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Cost-Effectiveness of Coronavirus Disease 2019 Policy Measures: A Systematic Review

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ABSTRACT

Objectives: The coronavirus disease 2019 pandemic has had a major impact on our society, with drastic policy restrictions being implemented to contain the spread of the severe acute respiratory syndrome coronavirus 2. This study aimed to provide an overview of the available evidence on the cost-effectiveness of various coronavirus disease 2019 policy measures.

Methods: A systematic literature search was conducted in PubMed, Embase, and Web of Science. Health economic evaluations considering both costs and outcomes were included. Their quality was comprehensively assessed using the Consensus Health Economic Criteria checklist. Next, the quality of the epidemiological models was evaluated.

Results: A total of 3688 articles were identified (March 2021), of which 23 were included. The studies were heterogeneous with regard to methodological quality, contextual factors, strategies' content, adopted perspective, applied models, and outcomes used. Overall, testing/screening, social distancing, personal protective equipment, quarantine/isolation, and hygienic measures were found to be cost-effective. Furthermore, the most optimal choice and combination of strategies depended on the reproduction number and context. With a rising reproduction number, extending the testing strategy and early implementation of combined multiple restriction measures are most efficient.

Conclusions: The quality assessment highlighted numerous flaws and limitations in the study approaches; hence, their results should be interpreted with caution because the specific context (country, target group, etc) is a key driver for cost-effectiveness. Finally, including a societal perspective in future evaluations is key because this pandemic has an indirect impact on the onset and treatment of other conditions and on our global economy.

Keywords: cost-effectiveness, COVID-19, policy measures, systematic review

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Introduction

Since December 2019, the coronavirus disease 2019 (COVID-19) pandemic has resulted in more than 128 million confirmed cases and caused more than 2.8 million deaths worldwide.1 As a result of the rapid spread of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), national authorities around the world had to implement drastic policy measures—ranging from limiting social contact, mandating the use of face masks, shutting schools and nonessential business activities, banning of public gatherings, and closing country borders to a countrywide lockdown—to contain transmission of the virus with the ultimate aim to prevent a healthcare system collapse.2,3

Most countries were caught in speed; hence, limited evidence was available on the effectiveness and even more so on the cost-effectiveness of the different measures to flatten the infection curve.4 Nevertheless, as time went by and because the pandemic continues to put pressure both on our healthcare system and our global economy, there is an urgent need for intelligent measures, that is, timely measures that can prevent our healthcare system from submerging in new COVID-19 waves; safeguard the physical, emotional and mental health, and well-being of the population; and protect risk groups. Nevertheless, to advise our decision makers in their decision-making process, up-to-date evidence is key.5

In the last few months, there has been a rapid increase in the number of COVID-19-related publications. Hence, this study aimed to systematically review the available cost-effectiveness studies on different policy measures to protect, detect, prevent/contain, and treat COVID-19 infections and to assess their quality,
Several inclusion criteria were formulated in advance (Table 1). A detailed search strategy is given in Appendix 1 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2021.05.013. Several inclusion criteria were formulated in advance (Table 1).

Methods

The methodology and reporting of this systematic review is consistent with the proposed methodology for systematic reviews of the Cochrane Collaboration.9

Search Strategy

A systematic search for peer-reviewed health economic evaluations published up to March 2021 was performed in 3 electronic databases: Web of Science, PubMed, and Embase. The following key terms were used in the search strategy: “cost-effectiveness,” “cost-benefit,” “cost-utility,” “health economic evaluation,” “COVID-19,” “corona,” “COVID19,” “COVID,” and “SARS-CoV-2.” In addition, reference lists of relevant articles were searched. The detailed search strategy is given in Appendix 1 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2021.05.013. Several inclusion criteria were formulated in advance (Table 1).

Study Selection

A detailed overview of the study screening and selection is given in Figure 1. Using a blinded web tool (Rayyan7), 2 independent reviewers (S.V. and D.D.S.) searched for relevant studies on the basis of titles and abstracts. Next, the full texts of the remaining articles were reviewed independently. In case of non-corresponding results, consensus was sought between both reviewers.

Quality Appraisal

The methodological quality of the included health economic evaluations was evaluated using the Consensus Health Economic Criteria (CHEC) checklist4 designed for assessing the methodological quality of health economic evaluations to be used in systematic reviews. Each criterion of the CHEC was scored either yes (1) or no (0), yielding a total score between 0 and 19. Next, an independent expert (T.A.) evaluated the quality of the included epidemiological models. This reviewer paid particular attention to the disease dynamics and to good modeling practice.9

Results

Overall, 23 articles were included in this systematic review (Fig. 1). Nine studies originated from the United States, 3 from the United Kingdom, 2 from South Africa, 2 from China, 2 from Germany, 1 from Ghana, 1 from India, and 1 from Israel; 1 study considered a group of 139 low- and middle-income countries, and 1 study did not focus on a particular country. The target population included the general population (13 studies), homeless adults (1 study), students (2 studies), patients who did not have COVID-19 (1 study), (hospitalized) patients with COVID-19 (4 studies), and healthcare workers (HCWs) (2 studies). Moreover, 5 studies focused on detection, 3 studies on protection, 12 studies on prevention/containment, and 3 studies on treatment. A comprehensive overview of the characteristics of the included articles can be consulted in Table 2 and in more detail in Appendix 2 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2021.05.013.

The CHEC quality assessment was performed for each included study (see Appendix 3 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2021.05.013). Nine studies scored high (>13/19), 10 studies scored moderate,19–25 and 4 studies scored low (≤6/19).26,27

Disease Models

Of the 23 studies, 1810–21,22–27 used a compartmental disease model to compute how SARS-CoV-2 spreads in the population. In contrast, 5 studies25–32 combined different approaches such as decision trees and life-table models to model disease impacts. Of the 16 compartmental disease models, 13 used an extended version of the classical Susceptible-Exposed-Infectious-Recovered-Deceased model (Table 2),10–12,15–21,24–26 They divided the infectious compartment (I) of the classical version into several compartments to account for presymptomatic infectiousness, asymptomatic COVID-19 infections, and/or different COVID-19 severities (examples in Appendix 4 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2021.05.013). Thunström et al13 and Zhao et al13 omitted the latent exposed (E) compartment and used the Susceptible-Infectious-Recovered-Deceased dynamics to model disease progression, whereas Risko et al12 used the World Health Organization Essential Supplies Forecasting Tool, which is based on the Susceptible-Infectected-Recovered model. Khajji et al27 started from a Susceptible, Exposed, Infectious, Quarantined, and Recovered model supplemented with a Susceptible-Infectected-Model for infected animals. Savitsky and Albright15 and Sheinson et al28 used decision tree models to compute the risk of SARS-CoV-2 transmission to HCWs. Cleary et al29 used a decision tree model to compute the short- and long-term effects of different treatment strategies in the hospital. Gandjour31 used a life-table approach to compute the number of life-years lost to COVID-19.

Six studies2,16,18,21,25,26 calibrated their models using COVID-19 incidence data in an attempt to replicate and extrapolate a real-world epidemiological situation. In contrast, 12 studies10,12,14,19,20,22,24,25,27–29 set up hypothetical epidemiological situations.

