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ARTICLE

Consequences of Restrictions, Therapies and Vaccines for Covid-19 Infection

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ABSTRACT

Herein, the available information about restrictions, therapies and vaccines for Covid-19 infection are summarized. Fatalities have not been less in countries adopting harsher, generalized, lockdowns. Similarly, dismissal of antiviral and immune therapeutic agents such as remdesivir, hydroxychloroquine, lopinavir/ritonavir and interferon, while supporting only corticosteroids as therapy hasn't translated into a reduced number of casualties. First data from the country where the number of partially and fully vaccinated has surpassed the 50% of the population suggests vaccines may not completely solve the Covid-19 emergency.

KEYWORDS

Covid-19, Restrictions, Therapies, Vaccine.

INTRODUCTION

The prevailing approach against Covid-19 infection in Europe has been the introduction of more or less severe restrictions, waiting for mass vaccination. There have been differences in the severity of the restrictions across Europe as well as the rest of the world. The efficacy of the measures is ultimately expressed by the number of fatalities attributed to Covid-19 or also by the excess mortality, of different countries. Regarding therapies for those infected, especially in Europe, most of the antiviral and immune therapeutic agents such as remdesivir, hydroxychloroquine, lopinavir/ritonavir and interferon has been dismissed, while supporting only corticosteroids as therapy, with the standard of care oxygen and ventilation when necessary in the late stages. Other countries have otherwise implemented protocols based on the available therapeutic agents. Also for what concerns therapies, the efficacy of the different approaches is ultimately expressed by the number of fatalities due to Covid-19 and the excess mortality. Finally, vaccination numbers start to be relevant in at least one country, where the number of partially or fully vaccinated has surpassed the 50% of the population. The time series of the number of new cases and the positive rate (number of positive vs. number of tested) phased with the vaccination numbers may be used for a first, preliminary assessment of the efficacy of vaccines.

EXPERIMENTAL

Analysis of the number of cases, tests performed, fatalities, excess mortality, partially and completely vaccinated vs. time,

as downloaded from public data providers such as ourworldindata.org and euromomo.org. Collection of public domain data about protocols by different health organizations across the world.

RESULTS AND DISCUSSION

Results are proposed hereafter in three separate sections, reporting on restrictions, therapies and vaccines.

Restrictions: The second wave of Covid-19 is ongoing in Europe, since the start of autumn 2020. It brings attention to the problem of efficacy and sustainability of the Covid-19 restrictions. The analysis of the time series of restrictions, new fatalities and new cases, despite the uncertainties of measuring these indicators, provides arguments to correlate them. The recorded cases and deaths are certainly rising across Europe and deaths are certainly following infections with a lag-time. The differences across countries are not inversely correlated to the severity of the generalized lockdown measures.

A second wave happened with the “Spanish flu” and it happens now with the Covid-19 infection. It has nothing to do with the relaxation of lockdowns and the public’s loosening of precautionary behaviours. The Spanish flu lasted from early 1918 to early 1920, infecting about 1/3 of the population at the time in four successive waves. Restrictions are aimed to reduce the number of infected.

It is evident in the data as the selective protection of the vulnerable and the adoption of more sustainable approaches produces better results in terms of fatalities. It must be mentioned that the number of tests now performed is much larger than the number of tests performed in the first wave of Covid-19, also detecting mild or asymptomatic cases. Working with an excessive cycle threshold of 40, also people that may only have viral fragments and thus are not infective, are counted as positive, adding further stress to the health system.

The number of fatalities is much less than what was experienced during the first wave, possibly because the vulnerable are protected more, or those who get infected are less vulnerable, but also because a much larger number of positive cases are counted because a much larger number of tests are performed. Despite not free of criticism for the methodology, data on the severity of restrictions starts to be available but can be coupled to data of positive cases and fatalities [1,2].

Ourworldindata [1] reports for every world country, the time series of positive cases and fatalities per million, 7-days moving averages and cumulative, as well as the time series of a government response severity index [2]. Fig. 1 shows the fatalities cumulative per million and this restriction severity index. Further insights into the pandemic are provided by the excess mortality. Ourworldindata provides some information, such as the p -score from the Human Mortality Database. Better data are available for the 26 European countries participating in euroMOMO [3]. Fig. 2 are the excess mortalities (z-index).

