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The challenge of estimating the direct and indirect effects of Covid-19 interventions: Toward an integrated economic and epidemiological approach

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The Challenge of Estimating the Direct and Indirect Effects of Covid-19 Interventions – Toward an Integrated Economic and Epidemiological Approach

Florian Dorn, Berit Lange, Martin Braml, David Gstrein, John L. Z. Nyirenda, Patrizio Vanella, Joachim Winter, Clemens Fuest, Gérard Krause

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Poschingerstr. 5, 81679 Munich, Germany
Telephone +49(0)89 9224 0, Telefax +49(0)89 985369, email ifo@ifo.de
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The Challenge of Estimating the Direct and Indirect Effects of Covid-19 Interventions – Toward an Integrated Economic and Epidemiological Approach*

Abstract

Decisions on public health measures to contain a pandemic are often based on parameters such as expected disease burden and additional mortality due to the pandemic. Both pandemics and non-pharmaceutical interventions to fight pandemics, however, produce economic, social, and medical costs. The costs are, for example, caused by changes in access to healthcare, social distancing, and restrictions on economic activity. These factors indirectly influence health outcomes in the short- and long-term perspective. In a narrative review based on targeted literature searches, we develop a comprehensive perspective on the concepts available as well as the challenges of estimating the overall disease burden and the direct and indirect effects of Covid-19 interventions from both epidemiological and economic perspectives, particularly during the early part of a pandemic. We review the literature and discuss relevant components that need to be included when estimating the direct and indirect effects of the Covid-19 pandemic. The review presents data sources and different forms of death counts, and discusses empirical findings on direct and indirect effects of the pandemic and interventions on disease burden as well as the distribution of health risks.

JEL Code: I15, I18, I19
Keywords: Covid-19, pandemics, health outcomes, disease burden, non-pharmaceutical interventions, economic decline, social distancing, healthcare access, integrated approach

Florian Dorn[a,d,e,1,**], Berit Lange[b,g,h,**], Martin Braml[a,c], David Gstrein[a,d], John L.Z. Nyirenda[b,f], Patrizio Vanella[b,g,i], Joachim Winter [d,e], Clemens Fuest[a,d,e], Gérard Krause[b,g,h]

[a] ifo Institute – Leibniz Institute for Economic Research, Munich, Germany, [b] Epidemiology Department, Helmholtz Centre for Infection Research (HZI), Braunschweig, Germany, [c] World Trade Organization, Economic Research and Statistics Division, Geneva, Switzerland[2], [d] Department of Economics, University of Munich (LMU), Germany, [e] CESifo Munich, Germany, [f] University Hospital Freiburg, University of Freiburg, Germany, [g] Hannover Medical School (MHH), Germany, [h] German Center for Infection Research (DZIF), Braunschweig, Germany, [i] Department of Health Reporting & Biometrics, aQua-Institut, Göttingen, Germany.

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[1] Corresponding author: Florian Dorn, ifo Institute, Poschingerstr. 5, 81679 Munich, Germany; Email: Dorn@ifo.de.
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1 Introduction

Disease burden and excess mortality are relevant parameters for decision-making on public health measures to contain a pandemic. During the COVID-19 pandemic, most studies assess the direct COVID-19 disease burden via data on reported cases and/or estimates of unreported cases (Liu, Magal et al., 2020; Zhao et al., 2020), transmission parameters (Anastassopoulou et al., 2020; Huang et al., 2020; Kucharski et al., 2020; Liu, Gayle et al., 2020), case fatality, the number of deaths, excess mortality (Rajgor et al., 2020; Russell et al., 2020; Spychalski et al., 2020; Wilson et al., 2020), and potential healthcare burden in terms of bed capacity constraints in intensive care unit (ICU) and hospital beds (an der Heiden & Buchholz, 2020; Hellewell et al., 2020; Ferguson et al., 2020). Various studies perform updated and context-specific evidence synthesis based on both statistics and mathematical models (Burns et al., 2020; Nussbaumer-Streit et al., 2020; Viswanathan et al., 2020). However, those approaches only cover the actual disease burden and excess mortality during the COVID-19 pandemic to a limited degree.

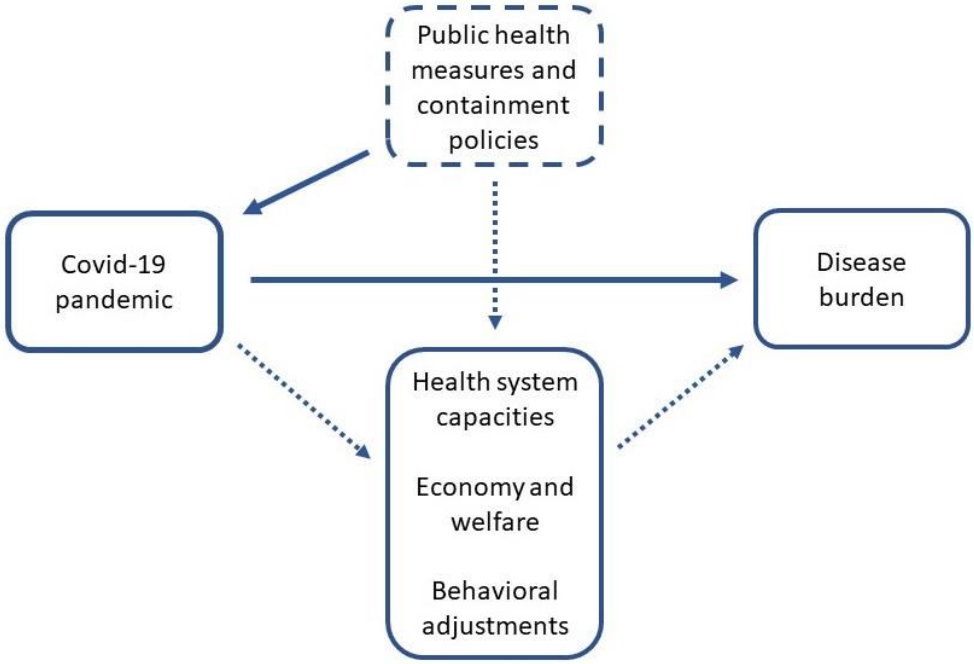
Containment measures may decrease the direct effect of the pandemic on mortality and long-term health consequences (Figure 1). However, both the pandemic and potential non-pharmaceutical measures against the pandemic generate considerable economic, social, and medical costs. Containment policies such as the lockdown of entire economic sectors and schools, the disruption of international supply chains due to border closures, or quarantine orders, also affect the short- and long-term economic well-being and the health of citizens (e.g., Walsh et al., 2021). For policy advice and modeling of intervention strategies, it is important to disentangle which costs are caused by the pandemic and which are a result of strategies of social distancing to fight the pandemic. Debates emphasizing a trade-off between the fight against the pandemic and its economic and social costs are, however, misleading (an der Heiden & Buchholz, 2020; Dorn et al., 2022; Hellewell et al., 2020; Ferguson et al., 2020). It is in the interest of both health and economic well-being to follow a balanced strategy to contain the pandemic (see Dorn et al., 2022).

Health and economic outcomes are interdependent. On the one hand, economic activity and economic well-being decrease because people get sick or are afraid of getting sick and therefore limit their consumption or their labor input. Full economic recovery is therefore impossible without containing the spread of the virus (e.g., Dorn et al., 2022). On the other hand, unemployment, structural economic decline, income and learning losses, or social distress due to the pandemic or social distancing measures have effects on health outcomes and mortality (e.g., Goolsbee & Syverson, 2021). Moreover, the capacities and resilience of healthcare systems depend on the economic performance of the economy as well as the financial leeway and the health expenditures of national governments (OECD, 2019). Therefore, today's decisions on public health measures to contain the pandemic have both short- and long-term effects on (economic) well-being, medical care, and the burden of disease.

