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Estimating the costs of Israel's four COVID-19 waves

Panagiotis TSIGARIS[1*], Jaime A. TEIXEIRA DA SILVA[2], Francesco CHIRICO[3]

Affiliations:

[1]Department of Economics, Thompson Rivers University, Kamloops, British Columbia, V2C 0C8, Canada. E-mail: ptsigaris@tru.ca. ***ORCID:*** *0000-0002-7965-4554.*

[2] Independent researcher, Ikenobe 3011-2, Kagawa-ken, 761-0799, Japan. E-mail: jaimetex@yahoo.com. ***ORCID:*** *0000-0003-3299-2772.*

[3] Università Cattolica del Sacro Cuore, Post-Graduate School of Occupational Health, Rome. Health Service Department, Italian State Police, Centro Sanitario Polifunzionale di Milano, Milano, Italy. E-mail: francesco.chirico@unicatti.it. ***ORCID:*** *0000-0002-8737-4368.*

****Corresponding Author***

Prof. Panagiotis Tsigaris. 805 TRU Way, Department of Economics, Thompson Rivers University, Kamloops, British Columbia, V2C 0C8, Canada. E-mail: ptsigaris@tru.ca.

Abstract

Introduction: This paper focuses on the health and economic costs of the COVID-19 pandemic to Israel during the first four waves (2020-2021) of the pandemic.

Methods: Four costs of the pandemic in Israel were assessed: economic losses, costs of premature mortality, mental health, and health impairment, estimated using IMF forecasts of GDP with COVID-19 relative to GDP without COVID-19 (i.e., the counterfactual) from 2019 until 2030, estimated number of deaths based on IHME data multiplied by VSL values, a Cutler and Summers method that assessed disutility using HRQoL, and the loss in VSL due to the disutility from suffering, respectively.

Results: The four primary waves of COVID-19 cases and deaths in Israel occurred between early 2020 and October 2021. After the first three waves between April and June 2021, excessive relaxation of stringency measures allowed the highly infectious delta variant (B.1.617.2) to spread, aided by an inability to vaccinate a high percentage of the population (never exceeding ~63%), leading to a fourth wave. Costs of the pandemic are estimated (in billions of 2017 constant Int$) at Int$81.7 for mental health, at Int$80.3 for economic losses, Int$53.3 for the cost of premature mortality, and Int$39.4 billion for health impairment. The total cost of the pandemic is estimated at Int$254.7 billion or 70% of the 2019 GDP of Israel but could be as high as Int$667 billion.

Discussion: Stringency policies to contain the virus' spread in Israel have been pro-cyclical, i.e., as infection rate increased so did stringency policies, and *vice versa*. Our study offers policymakers important suggestions regarding cost-effectiveness analysis for this and future pandemics. Balancing economic and health priorities is needed.

Take-home message: By October 2021, the estimated cost of the COVID-19 pandemic to Israel during the first four waves (2020-2021) was Int$254.7 billion, but as high as Int$667 billion.

Key words: Health and economic costs, health-related quality of life (HRQoL); mass vaccination; monetary value of quality-adjusted life years (MVQALY); stringency index (SI); value of a statistical life (VSL).

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INTRODUCTION

Since the Coronavirus disease 2019 (COVID-19) infection was declared as a pandemic on March 11, 2020, governments implemented many non-pharmaceutical interventions (NPIs) to address the spread of COVID-19 infection with varying results [1]. These measures include hygiene measures (mask usage, hand washing, avoiding crowded and closed areas, improved indoor air quality), lockdown measures (working from home, mobility restrictions, and social distancing), rapid and accurate testing, and vaccination, which represent relevant public policy measures against the COVID-19 pandemic [2]. Social distancing and mandatory lockdown were put in place in the first waves of the pandemic to protect not only the population, but also healthcare systems [3].

These measures were implemented to protect the most vulnerable strata of the population (i.e., old age, male sex, pre-existing morbidities, and racial/ethnic disparities) from severe and deadly forms of COVID-19 infections [4]. Initially, the absence of targeted treatments and a vaccine compelled every impacted nation to adopt different non-pharmacological strategies to curb the infection's spread. However, after the development and distribution of the COVID-19 vaccine, these measures were relaxed, allowing the resumption of socio-economic activities [5].

Despite lockdown measures also having contributed towards a temporarily cleaner environment [6] and certainly reducing the mortality rates of the COVID-19 pandemic [7], they forced countries to lockdown many cities and restrict transportation, industrial, and social activities [6]. The shutdown of economic activities led to high rates of unemployment, and a subsequent economic crisis and mental health issues [8]. This paper examines the costs of the pandemic in one country, namely Israel.

In early 2020, Israel showed a rapid and concerted response to COVID-19 due to the country's small size, its centralized healthcare system, its high degree of preparedness to emergencies, and rich data gathering, allowing it to implement nation-wide stringency measures without vaccinations in 2020 and in 2021 through the use of mass vaccination policies and measures [9-11].

There were four primary waves of COVID-19 cases and deaths in Israel between early 2020 and October 2021 (Supplementary Figure 1). In terms of new infections, each wave was higher than the previous one throughout this period, indicating that the pandemic was far from over, even with a mass vaccination campaign. The duration of the first wave was the shortest, while the other three waves lasted longer, the former mainly because of the almost complete lockdown of the economy.

The estimated cost of lockdowns to prevent one death by SARS-CoV-2 in Israel relative to "testing, tracing, and isolation" approach was estimated at US$45.1 million [12]. This high cost of preventing a death indicates why the Government followed a pro-cyclical stringency policy rather than a national lockdown in the four waves. However, the peak of new deaths in the fourth wave was below the third wave, suggesting that vaccinations reduced the risk of severe and critical illness, hospitalization, and ultimately death.