For western Europe, supposed to be a relatively homogeneous area, there are differences, in the cumulative fatalities per million, the restriction severity index, the excess mortality z-index. Some countries performed much better than others. Belgium and the United Kingdom were in between the worst-performing during the first phase and they are in between the worst-performing during the second phase. Countries that did well during the first phase, such as Austria or Switzerland, are not doing well during this second phase. The first peak of excess fatalities was much higher, but the second wave is lasting longer. This is also because the first wave started close to the beginning of spring, this second wave started at the beginning of autumn.

Countries that adopted more severe lockdowns during the first wave, such as Belgium and the United Kingdom and are using similarly harsh lockdowns now, did not perform better than Sweden, which never introduced complete lockdowns during the first wave [4,5] and is not using harsh lockdowns now. Countries that performed badly during the first phase of the Covid-19 infection, such as the United Kingdom and Belgium, are performing badly also during this second phase, likely because they did not address key issues.

Many commentators suggest that what is relevant is not only how many get infected (some countries managed very few cases), but who get infected and how to prevent the build-up of the viral load in these subjects, as well as the transmission of the virus to others. It should be time we learn about the effectiveness of restrictions by looking at the data and adopt evidence-based policies.

Policies should not have the only goal to generally slow the spread of the virus or protect the national health system (NHS). The policies should protect the vulnerable to limit fatalities. The measures restricting the freedom of individuals

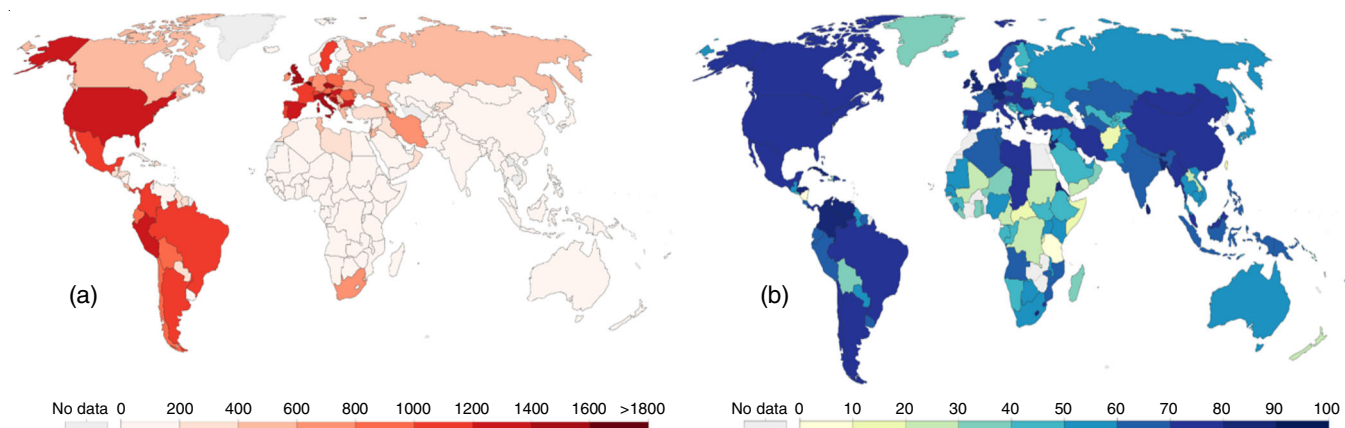


Fig. 1. Covid-19 fatalities per million (a) and restrictions severity index (b); Images from ourworldindata.org