In this paper, we present an overview of literature and data sources on relevant components and parameters that need to be considered when estimating the direct and indirect disease burden of the pandemic and measures to fight the pandemic from both epidemiological and economic perspectives, in particular during the early part of a pandemic. This is based on the topic knowledge of experts from infectious disease epidemiology and (health) economics. Moreover, we performed targeted literature searches using compound search strategies for the relevant topics in epidemiological and economic databases or paper series (e.g. MEDLINE, EMBASE, Web of Science, PreVIEW, Scholar, CESifo,

NBER, CEPR).[3] However, we do not provide a systematic review for any sub-topic or meta-analyses to identify pooled estimates of the direct and indirect effects of various relevant parameters.

Figure 1: ***Direct and indirect disease burden due to the pandemic and containment policies***



In our view, the components that need to be considered when discussing disease burden and excess mortality due to the pandemic in light of potential public health measures against the spread of the SARS-CoV-2 virus are the following:

Direct effects:

(A) **Direct burden of disease** caused by COVID-19, such as people dying from COVID-19 or suffering long-term consequences

Indirect effects, such as:

(B) Indirect disease burden due to **overloading the health system**, such as non-COVID-19 patients not being treated in ICU because of overloaded capacities

[3] We employed some criteria for searches in economics and in epidemiology. For example, in (health) economics, we searched in the following steps: First, we systematically reviewed Covid-19 related articles in leading working paper series (preprints) in economics (CESifo, CEPR and NBER Working Paper Series). In these paper series, we searched for the topics that we addressed in our review. These include the search for combinations of the words "health, deaths, unemployment, education, childcare, economic decline, containment policies, Covid-19, Corona, Sars-Cov-2, pandemic, epidemic etc.". We also reviewed the papers cited in these articles. Second, we extended our search on Scholar. We used the combination of the same keywords as mentioned above. In epidemiology, we used n two main databases to perform targeted literature searches on main concepts of direct burden of disease: Medline and PreView. We used simple search strategies in the combination of relevant key words.

(C) Disease burden due to **economic damage** (caused by the pandemic and by public health measures and interventions against the pandemic), such as raised cardiovascular mortality in those additionally unemployed, or long-term health consequences for younger cohorts because of learning and lifetime income losses

(D) Disease burden due to **social/physical distancing**, such as patients with oral anticoagulants (blood thinners, that require constant medical monitoring) not being regularly seen by their general physician, or fewer traffic accidents due to work-from-home orders

The main aim of policies implemented during the COVID-19 pandemic globally has been to minimize the disease burden possibly caused by a potential unmitigated scenario of a pandemic (an der Heiden &Buchholz, 2020; Ferguson et al., 2020), by implementing non-pharmaceutical interventions (NPIs), such as:

1. an increase in the capacity for case isolation and contact quarantine by official agencies (an der Heiden & Buchholz, 2020; Hellewell et al., 2020; Ferguson et al., 2020),
2. protection of population groups at higher risk of COVID-19 severe disease (Hellewell et al., 2020; Ferguson et al., 2020), and
3. physical distancing measures in all spheres of life (private, education facilities, home, and work) (Ferguson et al., 2020; Prem et al., 2020).

Pharmaceutical measures, such as vaccination and their associated strategies are crucial at a later stage during the pandemic, however, the effects of their use are only relevant in later estimations. In this paper we focus more on the effects of NPIs.

Estimating only the direct disease burden of COVID-19 for these different intervention scenarios is not sufficient. This applies to policy advice as well as to public and scientific debate. With epidemiological evidence being collected globally since the beginning of the pandemic, we can realistically include the indirect disease burden in the efficacy estimations of NPIs. In this paper, we discuss the main parameters that need to be considered to understand the direct disease burden caused by COVID-19. In addition, we review the literature on indirect disease burden due to changes in access to healthcare, due to social distancing during the pandemic, and due to economic decline. We show evidence of risks on disease burden for different groups in the population and emphasize the role of welfare state institutions and development levels of countries in mitigating adverse effects.

2 Direct disease burden caused by COVID-19

The main parameters that we need to consider understanding the disease burden caused by COVID-19 are the case and infection fatality estimates, excess mortality, and the proportion of severely sick patients needing ICU beds (e.g., Dudel et al., 2020; Klüsener et al., 2021; Vanella et al. 2021). For a comprehensive view of the disease burden due to COVID-19, it is additionally important to understand who is at a higher risk of severe disease and its long-term consequences. All of these parameters vary across demographics, regions, and different time points during infection dynamics.

2.1 Measuring direct disease burden using death counts

Different forms of death counts have been used during the epidemic, depending on the detail of information available. All of these share a numerator (deaths in the same population in the same region due to COVID-19) affected by potentially misclassifying deaths that are rather a consequence of impairment by other (infectious) diseases. This is, in particular, the case for those regions with high assumed seroprevalences (% of persons with positive antibodies against SARS-CoV-2), as was the case for early European outbreaks (Pollan et al., 2020) – meaning that initial death estimates due to the pandemic may well have underestimated the actual deaths associated with COVID-19 (e.g., as being associated with other types of pneumonia or other causes of venous embolism).

Crude *infection fatality risks (IFRs)* (those reported as dying from COVID-19 over everyone infected) have been estimated at between 0.5 and 2.4% in evidence synthesis of seroprevalence studies and estimations based on notified case data (Meyerowitz-Katz & Merone, 2020; Gornyk et al., 2021; Staerk et al., 2021). The IFR is age-specific, with infection fatality >1% in those above the age of 65 years (Levin et al., 2020). Estimates are therefore within originally assumed infection fatality estimates in modeling studies (an der Heiden & Buchholz, 2020; Ferguson et al., 2020), depending on the underlying age structure of the population (Verity et al., 2020). However, these estimates are still prone to uncertainties both in their numerator and in their denominator. For example, in a particular population-based serosurvey, the denominator "all infections" was initially based on tests that concluded that seroprevalence in the regions of the study was below 10% of the population. However, because of the low specificity of these initial tests and the low overall incidence of SARS-CoV-2 infection in the population, the positive predictive value was less than 60% (Lisboa Bastos et al., 2020).

Crude case fatality risk (CFR) estimates (those reported as dying from COVID-19 over those reported as infected) differ widely across countries and are skewed by the age structure and comorbidities of those infected, by underassessment of cases, by a time lag between case reporting and death of the respective individual, and by testing activity (Vanella et al., 2022).

COVID-19-specific mortality rates (those reported as dying from COVID-19 over the corresponding population) in those countries with more than 100,000 reported cases of COVID-19 vary between 3-98/100,000 inhabitants (Coronavirus Resource Center, 2020) and are similarly skewed by those parameters also skewing the CFR estimates. There is limited evidence indicating an association between lower mortality from COVID-19 and higher air pollution measures (Chen, Wang, Huang et al., 2020; Wu, Nethery et al., 2020).

Years of life lost (YLL) are measured as the number of deaths multiplied by the average remaining life expectancy at the age of death. Worldwide for 2020, estimates of YLL due to COVID-19 are at more than 20 million (Pifarré i Arolas et al., 2021); the 2020 estimate for Germany, for example, has been at more than 300,000 YLL (Rommel et al., 2021). A meta-analysis estimates a global YLL average of 16 for every person who dies of COVID-19 (Pifarré i Arolas et al., 2021). The main data sources to evaluate CFRs and mortality across countries remain national and international public health authorities, such as the European Centre for Disease Prevention and Control (ECDC) and the World Health Organization (WHO). However, data on the population structure corresponding tothe infected cases are often not part of these evaluations, thereby severely limiting the accuracy and interpretation of these estimates, which makes international comparisons difficult (Vanella et al., 2022). YLL estimates are relevant for a

comprehensive inclusion of demographics in the disease burden estimates, with first estimates showing a substantial burden of disease from COVID-19 also in terms of YLL (Hanlon et al., 2020).