Nine studies incorporated age stratification in their models,10,11,15,17,18,20,24,25,31 12 studies incorporated presymptomatic infectiousness,10–13,15,20,24,25,29 and 15 studies incorporated asymptomatic COVID-19 infections,10,12,15–22,24,25,30 whereas 4 studies did not incorporate differences in COVID-19 severity. Of the 16 compartmental disease models, 1012,15,17,19,22,23,26 models assumed homogeneous mixing of the entire modeled population. Khajji et al27 and Zhao et al13 built spatially explicit patch models, which divided the modeled territory into several subunits where homogeneous mixing was assumed. Zhao et al13 modeled SARS-CoV-2 during the initial outbreak in China with a model consisting of 2 spatial subunits, Hubei province and the rest of mainland China. Both authors accounted for mobility between the spatial subunits during the simulation. Heterogeneous population mixing was included in the individual-based models of Du et al26 who modeled 1000 US households and by the Imperial College COVID-19 Response Team Model used by Miles et al24,25 and Zala et al.10

Health Economic Models

Eighteen studies conducted a cost-effectiveness analysis,10–12,14–19,21,22,26,17,31,32 5 performed a cost-benefit analysis,1,19,20,23–25 and 1 discussed the budget impact alongside their cost-effectiveness analysis19 (Table 2 and Appendix 2 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2021.05.013). The health outcomes used in the models were diverse: deaths/deaths averted, infections/infections averted, quality-adjusted life-years (QALYs), quality-adjusted life-days, life-years...
saved, and hospital days. Cost outcomes were reported in $ or local currencies. The reported willingness to pay (WTP) thresholds differed substantially across studies depending on the health outcome used and country-specific contextual factors. Four studies did not report on WTP.

The time horizons (duration over which outcomes are projected) used in the studies ranged from 43 days to a lifetime with 5 studies not reporting on this aspect. Costs and health outcomes were discounted in 6 studies. Only 12 studies explicitly reported on the perspective used. Eight of them used a healthcare payer perspective. Five studies built their models on the basis of a societal perspective. Intervention costs related to protect, detect, and prevent/contain COVID-19 included costs of testing/screening, cost of quarantine/isolation, and cost of protective equipment, masks, and cleaning or disinfection. Disease and treatment costs accounted for the cost of the intervention and healthcare use including the costs of hospitalization days and intensive care unit (ICU) stay. Besides these direct costs, several studies included the cost of absenteeism (9 studies) or anticipated gross domestic product losses (4 studies).

Fourteen studies included multiple scenario analyses in their models. 11 conducted 1-way sensitivity analyses, 1,13,14,16–18,20,21,23,29–31 2 performed 2-way sensitivity analyses, and 2 performed multiway sensitivity analyses, whereas 7 conducted probabilistic sensitivity analyses, whereas 2 did not include any sensitivity analyses.

In the different scenario and sensitivity analyses, different model parameters were varied, such as the virus reproduction number ($R_0$), WTP, specificity and sensitivity of tests, intervention adherence, number of exogenous shocks, contact rates, different lockdown durations, and cost of interventions.

**Main Findings**

**Protection**

Three studies investigated the cost-effectiveness of protective measures for HCWs and concluded that personal protective equipment (PPE) can be cost-effective depending on the context.

Savitsky and Albright focused on PPE compared with COVID-19 screening to protect HCWs from COVID-19 transmission on a labor and delivery hospital unit in a US setting. Distinction was made in delivery mode (spontaneous labor, induced labor, or cesarean section). They concluded that universal screening is the preferred strategy for spontaneous and induced labor, whereas for a planned cesarean section universal PPE is cost saving.

Ebigbo et al compared 8 strategies related to testing and extensive PPE use (filtering facepiece-2 masks, goggles, and water-resistant gowns) for asymptomatic patients entering an

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**Table 1. Inclusion criteria.**

| Population                  | People susceptible for developing COVID-19 |
|-----------------------------|--------------------------------------------|
| Intervention                | All policy measures/strategies related to protection, detection, containment/prevention, or treatment of COVID-19 |
| Comparators                 | Doing nothing or alternative policy measures/strategies to protect, detect, contain/prevent, or treat COVID-19 |
| Outcomes                    | All outcomes related to cost-effectiveness, cost-utility, and cost-benefit analyses whereby a comparative analysis of alternative strategies is conducted in terms of both costs and effects |
| Context                     | COVID-19 pandemic |
| Study design                | Trial-based or model-based health economic evaluations or systematic reviews reporting on health economic evaluations |
| Evidence                    | Only peer-reviewed publications |
| Language                    | English, French, or Dutch |

COVID-19 indicates coronavirus disease 2019.
endoscopy unit aiming to protect HCWs, applying different prevalence rates. Incremental cost-effectiveness ratio (ICER) values decreased with increasing prevalence rates ($\geq 1\%$), but study findings were not clearly reported.

In addition, Risko et al$^{22}$ compared adequate PPE (including gloves, gowns, face shield, mask) with inadequate PPE (1 or more elements absent) in low- and middle-income countries. An ICER of $\$59/HCW infection averted, and an ICER of $\$4309/HCW life

### Table 2. Evidence table of the included studies.

| Author (Country)          | Intervention            | Population     | Strategies                                                                 | Epidemiologic model                                                                 |
|---------------------------|-------------------------|----------------|---------------------------------------------------------------------------|--------------------------------------------------------------------------------------|
| **1. Protection**         |                         |                |                                                                           |                                                                                      |
| Savitsky and Albright$^{30}$ (United States) | HCWs on labor and delivery | A. 1) Universal COVID-19 screening if vaginal delivery (spontaneous labor) | Decision tree to model transmission of SARS-CoV-2 to HCWs                             |
|                           |                         |                | A. 2) Universal PPE used if vaginal delivery (spontaneous labor)           |                                                                                      |
|                           |                         |                | B. 1) Universal COVID-19 screening if vaginal delivery (induced labor)      |                                                                                      |
|                           |                         |                | B. 2) Universal PPE used if vaginal delivery (induced labor)               |                                                                                      |
|                           |                         |                | C. 1) Universal COVID-19 screening if cesarean section                      |                                                                                      |
|                           |                         |                | C. 2) Universal PPE used if CD                                             |                                                                                      |
| Risko et al$^{22}$ (139) (LMIC) | HCWs                   | 1) Inadequate PPE: absence of one or more of the PPE elements             | SIR (ESFT)—(S) susceptible, (I) infected, and (R) recovered                          |
|                           |                         |                | 2) Full PPE on the basis of the WHO best practice guidelines (ESFT): gloves, gown, face shield and masks for all encounters involving a suspected case and enhanced precautions for aerosol generating procedures |
| Ebigbo et al$^{32}$ (Germany) | Patients presenting for endoscopy | 1) No routine pre-endoscopy virus test; use of surgical masks, goggles, gloves, and apron for all procedures | Decision tree to model transmission of SARS-CoV-2 from asymptomatic patients to HCWs in high-volume centers |
|                           |                         |                | 2) No routine pre-endoscopy virus test; additional use of FFP-2 and water-resistant gowns for all procedures |
|                           |                         |                | 3) Decentralized POC antigen test; use of surgical masks, goggles, gloves, and apron for all procedures |
|                           |                         |                | 4) Decentralized POC antigen test; additional use of FFP-2 and water-resistant gowns for all procedures irrespective of test result |
|                           |                         |                | 5) Centralized laboratory-based rapid PCR test; use of surgical masks, goggles, gloves, and apron for all procedures |
|                           |                         |                | 6) Centralized laboratory-based rapid PCR test; additional use of FFP-2 and water-resistant gowns for all procedures irrespective of test result |
|                           |                         |                | 7) Centralized laboratory-based standard PCR test; use of surgical masks, goggles, gloves, and apron for all procedures |
|                           |                         |                | 8) Centralized laboratory-based standard PCR test; additional use of FFP-2 and water-resistant gowns for all procedures irrespective of test result |

