review was based on an *a priori* defined protocol, as recommended²¹ and this can be accessed through the Open Science Framework (see link in Supplementary file S2).

Eligibility criteria

The Participants, Concept and Context (PCC) framework guided the eligibility criteria. The review included fully available publications in peer-reviewed journals. The year of publication was not limited as relevant papers from earlier pandemics were found. Primary research was preferred (i.e., not review articles or meta-analyses) and the analysis should be conducted with a health care or societal perspective. The study searched for articles with the following PCC criteria:

Participants: patients with emerging infectious virus causing outbreaks or pandemics (i.e., Ebola, Sika, SARS, MERS, H1N1, H5N1, or COVID 19) or a pandemic virus scenario.

Concept: cost-effectiveness analysis (CEA), where results were expressed in monetary units per case averted; cost-utility analysis (CUA), where results were expressed in monetary units per quality-adjusted life-years (QALYs) or disability-adjusted life-years (DALYs); cost-benefit analysis (CBA) or cost (minimisation) analysis, where results were expressed as an intervention's total saving or loss in monetary units.

Context: all contexts (i.e., all countries of origin) were included; however, the context should relate to health interventions and the perspective should be broader than the budget impact for a single hospital.

Information sources

The search was conducted in PubMed, EMBASE and Scopus,^{23–25} which are databases that include articles describing medical and health economic outcomes research.

Search strategy

The search strategy was developed using two databases, and the final search was conducted in all three databases, in accordance with guidelines.²¹ A preliminary search was conducted in PubMed and EMBASE using peer-reviewed clinical expert searches on relevant disease terms^{26–28} and costs. The complete search strategy is provided in Supplementary file S3.

Selection of sources of evidence

Studies were selected in two steps following the inclusion and exclusion criteria listed in Table 1.

Two reviewers (MKR and IF) conducted the selection; MKR first screened titles and abstracts using the Covidence online platform²⁹ and IF mainly assisted in sorting full-text references and in extracting results. Full-text articles were then screened by both reviewers independently. This was performed in Endnote³⁰ as some of the full-text articles could not be uploaded to Covidence due to copyright regulations. Disagreements were solved by discussion.

Data charting process

Full-text articles that were deemed relevant were examined and their data were entered into a predefined charting form. The following data were extracted: author and year, country and type of intervention, type of economic evaluation, study population, outcome measures, structure of economic model if relevant, perspective taken, types of costs assessed, measurement of productivity costs or indirect costs, and sources of data. The data chart was analysed using frequency tables, bar graphs and/or narrative summaries according to the focus of the research subquestions.

Results

This study identified 5410 references and, after screening of titles, abstracts and full-text, 36 articles were included in the review (see Fig. 1). The 36 articles were published between 2008 and 2021, and their main characteristics are summarised in Table 2.

All continents were represented, but over half of the studies were from North America (28%) and Europe (31%). Participants were mainly patients with COVID-19 (50%) or H1N1 (31%). The full data chart is available in Supplementary file S4.

The following sections present results on the research subquestions.

Types of economic evaluations

Cost effectiveness was reported in 22 studies (61%),^{31–55} four (11%) stated cost benefit,^{55–59} two (4%) a cost utility,^{53,55,60–62} three (8%) a cost-minimisation analysis^{63–66} and five (14%) reported multiple analyses.^{53–55,60,66}

Types of interventions

The interventions can be split into two groups according to World Health Organisation (WHO) objectives for epidemics:⁶⁷ (a) intervention strategies to suppress transmission; and (b) interventions to optimise care for patients with confirmed epidemic disease. Twenty-three studies (64%) analysed interventions to suppress transmission. These included use of face masks,^{60,65} insectoid-treated nets,⁴⁸ increased access to contraception,^{38,48}

suppression policies,⁵² lockdown,^{44,57} mitigation and movement restriction policies,^{53,55} hand hygiene,⁶⁰ school closure,^{35,49,50,56,63} workplace non-attendance,^{35,63} community contact reduction,^{35,63} social distancing,^{44,58} testing,^{32,36,40} and isolation strategies.⁴⁴ Eight studies (22%) analysed interventions for patients with confirmed epidemic disease. These comprised changes in organisation of medical treatment^{31,43,47,51} and treatment with specific pharmaceuticals.^{37,46,61,68} Five studies (14%) examined interventions in both of the WHO defined groups.^{35,39,45,63,66}

Perspective used when measuring costs

A societal perspective was stated in nine (25%) studies and a healthcare provider perspective in 12 (33%) studies. Four (11%) studies provided results from both perspectives. Nine studies did not state a perspective, but six (17%) included parameters referring to a societal perspective. A public payer perspective was used either alone or combined with private payer in two (6%) studies.