Excess mortality (the absolute number of deaths above the ex-ante expected number of deaths per inhabitant) is important for monitoring direct and indirect effects. Currently, excess mortality is estimated in Europe at the state level and is for many countries readily available in the form of excess mortality estimates, such as from the EuroMOMO network (Vestergaard et al., 2020) or via web-based applications (Németh et al., 2021). For example, Sinnathamby et al. show that excess mortality in England during the first months of the COVID-19 pandemic was higher than in the five previous years in all age groups (Sinnathamby et al., 2020). For real-time and current estimation and monitoring of the pandemic and pandemic measures, however, the estimation of *cause-specific excess mortality* as well as morbidity would be important (Vanella et al., 2021).

2.2 Measuring direct disease burden by assessing the severity of disease and populations at risk

The *proportion of patients in need of hospitalization and critical care,* including invasive and non-invasive ventilation, also depends on the demographic structure of the infected population (Fernández Villalobos et al., 2021). However, age- and sex-specific data for those with severe disease is only available in selected European countries (Vanella et al., 2022). The overall direct disease burden of COVID-19 largely depends on the incidents in the high-risk groups.[4] It is therefore important to quantify the risk of sub-populations with comorbidities to understand the specific severity of the disease burden of COVID-19. Knowledge of long-term complications in those persons surviving COVID-19 is increasing, with speculation about ongoing limitations of lung capacity as well as long-term neurological complications (Wu, Xu et al., 2020; Grobe et al. 2022).

Table 1 provides an evidence synthesis of relative risks associated with severe outcomes in COVID-19 patients by risk groups. Several comorbidities like hypertension, diabetes, cardiovascular or respiratory diseases as well as demographic factors like male sex and behavioral factors like smoking and obesity appear to increase the risk of severe disease progression with ICU admission and death (Fernández Villalobos et al., 2021). Population groups at a higher risk of a severe course and mortality have been identified as being mainly the elderly as well as individuals with chronic conditions or treatments affecting the cardiovascular or respiratory systems or immune status (Williamson et al., 2020; Vanella et al. 2021). There is an ongoing debate about whether the latter are mainly found due to confounding by age or whether age is modifying the association between predisposing conditions and severe COVID-19 (Fernández Villalobos et al., 2021).

For example, during the first wave of the COVID-19 pandemic in Spain, over 80% of deaths were related to patients over 70 years of age, but only 40% of all ICU patients were older than 70 years (Li et al., 2020). Moreover, evidence synthesis of the main comorbidities and other risk factors for case fatality and hospitalization and ICU admission shows that the relative risk for these population groups is higher for death than for hospitalization and ICU admission. This is important as it has implications for healthcare capacity calculations and disease burden estimation (Fernández Villalobos et al., 2021).

[4] Risks may also depend on intergenerational residence patterns (e.g., Fenoll & Grossbard, 2020) and the place of residence in the country (e.g., Armillei et al., 2021).

Table 1: ***Evidence synthesis of relative risks associated with severe outcomes in COVID-19 patients***

Risk group	Outcome	Number of studies	Calculated Relative Risk Ranges (95 %CI)	Pooled Analysis RR (95% CI)
Asthma	Death	1	0.9 (0.3-2.4)	0.9 (0.3-2.4)
	ICU admission	1	1.1 (0.7-1.6)	1.1 (0.7-1.6)
Cancer	Death	1	0.7 (0.1-4.9) - 4.8 (1.1-21.5)	2.0 (1.4-2.8)
	ICU admission	5	1.4 (0.7-3.0) - 4.9 (2.7-9.0)	2.3 (1.3-4.0)
Cardiovascular disease	Death	15	1.3 (0.2-8.9) - 6.7 (5.4-8.4)	3.3 (2.3-4.5)
	ICU admission	8	0.9 (0.4-2.1) - 4.1 (3.4-4.9)	2.1 (1.3-3.2)
Cerebrovascular disease	Death	7	1.2 (0.3-4.3) - 7.1 (3.3-15.4)	2.6 (1.7-4.1)
	ICU admission	4	0.8 (0.5-1.3) - 3.7 (2.4-5.8)	1.9 (0.9-4.0)
Chronic obstructive pulmonary disease (COPD)	Death	6	1.9 (0.4-10.1) - 6.0 (1.3-26.8)	2.4 (2.0-3.0)
	ICU admission	4	1.0 (0.4-2.8) - 10.6 (6.2-16.1)	2.4 (0.6-9.8)
Other respiratory diseases	Death	7	0.8 (0.3–2.2)–3.4 (2.4–4.9)	2.2 (1.5–3.0)
	ICU admission	3	0.4 (0.2–1.1)–2.6 (2.1–3.2)	1.3 (0.6–2.9)
Diabetes Mellitus	Death	18	1.1 (0.6-1.9) - 4.5 (1.9-10.6)	2.2 (1.7-2.9)
	ICU admission	12	0.3 (0.1-2.3) - 4.6 (2.8-7.5)	1.9 (1.4-2.6)
Hypertension	Death	17	1.1 (0.2-6.4) - 8.1 (2.9-22.3)	2.7 (2.1-3.4)
	ICU admission	9	0.9 (0.6-1.3) - 3.1 (1.8-5.4)	1.4 (1.1-1.7)
Male sex	Death	19	0.7 (0.1–7.5)–4.7 (1.4–15.1)	1.4 (1.3–1.6)
	ICU admission	11	0.7 (0.3–1.6)–2.0 (0.5–77)	1.3 (1.1–1.4)
Obesity	Death	2	2.1 (1.1–4.2)–4.0 (1.0–15.6)	2.4 (1.3–4.4)
	ICU admission	2	1.4 (1.0–1.8)–1.5 (0.9–2.3)	1.4 (1.1–1.8)
Smoking	Death	4	1.2 (0.8–1.7)–8.7 (3.7–20.1)	2.6 (1.0–6.8)
	ICU admission	5	0.9 (0.5–1.8)–2.9 (1.8–4.8)	1.8 (1.1–2.9)

Note: (selection adapted from Fernández Villalobos et al., 2021)

Additionally, to be able to evaluate the direct disease burden beyond case fatality, *the use of disability-adjusted life years (DALYs)* is important to include short- and long-term complications that do not end in death. This will be particularly important to better grasp the long-term complications that may be associated with COVID-19. There is now considerable evidence that different forms of long- and post-acute COVID-19 syndromes exist and this may imply persisting disease burden in adults and substantial pandemic-associated costs in the future (Davis et al., 2021; Michelen et al., 2021; Nalbandian et al., 2021; Taquet et al. 2021; Pavli et al., 2021). For children, this is less clear and evidence is still being gathered. And while, in particular, at the start of pandemics these long-term burdens might not be adequately quantifiable, epidemiological studies and models assessing direct disease burden ought to include these entities even early on. This is one of the advantages of the use of DALYs and similar measures as they allow an integration not only of the most severe patient outcomes like death but also of less severe patient outcomes, like milder disabilities. And while the actual – larger than expected burden of – long-term complications of COVID-19 only became clear during the second year of the pandemic, complications following ICU admittance and hospitalization were always expected and could have been included in estimations of disease severity from the beginning. This will then ensure that long-term complications are similarly included in later estimations as death counts or acute morbidities associated with the infectious disease.

3 Indirect disease burden due to changes in access to healthcare

There is broad consensus that there have been disease burden changes due to the COVID-19 pandemic that are not related to those infected but rather to the inability of the healthcare systems to adequately cover other diseases (Remuzzi & Remuzzi, 2020; Verelst et al., 2020). Similarly, NPIs aiming at physical and social distancing may also have effects on healthcare access when a part of the population cannot access or is afraid of accessing adequate care.

Most obvious has been *healthcare provider undercapacities* in those regions with a high burden of COVID-19 epidemics like Lombardy, Madrid, or Alsace during the first wave in the spring of 2020 (Buonanno et al., 2020; Grasselli et al., 2020; Magnani et al. 2020). This has been mirrored in relevant excess mortality in these regions, with excess mortality exceeding the isolated numbers reported for COVID-19 (Vestergaard et al., 2020).