ACS indicates alternative care site; CD, cesarean delivery; CEACOV, Clinical and Economic Analysis of COVID Interventions; CT, contact tracing; DALY, disability-adjusted life-year; DesigIsol, designated spaces; ESFT, Essential Supplies Forecasting Tool; FFP-2, filtering facepiece-2; GDP, gross domestic product; HCW, healthcare worker; HT, healthcare testing; IC, isolation center; ICER, incremental cost-effectiveness ratio; ICU, intensive care unit; INR, Indian rupee; LMIC, low- and middle-income country; LT, laboratory test; MCER, marginal cost-effectiveness ratio; NA, not applicable; NMB, net monetary benefit; PCR, polymerase chain reaction; POC, point of care; PPE, personal protective equipment; QALY, quality-adjusted life-year; QC, quarantine center; Re, reproduction number; ResIsol, residence-based isolation; RLT, routine laboratory testing; ROI, return on investment; RT-PCR, real-time polymerase chain reaction; SALIRD, Susceptible-Asymptomatic-Presymptomatic-Infectious-Recovered-Deceased; SEIRD, Susceptible-Exposed-Infectious-Recovered-Deceased; SEIQR, Susceptible-Exposed-Infectious-Quarantined-Recovered; SI, Susceptible-Infected; SIR, Susceptible-Infected-Recovered-Deceased; SIRD, Susceptible-Infectious-Recovered-Deceased; SQIRD, Susceptible-Quarantined-Infectious-Recovered-Deceased; SxScreen, symptom screening; TempHousing, temporary housing; WHO, World Health Organization; WTP, willingness to pay; YLL, years of life lost; YLS, years of life saved.
| Primary outcome measure | Type of evaluation | Time horizon | Perspective | Author conclusion |
|-------------------------|--------------------|--------------|--------------|-------------------|
| ICER: cost/prevent one COVID-19 infection in an HCW (WTP = $25,000; estimate of immediate cost of a COVID-19 infection of a HCW) | Cost-effectiveness | NA | Not reported (only cost of testing + costs of PPE are included, limited/restricted healthcare perspective) | At relatively low prevalence of disease (<10%), universal screening is the preferred strategy for women presenting in spontaneous labor and for labor induction. Interestingly for a planned CD universal PPE was more often cost-effective, and therefore, the preferred strategy as long as the cost of PPE remained stable. At high disease prevalence, universal PPE is the best strategy to protect HCW. |
| ICER: cost/HCW death averted; ICER = cost/HCW case averted (no WTP reported) | Cost-effectiveness; ROI analysis | 30-week period | Societal perspective | Immediate investment in the wide-scale production and distribution of PPE for LMICs yields a significant benefit in lives saved and ROI. The authors also conclude that this public health strategy is required to prevent massive depletion of the healthcare workforce. |
| ICER: cost/positive test (no WTP reported) | Cost-effectiveness | Not reported | Not reported (on the basis of included costs it can be considered a limited societal perspective) | ICER values for universal testing decreased with increasing prevalence rates. For higher prevalence rates (>1%), ICER values were the lowest for routine pre-endoscopy testing coupled with the use of high-risk PPE, whereas cost per endoscopy was the lowest for routine use of high risk PPE without universal testing. In general, routine pre-endoscopy testing combined with high-risk PPE becomes more cost-effective with rising prevalence rates of COVID-19. |
Table 2. Evidence table of the included studies.

| Author (Country) | Intervention | Population | Strategies | Epidemiologic model |
|------------------|--------------|------------|-------------|---------------------|
| Neilan et al\(^1\)
(United States) | People with COVID-19 symptoms | People with COVID-19 symptoms | 1) PCR testing only in patients with severe/critical symptoms warranting hospitalization. \((R_e = 0.9, 1.3, 2.0)\)  
2) PCR testing for any COVID-19 consistent symptoms with self-isolation when positive. \((R_e = 0.9, 1.3, 2.0)\)  
3) PCR testing for symptomatic patients and one-time PCR for entire population. \((R_e = 0.9, 1.3, 2.0)\)  
4) PCR testing for all symptomatic persons and monthly re-testing for the entire population. \((R_e = 0.9, 1.3, 2.0)\) | Extended SEIRD (CEACOVID)-(S) susceptible, (E) exposed (latent, noninfectious), (Ip/IA) pre- and asymptomatic, (Im) mildly infected, (Is) severely infected, (Ic) critically infected, (Ir) recovery after critical infection, (R) recovered, and (D) deceased |
| Jiang et al\(^2\)
(China) | People suspected of having COVID-19 | People suspected of having COVID-19 | 1) Two RT-PCR tests for diagnosing and discharging people with COVID-19  
2) Three RT-PCR tests for diagnosing and discharging people with COVID-19 | Extended SEIRD (SALIRD)-(S) susceptible, (A) asymptomatic, (L) presymptomatic, (I) infectious (R) recovered, and (D) deceased |
| Paltiel et al\(^3\)
(United States) | Students (<30 years old and nonimmune, living in a congregate setting) | Students (<30 years old and nonimmune, living in a congregate setting) | 1) Weekly screening \((R_e = 1.5, 2.5, 3.5;\) sensitivity = 70%, 80%, 90%)  
2) Every 3 days screening \((R_e = 1.5, 2.5, 3.5;\) sensitivity = 70%, 80%, 90%)  
3) Every 2 days screening \((R_e = 1.5, 2.5, 3.5;\) sensitivity = 70%, 80%, 90%)  
4) Daily screening \((R_e = 1.5, 2.5, 3.5;\) sensitivity = 70%, 80%, 90%) | Extended SEIRD—(S) susceptible, (E) exposed (latent, noninfectious), (A) asymptomatic infectious, (Is) symptomatic infectious, (R) recovered, (D) deceased |
| Paltiel et al\(^4\)
(United States) | General population | General population | A. 0) \(R_e = 0.9\): no test scenario  
A. 1) \(R_e = 0.9\): weekly home-based SARS-CoV-2 antigen testing  
B. 0) \(R_e = 1.3\): no test scenario  
B. 1) \(R_e = 1.3\): weekly home-based SARS-CoV-2 antigen testing  
B. 2) \(R_e = 1.7\): no test scenario  
B. 1) \(R_e = 1.7\): weekly home-based SARS-CoV-2 antigen testing  
B. 0) \(R_e = 2.8\): no test scenario  
B. 1) \(R_e = 2.8\): weekly home-based SARS-CoV-2 antigen testing | Extended SEIRD—(S) susceptible, (E) exposed (latent, noninfectious), (A) asymptomatic infectious, (Is) mildly symptomatic infectious, (R) critically symptomatic, (D) deceased |
| Du et al\(^5\)
(United States) | General population-households | General population-households | A. 1) \(R_e = 1.2\): daily test plus 1-week isolation  
A. 2) \(R_e = 1.2\): daily test plus 2-week isolation  
A. 3) \(R_e = 1.2\): test every 7 days plus 1-week isolation  
A. 4) \(R_e = 1.2\): test every 7 days plus 2-week isolation  
A. 5) \(R_e = 1.2\): test every 14 days plus 1-week isolation  
A. 6) \(R_e = 1.2\): test every 14 days plus 2-week isolation  
A. 7) \(R_e = 1.2\): test every 28 days plus 1-week isolation  
A. 8) \(R_e = 1.2\): test every 28 days plus 2-week isolation  
B. 1) \(R_e = 2.2\): daily test plus 1-week isolation  
B. 2) \(R_e = 2.2\): daily test plus 2-week isolation  
B. 3) \(R_e = 2.2\): test every 7 days plus 1-week isolation  
B. 4) \(R_e = 2.2\): test every 7 days plus 2-week isolation  
B. 5) \(R_e = 2.2\): test every 14 days plus 1-week isolation  
B. 6) \(R_e = 2.2\): test every 14 days plus 2-week isolation  
B. 7) \(R_e = 2.2\): test every 28 days plus 1-week isolation  
B. 8) \(R_e = 2.2\): test every 28 days plus 2-week isolation | Extended SEIRD—(S) susceptible, (E) exposed (latent, noninfectious), (Ip/IA) pre- and asymptomatic, (Im) mildly symptomatic, (Ih) hospitalized, (R) recovered, (D) deceased |
| Primary outcome measure | Type of evaluation | Time horizon | Perspective | Author conclusion | CHEC |
|-------------------------|--------------------|--------------|-------------|-------------------|------|
| ICER: cost/QALY (WTP: $100,000/QALY) | Cost-effectiveness | 180-day horizon | Healthcare system perspective | Testing people with any COVID-19-consistent symptoms would be cost saving compared with testing only those whose symptoms warrant hospital care. Expanding PCR testing to asymptomatic people would decrease infections, deaths, and hospitalizations. Despite modest sensitivity, at low-cost, repeated screening of the entire population could be cost-effective in all epidemic settings. | 18 |
| ICER: cost/QALY (WTP = CNY64 644); NMB | Cost-effectiveness | January 2020 to March 2020 (43 days) | Healthcare system perspective | The three-test strategy is a dominant strategy in all scenarios. | 18 |
| ICER: screening costs/infection averted (WTP = $100,000 per year-of-life gained; a maximum WTP to avert 1 infection ranging from $7500 (R_e = 1.5) to $10,500 (R_e = 2.5) to $13,500 (R_e = 3.5) = budget impact) | Cost-effectiveness/budget impact | 80 days | Not reported (only costs of screening were considered. On the basis of the included costs it can be considered a restricted approach/perspective) | There is a safe way for students to return to college in the Fall of 2020. The question is whether it is feasible today on a large scale. Coupled with strict behavioral interventions that keep R_e below 2.5, a rapid, inexpensive and even poorly sensitive (~70%) test, conducted at least every 2 days, would produce a modest number of containable infections and would be cost-effective. | 13 |
| ICER: costs/infections averted and costs/deaths averted (Value of statistical life saved = $5.3 million) | Cost-effectiveness | 60 days | Societal perspective | High-frequency home testing for SARS-CoV-2 with an inexpensive, imperfect test could contribute to pandemic control at a justifiable cost and warrants consideration as part of a national containment strategy. | 15 |
| Net benefit (WTP = $100,000 per YLL averted) | Cost-benefit | Not reported | Not reported (on the basis of included costs it can be considered a limited societal perspective) | Assuming a WTP of $100,000 per YLL averted and a price of $5 per test, the strategy most likely to be cost-effective under a rapid transmission scenario (R_e = 2.2) is weekly testing followed by a 2-week isolation period subsequent to a positive test result. Under low transmission scenarios (R_e = 1.2), monthly testing of the population followed by 1-week isolation rather than 2-week isolation is likely to be most cost-effective. Expanded surveillance testing is more likely to be cost-effective than the status-quo testing strategy if the price per test is less than $75 across all transmission rates considered. | 11 |