Similar to other nations around the world, COVID-19 inflicted socio-economic and health-related costs. For the US, Cutler and Summers [13] estimated a US$16.1 trillion cost for the COVID-19 pandemic, a cost that exceeded 90% of the annual gross domestic product (GDP) of the US. Economic losses for the US were highest, estimated at US$7.59 trillion, the second highest cost was that of premature mortality at US$4.37 trillion, followed by health impairment cost at US$2.57 trillion, and finally mental health cost, which was assessed at US1.58 trillion. López-Valcárcel and Vallejo-Torres [14] found that GDP (economic costs) outweighed all other costs, with a global cost of 14% of GDP and in the case of Spain, 24% of the 2019 GDP (€397.3 million). The global cost of premature mortality caused by the COVID-19 pandemic for high-income nations, including Israel, was estimated at Int$ $4.4 trillion or $3,700 per person, increasing to Int$18.4 trillion or $15,500 per person by March 1, 2021 if policies were relaxed [15]. In addition, COVID-19 and lockdown policies negatively impacted the health-related quality of life (HRQoL) in two regions of China [16], Turkey [17], and Morocco [18].

Following the Cutler and Summers [13] methodology, this paper focuses on the health and economic costs of the pandemic to Israel during the first four waves (2020-2021) of the pandemic.

METHODS

Study procedure and measurements

In this paper, the costs of COVID-19 that we measured were relative to the absence of the pandemic, i.e., the counterfactual. Costs considered were economic losses, premature mortality, long-term health impairment, and mental health.

Economic costs were the difference between the time path of GDP with COVID-19 relative to GDP without COVID-19 (i.e., the counterfactual) from 2019 until 2030 (see Table 1). GDP with COVID-19 was assumed to take the path as forecast by the International Monetary Fund (IMF) until 2026, with a constant long-term growth rate of 3.1% per year thereafter until 2030 [19]. The counterfactual assumed a constant annual economic growth starting from 2019 based on the range of the average historical annual growth rate of GDP without the pandemic. Future losses were discounted to 2019 at a social discount rate of 3.5%.

Premature mortality costs were estimated using the estimated number of deaths until January 1, 2022 from the Institute for Health Metrics and Evaluation (IHME) [20], and multiplied by the value of a statistical life (VSL). VSL measures how much people are willing to pay to reduce their risk of premature mortality. The purpose of VSL is to measure the benefits associated with regulatory and health policy, so it can also assess the benefits of being prepared for pandemics such as COVID-19. This approach was also used by Teixeira da Silva and Tsigaris [15] to estimate the worldwide cost of premature mortality due to COVID-19. The VSL for Israel is US$6.154 million per life saved [21].

Estimating health impairment is not easy. The cost was estimated using the Cutler and Summers [13] approach. Pandemic survivors may encounter significant long-term health impairments such as lung, cardiac, and mental health disorders such as anxiety, depression, and post-traumatic stress disorder [22]. To estimate these costs requires forecasting the cumulative number of people that experienced severe or critical illness due to the virus. Health impairment may appear in one third of such survivors [23]. Such people suffer and thus have a disutility caused by this health impairment. Disutility can be represented by a reduction in HRQoL arising from the pandemic or based on health indices such as the 5-level EQ-5D version (EQ-5D-5L) [24,25]. A reduction in HRQoL due to COVID-19 reduces VSL depending on the disutility from long-term mental and physical health issues.

Thus, health impairment costs are the expected number of people with such health issues multiplied by the loss in VSL due to the disutility from suffering (i.e., measured by the reduction in HRQoL or the disutility factor × VSL). This cost was estimated until January 1, 2022 (see "Health impairment costs" section for details).

The final cost estimate was the cost of mental health of the population of adults due to COVID-19 over the two years of the pandemic. This cost requires estimating the fraction of the adult population that may suffer from mental health issues due to COVID-19. In this assessment, based on existing evidence, 30% of the adult population was assumed to be suffering from psychological health issues.

The pandemic and stringency regulations caused significant mental health problems, and many people suffered from anxiety and depression, even if they had not been infected by the virus or fallen critically ill, with 37.5% of elderly participants in Israel being classified with depression [23,26]. Globally, economic suffering due to job loss, insecurity, fewer social interactions, fear, the loss of someone close, and other anxiety-related events affect a population's mental health [27]. For example, anxiety and depression within the adult population in the US increased from 11% in 2019 to 40% since April 2020 [28]. Fear, psychological distress – including anxiety and depression – were also very significant in Israel, ranging from 26–34%, as assessed from online survey participants [29-31], and lowered the HRQoL [32,33].

To estimate the mental health cost also requires obtaining from the literature, disutility or the reduction in HRQoL values for people with mental health issues. Shiroiwa et al. [34] found that "the disutility for depression was approximately 0.18" in a sample of 10,183 respondents in Japan. Cutler and Summers [13] assumed a quality-of-life disutility or loss in HRQoL of approximately –0.25 to –0.35. An early study noted that severe depression was associated with a disutility of between –0.2 and –0.6 [35]. Two studies indicated a -0.40 disutility for people suffering from depression, while anxiety has a disutility of about –0.15 [13,26]. In this paper, we used a disutility of –0.2 for mental health suffering in the base case.