Besides these immediate consequences during the peak times of the epidemic, however, there are less obvious consequences resulting in indirect disease burden due to *changes in healthcare use*. There is now considerable evidence of *reduced or delayed healthcare access* for chronic conditions where a) healthcare access was reduced due to the treatment of COVID-19 patients (Aziz et al., 2020; Krenzlin et al., 2020; Verelst et al., 2020), b) elective procedures were suspended for a considerable amount of time (Krenzlin et al., 2020; Latz et al., 2020; Rimmer et al., 2020), and c) healthcare access was reduced due to NPIs or precautions against COVID-19 (Lazzerini et al., 2020).

4 Indirect disease burden due to social distancing during the pandemic

Evidence synthesis assessing *mental health and psychiatric issues* during the pandemic and anti-pandemic measures indicates a high load of mental health burden in high-income countries for COVID-19 survivors (Rogers et al., 2020) among those having to undergo quarantine and isolation (Hossain et al., 2020) as well as for healthcare workers treating COVID-19 patients (Shaukat et al., 2020). Several studies report a higher mental health burden for females (Shaukat et al., 2020; O'Connor et al., 2021). Parents, adolescents, and children are also heavily affected by the mental health impact of the pandemic and the containment measures, a finding with evidence from several countries (Gassman-Pines et al., 2020; Orben et al., 2020; Orgilés et al., 2020; Ravens et al., 2021). For example, a nationwide representative study from Germany shows that two-thirds of children and adolescents reported being negatively affected by the pandemic. They experience a significantly lower health-related quality of life (40.2% vs. 15.3%), more mental health problems (17.8% vs. 9.9%), and higher anxiety levels (24.1% vs. 14.9%) than before the pandemic. Children with low socioeconomic status, a migration background, and limited living space are affected significantly more (Ravens et al., 2021). Mental health of children was affected both by social distancing but also by the pandemic itself, with a relevant number of children experiencing the loss of a parent or caregiver (Hills et al. 2021). Moreover, Google searches for boredom, loneliness, worry, and sadness increased significantly during the pandemic, while searches for suicide and divorce decreased (Brodeur, Clark et al., 2021).

Both stress caused by the pandemic and by anti-pandemic measures, economic consequences, and social distancing are factors that will likely lead to an increase in *intimate partner violence (IPV)* (Buttell & Ferreira, 2020; Usher et al., 2020). In the US, police calls for domestic violence increased by 7.5%

between March and May 2020, starting even before stay-at-home orders went into effect (Leslie & Wilson, 2020). Using data from the US state of Michigan, Chalfin et al. (2020) show that the relationship between alcohol consumption and IPV has strengthened since the start of the pandemic, most likely because of an increase in alcohol consumption at home. Baron et al. (2020) show that teachers are crucial for reporting child maltreatment and that school closures have led to increases in underreporting, making it difficult to assess the full extent of the problem. Anderberg et al. (2022) develop an internet search-based measure of domestic violence to circumvent the bias of underreporting. They find that domestic violence in the Greater London area peaked at a 40% increase compared to pre-pandemic levels, much larger than the rise recorded by the police. While interventions against IPV are well established and can be continued digitally (Emezue, 2020), their effectiveness was constrained by anti-pandemic measures (Johnson et al., 2020).

By contrast, there are examples of the pandemic and the NPIs used resulting in *a reduction of disease burden.* Most notably, a reduction in *air pollution* has been identified as a source of declining mortality during this pandemic because of lockdowns and the economic downturn. Studies from China and the US, for example, have estimated that the number of premature deaths from air pollution could drop by a few thousand deaths per year (Achebak et al., 2020; Chen, Wang, Huang et al., 2020; Chen, Wang, Kinney et al. 2020; Wu, Nethery et al., 2020; Brodeur, Cook et al., 2021).

Similarly, *mortality rates from accidents*, both work-related and transport-related, have decreased due to social distancing or increased unemployment and work-from-home orders. First studies suggest a decline in emergency department visits for orthopedic hand and trauma reasons of between 20% and 60% during the months of social distancing measures and stay-at-home regulations (Lubbe et al., 2020; Morris et al., 2020; Regas et al., 2020; Stoker et al., 2020). Similarly, traffic accidents have fallen significantly by 74% during the strict lockdown in Spain (Saladié et al., 2020), or, depending on the exact time frame and state, by 20% to 47% in the US (Barnes et al., 2020; Brodeur, Cook et al., 2021).

And finally, considerable reductions in disease burden were observed in 2020 due to reductions in other infectious diseases, like influenza and other infectious diseases (Fricke et al., 2021). However, some studies predict larger outbreaks of respiratory viruses that affect children, such as RSV and influenza, following the relaxation of NPIs (Baker et al., 2020), and there is some evidence that they are already occurring (Weinberger Opek et al., 2021).

Table 2: ***Parameters to estimate direct and indirect disease burden used by epidemiologists***

	Definition	**Other names**	**Potential bias in this estimate**	**Data source and examples of current estimates for COVID-19 if available**
Disease counts				
Number of visits to healthcare providers	Visits/period		**Underestimate** of actual disease incidence if lower proportion of those with the disease attend healthcare providers	Single sources from hospitals, healthcare providers
Incidence	Incidence: Events/person-time	Rate	**Underestimate** if notification is decreased **Overestimate** if notification is increased	Reported from official sources like ECDC, WHO
Prevalence	Events/population at a specific time point	Cumulative incidence	**Underestimate** if notification is decreased **Overestimate** if notification is increased	Reported from official sources like ECDC, WHO
Proportion of cases in ICU	Persons admitted to ICU/different denominators are used: hospitalizations, all reported cases, all infected	ICU cases	**Underreporting** of cases **Misclassification** of disease cause as COVID-19 (both negative/positive)	Reported from official sources like ECDC, WHO
Disability adjusted life years (DALY)	Sum of the years of life lost (YLL) due to premature mortality in the population and the years lost due to disability (YLD) (WHO definition: https://www.who.int/healthinfo/%20global_burden_disease/metrics_daly/en/)		**Underestimate** if death counts or disease prevalence misclassified **Overestimate** if alternative explanations of attributed disease burden	**IHME (http://www.healthdata.org/)**; global burden of disease estimations, World Health Organization's global reports
Death counts				
Case fatality estimate (CFR)	Deaths caused by COVID-19/reported cases in one population	Often misnamed case fatality *rate* (though not a rate), case fatality risk	**Misclassification** of death causes, both as being from COVID if in reality a comorbidity was to blame, as well as being not from COVID if this was not tested **Underreporting** of cases	Reported from official sources like ECDC, WHO (Vanella et al., 2021)
Infection fatality estimate (IFR)	Deaths caused by COVID-19/all infections in one population	Infection fatality rate	**Misclassification** of death causes, both as being from COVID if in reality a comorbidity was to blame, as well as being not from COVID if this was not tested **Low positive predictive values** of current serology assays	Serosurveys in several countries have reported this (Levin et al., 2020; Meyerowitz-Katz & Merone, 2020) IFR: 0.4-0.9%
Mortality estimate	Deaths caused by COVID-19/number of people in one population	Mortality rate	**Misclassification** of death causes, both as being from COVID if in reality a comorbidity was to blame, as well as being not from COVID if this was not tested	Reported from official sources like ECDC, WHO
Years of life lost (YLL)	Number of cause-specific deaths multiplied by a loss function specifying the years lost for deaths as a function of the age at which death occurs	YLL	**Misclassification** of death causes, both as being from COVID if in reality a comorbidity was to blame, as well as being not from COVID if this was not tested	Single reports from several sources, 14 years for men and 12 years for women in Scotland (Hanlon et al., 2020)
Excess mortality	Deaths over time in a particular population in relation to deaths over time in the same population from previous time periods	Excess deaths, excess mortality	**Underreporting** of deaths in principle possible but not likely in most European countries **Seasonal effects** have to be taken into account	European sources (EuroMOMO), influenza monitoring (Vestergaard et al., 2020); Vanella et al. (2021)
Cause-specific excess mortality	Cause-specific deaths over time in a particular population in relation to same cause-specific deaths over time from previous periods in the same population	Excess deaths, cause-specific excess deaths	**Misclassification** of death causes **Underreporting** of deaths in principle possible but not likely in most European countries **Seasonal effects** have to be taken into account	No sources yet

5 Disease burden due to economic decline

The pandemic and shutdown measures have had a severe impact on worldwide economic activity and well-being. Countries all over the world were affected by a massive slump in economic output, which gave rise to unemployment, bankruptcies, income losses for many households, and increasing public and private debt (OECD, 2021a). In 2020, the global gross domestic product (GDP) fell by 3.1%, with large cross-country differences.[5]

Increases in unemployment and short-time work were substantial in many countries, but effects on household incomes varied across countries depending on welfare systems and unemployment insurance schemes and policies (OECD, 2021a). Expanded government spending and declining GDP led to an increase in debt-to-GDP ratios by 16 percentage points across OECD countries (OECD, 2021c). Notably, a persistent decline in economic well-being and the need for fiscal consolidation may have effects on disease burden and life expectancy in the long-term perspective (Schnabel & Eilers, 2009).