continued on next page
saved was calculated. Furthermore, the societal return on investment amounted to 7.93%.

**Detection**

Five studies calculated the cost-effectiveness of different detection strategies.12,16,18–20 In general, testing is a cost-effective strategy and more extensive testing becomes more efficient with increasing $R_e$.

Jiang et al16 compared the use of 2 polymerase chain reaction (PCR) tests versus 3 PCR tests in people susceptible of having COVID-19 in the Wuhan area (China) and concluded that a 3×-testing strategy was dominant (a net benefit of CNY 104.0 million).

Neilan et al18 compared 4 PCR testing strategies (only patients with severe/critical symptoms warranting hospitalization to symptomatic patients and monthly tests for the entire population) using different $R_e$ (0.9; 1.3; 2.0). At lower $R_e$, testing of patients

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**Table 2. Evidence table of the included studies.**

| Author (Country) | Intervention | Epidemiologic model |
|------------------|--------------|---------------------|
| **3. Prevention/containment** | | |
| Miles et al24,25 (United Kingdom) | General population | 0) Doing nothing (no change in behavior) 1) Lockdown | Extended SEIRD (Imperial College COVID-19 Response Team model)38 (Ferguson et al) |
| Zala et al10 (United Kingdom) | General population | 0) No measures 1) Mitigation policy: individual case isolation, home quarantine (ie, quarantine of a household with a suspected case), and social distancing advice for people over 70 years of age 2) Suppression strategy 1 = mitigation policy plus general social distancing and closure of schools and universities: triggered “on” when there are 100 ICU cases in a week and “off” when weekly cases halve to 50 cases 3) Suppression strategy 2 = suppression strategy 1 triggered “on” when there are 400 ICU cases in a week and “off” when weekly cases halve to 200 cases | Extended SEIRD (Imperial College COVID-19 Response Team model)38 (Ferguson et al) |
| Asamoah et al26 (Ghana) | General population | 1) Effective testing and quarantine when boarders are opened 2) Intensifying the usage of nose masks and face shields through education 3) Cleaning of surfaces with home-based detergents 4) Safety measures adopted by the asymptomatic and symptomatic individuals such as; practicing proper cough etiquette (maintaining a distance, cover coughs and sneezes with disposable tissues or clothing and wash hands after cough or sneezes) 5) Fumigating commercial areas such as markets 6) Combines the use of controls of strategy 1 to 5 | Extended SEIRD(CEACOV)–(S) susceptible, (E) exposed (latent, noninfectious), (Ip/Ia) pre- and asymptomatic, (im) mildly infected, (is) severely infected, (Ic) critically infected, (Ir) recuparation after critical infection, (R) recovered, and (D) deceased |
| Reddy et al17 (South Africa) | General population | 1) HT ($R_e = 1.2; R_u = 1.5$) 2) $= 1 + CT (R_e = 1.2; R_u = 1.5)$ 3) $= 2 + IC (R_e = 1.2; R_u = 1.5)$ 4) $= 3 + mass SxScreen (R_e = 1.2; Re = 1.5)$ 5) $= 3 + QC (R_e = 1.2; R_u = 1.5)$ 6) $= 4 + quarantine center (R_e = 1.2; R_u = 1.5)$ | Extended SEIRD(CEACOV)–(S) susceptible, (E) exposed (latent, noninfectious), (Ip/Ia) pre- and asymptomatic, (im) mildly infected, (is) severely infected, (Ic) critically infected, (Ir) recuparation after critical infection, (R) recovered, and (D) deceased |
with COVID-19-consistent symptoms was the preferred (dominant) strategy. With a higher Re, PCR testing for all symptomatic persons and monthly PCR testing for the entire population was the most cost-effective strategy (ICER = $33 000/QALY).