To arrive at an estimate of mental health cost, the monetary value of a quality-adjusted life year (MVQALY) from the literature was used to place a cost for not having one good year of mental health [36,37]. The estimated values for MVQALY come from contingency valuation studies. They vary depending on whether the hypothetical policy scenarios extend or save a life or improve the quality of life and the severity of the problem, its duration, and the funding sources for the policy [37]. MVQALY was estimated using the average ratio of willingness to pay (WTP) per QALY and GDP per capita as in Nimdet et al. [37] combined with those used by Cutler and Summers [13]. Using Israel's GDP per capita in 2019 at approximately Int$40,000, MVQALY ranges from Int$23,600 to Int$81,200 per year. In contrast, Cutler and Summers (2020) for the USA assumed a range from US$100,000–200,000 for one good health year. Thus, taking the average of the lower end of the two estimates yields Int$61,800 in mental health costs per year for Israel. However, if disutility is –0.40 then the MVQALY is Int$140,600 (i.e., the average of the upper end of the two studies). These lower and upper values are also consistent if, instead, the ratio of the VSL of Israel to that of the USA is adjusted using the Cutler and Summers [13] US$100,000–200,000 range. With a VSL of USA at US$9.631 million per life saved [38] the MVQALY for Israel would be $63,960 at the lower end and $127,920 at the upper end. In addition, Chernichovsky and Bental [39] estimated the value of NIS 340,000 for a life-year for Israel. The exchange rate (January, 2022) of $US0.31 = 1 NIS translates to US$105,400 for a life-year.

Thus, the mental health costs are the expected number of people experiencing mental health multiplied by MVQALY for not having good mental health for two years (i.e., the examined period of the pandemic), and the result is weighted by the disutility value they receive.

Data sources and definitions

Data on infections, deaths and vaccination rate were retrieved from Our World in Data (2021) while the stringency measure to contain the spread of the virus, including its eight sub-components and facial coverings [40], were obtained from Hale et al. [41] on October 10, 2021. Population and GDP data were derived from the IMF World Economic Outlook database [42]. GDP was adjusted for purchasing power parity and expressed in constant 2017 international dollars (Int$). The IMF provides GDP forecasts until 2026, which were used in this study.

Four waves and stringency measures

The first two waves, roughly from March to May 2020, and from September to November 2020, with some uncertainty in the wave pattern from May to September, were battled using stringency policies, as classified by the IHME stringency index (SI) (Supplementary Figure 1) [43], since vaccinations were not yet available. Stringency policies included school and workplace closures, cancellation of public events and forbidden use of public transport, restricted gatherings, stay-at-home requirements, restrictions on movement, control of international travel, and mandatory facial coverings (masks) (Supplementary Figure 2). Supplementary Figure 1 shows that SI peaked on April 9, 2020 at 94.4 as infections peaked on March 25, 2020 with 1,117 people infected. However, as infections started to fall, so too did stringency restrictions. Stringency reached a low value of 34.4 on August 19, 2020 but as restrictions were loosened, infections started to increase. By July 27, 2020 cases were almost double than the peak of the first wave at 2,048 infected people and rising, marking the start of the second wave. The Israeli Government reacted by tightening policy and by September 25, 2020 SI had reached 85.2 and COVID-19 cases peaked five days later on September 30, 2020 at 9,078 cases after which they started to fall, as did stringency measures, which were relaxed, falling to 40.7 by October 31, 2020. As a result of the relaxation of stringency measures, the third wave started in November of 2020 and stringency measures were again tightened with SI reaching the highest level of 87.1 on February 4, 2021.

The third wave, in the first quarter of 2021, was also tackled by initiating the mass vaccination program, primarily using the Pfizer-BioNTech mRNA (BNT162b2) vaccine, which conferred an almost population-wide level of protection against the alpha variant (B.1.1.7) of SARS-CoV-2 [44]. The B.1.1.7 variant accounted for almost 95% of cases between January 24 and April 3, 2021 [45]. Protection was mainly due to a rapid and highly coordinated effort to vaccinate the population, stricter stringency measures (Supplementary Figure 2), including lockdowns, an efficient universal health care system, and mass-media campaigns [46,47]. Consequently, cases fell from a peak on January 27, 2021 at 11,934 cases, stringency measures were reduced, and by mid-June of 2021, the number of daily cases dropped to < 10 [48]. However, a slump in stringency measures between May and July of 2021, compounded by an inability to increase full vaccinations to more than 63% of the total population, and spread of the delta variant (B.1.617.2) among vaccinated and unvaccinated individuals [49], saw cases and deaths rise in early August, peaking on September 8, 2021 at 22,291 cases, then dropping in October of 2021 (Supplementary Figure 1). At the end of July of 2021, a third dose of the vaccine (i.e., booster) was administered only to individuals in the 60+ age group that had already received two prior doses [50]. At the time of our analysis (October 23, 2021), according to Our World in Data [51] (2021), about 65% of the population was fully vaccinated. We attribute the change in Israel's status in the fourth wave to a combination of factors. Firstly, mRNA vaccines might only be effective for 4-5 months against the highly transmittable delta variant [52,53]. In addition, vaccine hesitancy remains high, including in some population sectors such as minority [54] groups, with a concomitantly low level of vaccination [52,55,56]. The SI reached the lowest level, over the entire period, and was 22.2 on June 15, 2021, indicating almost a return to a pre-COVID-19 environment. Coupled with possible long-term fatigue caused by non-pharmaceutical interventions (i.e., stringency measures) [57,58], these may have led to the rapid rise in the numbers noted above.

RESULTS

Economic costs

Economic losses are expressed in terms of GDP with COVID-19 as projected by the IMF in April 2021. IMF was projecting for a V-shape recovery from 2020 until 2026 [51]. From 2020 until 2026, IMF projections are used showing GDP recovering in 2021 with a growth rate of 5%, from a 2.4% drop in 2020, and falling steadily to 3.1% in 2026 and assumed to converge to 3.1% afterwards, which is significantly lower than the historical average from 1981 until 2019 of 4.1% per year.