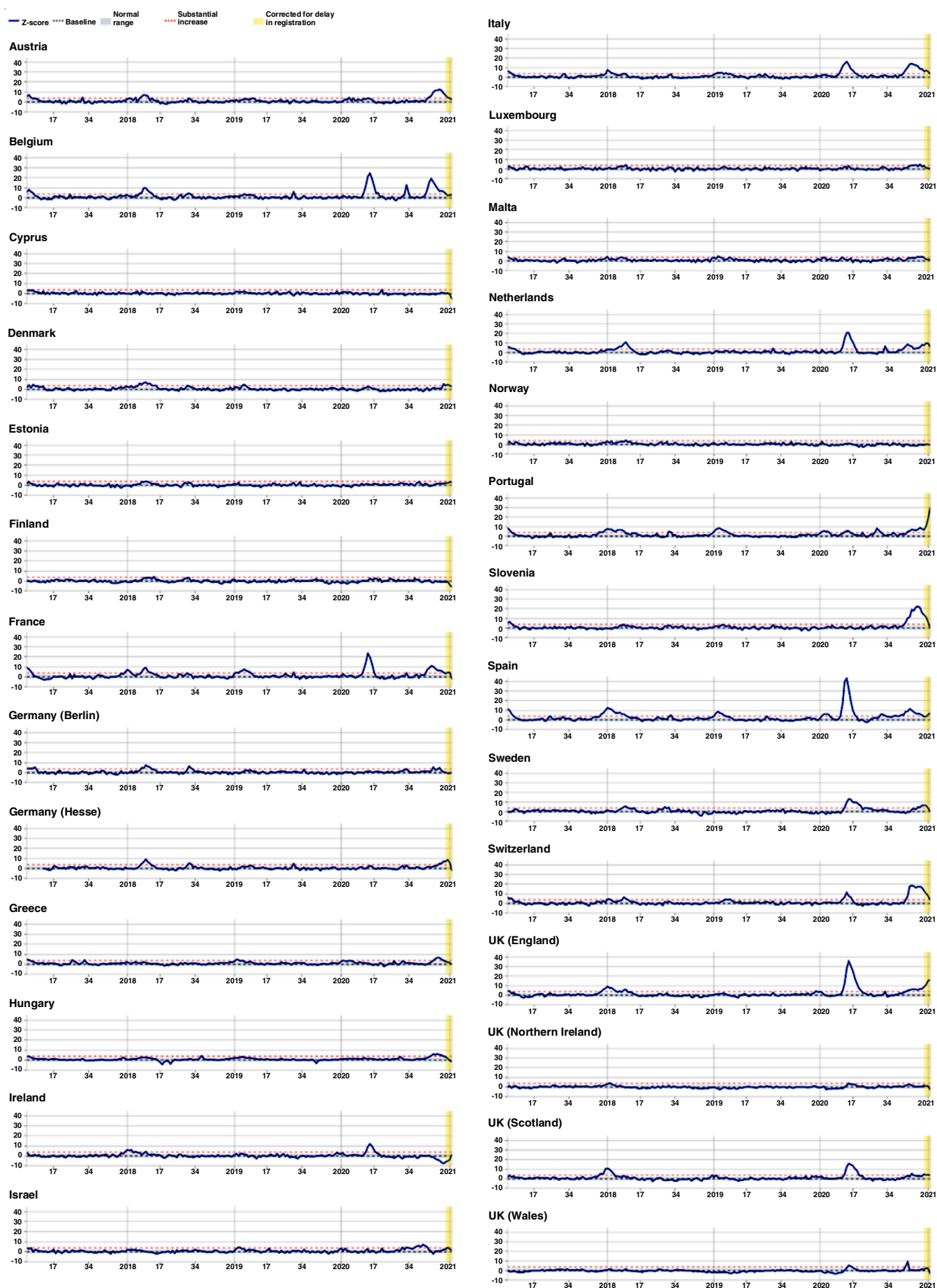


Fig. 2. Excess fatalities from EUROMOMO. Credit EUROMOMO.

are socially and economically very costly and have long term consequences that must be considered in picture [4,6].

Some commentators have noticed as especially countries that experienced stagnation or regression of life expectancy, as well as the economy, with also high non-communicable diseases and income rates, had the highest fatalities for Covid-19 [7]. This problem was not relieved by adopting more stringent restrictions [7] as intrinsic reasons drive the fatality of Covid-19. Only a better understanding of these intrinsic reasons could improve the strategies for prevention.