In line with Neilan et al,18 Paltiel et al12,19 performed 2 studies in a US setting (2020 and 2021). In their first study, they focused on the cost-effectiveness of a screening strategy on a college campus, thereby comparing 4 different screening strategies with “doing nothing” going from daily to weekly screening, again using different Re and different test sensitivity values. They also concluded that, with higher Re, more frequent testing becomes the preferred strategy. In their second study, they investigated the cost-effectiveness of weekly home-based SARS-CoV-2 antigen testing compared with a no testing strategy, again using different Re (0.9, 1.3, 1.7, 2.8) whereby high-frequency home testing was considered cost-effective for all reproduction rates.

Du et al20 compared 8 testing strategies using rapid antigen testing at different frequencies going from daily to monthly (every 1, 7, 14, and 28 days) followed by a 1-week or 2-week isolation period for confirmed cases assuming 2 different Re (1.2 and 2.2).

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**Table 2. Continued**

| Health economic evaluation | Type of evaluation | Time horizon | Perspective | Author conclusion |
|----------------------------|--------------------|--------------|-------------|-------------------|
| Total damage (WTP = £30 000/ QALY) | Cost-benefit | March-July 2020 | Not reported (on the basis of the included costs it can be considered as a partial societal perspective) | The costs of the 3-month lockdown in the UK are likely to have been high relative to the benefits. According to the authors there is a need to normalize how we view COVID-19, because its costs and risks are comparable with other health problems (such as cancer, heart problems, diabetes). |
| ICER (WTP = £20 000-30 000; according to NHS or more general estimates of the social value of a QALY between £10 000 and £70 000) | Cost-effectiveness | March-July 2020 | Not reported (on the basis of the included costs it can be considered a societal perspective) | Suppression policies were compared with an unmitigated pandemic. Even the most pessimistic National income loss scenarios under suppression (10%), give ICERs below £50 000 per QALY. Assuming a maximum reduction in national income of 7.75%, the ICERS of suppression vs mitigation are below 60 000 per QALY. |
| ICER: cost of control strategies/ averted infections by control strategies (No WTP reported) | Cost-effectiveness | March 12 to May 7, 2020 | Not reported (on the basis of included costs it can be considered a limited/restricted healthcare perspective) | Strategy 4 is the most cost-effective strategy: safety adopted by the asymptomatic and symptomatic individuals such as practicing proper cough etiquette by maintaining a distance, covering coughs and sneezes with disposable tissues or clothing and washing hands after coughing or sneezing. |
| ICER: the difference in healthcare costs divided by the difference in life years between strategies (WTP: $3250/YLS) | Cost-effectiveness | 360 days | Public/private health sector perspective | A strategy combining all interventions would cost an additional $340 per year-of-life saved, which compares favorably with the cost-effectiveness of many established public health interventions in South Africa. With low epidemic growth (Re = 1.1-1.2): HT + CT + IC + QC was the optimal strategy; QCs remained cost-effective but adding MS was not cost-effective. With high epidemic growth (Re = 2.6), when the epidemic outpaced control measures and costs increased substantially, no combination of the modeled interventions was cost-effective compared with HT alone. |

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Under high $R_e$, weekly testing coupled with 2-week isolation for confirmed cases was preferred, assuming lower $R_e$ monthly testing with 1-week isolation was preferred.

**Prevention/containment**

A total of 12 studies assessed the cost-effectiveness of prevention or containment strategies of which 1 study was published twice with a slightly different approach. Most of the studies combined multiple policy measures using various $R_e$. In general, maintaining social distancing, undergoing quarantine/isolation, using a mask, using hygienic measures, and having movement restrictions was cost-effective. As $R_e$ increase, strategies should be adopted simultaneously and in a timely manner.

The studies by Miles et al\textsuperscript{24,25} assessed the cost-benefit of a 3-month lockdown in the United Kingdom compared with “doing nothing” on the basis of different gross domestic product loss assumptions and QALY loss assumptions. In the best case, the lockdown was associated with £68 billion loss, in the worst case with £547 billion loss. In their second study, they accounted for approximately £20,000 additional healthcare benefits for each death avoided through the lockdown; hence, the total damage decreased to £59 billion in the best case.

Table 2. Evidence table of the included studies.

| Author (Country) | Intervention | Strategies | Epidemiologic model |
|------------------|--------------|------------|---------------------|
| Khajji et al\textsuperscript{27} (not reported) | General population | 1) Awareness campaign to protect susceptible individuals from contacting the infected individuals in the same region | SEIQRD with SI model for animals—susceptible (S), exposed (E), infectious (I), quarantined (Q) and recovered (R); (D) discrete time |
| | | 2) Security campaigns and health measures protecting and preventing susceptible individuals from contacting the infected individuals in the same region or in other regions | |
| | | 3) Protecting susceptible individuals, preventing their contact with the infected individuals, and encouraging the exposed individuals to join QCs | |
| | | 4) Protecting susceptible individuals, preventing their contact with the infected individuals, encouraging the exposed individuals to join quarantine centers, and the disposal of the infected animals | |
| Thunström et al\textsuperscript{23} (United States) | General population | 1) Without social distancing | SIRD—susceptible (S), infectious (I), recovered (R), and deceased (D) |
| | | 2) With social distancing | |
| Shlomai et al\textsuperscript{21} (Israel) | General population | 1) National lockdown + individuals who have essential occupations (as determined by government decisions) will not be quarantined and will be required to maintain social distancing. All known exposed individuals will be completely isolated for a 14-day period | Extended SEIRD—(S) susceptible, (E) exposed, (Ia) asymptomatic, (Is) symptomatic and infectious, (R) recovered, (D) deceased |
| | | 2) Testing, tracing, isolation (focused isolation of individuals at high exposure risk who will return to the workforce under social distancing measures after a 14-day isolation period) | |
| Zhao et al\textsuperscript{13} (China) | General population | 1) Current practice: the real-world scenario in China, where the first movement restriction policies started on January 23, 2020 and ended on March 25, 2020 | Extended SIRD—(S) susceptible, (Ip) presymptomatic, (Im) infectious with mild symptoms, (Ih) hospitalized, (R) recovered, and (D) deceased |
| | | 2) 1-week delay in the imposition of movement restriction policies (MRPs) (MRPs end on the day when national newly confirmed cases reach zero) | |
| | | 3) 2-week delay in the imposition of MRPs (MRPs end on the day when national newly confirmed cases reach zero) | |
| | | 4) 4-week delay in the imposition of MRPs (MRPs end on the day when national newly confirmed cases reach zero) | |
In line, Shlomai et al.\textsuperscript{21} compared a national lockdown with a testing-tracing-isolation strategy (including social distancing) in Israel with an ICER of $45,104,156$ per life saved and an ICER of $4.5$ million per QALY and concluded that a national lockdown was not cost-effective.

Zala et al.\textsuperscript{10} compared 3 preventive strategies compared with doing nothing across the general population in the United Kingdom: (1) “Mitigation policy” including individual case isolation, home quarantine, and social distancing advice for people older than 70 years; (2) “Suppression strategy 1”: a mitigation policy + general social distancing and closure of schools and universities that was triggered “on” when there were 100 ICU cases in a week and “off” when weekly cases halved to 50 cases; and (3) “Suppression strategy 2”: the suppression strategy 1, this time triggered “on” when there were 400 ICU cases in a week and “off” when weekly ICU cases halved to 200 cases. Compared with the unmitigated and mitigated strategy, both suppression strategies 1 and 2 were cost-effective.