The growth rates assumed under the counterfactual are 3.1% and 4.1%, respectively, from 2020 until 2030. The average growth rate of GDP from 1981 to 2019, excluding 2020, is 4.1% per year with a 99% CI [3.1,5.0]. COVID-19 is the largest shock Israel has observed since 1981 (Figure 1).

Economic losses are computed for the period 2020 to 2030. Table 1 shows the values of GDP with COVID-19 and without COVID-19 growing at 3.1% per year (the lower bound of the 99% CI) and 4.1% per year (i.e., the historical average growth rate from 1980–2019). GDP under COVID-19 reaches Int$501.0 billion by 2030, while under 3.1% growth without COVID-19 it reaches Int$507.7 billion by 2030 and Int$564.5 billion by 2030 with a 4.1% annual growth rate during this decade. Future losses are discounted at the social discount rate of 3.5% [59]. The economic cost, assuming a 3.1% growth on average, over the decade under the counterfactual, yields an economic loss of Int$80.3 billion. Assuming the economy over the next decade continued to grow at 4.1% per year in the absence of the pandemic, the cost will be Int$313.3 billion.

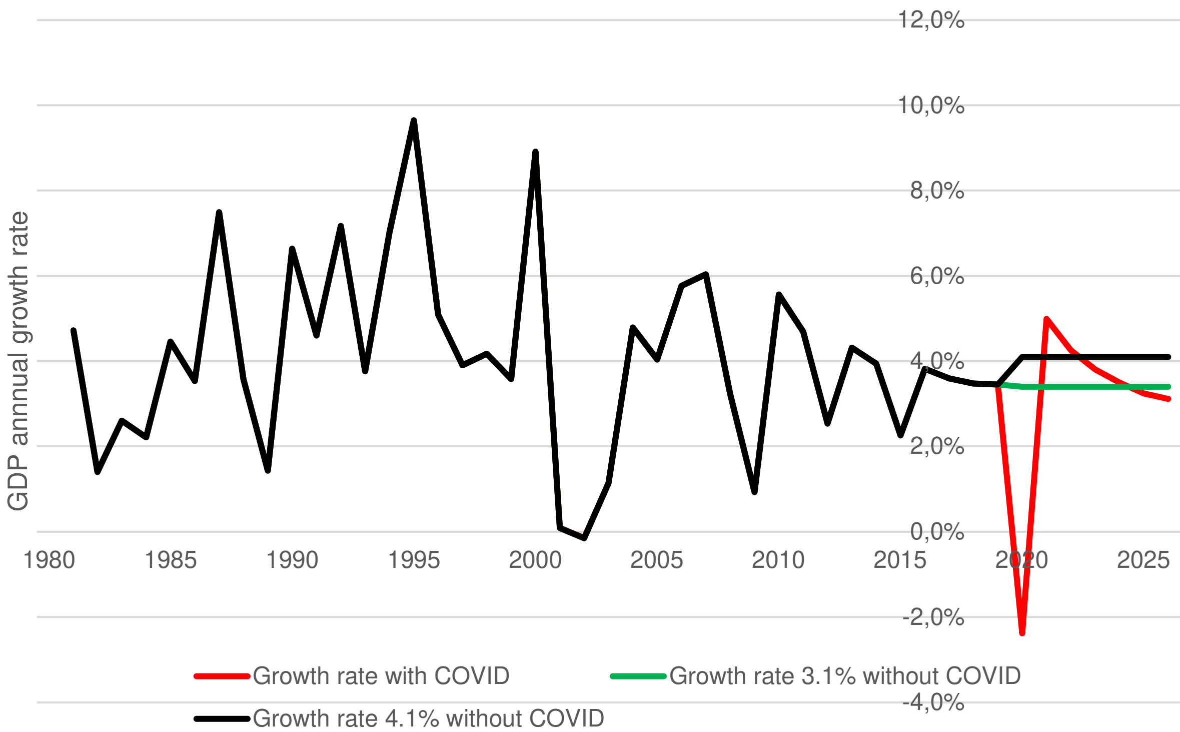


Figure 1. Economic growth from 1981 to 2026. Economic growth from 1981 to 2020 (black). Growth rate with COVID-19 is from the IMF projection for a V-shaped recovery (red). The growth rates assumed under the counterfactual in the absence of the 2020 negative growth and continued at a healthy average growth rate of 3.1% (green) and 4.1% (black), respectively.

Table 1. Economic losses for Israel, 2020 to 2030.

	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	Total cost
GDP per capita	39,503	40,090	38,436	39,632	40,579	41,365	42,047	42,630	43,169					
Population	8.879	9.051	9.216	9.384	9.555	9.73	9.907	10.088	10.272					
GDP with COVID-19	350.8	362.9	354.2	371.9	387.7	402.5	416.6	430.0	443.4	457.2	471.4	486.0	501.0	
Change in GDP		12.1	–8.6	17.7	15.8	14.8	14.1	13.5	13.4	13.7	14.2	14.6	15.1	
Growth rate of GDP		3.45	–2.38	4.99	4.26	3.80	3.50	3.24	3.11	3.10	3.10	3.10	3.10	
GDP at 3.1% growth	350.8	362.9	374.1	385.7	397.7	410.0	422.7	435.8	449.3	463.2	477.6	492.4	507.7	
Economic cost			19.2	12.9	9.0	6.5	5.2	4.7	4.6	4.6	4.6	4.6	4.5	80.3
GDP at 4.1%	350.8	362.9	377.7	393.2	409.3	426.1	443.6	461.8	480.7	500.4	520.9	542.3	564.5	
Economic cost	0	0	22.7	19.9	19.5	20.6	22.8	25.8	29.3	32.8	36.4	39.9	43.5	313.3

Notes: GDP is in billions of constant 2017 international dollars adjusted for purchasing power parity. Population is in millions of people. Estimates are after 2019. The average growth rate is 3% per year with COVID-19. Future economic losses are discounted at the social discount rate of 3.5%. Source: IMF [42].