What is clear in Europe, for already some time, is that lockdowns do not work as they are portrayed to do. Similarly, by looking at the United States [8], in the states with the most extreme policies, there is no evidence locking down harshly saves lives. The primary purpose of lockdowns is the flattening of the curve and make the situation manageable by the health service. There is however different effectiveness of lockdowns in different countries and more severe policies alone are not associated with better results. Personal responsibility may be more important than restrictions, same of sustainability and societal responsibility.

Therapeutic agents: The analysis of the second wave of Covid-19 ongoing in Europe and other countries especially in the Northern Hemisphere also brings attention to the problem of the therapies for Covid-19 infection. There are indeed very large differences in between the case fatality rates (number of fatalities to number of infected). There are some differences between the many European countries adopting similarly restrictive approaches on the permitted therapies. There are much larger differences between countries in Europe and other parts of the world that adopt different therapeutic approaches involving the combination of antiviral and immunotherapeutic agents. Fig. 3 shows the Covid-19 cases per million and the fatality rate.

Based on a very subjective view of the available evidence, the World Health Organization (WHO) has deliberated [9] against the use of therapeutic agents, with the only exception of corticosteroids that are however only adjuvants. The solidarity Trial [9] found that all the four treatments they evaluated (remdesivir, hydroxychloroquine, lopinavir/ritonavir and interferon) had little or no effect on overall mortality, initiation of ventilation and duration of hospital stay in hospitalized patients.

Most of the European countries strictly followed the WHO direction. Other countries preferred to keep using the available

agents, often sorting out best practices through direct experience. These other countries generally performed better under the case fatality rate criterion. While the case fatality rate is certainly not only driven by therapies, surely it also depends on therapies. Countries such as Belgium or the United Kingdom have cumulative case fatality rates of 3% and 2.7%. Countries like Qatar and the United Arab Emirates have 0.2% and 0.3%. There is a factor of 10 in between the numbers, with patients also belonging to the same categories for age or co-morbidities experiencing different outcomes.

The protocols of the United Arab Emirates are based on antiviral agents not recommended by the WHO [10]. These protocols suggest to administer: (i) chloroquine phosphate to high-risk asymptomatic patients [10]; (ii) hydroxychloroquine or chloroquine phosphate or Favipiravir or Lopinavir-Ritonavir plus eventually Camostat to patients without pneumonia for 5 days [10]; (iii) combinations of Favipiravir (Lopinavir-Ritonavir) + Hydroxychloroquine (Chloroquine Phosphate) ± Camostat or Remdesivir, plus eventually interferon nebulized therapy to patients with pneumonia for 7 days [10]; (iv) Favipiravir + Camostat ± nebulized Interferon or Lopinavir-Ritonavir + Ribavirin ± nebulized Interferon to patients with severe pneumonia/critically ill patients [10]. This seems to dramatically decrease mortality, rather than the opposite.

Vaccines: Israel is the leading country for Covid-19 vaccines with 34% of the population having received one vaccine dose and 19% of the population fully vaccinated, as of January 29, 2021. The share of positive cases is however growing since the time the mass vaccination started mid-December 2020 [1].

Correlation is not causation and the coincidence can be purely casual. Fig. 4 shows the latest data of the number of cases, number of tests, positive rate, number of vaccine doses, number of partially and fully vaccinated. The number of new positive cases in isolation does not represent the state of infection, as it may be an artifact of an increased number of tests. The share of positive cases provides a better assessment of growing or reducing infections. The number of tests has been increasing until January 14, 2021. Then, it has been decided to reduce this number.