Study designs for cost estimation

Overall, 32 studies (89%) were model based, two studies were based on clinical studies^{59,64} and two studies had no described study design. In 15 (42%) studies, expected values were derived from a transmission model (e.g., the SEIR [Susceptible, Exposed, Infected, Recovered] Model) and thereafter attached to costs. Decision trees were used in 10 (28%) studies; this was alongside either Markov or other simulation models in three (8%) studies.

Data sources

Nineteen studies included estimates acquired from published literature.^{34–37,39,40,46–52,55–57,60–63,65,66} National or official statistical resources were used in 17 studies.^{31,34,36,40,41,43–45,47,49,50,54,56–58,60,66} Five studies used aggregate or patient-level data from local hospital resources.^{37,42,46,64,66} A few studies included prices from private insurance companies^{38,43} or market prices,^{42,60,64} questionnaires,⁵⁹ or interviews with individuals (e.g., patients, household and healthcare personnel).^{59,64}

Types of costs

Costs were grouped into direct health care costs, (89%) intervention costs, (69%) productivity costs, (58%) direct costs to the patient (11%) and direct non-health care costs (14%). Fig. 2a–c presents the most common types of costs in more detail; all cost data are available in Supplementary file S5 (Tables S2d–e).

Productivity costs or indirect costs

Productivity costs were included in 21 (58%) studies, often measured as costs of lost labour incurred by the patient due to illness or premature death (25% and 11%), as absenteeism of

Table 1
Inclusion and Exclusion Criteria.

Inclusion criteria	Exclusion criteria
<ul style="list-style-type: none"> • Studies describing patients with an emerging infectious virus causing outbreaks or pandemics • Studies conducting a cost-effectiveness analysis, cost-utility analysis, cost-benefit analysis or cost minimisation analysis • The perspective of analysis should be health care, payer or societal • Full publication in peer-reviewed journal • Primary research 	<ul style="list-style-type: none"> • Literature reviews, letters, editorials, unpublished grey literature, guidelines, conference proceedings, case reports • Narrow perspective, e.g., single hospital • Studies that did not adopt a comparator • Not published in English • Studies of vaccines • Cost of illness studies