Cost of health impairment

The literature indicates that severe or critical conditions from prior pandemics (e.g., SARS and MERS) result in infected individuals experiencing long-term health issues [60]. In order to estimate the number of individuals with severe and critical conditions for Israel, we followed the Cutler and Summers [13] approach. The estimation uses the probabilities of those in a severe condition (Table 2, column 2), in a critical condition (Table 2, column 3), and death (Table 2, column 4) by age group (Table 2, column 1) based on the COVASIM model [61]. With this information, the ratio of critical or severe conditions to death can be obtained (Table 2, column 5). This ratio is the net probability of severe or critical condition relative to the probability of death (i.e., [column 2 + column 3 – column 4]/column 4). Using the existing deaths by age group from the Ministry of Health Report on June 10, 2021 (Table 2, column 6), the estimated number of individuals with severe or critical conditions is the ratio of severe or critical to death multiplied by deaths in Israel, and multiplied by age, resulting in a total of 70,509 severe or critical cases. To project these severe or critical cases to January 1, 2022, 70,509 was multiplied by the ratio of the future expected deaths (i.e., 8,655) to the current level of deaths (i.e., 7,950) to arrive at 76,762 individuals.

Table 2. Israel's estimated severe or critical.

Age group	Severe condition	Critical condition	Death	Critical or severe to death ratio	Deaths by age in Israel	Severe or critical conditions
	Probabilities					
0-9	0.0005	0.00003	0.00002	25.5	0	0
10-19	0.00165	0.00008	0.00002	85.5	0	0
20-29	0.0072	0.00036	0.0001	74.6	31	2,313
30-39	0.0028	0.00104	0.00032	11.0	51	561
40-49	0.0343	0.00216	0.00098	36.2	124	4,489
50-59	0.0765	0.00933	0.00265	31.4	376	11,802
60-69	0.1328	0.03639	0.00766	21.1	947	19,970
70-79	0.20655	0.08923	0.02439	11.1	1629	18,126
80+	0.2457	0.1742	0.08292	4.1	3260	13,248
				total to date	6418	70,509

Notes: The probabilities of severe/critical and death by age group are obtained from Kerr et al. [61]. The deaths by age group from Ministry of Health Report, June 10, 2021 report at: https://www.science.co.il/medical/coronavirus/Death-statistics.php. To arrive at the estimated costs in the main document, the following equation was used:
Cost = 1/3 × of 70,509 × adjustment to Jan 1 2022 × % of disutility × VSL

The number of survivors from severe or critical COVID-19 illness is much larger than COVID-19 deaths. As a result, people with health impairment could be significantly more than the people dying from COVID-19. Using the Cutler and Summers [13] approach, Israel's estimated number of severe and critically ill is 76,762 people as stated above, about ten-fold more than total deaths. Assuming that one-third, or 25,587 people, encounter some long-term health impairment, these suffering survivors are assumed to have a quality-of-life disutility or loss in HRQoL of approximately –0.25 to –0.35 [13]. Assuming a 25% disutility, it represents a loss of $1.5 million per impacted person given that the VSL is estimated at Int$6.154 million (i.e., 25% of $6.154 million). Thus, the health impairment costs are estimated at Int$39.4 billion but using 35% disutility increases and the worse-case scenario from IHME, the cost increases to Int$73.3 billion.

Cost of mental health impairment

Assuming a 30% increase in mental distress in the estimated adult population of 6.8 million in Israel, this translates to 2 million people suffering from some form of mental health issues (see methods). For this estimation, a –0.20 weight is the assignment for disutility from a mental disorder.

In addition, mental health problems can last for two years on average as COVID-19 is completing its second year, while Cutler and Summers [13] assumed a one-year impact of COVID-19 on mental health. Finally, with an MYQALY of US$105,400 per year per person [38], the cost of mental health with a disutility of –0.20 is Int$81.7 billion making it similar to the economic cost of the pandemic. For the upper end, costs a disutility of –40 and an MYQALY of $140,600 result in total mental health costs of Int$218 billion.

Cost of premature mortality

As of October 17, 2021, Israel reported 7,950 deaths [40], while the IHME projects 8,655 deaths by January 1, 2022 [62]. Hence, the estimated cost of premature mortality by January 1, 2022 is Int$ 53.3 billion (Table 3) using a VSL for Israel at Int$6.154 million per life saved. Assuming a worse-case scenario from the IHME projected deaths, the cost would increase to $62.3 billion as IHME projects deaths to increase to 10,121 from 8,655.

Summary of costs

The cost of economic losses, premature mortality, health impairment and mental health of the Israeli adult population from the COVID-19 pandemic was estimated (Table 3).

Table 3. Projected costs (2017 Int$ billions) of COVID-19 to Israel.

Types of costs	Lower-end costs	% of total	Upper-end costs	% of total
Health impairment	39.4	15.5%	73.7	11.0%
Mental health impairment*	81.7	32.1%	218.0	32.7%
Premature mortality	53.3	20.9%	62.3	9.3%
Economic costs	80.3	31.5%	313.3	47.0%
Total cost	254.7	100%	667.15	100%

Note: Mental health impairment assessed at US$105,400 and –0.20 disutility at the lower end cost.

Thus, the estimated total cost of the pandemic, including economic and health/mental health impact, is conservatively at Int$254.7 billion or 70% of the 2019 GDP of Israel. However, at the upper end, the costs are Int$667 billion.