More than the new positive cases and the share of positive cases per day, it makes sense to use moving averages as the positive cases reported on a specific day are the result of the test performed in the days before. Especially those who received only the first of two shots are more prone to test positive, but

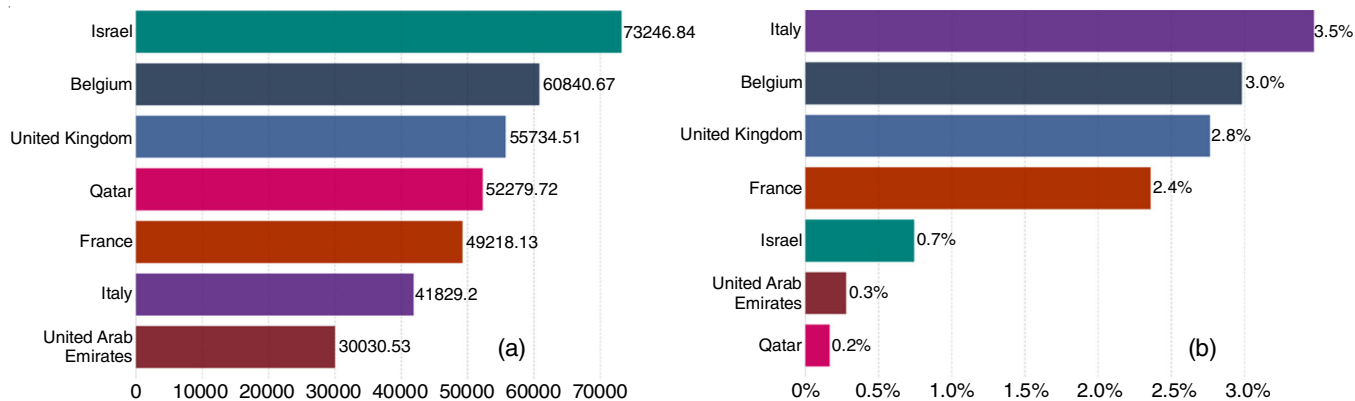


Fig. 3. Covid-19 cases per million (a) and fatality rate (b). Images from ourworldindata.org