We disentangle different but related channels that transmit economic effects into individual health outcomes. First, we review the general relationship between health outcomes and unemployment during times of recession as well as the general effect of household income and unemployment shocks on general and cause-specific mortality. Then, we discuss some first studies on the effect of the COVID-19 related economic decline on health outcomes.

5.1 Health and mortality during times of recessions and high unemployment

There is a large body of evidence showing that aggregate-level mortality is procyclical – rising when overall economic conditions improve and falling when they deteriorate. In an influential study, Ruhm (2000) shows that total mortality and eight out of ten main sources of fatalities exhibit a *procyclical fluctuation*, i.e., mortality rates tend to be lower in recessions. One exception is the suicide rate, which was shown to be higher in recessions. These results were based on a state-level fixed effects analysis for the US. Further, Ruhm (2017) argues that more severe economic crises affect mortality and other dimensions of health in the same way as less severe downturns, also leading to improved physical health.

Several *macro-level studies* following the approach of the seminal work of Ruhm (2000) support his finding of a procyclical relationship. Ruhm (2000) and subsequent studies argue that harmful behaviors such as smoking and drinking as well as traffic accidents become less prevalent in a recession. Studies using state-level data from Canada, Germany, and the US suggest a negative relationship between *unemployment* and total mortality rates once controlled for time-invariant state-fixed effects and other confounding factors (Ruhm, 2000; Neumayer, 2004; Miller et al., 2009; Ariizumi & Schirle, 2012). According to these results, the overall mortality rate, ceteris paribus (c.p.), decreases by about 0.5-1.1% when the unemployment rate increases by one percentage point (p.p.). For young adults (20-44 years of age), who make up the largest share of the working-age population, the effect is the strongest: a one p.p. rise in state unemployment rates lowers the predicted death rate of 20-44 year-olds by about 1.0-2.0% (c.p.).

[5] While it increased by 2.3% in China, it fell by 7.3% in India, by 6.3% in the Euro area, by 9.8% in the UK, and by 3.4% in the US (IMF, 2021). However, all countries saw substantial losses compared to their initial GDP growth projections for 2020 as expected before the crisis in 2019 (IMF, 2019): World GDP in 2020 is 6.5 percentage points (p.p.) lower than expected. While it is 3.5 p.p. lower in China, losses are higher in India (14.3 p.p.), the Euro area (7.7 p.p.), the UK (11.2 p.p.), and the US (5.1 p.p.).

Conversely, a macro-level study conducted in a panel of EU member states shows a positive relationship between adverse economic conditions and total mortality rates (Economou et al., 2008). According to the authors, a 1% increase in national unemployment rates c.p. gives rise to approx. 1.54 deaths per 100,000 inhabitants. The positive relationship is largest for the 45-54 age group, while the study confirms that unemployment is associated with decreases in mortality for the youngest working-age cohort. By contrast, another cross-country study among OECD countries suggests that a one p.p. decrease in the national unemployment rate is on average, c.p., associated with a rise in total mortality of 0.4%. The results suggest variation across countries, with larger adverse health effects of rising unemployment in countries with relatively weak welfare states (Gerdtham & Ruhm, 2006). Other studies support the notion that lower public health expenditure and a lack of health institutions like universal health coverage are correlated with larger cause-specific mortality rates, such as treated cancer deaths during economic recessions (Maruthappu et al., 2016).

Micro-level studies that use individual-level data (from natural experiments) to estimate the causal effects of unemployment on health outcomes consistently find that these are negative, on average. These studies require administrative datasets which cover large populations. Such datasets are accessible only in some countries, including the US and Scandinavian countries. In the following, we illustrate the research designs and main findings of selected studies. It remains an open question whether these results are representative for other countries, but the fact that negative effects of individual-level unemployment on health outcomes have been found in countries with very different labor market intuitions and healthcare systems suggests that they do.

As pointed out by Sullivan and von Wachter (2009a), "the situation of an individual displaced worker differs qualitatively from that of the average worker during a recession" (p. 1269). Using administrative employment data from the US state of Pennsylvania, Sullivan and von Wachter (2009a) estimate that mortality rates in the year after *displacement* are 50 to 100% higher for older male workers. While the effect of becoming unemployed on mortality hazards declines over time, it can still be detected twenty years after job displacement. The authors estimate a loss in life expectancy of 1.0 to 1.5 years for a worker displaced at age 40. Similar results have been established for the Scandinavian countries. Using administrative data covering the entire Danish workforce, Browning and Heinesen (2012) exploit plant closures as a natural experiment. They show that job loss increases the risk of overall mortality and cause-specific mortality for circulatory disease, suicide and suicide attempts, and death and hospitalization due to traffic accidents, alcohol-related disease, and mental illness. The latter study estimates the average risk of overall mortality associated with unemployment at 79% higher in the year of displacement and 11% higher over the twenty-year period after the base year.[6] Based on Swedish data, Eliason and Storrie (2009) confirm the magnitude of such short-term effects but identify larger long-run effects. The findings for Denmark and Sweden suggest smaller effects than those found by Sullivan and von Wachter for the US. Institutional differences such as whether access to the healthcare system is linked to the job, and differences in income insurance and welfare programs, could explain differences in health-related outcomes across countries. More generous welfare institutions with unemployment benefits and tighter labor market institutions seem to attenuate the negative health effects

[6] Browning and Heinesen (2012) mention that it is very difficult to assess the social costs of the estimated increase in mortality and incidence of serious diseases caused by plant closures. These costs are borne by a small share of the displaced workers. Presumably, a larger share experience negative health effects which are less serious and do not lead to hospitalization or death, so they are more difficult to detect. We are not aware of reliable estimates of these effects.

of job losses. For the US, Cylus et al. (2015) find that the impact of job losses on health is lower in states with more generous unemployment benefits. Riumallo-Herl et al. (2014) find that the effect of job loss on depression is significantly larger in the US than in Europe. In addition, the effect is moderated by pre-existing wealth in the US but not in Europe. Browning and Heinesen (2012) also find that the effects are larger in local labor markets with higher unemployment.

5.2 Income shocks and mortality

There is evidence of an association between income (and wealth) levels and mortality rates, as in Chetty et al. (2016) for the US and in von Gaudecker and Scholz (2007) for Germany.[7] Evidence for the effects of *income shocks* on health is mixed and findings seem to depend on the specific measure of income, or economic resources more generally. For example, Ahammer et al. (2017) find a zero effect of short-run variations in labor income on 10-year death rates for workers aged 40-60 years using administrative social security data from Austria.

The effects of shocks on lifetime income are likely larger. Sullivan and von Wachter (2009b) argue that estimates based on single years of earnings data are likely to understate the strength of the association between income and mortality. Using the same data as Sullivan and von Wachter (2009a, see above), they find that relative to a single year of earnings, the average of earnings over six years predicts a 70% larger impact of income on mortality. One of their main results is that for the group of workers younger than age 60, a 10% increase in income over five years c.p. lowers the probability of death in the following year by approximately 5%. These findings suggest that recessions and shocks to GDP are more harmful to health and life expectancy with increasing duration of the economic shock.