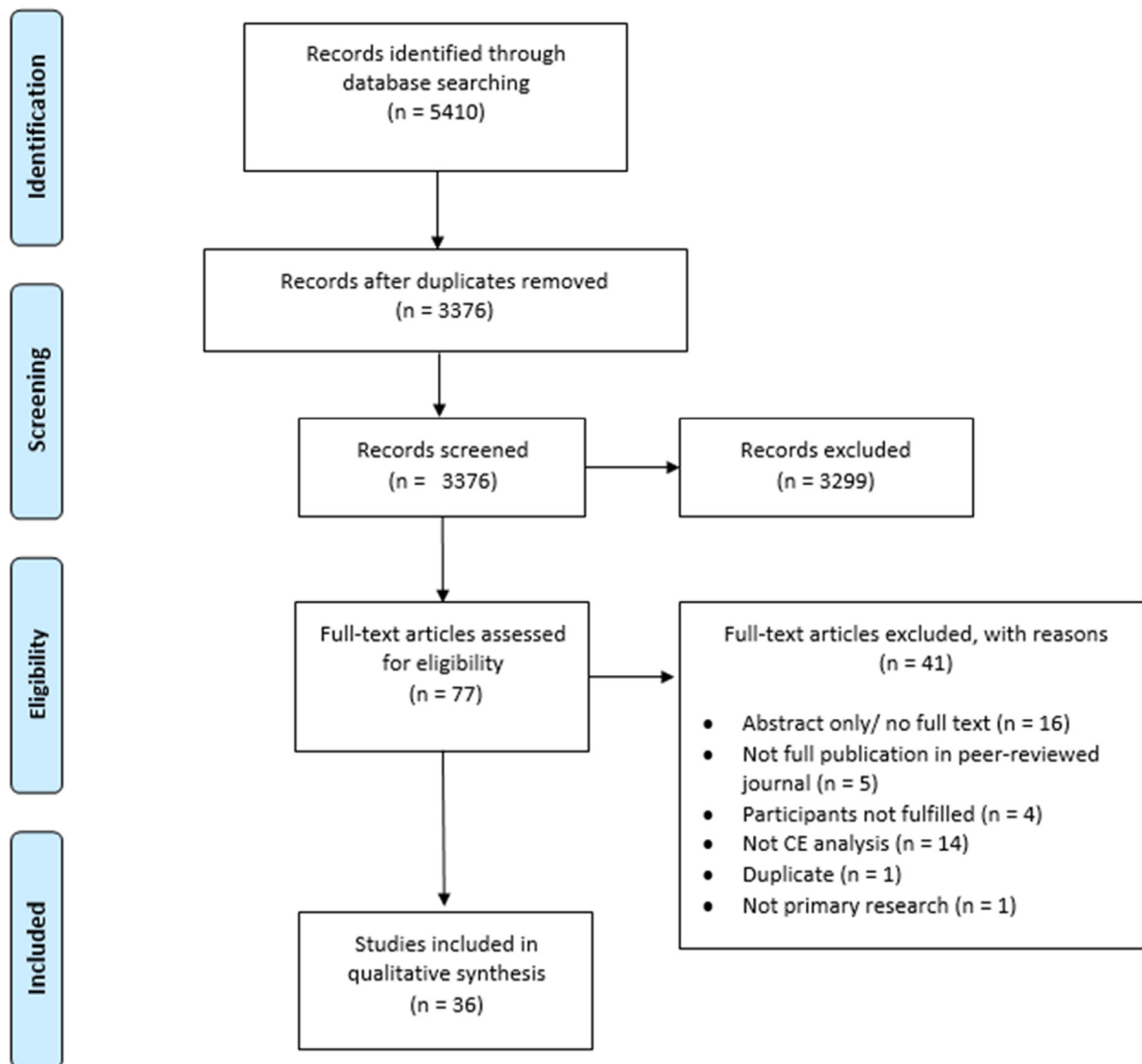


Fig. 1. Flow diagram of selection of sources of evidence.

relatives, close contacts and teachers (14%) but also, in some studies (11%), not explained further.

Six studies included daily wages of parents or relatives absent from work to take care of healthy or ill children.^{35,49,50,56,63,65} Two studies analysed different testing strategies and included loss of salary for close contacts (e.g., during household quarantine).^{32,55} One study included costs of work delay plus transportation for family members of sick individuals.⁵⁹

Two studies included productivity costs for the health care sector as costs of quarantine and sick leave in terms of income for personnel in the hospital ward.^{33,42}

Zala et al. modelled the cost effectiveness of suppression policies. These included productivity costs based on a macroeconomic model in which a pandemic influences GDP through (i) a reduced labour supply owing to death, illness (i.e., direct absenteeism), school closures and prophylactic absenteeism; (ii) consumption

shocks owing to illness and precautionary avoidance; and (iii) modest investment deferment.⁵²

Four studies (11%)^{43,59,62,63} stated a specific approach to value productivity: the human capital approach. In this approach, income acts as a proxy for the production value of the individual.¹ Thirteen studies (36%) included productivity costs by multiplying days of absence due to illness, mortality or interventions by average income, GDP per capita/day or similar value per day. These studies did not state a specific approach, but their method of valuation was similar to the human capital approach.^{32,33,35,40,42,44,49,50,52,56,61,64,65} Three studies (8%) did not explain their approach nor method of valuation.^{39,54,58}

Different assumptions were applied when estimating productivity costs. Studies analysing school closure most often included productivity costs of at least one parent, but Brown et al. assumed that only parents of children aged 6–11 years would incur

Table 2
Characteristics of included studies.

Characteristic	No. of studies	%
Origin (Continent)		
Global	1	3%
Oceania	1	3%
South America	2	6%
Africa	4	11%
Asia	7	19%
North America	10	28%
Europe	11	31%
Disease		
Ebola	2	6%
Zika	2	6%
Pandemic Influenza scenario	3	8%
H1N1 (pandemic influenza A)	11	31%
COVID-19	18	50%
Study type		
Cost-minimisation & 'ACER' ^a cost-effectiveness	1	3%
Cost-effectiveness & cost-benefit	1	3%
Cost-effectiveness & return on investment-analysis	1	3%
Cost-utility & cost-effectiveness	2	6%
Cost-utility	2	6%
Cost-minimisation analysis	3	8%
Cost-benefit	4	11%
Cost-effectiveness	22	61%
Study design		
Patient simulation model (SEIR) with attached costs	15	42%
Decision tree	10	28%
Decision tree and Markov	2	6%
Decision tree and simulation model	1	3%
Simulation model, e.g., Monte Carlo simulation	4	11%
Others (survey, micro costing, not described)	4	11%
Perspective		
Societal perspective	9	25%
Healthcare provider perspective	12	33%
Health care and societal perspective	4	11%
Public payers' perspective	1	3%
Combined health sector perspective (public and private)	1	3%
Not explicitly given (societal perspective)	6	17%
Not explicitly given	3	8%