Zhao et al.\textsuperscript{13} used another approach by investigating the cost-effectiveness of early versus late implementation of movement restriction policies: no delay versus 1-week, 2-week, and 4-week delay, resulting in a net monetary benefit of $\text{2636 billion RMB}$, $\text{24549 billion RMB}$, $\text{26289 billion RMB}$, and $\text{22699 billion RMB}$, respectively. Early implementation dominated all other strategies.

\begin{table}[h]
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\begin{tabular}{|l|c|c|c|c|c|}
\hline
\textbf{Primary outcome measure} & \textbf{Type of evaluation} & \textbf{Time horizon} & \textbf{Perspective} & \textbf{Author conclusion} & \textbf{CHEC} \\
\hline
ICER: delta cost/delta averted infections (No WTP reported) & Cost-effectiveness & Not reported & Not reported (unclear what costs are included) & Strategy 3 is most cost-effective. & 6 \\
\hline
Net benefit (incremental GDP loss vs value of lives saved) & Cost-benefit & 30 years & Not reported (on the basis of the included costs it can be considered a limited societal perspective) & The authors conclude that social distancing likely generates net social benefits ($5.16$ trillion). & 9 \\
Value of statistical life = $10$ million & & & & & \\
\hline
ICER: cost/life saved (WTP for statistical life saved = $10,000,000$; WTP per QALY $= 15,243-17,366$) & Cost-effectiveness & 200 day period & Not reported (on the basis of included costs it can be considered a limited societal perspective) & Over time a strategy of national lockdown is moderately superior to a strategy of focused isolation in terms of reducing death rates but involves extremely high economic costs to prevent 1 case of death. A national lockdown has a moderate advantage in saving lives with tremendous costs and possible overwhelming economic effects. & 8 \\
\hline
Net benefit (WTP = 70,892 RMB) & Cost-benefit & Period less than a year & Societal and healthcare perspective & Strategy A (“current practice”) dominates all other strategies, from both a healthcare perspective and societal perspective. At a WTP of 70,892 RMB per DALY averted, the probability that strategy A is more cost-effective compared with strategy B, C, and D is 96%, 99%, 100%, respectively. Delay in initiating MRPs leads to exponential growth in DALY loss and societal cost: a 4-week delay resulted in 3.7 million more DALYs and 2942 billion USD additional societal cost, compared with no delay. & 16 \\
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\end{tabular}
\caption{Continued}
\end{table}

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Asamoah et al\textsuperscript{26} also considered a wide range of prevention strategies targeting the general population in Ghana whereby safety measures, such as proper cough etiquette were the preferred strategy over the following 5 other strategies: (1) testing and quarantine, (2) cleaning of surfaces, (3) using nose masks and face shields, (4) fumigating commercial areas, and (5) a combination of all, but the exact results were not clearly reported.

Reddy et al\textsuperscript{17} also compared a range of strategies that were combined in a stepwise approach across the general population in South Africa assuming different $R_e$: (1) testing, (2) contact tracing, (3) $1 + 2 + 3 + 4 + 5$, assuming an $R_e$ of 1.2, strategy 5 was the most cost-effective strategy. Applying an $R_e$ of 1.5, combining all interventions was the most cost-effective strategy ($\text{ICER} = $340/LY saved).

Khajji et al\textsuperscript{27} also compared prevention strategies, again using a stepwise approach adding more restrictions in the general population ranging from awareness/security campaigns (to avoid contact with infected people) to joining quarantine centers whereby protecting susceptible individuals, preventing their contact with the infected individuals, and encouraging the exposed individuals to join quarantine centers were the preferred strategies.

Losina et al\textsuperscript{15} considered 4 prevention/containment strategies among college students: social distancing, wearing a mask, isolation, and laboratory testing (going from no testing of asymptomatic students to routine laboratory testing of asymptomatic students at 14-, 7-, or 3-day intervals) in various combinations compared with campus closure and campus opening as usual (24 strategies in total). Extensive social distancing with mandatory use of a mask seemed to be the most cost-effective strategy ($49,200/QALY$).

Baggett et al\textsuperscript{11} compared 7 strategies in homeless US adults, including different combinations of symptom screening, PCR

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**Table 2. Evidence table of the included studies.**

| Author (Country) | Intervention Epidemiologic model |
|------------------|---------------------------------|
| Losina et al\textsuperscript{15} (United States) | College students | 0) No intervention |
|                  | 1) Minimal social distancing + ResIsol (residence isolation in student dorm room) + self-screen |
|                  | 2) Masks + ResIsol + self-screen |
|                  | 3) Minimal social distancing + DesigIsol (student quarantine in separate location) + self-screen |
|                  | 4) Masks + DesigIsol + Self-screen |
|                  | 5) Minimal social distancing + DesigIsol + 1-time LT |
|                  | 6) Extensive social distancing + ResIsol + self-screen |
|                  | 7) Masks + DesigIsol + 1-time LT |
|                  | 8) Extensive social distancing + DesigIsol + self-screen |
|                  | 9) Extensive social distancing + masks + ResIsol + self-screen |
|                  | 10) Extensive social distancing + DesigIsol + 1-time LT |
|                  | 11) Extensive social distancing + masks + DesigIsol + self-screen |
|                  | 12) Extensive social distancing + masks + DesigIsol 1-time LT |
|                  | 13) Minimal social distancing + DesigIsol + RLTq14 (routine LT every X days) |
|                  | 14) Masks + DesigIsol + RLTq14 |
|                  | 15) Extensive social distancing + DesigIsol + RLTq14 |
|                  | 16) Campus closed |
|                  | 17) Extensive social distancing + Masks + DesigIsol + RLTq14 |
|                  | 18) Minimal Social Distancing + DesigIsol + RLTq7 |
|                  | 19) Masks + DesigIsol + RLTq7 |
|                  | 20) Extensive social distancing + DesigIsol + RLTq7 |
|                  | 21) Extensive social distancing + Masks + DesigIsol + RLTq7 |
|                  | 22) Minimal social distancing + DesigIsol + RLTq3 |
|                  | 23) Masks + DesigIsol + RLTq3 |
|                  | 24) Extensive social distancing + DesigIsol + RLTq3 |

*Extended SEIRD (CEACOV)—(S) susceptible, (E) exposed (latent, noninfectious), (Ip/Ia) pre- and asymptomatic, (Im) mildly infected, (Ic) critically infected, (Ir) recuperation after critical infection, (R) recovered, and (D) deceased.*
testing, nonhospital alternative care sites (ACSs), and relocating all shelter residents to temporary housing compared with doing nothing using different $R_e$ (0.9, 1.3, 2.6). Assuming an $R_e$ of 0.9 or $R_e$ of 1.3, daily symptom screening and ACSs for sheltered homeless adults was the preferred strategy. With a $R_e$ of 2.5, shelter-based universal PCR testing every 2 weeks for those without symptoms should be added.

Bagepally et al.\textsuperscript{14} assessed the cost-effectiveness of the use of surgical mask with hand hygiene, hand hygiene alone, surgical mask alone, and N95 respirator (fit tested and nonfit tested) compared with doing nothing from an Indian perspective; none of the proposed interventions was cost-effective.

In contrast, Thunström et al.\textsuperscript{23} conducted a cost-benefit analysis by only comparing social distancing with no social distancing in a US context. They found that, in the base case, social distancing generates a net social benefit of $5.16 trillion.