5.3 Variation in cause-specific mortality

The evidence on overall mortality and cause-specific mortality rates such as cardiovascular, respiratory, or liver diseases as well as homicides and infant mortality is mixed. However, there is strong evidence that economic decline and a rise in unemployment are associated with increases in several cause-specific mortality rates, such as suicide rates, while empirical evidence is also strong for declining death rates from other causes such as (motor) vehicle accidents during economic downturns. In the following, we highlight findings from this literature, focusing on the effects of economic decline and individual-level unemployment. We acknowledge that during a pandemic such as COVID-19, other mechanisms will also affect suicide rates. Most importantly, in contrast to recessions, major crises often induce policy interventions that support individuals that are at risk. For instance, a recent study by Alvarez-Galvez et al. (2021) highlights the mediating role of social cohesion and community values during a major crisis – in their analysis, the 2011 financial crisis in Spain. The following studies typically analyze economic

[7] Macro-level data is often employed to examine the long-run relationship of cross-country income levels and life expectancy (e.g., Swift, 2011; Biggs et al., 2010; Bilas et al., 2014; Felice et al., 2016). Some scholars use correlations to predict the influence of real GDP growth on life expectancy. The direction of causality is, however, ambiguous. Both wealth and health positively influence each other at the personal as well as at the country level. Using correlations as a predictor would therefore overestimate the effect of GDP on health. Moreover, positive correlations between the two variables could also result from third variables, such as technological progress, that positively impact health and income. These interdependencies need to be interpreted cautiously as they only report (simple or conditional) correlations. We suggest that scholars should avoid using estimates of correlations to predict effects of GDP on life expectancy. By contrast, Acemoglu and Johnson (2007) use an instrumental variable approach and find no evidence that a rise of life expectancy (due to health improvements) increases GDP per capita.

downturns and individual unemployment as determinants of suicide in periods with the implicit assumption that the social environment remains stable.

Suicide mortality: Economic theory suggests that social living conditions such as income and unemployment are determinants of suicidal behavior (Hammermesh & Soss, 1974). Several empirical studies find evidence, both across countries and time, supporting this hypothesis. These studies show that recessions are correlated with short-term increases in suicide mortality rates (Chang et al., 2009; Tapia Granados & Diez Roux, 2009; Stuckler et al., 2009; Stuckler, 2011a; Stuckler et al., 2011b; Reeves et al., 2012; Sullivan et al., 2013; Baumbach & Gulis, 2014). Empirical studies show that both a rise in *unemployment* and a decline in *economic growth* influence suicide mortality. Using data from 63 countries, Nordt et al. (2015) find a positive association between unemployment and suicide mortality that is stronger in countries with lower levels of baseline unemployment. Findings based on US state-level data show an increase in suicide rates by 1.3-1.6% for each one-p.p. rise in state-level unemployment rates (Ruhm 2000; Phillips & Nugent, 2014). However, studies show that the conditional correlation is lower in European countries than in the US, or even lacks statistical significance (Neumayer, 2004; Andrés, 2005; Breuer, 2015; Tapia Granados & Ionides, 2017). Using panel data of European countries or regions, Breuer (2015) and Tapia Granados and Ionides (2017) show that suicide rates are predicted to rise within a range of 0.4-1.3% for each one-p.p. increase in the unemployment rate. Similarly, a decline in the real growth rate of gross value added in European regions of 1% would increase regional suicide rates by about 0.3-0.5% (Breuer, 2015). Some studies which examine the relationship between unemployment and suicides in European countries by using more aggregated data suggest a negative correlation or do not find significant correlations between unemployment and suicide rates (Neumayer, 2004; Andrés, 2005; Gerdtham & Ruhm, 2006).

However, studies relying on micro-level data support a causal inference that unemployment and job displacement increase suicide risks in European countries (Gerdtham & Johannesson, 2003; Browning & Heinesen, 2012). Other global regions report similar findings. Christian et al. (2019) find that the rollout of cash transfers and agricultural productivity shocks influence suicide rates in Indonesia. Other scholars also find evidence that a rise in unemployment implies higher suicides at the Japanese subnational and local levels (Kuroki, 2010).

Reflecting the differences between elasticities of changes in the economic situation on health outcomes in the US and Europe, scholars suggest variation in the rise of suicide rates depending on social integration and the size of the welfare state (Brainerd, 2001; Baumbach & Gulis, 2014).[8] Besides regional differences, empirical evidence reveals relevant heterogeneity across demographics. First, the elasticity of suicide behavior of men tends to be somewhat larger than for women during economic downturns (Brainerd, 2001; Breuer, 2015). Second, economic recessions only influence suicide rates of the working-age population, as they suffer a negative shock in expected income. Findings based on a panel of European regions indicate a one-p.p. increase in unemployment to be associated with an approx. 1% increase in suicides among individuals aged younger than 65 years, while old-age suicides do not respond to fluctuations in unemployment (Breuer, 2015).

[8] For a sample of 22 economies during transition and lack of generous welfare system in the 1988-1998 period, the effect was even larger: a one p.p. increase in the national unemployment rate is associated with a rise in suicides rates by about 3%; and a decline of GNP per capita of USD 100 raised the predicted male suicide rate by 0.1-0.2% (Brainerd, 2001).

Preliminary findings for the COVID-19 pandemic have shown that suicides generally decreased in the US and several other countries during the first infection wave (Ahmad & Anderson, 2021; John et al., 2020). However, some evidence from Japan suggests increases in subsequent waves or when governmental (income) support has come to an end (Tanaka & Okamoto, 2021).

Vehicle accidents: Economic downturns go along with a reduction of traffic volume for two reasons: first, the need for commuting declines when unemployment rises, or when plants are suspended (e.g., by short-time work). Second, the shrinking of disposable household incomes typically leads to a reduction of expenditure on non-work-related transportation. During the COVID-19 pandemic, traffic was additionally reduced due to work-from-home orders (see Section 2.3). The negative effect of unemployment on commuting and thus on vehicle accident fatality has also been the subject of empirical research. Ruhm (2000) quantifies that an increase in the unemployment rate by one p.p. reduces traffic accident fatalities by c.p. 2.4% in the US. Examining the same relationship for the US during the Great Depression, He (2016) estimates an elasticity of 2.9%. Wegman et al. (2018) emphasize that this effect is mainly driven by a disproportionate reduction of traffic exposure by high-risk drivers (especially young men).

5.4 COVID-19 economic decline and health outcomes

5.4.1 Economic decline because of the pandemic and containment policies

To evaluate and model the effects of the pandemic and health policy interventions on disease burden during a pandemic, it is necessary to disentangle economic losses that are caused by the pandemic from those caused by policy reactions to the pandemic, in particular NPIs. Evidence from the US and Europe in the first COVID-19 wave suggests that the decline in economic activity was mainly caused by behavioral adjustments, and only a minor part of the economic decline can be explained by NPI measures (Rojas et al., 2020; Goolsbee & Syverson, 2021; Juranek et al., 2021; Sheridan et al., 2020; Chetty et al., 2020).[9]

For example, legal restrictions explain less than 10% of the overall decline in consumer traffic in the US during the first infection wave; the rest is likely due to voluntary behavioral changes because of fear of infection with the virus (Goolsbee & Syverson, 2021). Similarly, earlier reopening policies in US states did not have significant effects on consumer spending and employment compared to states with stricter measures while the virus continued to rage (Chetty et al., 2020). In-person consumption in China decreased more in cities that experienced more cases and deaths, even when mitigation policies were the same across both groups of cities (Chen, Qian, & Wen, 2021). Similarly, Swedish VAT (value-added tax) revenues fell more in municipalities with more infections, while NPIs were at the same level (Angelov & Waldenström, 2021b). Sheridan et al. (2020) find that Danish customers reduced their spending by 29%, while Swedish spending fell by 25% during the pandemic, although Sweden did not implement a strict lockdown like Denmark. They conclude that the 4-p.p. difference between both countries was likely caused by the Danish shutdown, while the 25% decrease happened because of the pandemic and voluntary behavioral changes. Similar effects are found in the labor market when comparing Denmark, Finland, Norway, and Sweden (Juranek et al., 2021). Sweden experienced a 25% to 50% lower rise in unemployment than the other countries, suggesting that between 50% and 75% of

[9] Behavioral responses could have been different in other infection waves, for example because of better knowledge about the risks and mitigation measures, or because of different infection and fatality risks.

the rise in unemployment was caused by the pandemic, not by the NPI policies. Moreover, it is important to disentangle the effect of different NPI strategies on the economy.[10]

Other studies have focused on separating policy-induced and voluntary mobility reductions and their impact on death counts. Both containment policies and voluntary behavioral adjustments led to substantial reductions in death growth rates in the US (Chernozhukov et al., 2021). Depending on the specification, between 33% and 66% of the decline in deaths can be attributed to political orders, while the rest is likely due to voluntary changes in behavior. Gupta et al. (2020) show that mobility began to fall even before policies were enacted and did not respond strongly to the lifting of those policies. Their estimates suggest that state emergency declarations account for 65% of the decline in mobility, while the remaining 35% is explained by personal behavioral decisions.