^a Average cost-effectiveness ratio.

production loss due to absenteeism from work.⁵⁶ Neilan *et al.* assumed that a day in self-isolation would only halve productivity as some people would be able to work from home while moderately ill or taking care of an ill child.⁴⁰ Kelso *et al.* assumed costs to children as a school day lost would incur additional educational expense in the future.⁶³ Three studies assumed that seniors or persons aged over 65 years do not work and used a valuation of zero for time in this group.^{40,50,65} In contrast, two studies referred to growing evidence that elderly individuals contribute to non-market productivity and thus included a value for all age groups over 18 years.^{43,49} Four studies included productivity costs due to premature death, but only Kellerborg *et al.* assumed that life-years spent in poor health do not result in productivity gain.⁶²

The proportion of total costs attributed to productivity costs ranged from 10% to 90% in the studies that included productivity costs. In studies with productivity costs around 90% of the total cost, the interventions included workplace or school closure, an unmitigated pandemic or high transmission scenarios. In studies with productivity costs around 10% of the total cost, the interventions included antiviral drugs or acute treatments for hospitalised patients, lower transmission scenarios or less severity of illness.^{35,40,43,63}

Discussion

This scoping review identified 36 studies that included economic evaluations of interventions against viral pandemics. Most

studies included costs of the intervention and economic consequences for the health care system. The costs to the health care system varied from costs of hospital resource use only to including GP visits, utensils or devices, pharmaceutical costs and costs of quarantine. Other studies reported consequences at a societal level, including productivity costs. Studies varied in reporting productivity costs, where the most common item was costs to the patient. Others included costs to relatives and to the health care sector.

Inclusion of productivity costs impacts the estimated total cost. Studies noted that the largest contribution to total cost was productivity losses, which arose from mortality at a young age or from widely applied interventions, such as lockdowns.^{35,62} Severity of illness and degree of transmission were also contributing factors.⁶¹

The result of each cost-effectiveness analysis may be impacted by the approach used for measuring productivity costs. For example, placing a zero value on the time of older people implicitly gives a higher weight to interventions aimed at the working population who would incur productivity costs from illness while older people would not. Another example is deciding whose productivity costs should be measured. Some studies included productivity costs for the patient only or for the relatives. A few studies used the human capital approach for estimating productivity costs and although most other studies did something similar, they did not report a specific approach. The inconsistency in estimating costs, particularly productivity costs, is a challenge for decision-makers when selecting which interventions to implement. To improve consistency in methods and reporting of cost-effectiveness analyses, an updated guideline is needed specifically for interventions aimed at viral pandemics.

Study limitations

This review excluded studies of immunisation programmes as these were described in two recent systematic reviews.^{15,19} Vaughan *et al.* reviewed 68 costing studies and found inconsistent practices in reporting on types of immunisation costs, and that vaccine and delivery cost details were frequently not reported. The authors also reported insufficient methodological detail on data analysis and provided a checklist with specific guidance on how to write up a costing study in the field of immunisation economics. Yuasa *et al.* reviewed 208 studies and found that most of the studies that included productivity costs only considered patients' absenteeism, while ignoring time lost by caregivers. The approach used to estimate productivity losses/gains was not commonly reported or not sufficiently detailed, but this may be partly due to varying country guidelines.¹⁵ Similarly, the current scoping review found that the impact and method of calculation of productivity costs was sometimes unclear or not reported.

Cost of illness studies were not included because this review was limited to economic evaluations as defined by Drummond *et al.*;¹³ thus, some relevant information might be omitted as a result.