### Table 2. Continued

| Health economic evaluation | Type of evaluation | Time horizon | Perspective | Author conclusion | CHEC |
|---------------------------|--------------------|--------------|-------------|-------------------|------|
| ICER: cost/QALY (WTP: $150,000/QALY) | Cost-effectiveness | One semester (105 days) | Modified societal perspective | Extensive social distancing with mandatory use of a mask could prevent 87% of COVID-19 cases on college campuses and be very cost-effective. Routine LT would prevent 96% of infections and require low-cost tests to be economically attractive. | 18 |

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**Treatment**

Three studies investigated the cost-effectiveness of different treatment strategies. Sheinson et al.\textsuperscript{28} compared treatment in hospitalized patients with COVID-19 (no oxygen support, oxygen support without ventilation, oxygen support with ventilation) with supportive care; all ICERs (payer [bundled and fee for service payment] and societal perspective) were below the WTP = 50,000$/QALY and thus considered cost-effective. Cleary et al.\textsuperscript{29} analyzed the cost-effectiveness of intensive care management in South Africa, a country that experienced shortages of critical care capacity in public hospitals. With an ICER of ZAR 73,091/disability-adjusted life-year averted, purchasing ICU capacity from the private sector was not cost-effective. In contrast, Gandjour\textsuperscript{31} investigated the cost-effectiveness of expanding the ICU capacity in Germany, resulting in a cost-effective ICER of €21,958/life-year gained and a return on investment equal to 4.6.
**Discussion**

This systematic review summarizes the cost-effectiveness evidence of the different COVID-19 policy measures and provides a detailed overview of the quality, strengths, and limitations of these published studies. The ultimate goal of our healthcare system is to improve health. Nevertheless, because financial resources are scarce, we aim to produce as much health gain as possible with our restricted means. To do this, information on the “best buy” is extremely important. This review can be used by decision makers worldwide to gain insight in the optimal trajectory of implementing timely interventions providing best value for money to tackle pandemics. Furthermore, it can also guide researchers on the existing evidence gaps and flaws when developing their own health economic evaluations in the future.

### Table 2. Evidence table of the included studies.

| Author (Country) | Intervention | Population | Strategies | Epidemiologic model | COVID-19 model |
|------------------|--------------|------------|------------|---------------------|----------------|
| Baggett et al11 (United States) | Homeless adults | A. 0) $R_0 = 0.9$: No intervention: only basic infection control practices are implemented in shelters A. 1) $R_0 = 0.9$: SxScreen/PCR/ACS: CDC-recommended SxScreen daily in shelters. Screen-negative individuals remain in shelters. Screen-positive individuals are sent to an ACS for people under investigation, where they undergo PCR testing and await results. PCR-positive individuals with mild/moderate illness are transferred to ACSs for confirmed COVID-19 cases. PCR-negative individuals return to shelter A. 2) $R_0 = 0.9$: universal PCR/hospital: universal PCR testing every 2 weeks in shelters. Those with symptoms at the time of testing await results at the hospital; individuals without symptoms await results in shelters. PCR-negative individuals return to or stay in shelters. PCR-positive individuals, regardless of illness severity, remain in or are sent to the hospital A. 3) $R_0 = 0.9$: SxScreen/PCR/hospital: CDC-recommended SxScreen daily in shelters. Screen-negative individuals remain in shelters. Screen-positive individuals are sent to the hospital for PCR testing. PCR-positive individuals remain in hospital; PCR-negative individuals return to shelter A. 4) $R_0 = 0.9$: universal PCR/ACS: universal PCR testing every 2 weeks in shelters. Those with symptoms at the time of testing are sent to an ACS for people under investigation while awaiting results; individuals without symptoms await results in shelters. PCR-negative individuals return to or stay in shelters. PCR-positive individuals with mild/moderate illness are transferred to ACSs for confirmed COVID-19 cases A. 5) $R_0 = 0.9$: universal PCR/TempHousing: All shelter residents are pre-emptively moved to TempHousing for the duration of the 4-month period. Universal PCR testing occurs every 2 weeks. PCR-positive individuals with mild/moderate illness remain in TempHousing and are transferred to the hospital if they progress to severe or critical disease A. 6) $R_0 = 0.9$: hybrid/hospital: this includes the SxScreen/PCR/hospital strategy and adds shelter-based universal PCR testing every 2 weeks for those without symptoms A. 7) $R_0 = 0.9$: Hybrid/ACS: this includes the SxScreen/PCR/ACS strategy and adds shelter-based universal PCR testing every 2 weeks for those without symptoms B. 0) $R_0 = 1.3$: No intervention B. 1) $R_0 = 1.3$: SxScreen/PCR/ACS B. 2) $R_0 = 1.3$: Universal PCR/Hospital B. 3) $R_0 = 1.3$: SxScreen/PCR/Hospital B. 4) $R_0 = 1.3$: Universal PCR/ACS B. 5) $R_0 = 1.3$: Universal PCR/TempHousing B. 6) $R_0 = 1.3$: Hybrid/Hospital B. 7) $R_0 = 1.3$: Hybrid/ACS C. 0) $R_0 = 2.6$: No intervention C. 1) $R_0 = 2.6$: SxScreen/PCR/ACS C. 2) $R_0 = 2.6$: Universal PCR/Hospital C. 3) $R_0 = 2.6$: SxScreen/PCR/Hospital C. 4) $R_0 = 2.6$: Universal PCR/ACS |

Extended SEIRD (CEACOV) — (S) susceptible, (E) exposed (latent, noninfectious), (Ip/Ia) pre- and asymptomatic, (Im) mildly infected, (Ic) critically infected, (Ir) recuperation after critical infection, (R) recovered, and (D) deceased
On the basis of the results of this systematic review, several conclusions can be drawn about the cost-effectiveness of different policy measures. First, there is a consensus that testing is a cost-effective strategy. Moreover, the higher the $\mathcal{R}_e$, the more cost-effective frequent testing of the entire population becomes. Second, PPE can be cost-effective depending on the context and on the $\mathcal{R}_e$ (higher $\mathcal{R}_e$, more cost-effective). Third, evidence indicated that undergoing quarantine, using a mask, and maintaining social distancing are also efficient strategies to contain COVID-19. Fourth, 2 high-quality studies indicated that with increasing $\mathcal{R}_e$, a combination of restrictive measures (from testing, social distancing, and quarantine to closures) together is most efficient in tackling this crisis. Even more, another study also pointed out the

| Health economic evaluation | Primary outcome measure | Type of evaluation | Time horizon | Perspective | Author conclusion | CHEC |
|----------------------------|-------------------------|--------------------|--------------|-------------|------------------|------|
| ICER: cost/COVID-19 case prevented (whereby $1000/case prevented is approximately equivalent to $61 000/QALY gained) | Cost-effectiveness | 4 months time horizon (April to August 2020) | Healthcare system perspective | Daily SxScreen and ACSs for sheltered homeless adults will substantially decrease COVID-19 cases and reduce costs compared with no intervention. In a surging epidemic, adding universal PCR testing every 2 weeks further decreases cases at modest incremental cost and should be considered. | 18 |

continued on next page
importance of early implementation of movement restrictions compared with a delayed response. Next, according to 3 studies, the high economic societal cost of lockdown did not outweigh the health benefits; however, none of these studies accounted for the potential health consequences of a healthcare system collapse. Comparison across studies is challenging and should be done with caution, not only because of contextual differences but also because of methodological variation, such as the use of different health outcomes, variation in included costs, and the differences in methodological quality. Indeed, the quality appraisal indicated that the current health economic evaluations are plagued by several methodological issues. A major limitation is the high uncertainty and preliminary nature of most input parameters because of the sparsity of available COVID-19 data. Because many health and economic consequences are not yet known, correctness of the evaluations highly depends on the accuracy of the projections and assumptions made by the used epidemiologic models. In addition, many studies had generalizability issues because studies were often very context specific. Moreover, future healthcare costs and health effects that were directly related to the pandemic were often not accounted for. Indeed, Savitsky and Albright and Reddy et al mentioned the lack of evidence about the long-term effects of COVID-19, including the lifetime healthcare costs among survivors. In addition, the costs and healthcare losses related to other untreated chronic diseases because of limited healthcare capacity during epidemic waves were not covered. Furthermore, the use of inadequate perspectives also affected the included costs. Some studies had incomplete inclusion of relevant costs (only including the cost of testing, not including healthcare costs and only included nondetailed short-term direct healthcare cost consequences). Furthermore, most studies did not report on potential side effects, such as the economic impact, the mental health impact, and educational regression of the different strategies investigated or only did so for a particular intervention instead of for all usual care. Another