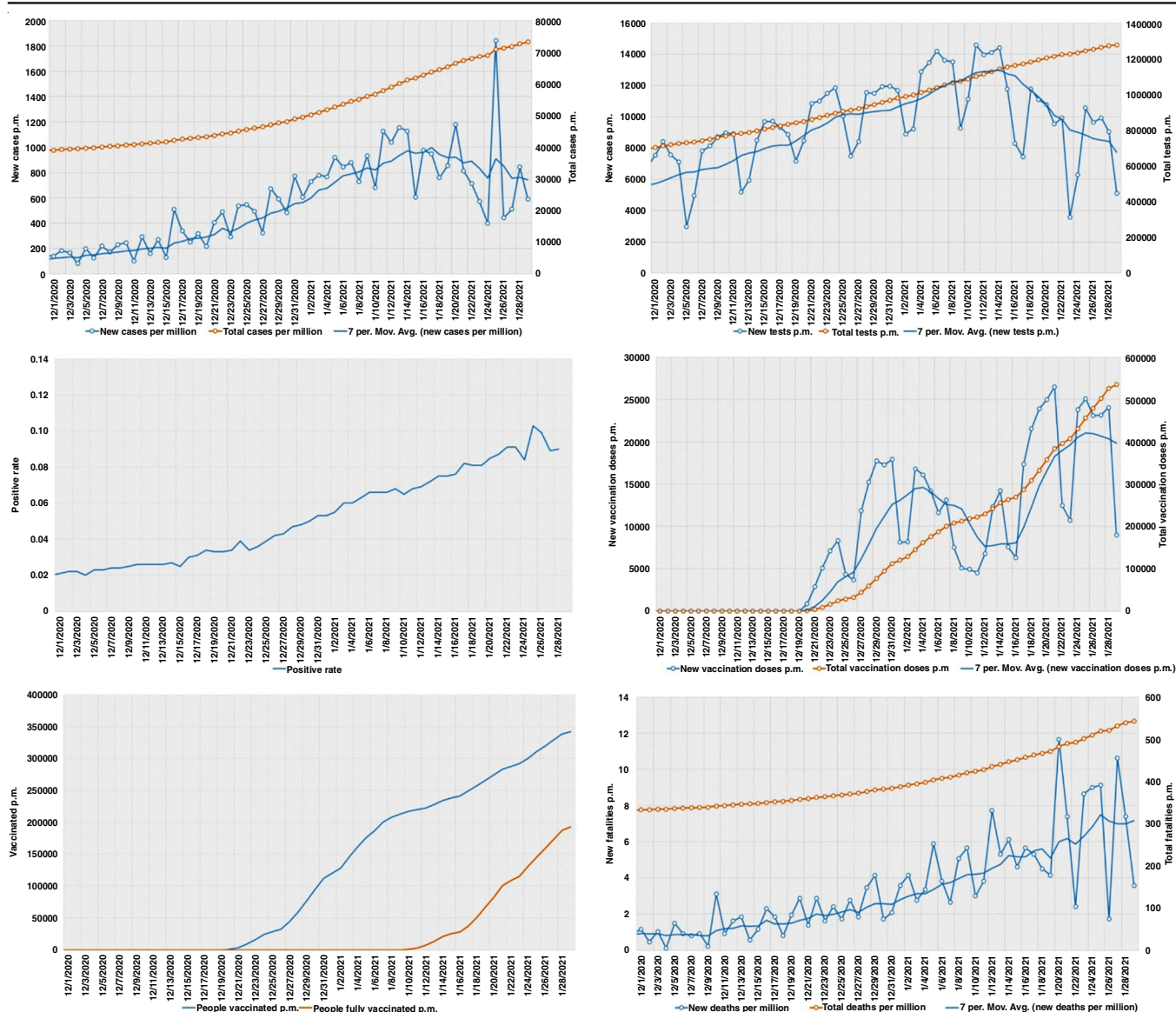


Fig. 4. New and total cases per million, new and total tests per million, positive rate, new and total vaccination doses per million, partially and fully vaccinated per million, in Israel. Data from ourworldindata.org

positive cases are also detected in between those who received two shots. This is partially acknowledged by official reports.

According to ministerial data reported by media outlets on January 19, 2021 [11,12], 6.6% of those tested after having received a vaccine dose, or 12,400/189,000, resulted positive. Most of them were tested shortly after they received the first of the two jabs, but everything but a negligible number, 1,410, tested positive two weeks after the first injection and 69 tested positive after being administered both shots. It is unknown how many were tested in the different categories immediately after the first shot, two weeks after the first shot and after the second shot, to make a better statistic.

To better understand the trend in the number of infected, it would be necessary to have the share of those tested after having received vaccine doses and those having not received any vaccine doses and have the positive rate computed in both groups. These data are unfortunately unavailable. The choice of the population to test makes difference in the positive rate. To have the breakdown of positive rates in every category,

partially, completely, or not vaccinated, would help enormously other countries to properly plan their vaccination campaigns. A full share of data would be welcomed to understand how protective are specific vaccines over time.

Despite claims of reducing cases because of vaccinations [13,14], the growing number of infected has only been recently masked by reducing the number of tests, as the positive rate is still about a 9% peak. The positive rate here considered is the rolling 7-day average of the share of daily Covid-91 tests that are positive. The positive rate dropped to about 1.7% about November 24, 2020. Then, it started to grow. On December 20, 2020, when mass vaccination started, it was 3.3%. It is now (January 31, 2021) 9.3%.

The impact on the severity of infection and fatalities, is still impossible to be determined. The expectation that vaccines will solve the Covid-19 emergency is not confirmed yet by the data. The first work that appeared in preprint to demonstrate the efficacy of the vaccine [15] is a questionable retrospective cohort study claiming the effectiveness of 51% of BNT162b2

vaccine against Covid-19 infection 13-24 days after immunization with the first dose, recommending for a second dose. Ultimately, the efficacy of the vaccine will have to be confirmed by a reducing positive rate.

The latest information (January 31, 2020) is confusing [16], as the positive rate does not reduce from the about 9% peak despite lockdowns being made harsher and the reducing number of new cases is only an artifact of the reduced number of tests. The efficacy of the vaccines will be clear after complete vaccination and removal of restrictions.

Conclusion

Data of new cases, tests, fatalities and vaccines permit to test the different hypotheses formulated about restrictions and therapies and the solution of the emergency by mass vaccination. The containment and therapeutic choices of many European countries are not based on the best available science, as evidence suggests. While data for vaccines are still preliminary, with about 50% of the population fully or partially vaccinated, the positive rate is still growing. The number of cases is expected to drop any way in March 2021 across the northern hemisphere countries because of spring.