DISCUSSION

This study, just as in Cutler and Summers [13], found the cost of this pandemic to be staggering. The cost of the pandemic, which is measured relative to its absence, was estimated with the nation of Israel taking nation-wide stringency measures in 2020, and with mass vaccination campaigns and stringency measures in 2021. Stringency policies were pro-cyclical throughout this 2-year period, implying that as infections rose at the start of a wave, policies were tightened, and when infections fell, policies were relaxed. The loosening of stringency policies was necessary to reduce the economy's impact and social network fabric. However, this reduction in stringency measures came at the expense of allowing the virus to spread, creating another wave of infections, and retightening of stringency measures (Supplementary Figure 1).

Furthermore, the economic cost in 2021 is estimated at Int$19.2 billion while the economic cost is estimated at $12.9 billion, indicating a reduction in the economic cost by $6.3 billion (Table 1). The main difference in policies between the two years is the mass vaccination campaign and the very lax policies from April to June in 2021 due to the almost absence of new infections. However, the gain in economic cost in 2021 relative to 2020 came at the expense of more deaths in 2021 than in 2020. Namely, there were 3,325 deaths in 2020, but 5,330 deaths are projected to occur in 2021.

The COVID-19 pandemic in Israel

The first COVID-19 wave in Israel started when the SARS-CoV-2 arrived in March 2020 and persisted until May 2020. The subsequent wave occurred from June to October 2020, and the next wave commenced in November 2020. Israel was one of the first countries to offer vaccinations to its entire adult population. Beginning on December 19, 2020, the Pfizer BNT162B2 vaccine was first administered to healthcare workers and those with elevated risk of infection. This vaccine was then extended to seniors aged 60 and above before being progressively offered to other adults, descending by age groups. As a result, there was a swift decline in COVID-19 cases starting from February 2021 [46]. The appearance of the Delta variant in India in early 2021, which soon became the prevailing variant globally, combined with the diminishing efficacy of the vaccine, resulted in a fourth surge that began in Israel in June 2021. From December 2021, the omicron strain, together with the waning protection of the booster, led to a fifth wave [56].

In the initial two waves of the outbreak, the Israeli authorities imposed rigorous control measures, beginning with restrictions on public events and festivities, limiting the use of public transport, closing non-essential shops, closing schools and places of worship, and finally, lockdown [63]. During the first wave, Israel's excess death rate was relatively low in comparison to numerous other nations [63]. but scholars were not able to prove a direct connection between these measures and mortality rates [64].

According to Haklai [63,64], the excess mortality of the second and third waves was halted by the second strict lockdown and by a swift and comprehensive vaccine program, respectively. During the fourth wave of COVID-19, Israel experienced a severe impact from the Delta variant, resulting in high excess deaths between August and October 2021. The restrictions during this wave were more lenient than before, and the mortality rate approached that of the second wave for all demographics.

The advent of mass vaccination campaigns in Israel, one of the earliest adopters and fastest inoculators globally, marked a pivotal turning point, because vaccinations undeniably reduced the severity of infections, as reflected in the reduced peak of new deaths during the fourth wave.

However, the resurgence of infections post-vaccination campaign and following the relaxation of restrictions has highlighted the limits of vaccination as a solitary containment measure [65]. This raised questions about the need for accompanying measures such as booster shots, sustained public health measures, or a more adaptable health policy framework that can respond swiftly to changing scenarios.

As shown in the literature, mass vaccination against COVID-19 has been cost-saving, by saving more lives and incurring less costs [66], as well as to decrease healthcare expenses and boost QALYs in comparison to inaction [67]. In Padula's research, the cost-effectiveness analysis was based on the known clinical advantages of COVID-19 vaccines, even though long-term definitive efficacy data is still pending [67].

The economic impact and the cost-effectiveness of the non-pharmaceutical interventions (NPIs) implemented against the COVID-19 pandemic

The COVID-19 pandemic has placed unparalleled stress on governments to sustain vital health and social services and to keep their economies operational. This challenge persists even as the virus affects every facet of daily life.

This pandemic has undoubtedly inflicted both immediate and prolonged harm to economies and the quality of life for numerous individuals. While there are projections regarding this harm, the precise extent remains uncertain [68].

COVID-19 was cited as the largest challenge since World War II and the century's most severe health catastrophe [69]. Worldwide, this pandemic has presented major health, economic, and societal hurdles for all countries, including Israel. Most countries adopted complete or partial lockdowns to curb the disease's progression. This has considerably affected the global economy, especially sectors like services, food, education, sports, and entertainment, generated a global financial crisis, damaged enterprises, and led to unemployment [69].

In Israel, the cyclic approach to stringency, while aimed at alleviating economic burdens, inadvertently contributed to successive waves of infection. Our study showed that while there were economic gains made in 2021 relative to 2020, these were accompanied by a heavier toll on human life.

Therefore, attempting to assess the detrimental economic effects of the pandemic is a crucial aspect of safeguarding the livelihoods and well-being of individuals. This underscores the complex and other difficult decisions policymakers faced at the height of the pandemic.

In the literature, there are many studies, including cost-effectiveness analyses, on public health strategies against COVID-19. According to Mol and Karnon [70], who compared the strict lockdown strategy followed by Denmark with the flexible social distancing policy as was applied by Sweden, stratified protection, where vulnerable groups were safeguarded while the infection's spread was tolerated, serving as a balanced approach.

A review of 12 studies on the economic assessment of NPIs released between January 2020 and December 2021, revealed that individual protection, social distancing, and testing-tracing-isolation strategies were financially viable. Nevertheless, various NPI combinations could yield varying outcomes. Conversely, the financial implications of lockdowns were significant, potentially resulting in substantial economic strain [71]. According to a global analysis based on country-level daily time series from Our World in Data, masks were the most economically efficient non-pharmaceutical intervention, four times more effective than closing schools and about twice the impact of policy restrictions [72]. Limiting gatherings came in as the second most effective measure. On the contrary, international travel controls and public information campaigns had negligible effects in reducing the number of COVID-19 cases [1].