Conclusions

The current scoping review showed that economic evaluations of interventions against viral pandemics may include productivity costs for both ill and non-ill individuals. In several studies, costs to parents or relatives were included, but also productivity losses within the health care sector and on a societal level were sometimes described. The estimation methods and reporting of productivity costs differed, even for similar interventions. The conclusion of a cost-effectiveness analysis can be greatly impacted by the approach used for measuring productivity costs, and this poses a challenge to decision-makers facing the choice of which

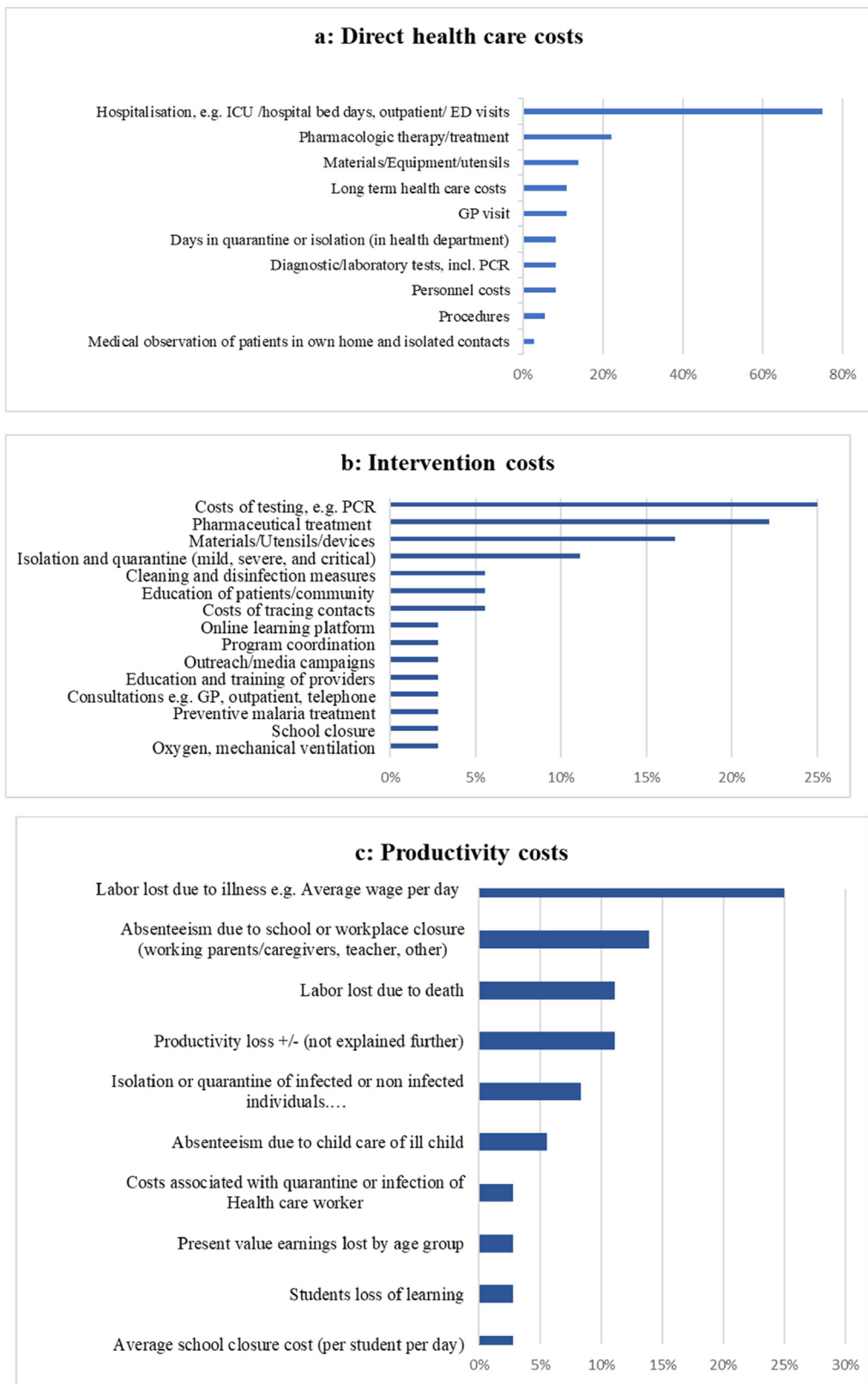


Fig. 2. a–c: Types of costs included in analyses.

interventions to implement. To improve consistency in the conduction and reporting of economic evaluations, an updated guideline is needed for interventions against viral pandemics.

Author statements

Ethical approval

None required.

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Competing interests

The authors declare no conflicts of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.puhe.2022.05.001>.

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