While the studies discussed so far in this section focus on the role of "voluntary" behavioral adjustments versus government intervention to contain the pandemic at a given point in time, it should be noted that there is an important intertemporal dimension. In particular, early NPIs may have had immediate costs due to limited economic activity but may enable more economic activity later because infection rates had been reduced earlier (Dorn et al., 2022; König & Winkler, 2021).

5.4.2 Disease burden caused by COVID-19-associated economic decline

Research on the indirect effects of a COVID-19-associated economic shock on health outcomes is still scarce. Data availability is limited and causal inference is challenging. Some first studies use parameters from earlier recessions to predict adverse effects on disease burden. For the US, Bianchi et al. (2021) apply vector autoregression to historical time series data on unemployment, life expectancy, and death rates. Their simulations show that macroeconomic *unemployment shocks* give rise to a reduction in *life expectancy*. The model predictions suggest a sizeable decline in life expectancy over the following 20 years due to a large unemployment shock. They estimate that job losses will be greatest for women and the African-American population, but the adverse effects on life expectancy are assumed to be the largest for the latter. For the UK, the British Office for National Statistics (2020) estimates the *long-run health impact of the economic decline* caused by the pandemic. Their baseline scenario suggests a loss of 1.3 million QALYs (quality-adjusted life years), with a range from 0.23 million to 2.7 million in the upside and downside scenarios. Such estimates are highly volatile, which makes external validity critical as the economy, for example, may recover faster or slower than expected.

Welfare and unemployment insurance programs may moderate the unemployment shock as well as its health consequences. Donnelly and Farina (2021) show that the relationship between income losses and deteriorations in mental health was strong in US states with less supportive policies such as Medicaid or unemployment and income insurance schemes. Several studies from Europe and the US show that relative wage declines (before tax and transfers) were largest at the bottom of the income distribution during the pandemic crisis (Palomino et al., 2020; Chetty et al., 2020; Crossley et al., 2021; Angelov & Waldenström, 2021a; Almeida et al., 2021). Inequality after redistribution programs has, however, only increased in some countries as government programs cushioned adverse economic effects in many advanced economies during the crisis (see Angelov & Waldenström, 2021; Clark et al., 2021). This

[10] For example, restaurant and bar limitations and non-essential business closures had an effect on unemployment claims, responsible for around 6% (Kong et al., 2020). However, findings for other mitigation policies, such as stay-at-home orders, large-gatherings bans, school closures, and emergency declarations do not seem to affect unemployment to a significant size.

underlines the importance of unemployment and income insurance programs to avoid adverse economic outcomes and their health consequences during a crisis. Longer-lasting adverse effects might become more visible once such programs expire (Stantcheva, 2022).

Another specific effect of the COVID-19 pandemic and its social distancing measures is the *disruption of education and childcare.* Gassmann-Pines et al. (2022), for example, find that families with children reported disruptions to their schooling and care arrangements on 24% of days. Such disruptions have led to worse mental health for children and parents as well as substantial learning losses, especially among students from disadvantaged backgrounds (Agostinelli et al., 2021; Gassmann-Pines et al. 2022; Grewenig et al., 2020). These disruptions might create substantial losses in the lifetime income of the affected students (Wößmann, 2020; Hanushek & Wößmann, 2020). Hanushek and Wößmann (2020) estimate that a learning loss of one school year is, on average, c.p., associated with (cumulated and discounted) future GDP losses to its present value of more than 4%. As such, the pandemic may have a long-term effect on economic growth, individual income opportunities, and ultimately the health outcomes of today's students.

At a more general level, severe diseases and shocks such as economic crises that are experienced by children and young adults are known to have adverse long-run effects in such diverse outcomes as mental health, human capital formation, family formation, lifetime incomes, and more. A large literature studies the effects of wars, recessions, and early childhood diseases on long-run outcomes (e.g. Almond et al., 2018; Bleakly 2007; Currie 2020). By their long-run nature, these effects are difficult to quantify and to generalize but empirical evidence suggests that even relatively small shocks to parent's or children's (mental) health can have large long-term consequences on children's health, educational attainment, and income (see Almond et al., 2018; Goodman et al., 2011; Currie & Stabile, 2006; Currie et al., 2010; Currie 2020).[11]

6 Economic development, public debt, and long-term implications of a pandemic´

Finally, we consider fiscal conditions and the level of economic development across countries as relevant pre-conditions for the effect of economic decline on disease burden.

6.1 Public debt and fiscal consolidation

The COVID-19 pandemic revealed substantial differences in hospital bed and ICU capacities across advanced economies. Economic determinants for differences in capacities in the health system and health spending levels constitute another relevant pre-condition for effects on indirect disease burden. Capacities and resilience of healthcare systems depend on the performance of the economy, the financial leeway, and the spending of national governments.[12] Public debt and fiscal consolidation may lead to decreasing government expenditures in the healthcare sector with potentially negative effects on intertemporal healthcare provision. While health expenditures may increase in high-income countries during economic slowdowns (Keegan et al., 2013), a rise in public debt can force governments to

[11] For instance, childhood psychological problems by age 16 are associated with 28% lower family income at age 50 (Goodman et al., 2011).

[12] Blum et al. (2021) show that political institutions also influence government health spending.

consolidate and cut spending in the future. Debates on fiscal consolidation and its adverse effects on health outcomes have intensified since many EU member states implemented budget consolidation measures in the aftermath of the global financial crisis (Reeves et al., 2013; Stuckler et al., 2017). Several scholars argue that fiscal consolidation policies in Europe have exacerbated short-term negative public health effects of the financial crisis (Karanikolos et al., 2013). For example, European countries with large fiscal adjustments exhibit a rise in suicide rates (McKee et al., 2012; Karakinokolos et al., 2013; Antonakakis & Collins, 2014). Studies for Greece also suggest that the reduction in government health expenditure is correlated with a rise in infant mortalities, stillbirths, and the number of low-birth-weight infants (Ifanti et al., 2013; Kentikelenis et al., 2014). By contrast, countries that failed to consolidate their public finances in the aftermath of the financial crisis had higher debt-to-GDP ratios and lower fiscal leeway to support the health system, the economy, and the most vulnerable members of the population during the pandemic crisis. There might be an intertemporal trade-off between fiscal consolidation including health spending cuts in the present, and higher future spending capabilities which might help to mitigate negative health outcomes during a future crisis.