Another systematic review of 23 articles published from 2020 to March 2021 showed that testing/screening, social distancing, personal protective equipment, quarantine/isolation, and hygienic measures were cost-effective measures, but the most optimal choice and combination of strategies depended on the context and reproduction number of the infection [73]. However, evidence showed the importance of gradual reopening strategies with a careful sequencing of sectoral openings based on their infection amplification risks [74].

Considering the broader impacts beyond health and understanding the distributional effects are crucial for a thorough evaluation of intervention outcomes. This approach is vital to produce evidence on cost-effectiveness for present and upcoming pandemics.

Study strengths and limitations

Our study is not without limitations. Indeed, this study did not incorporate the impact of the Omicron variant, which would merely add to the staggering costs estimated above.

Furthermore, we did not include in our cost-effectiveness evaluation the indirect health effects of the pandemic, including the mental health strain caused by the pandemic in the most vulnerable strata of the populations and in certain working groups like healthcare professionals. Prolonged periods of isolation, anxiety and post-traumatic stress symptoms from the ever-present threat of infection, economic uncertainties and the collective trauma of witnessing a global catastrophe have all likely contributed to a high mental health burden, which we can better quantify in upcoming years.

Nevertheless, it reaffirms the importance of balancing economic and health priorities, and the necessity for heightened attention to mental health in a global health crisis. For example, a study carried out in Israel indicated that lockdown measures did not adversely impact the mental health of older individuals, so such studies should consider the possible balancing impact of financial assistance initiatives [75].

Our study has some strengths, too. The intricate dynamics of the COVID-19 pandemic, with its interplay of health, economic, and societal dimensions, underscores the multifaceted challenges faced by Israel and by countries worldwide. Our assessment of the cost of the pandemic to Israel offers insights not just into the immediate tangible impacts, but also serves as an important contribution for future policy considerations, in the event of a new pandemic or major health crisis [76,77].

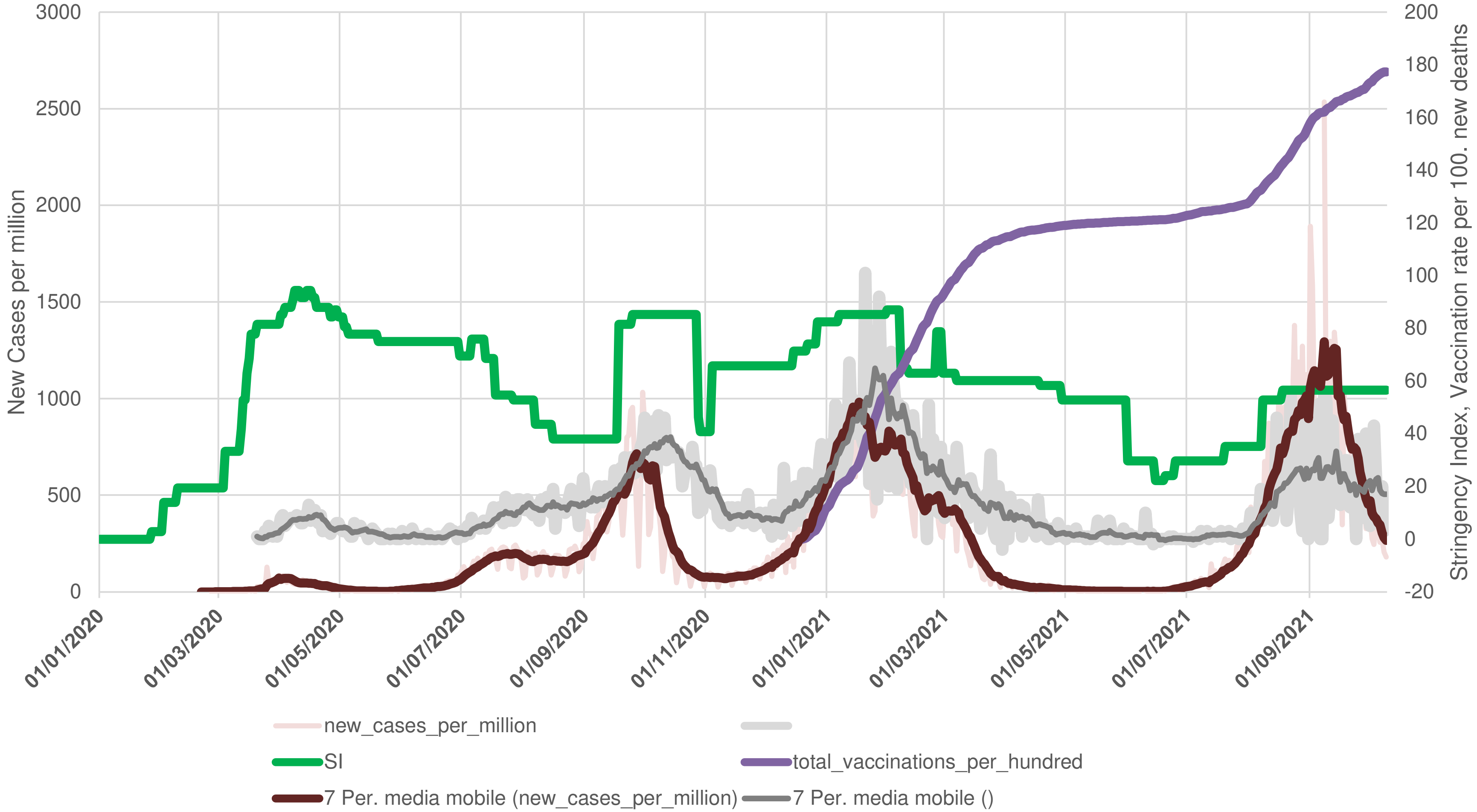
CONCLUSION

Our study offers to policymakers important suggestions in terms of cost-effectiveness analysis for this and future pandemics, as it underlines the need to balance economic and health priorities.