Table 2. Evidence table of the included studies.

| Author (Country) | Intervention | Population | Strategies | Epidemiologic model |
|------------------|--------------|------------|------------|---------------------|
| Bagepally et al14 (India) | General population | 0) Doing nothing <br> 1) Surgical mask + hand hygiene <br> 2) Hand hygiene <br> 3) Surgical mask <br> 4) N95 respirator (fit tested) | SQIRD—(S) susceptible, (Q) quarantined, (Im) mild infection, (Is) severe infection, (Ic) critical infection, (R) recovered, and (D) deceased |
| Sheinson et al28 (United States) | Hospitalized patients with COVID-19 | 1) Treatment (no oxygen support; oxygen support without ventilation; oxygen support with ventilation) <br> 2) Best supportive care | Acute care, short-term decision tree to model hospital treatment with 3 states: 1) No oxygen support, 2) oxygen support w/o ventilation, 3) oxygen support with ventilation, and 2 outcomes for every treatment: (A) alive or (D) deceased. Discharged patients advance to a long-term, post-discharge, life-table model with 2 states: 1) Alive and has not received ventilation during inpatient stay and 2) alive and has received ventilation during inpatient stay |
| Cleary et al29 (South Africa) | Hospitalized patients with COVID-19 | 1) General ward <br> 2) General ward + ICU | Acute care, short-term decision tree to model health outcomes (recovered/deceased) of different hospital treatments |
| Gandjour31 (Germany) | Hospitalized patients with COVID-19 | 0) Maintaining ICU bed capacity (do nothing) <br> 1) Expanding ICU bed capacity | Life years gained computed using life-table model |
barrier was the lack of data on acceptability among the population and the variable uptake of containment measures. Furthermore, some studies lacked the basic knowledge of health economic evaluations, such as the proper calculation of ICERs. As such, 3 studies reported negative ICERs without computing incremental effects. In addition, several studies experienced a lack of transparency about the included costs and their data source. Next, several shortcomings of the epidemiological models used in the evaluations should be addressed. Many studies assumed homogeneous population mixing of large and spatially heterogeneous territories or have used nonage-dependent disease characteristics. Both are drastic simplifications of reality that result in an overestimation of COVID-19 prevalence. Others did not include a mathematical model description, an overview of the chosen disease parameters, or a flowchart of the disease model compartments, which compromised reproducibility and tangibility of the disease model. Finally, this systematic review itself has several limitations as well. First, because the literature on COVID-19 evolves very fast, this systematic search should be updated regularly to include new evidence. As such, this systematic review updates the review of Rezapour et al. which included articles until July 2020. Nevertheless, their review used a slightly different approach by including many nonpeer-reviewed articles. Despite the potential loss of high-quality articles, the authors are convinced that the current approach is preferred because a peer review process assures a minimum level of quality, which is of particular importance in this crisis because of the rapid spread of poor quality publications.

On the basis of the main findings of this review, several recommendations can be formulated. First, the findings mentioned above call for a “triggered” stepwise approach, where policy makers should timely shift from one strategy to another on the basis of predefined thresholds. Moreover, it is also important to prevent delay in implementing those “shifts.” Second, future research should deal with the current methodological problems in this field. As such, adopting a broad societal perspective is key, not only considering short- and long-term COVID-19 health losses and costs but also other health losses and costs associated with untreated chronic diseases because of limited healthcare capacity.

### Table 2. Continued

| Health economic evaluation                                                      | Type of evaluation | Time horizon | Perspective                        | Author conclusion                                                                 | CHEC |
|--------------------------------------------------------------------------------|--------------------|--------------|------------------------------------|-----------------------------------------------------------------------------------|------|
| **ICER: cost/QALY (WTP: INR 142,719 ($1921)/QALY gained)**                     | Cost-effectiveness | 1 year       | Health system perspective          | None of the interventions were cost-effective using the WHO WTP threshold. Among the interventions, hand hygiene appeared to be less expensive compared with other interventions but with similar effectiveness. The use of surgical mask with hand hygiene prevented the largest number of COVID-19 deaths. | 15   |
| **ICER: cost/QALY (WTP: $50,000/QALY; $100,000/QALY; $150,000/QALY)**           | Cost-effectiveness | 5 years      | Healthcare payer perspective and societal perspective | Effective COVID-19 treatments for hospitalized patients may not only reduce disease burden but also represent good value for the health system and society. Post-COVID treatments were included. | 10   |
| **ICER: cost/DALY averted (WTP: $38,465.46/DALY averted)**                      | Cost-effectiveness | Not reported  | Healthcare system perspective      | ICU use for patients with COVID-19 was unlikely to be cost-effective on the margin, and therefore an expansion of ICU capacity during COVID-19 surges through government purchase of private services for use by public sector patients (at current prices and evidence of effectiveness) may not be the best use of limited health resources. | 12   |
| **MCER of the last bed added to the existing ICU capacity (WTP: €101,493 per life-year gained)** | Cost-effectiveness | Lifetime     | Societal perspective               | Extending the existing ICU bed capacity seems acceptable on the basis of the MCER but also from a budgetary perspective. That is, extending capacity by more than 100% is forecast to result in a one-time increase in healthcare expenditure of 13%. If, however, the additional capacity remains entirely unused, the value of the investment becomes negative because of the presence of fixed costs. Nevertheless, it is reassuring that even a vacancy rate of 98% still allows for a positive return because of the low share of infrastructure costs. This is equivalent to a 2% probability of having full utilization. | 6    |
the broader economic impact, mental health losses because of social and material deprivation, and educational regression. Third, it is unfortunate that none of the evaluations focused on how a healthier lifestyle could protect against severe COVID-19 outcomes. In this light, cost-effectiveness of lifestyle strategies should also be investigated. Fourth, because each country has different characteristics and societal challenges, such as a different population density, a different population structure (more elderly population in western countries), differences in healthcare system capacity, or cultural differences, local policy makers must never blindly adopt containment measures from other countries. Fifth, best modeling practices should be adopted in future studies, such as providing a complete mathematical description of the disease model and its parameters, demonstrating goodness-of-fit and confidence bounds when the model is calibrated to data, and demonstrating the tangibility of the epidemic growth scenarios, including sensitivity analyses to test robustness of the models and at the same time transparent reporting on included strategies. As such, existing models can be further adapted by others to model particular context-specific factors.

Conclusion

Future cost-effectiveness analyses should respect good modeling practices and should adopt a broad societal perspective considering: long-term COVID-19 health impact, health losses and costs associated with untreated chronic diseases because of limited healthcare capacity, the broader economic impact, mental health losses because of social and material deprivation, and educational regression. Meanwhile, stepwise and timely extending the testing strategy and implementing multiple restriction measures seem most cost-effective to mitigate rising SARS-CoV-2 spread.

Supplemental Material

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.jval.2021.05.013.

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