6.2 Pandemic disease burden in low- and middle-income countries

Thus far, we have focused on sources related to high-income countries (HIC) – mainly from a European or US perspective. Both the direct and indirect disease burden of the pandemic *in low- and middle-income countries (LMIC)* were originally estimated to exceed those in HICs (Hogan et al., 2020). Several studies initially discussed the import of cases, vulnerability, and the preparedness of low-income countries especially in Africa (Gilbert et al., 2020). Shortages of medical supplies were predicted to affect LMICs more severely in terms of the direct COVID-19 burden since the facilitation of sensitive imports from China and Europe is not granted due to lockdown measures. With already overburdened health systems in several African countries and less financial leeway in the WHO budget, a shift of resources away from other diseases such as malaria, tuberculosis (TB), noncommunicable diseases (NCDs), and HIV to tackle COVID-19 was projected to intensify indirect disease burdens (Hogan et al., 2020). Studies from epidemics in African countries, however, indicate a considerable but less than expected direct disease burden from COVID-19 in these countries. This is mainly explained by a younger age structure in those regions (Diop et al., 2020; Kirenga et al., 2020; Mbow et al., 2020). However, the indirect disease burden due to physical distancing and lockdown policies implemented seems to be just as high as projected. First surveys and studies from tuberculosis and HIV treatment and diagnostic programs, for example, reveal substantial interruptions of these programs. (Lagat et al., 2020; Louie et al., 2020; Watts et al., 2020). These interruptions are not always as large as initially predicted by models (Kessel et al, 2022), but they are substantial and have set programmatic efforts to eliminate poverty-related but essentially well-treatable diseases like tuberculosis importantly (Jeremiah et al. 2022).

Scholars, moreover, have shown that citizen compliance with interventions against the pandemic depends on household incomes and economic incentives or financial support from the government (e.g., Trudeau et al. 2020). Unemployment in LMICs also leads to a deterioration of personal health due to increased exposure to unhealthy behavior (e.g., Kwon et al., 2010). This relationship is similar to findings in HIC countries. However, the effect is even more pronounced in countries with a lack of universal health or income insurance systems. Health insurance coverage in the Philippines, for example, decreased significantly during the global financial crisis (Weber & Piechulek, 2010). Moreover, LMICs suffer from the tendency of HICs to reduce donor funding for the treatment of typical third-world

diseases, e.g., when HIV prevention programs are not prolonged. At the beginning of the COVID-19 pandemic, for example, the US suspended their contributions to the WHO starting in March 2020. As the US contributed about 15% to the budget of the WHO in recent years, the large budget cut likely exacerbates the problematic healthcare situation in LMICs.[13]

Other research has highlighted negative income shocks for LMICs during economic crises with the consequence of a decline in remittance payments received (Weber & Piechulek, 2010). Another, yet underexposed income channel, relates to terms-of-trade deterioration effects: recessions in emerging markets often go hand in hand with sharp currency devaluations (Obstfeld et al., 2019). As these economies' supply of drugs relies heavily on imports, currency devaluations increase prices for medicines disproportionately and make them even less affordable.

7 Conclusion

The COVID-19 pandemic gives rise to a notable short- and long-term disease burden and excess mortality. We present an overview of different death counts and an evidence review of the severity of direct disease burden from COVID-19 and populations at risk. The actual disease burden and expected additional mortality during a pandemic are, however, dependent on more than these direct estimates. While our review is limited by not being an actual systematic review, we conduct a comprehensive evidence review of parameters that need to be considered when estimating the overall disease burden from both epidemiological and economic perspectives (see Table 3 for a summary of the range of effects). Furthermore, the pandemic influences health outcomes indirectly through changes in access to healthcare, social distancing, and economic decline. Future research on the effect of mitigation policies in pandemics therefore should examine the effect of policies on both direct and indirect disease burdens. While our results are mainly based on the COVID-19 pandemic and not all parameters and estimates presented will be relevant in future pandemics of different pathogens, we still think the following is crucial for any pandemic: When evaluating policy measures implemented to contain the pandemic, it is important to disentangle effects that are influenced by NPIs and those that are caused by the pandemic itself. Empirical findings in our review moreover suggest that established welfare systems and labor market institutions providing income insurance and other support during a crisis may help to moderate the negative (indirect) effects of a pandemic.

We conclude that a thorough assessment of a pandemic's disease burden requests the following four aspects:

(1) Interdisciplinary groups from epidemiological, economics and further health and social science backgrounds should focus on collaboratively synthesizing the now emerging evidence on indirect disease burden during this pandemic using rapid, systematic, and living review methodologies.
(2) Mathematical modeling and simulations going beyond the direct burden of disease from COVID-19; both positive and negative indirect effects on a regional and local scale should be included to gain reusable models of disease burden in pandemic situations.

[13] Though, the US withdrawal from the WHO was compensated by increased contributions from other members such as Germany.

(3) Real-time monitoring tools that cover direct as well as indirect disease burden, including cause-specific excess mortality estimates (Parks et al. 2018) as well as morbidity estimates using measures like DALYs need to be installed wherever possible.
(4) The role of the design of (public) health systems, welfare programs, institutions, mitigation and containment policies as well as economic policies needs to be examined with respect to their impact on both direct and indirect disease burden during a pandemic.

Table 3: ***Range of effects expected in direct and indirect effects***

	Effect	Direction of disease burden due to the pandemic	Direction of disease burden due to NPIs	Range of expected effect
Direct				
Direct COVID-19 burden	Additional deaths due to COVID-19 (excess mortality)	▲	▼	Suppression: 10-15,000 additional deaths No suppression: 150,000 – 500,000 additional deaths/year until 2021
Indirect effects				
Limited health access	Indirect effect due to limited healthcare access	▲	▲	Unclear
Indirect burden due to economic effect	Unemployment rate	▲/▼	▲/▼	Direction of the effect is unclear and depends on the country, time span, and age group examined. A one p.p. increase in the unemployment rate is associated with a short-run reduction in total mortality of 0.4 to 1.1%. Mortality is decreasing for young adults (20-44 y.) by about 1.0 to 2.0%. Other studies suggest a rise in total mortality of about 1.5/100,000 people, while the positive relationship is largest for the 45-54 age group.
	Job displacement	▲	▲	For male workers, the risk of mortality in the year after displacement is 50-100% higher and at least 11% higher over the twenty-year period after the displacement. A displaced worker at age forty has a loss in life expectancy of 1.0 to 1.5 years.
	Income shock	▲	▲	No short-term effects, but recessions and shocks to GDP are more harmful to life expectancy the longer they last. For the group of workers younger than age 60, a 10% increase in income over a five-year period lowers the probability of death in the following year by approx. 5%.
	Intimate partner violence	▲	▲	Increase, with high variation across countries (Muldoon et al, 2021; Lausi et al., 2021).
	Suicide	▲	▲	0.4-1.3% (1.3-1.6%) increase for each one p.p. increase in the unemployment rate in Europe (USA); and 1.0% increase in suicides among individuals aged younger than 65 years (while old-age suicides do not respond to economic downturns). *Data on suicide mortality* in the European Union is, for example, released by Eurostat. In the post-financial-crisis period 2011 to 2016, suicide mortality in the EU27 ranges between 12.3 suicides per 100,000 inhabitants in 2011 and 10.8 in 2016. Suicide rates are lower for people aged below 65 and range between 9.2 in 2016 and 10.8 in 2011. There is, however, much variation across the member states of the European Union, with large numbers above 30 suicides per 100,000 inhabitants in Lithuania and about 4.2 suicides per 100,000 inhabitants in Greece. In Germany, as the largest member state, suicides range between 11 and 12 per 100,000 inhabitants in the period 2011-2016.
	Air pollution	-▼	▼	Unclear
	Vehicle accidents	▼	▼	Traffic accidents have fallen significantly during the months of social distancing and stay-at-home regulations and because of unemployment. Depending on the country, time span, strength of lockdown, and economic impact, traffic accidents decreased by up to 74%. Emergency department visits for orthopedic hand and trauma reasons declined by up to 60%. An increase in the unemployment rate by one p.p. reduces traffic accident fatalities by between 2.4 and 2.9%. *Data on mortality due to vehicle accidents* in the European Union is, for example, released by Eurostat. In the period 2011 to 2016, the number of persons killed in road accidents in the EU27 decreased from 6.5 to 5.3/100,000 inhabitants. The rates are highest in Romania and lowest in Sweden. In Germany, as the largest member state, the rate was 5.0/100,000 in 2011 and 3.9/100,000 in 2016.

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