Israel's experience, indeed, while unique in its own right, offers lessons for other nations and underscores the need for global collaboration in data-sharing, best practices, and resource pooling, as well as the importance to invest more heavily in preparedness and resilience measures. These include strengthening healthcare infrastructures, investing in research and development for rapid medical responses, fortifying economic cushions, and enhancing data surveillance systems to mitigate the economic impact of future global emergencies [76-78]. At the same time, it is essential for governments to prioritize enhancing healthcare infrastructure and supporting coverage to ensure efficient and equal vaccine and pharmaceutical distribution against COVID-19 and future pandemics. Addressing economic inequalities within and between countries is urgent to tackle new global emergencies like the COVID-19 pandemic.

In conclusion, the COVID-19 pandemic and its staggering costs to Israel illustrate the benefits of being prepared in the future for another pandemic.

Supplementary Materials



Supplementary Figure 1. Primary (left) Y-axis plots new cases per day per million (pink) and its 7-day moving average (brown). Secondary (right) Y-axis plots new deaths per day (gray) and its 7-day moving average (dark gray), the stringency Index (green), and total number vaccinated per 100 (yellow). Population from Our World in Data (2021) is reported at 8,789,776.

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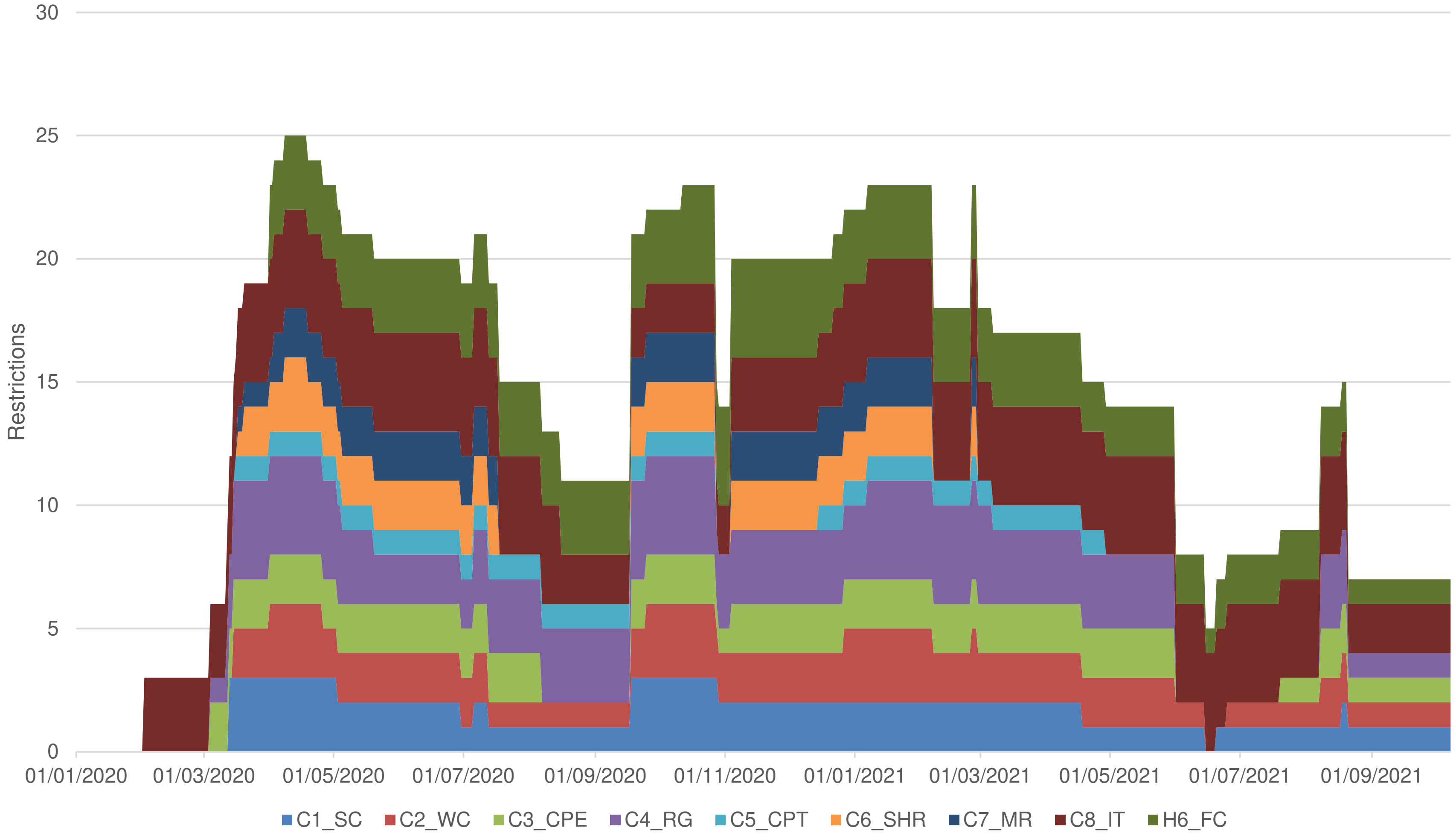

Supplementary Figure 2. School closure (C1_SC), workplace closing (C2_WC), cancellation of public events (C3_CPE), restrictions of gathering (C4_RG), cancellation of public transport (C5_CPT), stay at home requirements (C6_SHR), Movement restrictions (C7_MR), International travel control (C8_IT) and facial coverings (H6_FC).

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