REFERENCES

1. M. Roser, H. Ritchie, E. Ortiz-Ospina and J. Hasell, Coronavirus Pandemic (COVID-19). 2020. ourworldindata.org/coronavirus (Accessed January 28, 2021).
2. T. Hale, S. Webster, A. Petherick, T. Phillips and B. Kira, Oxford COVID-19 Government Response Tracker. 2020. www.bsg.ox.ac.uk/research/research-projects/oxford-covid-19-government-response-tracker (Accessed January 28, 2021).
3. Euromomo, data and graphs. www.euromomo.eu (Accessed January 28, 2021).
4. A. Boretti, Sustainable Post Covid19 Lockdown Strategy Through Evidence-Based Policy: Analysis of Covid19 Fatalities Across Europe, *Int. J. Med. Sci.*, **7**, 172 (2020); <https://doi.org/10.15342/ijms.7.172>
5. A. Boretti, After Less than 2 Months, the Simulations that Drove the World to Strict Lockdown Appear to be Wrong, the Same of the Policies They Generated, *Health Serv. Res. Manag. Epidemiol.*, **7**, 2333392820932324 (2020); <https://doi.org/10.1177/2333392820932324>
6. M. Kulldorff, S. Gupta and J. Bhattacharya, Great Barrington Declaration. 2020. gbdeclaration.org (Accessed January 28, 2021).
7. Q. De Laroche Lambert, A. Marc, J. Antero, E. Le Bourg and J.F. Toussaint, Covid-19 Mortality: A Matter of Vulnerability Among Nations Facing Limited Margins of Adaptation, *Front. Public Health*, **8**, 604339 (2020); <https://doi.org/10.3389/fpubh.2020.604339>
8. US CDC, excess deaths. www.cdc.gov/nchs/nvss/vsrr/covid19/excess_deaths.htm (Accessed January 28, 2021).
9. WHO, solidarity clinical trial for covid-19 treatments. www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments (Accessed January 28, 2021).
10. UAE Department of Health, Updates of Comprehensive COVID-19 Guideline for the Use of Healthcare Professionals in the Emirate of Abu Dhabi. doh.gov.ae/-/media/7BD7B077D8F846B48A70C5872902DD1C.ashx (Accessed January 28, 2021).
11. RT.com, Thousands of Israelis test POSITIVE for Covid-19 despite receiving Pfizer/BioNTech jab. www.rt.com/news/513139-israel-pfizer-vaccine-coronavirus/ (Accessed January 28, 2021).
12. I. Efrati and R. Linder, Thousands of Israelis Tested Positive for Coronavirus After First Vaccine Shot. www.haaretz.com/israel-news/thousands-of-israelis-tested-positive-for-coronavirus-after-first-vaccine-shot-1.9462478 (Accessed January 28, 2021).
13. I. Levingston, Israel is leading the world in COVID vaccinations—and its cases and hospitalizations are starting to decline. fortune.com/2021/01/24/israel-covid-vaccine-cases-hospitalizations-decline/ (Accessed January 28, 2021).
14. C. Perret, Coronavirus cases in Israel are finally beginning to decline from record highs after it vaccinated 27% of its population. www.businessinsider.com/israel-has-vaccinated-27-of-its-population-for-covid-19-2021-1 (Accessed January 28, 2021).
15. G. Chodcik, L. Tene, T. Patalon, S. Gazit, A.B. Tov, D. Cohen and K. Muhsen, The Effectiveness of the First Dose of BNT162 b 2 Vaccine in Reducing SARS-CoV-2 Infection 13-24 days After Immunization: Real-world Evidence, *Medrxiv* (Pre-print) January 29 (2021); <https://doi.org/10.1101/2021.01.27.21250612>
16. TOI, Health Ministry expected to seek week-long lockdown extension as virus rages on. www.timesofisrael.com/health-ministry-expected-to-seek-week-long-lockdown-extension-as-virus-rages-on/ (Accessed January 31, 2021).