

The effect of a national lockdown in response to COVID-19 pandemic on the prevalence of clinical symptoms in the population

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Abstract

'SARS-CoV-2', a novel coronavirus and the cause of COVID-19, was isolated in December 2019 and has since been declared a pandemic by the World Health Organization (WHO). The vast and rapid spread of COVID-19 calls for immediate action from policy-makers and in many countries, various lockdown measures were implemented. Here, we utilized nationwide surveys that assess COVID-19 associated symptoms to analyse the effect of the lockdown policy in Israel on the prevalence of clinical symptoms in the population. Daily symptom surveys were distributed online and included fever, respiratory symptoms, gastrointestinal symptoms, anosmia and Ageusia. A total of 1,003,298 surveys were filled up to date. We used a single measure of symptoms, Symptoms Ratio (SR), defined as a weighted mean of symptoms found to be prevalent in COVID-19 patients. Notably, following severe lockdown measures, we found that between March 15th and April 22nd, the mean SR sharply declined by 78.9%, as did every individual symptom, including our most common symptoms of cough and rhinorrhea or nasal congestion, which decreased from 14.5% and 13.8% of the survey responders, respectively, to 2.4% and 2.5%. We also observed reduction in symptoms separately in the vast majority of cities in Israel. Overall, these results demonstrate a profound decrease in a variety of clinical symptoms following the implementation of a lockdown in Israel. As our survey symptoms are not specific to COVID-19 infection, this effect likely represents an overall nationwide reduction in the prevalence of infectious diseases, including COVID-19. This quantification may be of major interest for COVID-19 pandemic, as many countries consider implementation of lockdown strategies.

Introduction

Since its isolation in December 2019, the novel coronavirus COVID-19 has spread to almost every country in the world ¹. In Israel, the first infection of COVID-19 was confirmed on February 21st 2020, and in response, the Israeli Ministry of Health (MOH) employed a series of steps in an attempt to mitigate the spread of the virus in Israel. These steps were gradually aggravated; on March 9th all Israelis returning from abroad were instructed to begin a 14-day home-isolation period upon their arrival; on March 11th gatherings were limited to a maximum of 100 people; on March 12th educational institutions were closed; on March 25th new regulations instructed Israeli citizens to remain in their homes, with permission to leave only to a distance of 100 meters; and on March 31st the above regulations were further exacerbated forbidding any gatherings of people from different households. Policy changes in Israel thus far were enforced on the entire Israeli population. In several cities with high infection rates, stricter regulations were implemented. April imposed new challenges for the Israeli population and the government, given the Jewish holiday Passover which is traditionally celebrated with family. To prevent gatherings during the holiday period, between April 8th and 15th, harsher restrictions were imposed, with a national quarantine declared on the eve of Passover. On April 19th, a few of the restrictions were lifted and more employees were allowed to return to work and limited social events such as prayers and weddings were allowed to take place but under severe restrictions on the numbers of people.

Policy-makers in Israel, as well as others worldwide, struggle to find the most suitable policy which will slow the rate of infection while maintaining the functionality of the economy. In the absence of a vaccine against COVID-19, control of disease spreading through large-scale physical distancing measures appears to be an effective means of mitigation (1). These may include closures of workplaces, schools, and general lockdown. While many countries have implemented different policies and various degrees of lockdowns (1–3), the effect of these measures on the prevalence of clinical symptoms in the general population has not been quantified to date. Here, we utilize data obtained from nationwide, daily, one minute surveys, deployed by us from the early stages of COVID-19 spread in Israel ³, to analyse the effect of different actions implemented in Israel on the prevalence of different clinical symptoms and at high geographical resolution.

Methods

Data

To obtain real-time information on symptoms across the entire Israeli population, we developed a simple one-minute online questionnaire (4). The survey was posted online (<https://coronaisrael.org/>) on March 14th, and participants were asked to fill it on a daily basis and separately for each family member, including those who are unable to fill it out themselves (e.g., children and elderly). The study protocol was approved by the institutional review board (IRB). The survey is filled anonymously to maintain individual privacy and was filled out 1,003,298 times to date.

The survey includes questions on respondents age, gender, geographic location (city and street), isolation status, smoking habits, prior medical conditions, body temperature measurement and self-reporting of symptoms. All prior medical conditions and symptoms included in the questionnaire were meticulously chosen by medical professionals, taking symptoms which were described as prevalent in patients with COVID-19 infection (e.g. cough and fatigue) as well as symptoms which were less prevalent in these patients (e.g. nausea

and vomiting) (5) to allow better discrimination of individuals with possible COVID-19 infection. The complete questionnaire can be found in Section 1 of the Supplementary Appendix.

The initial symptoms included cough, fatigue, myalgia (muscle pain), shortness of breath, rhinorrhea or nasal congestion, diarrhea and nausea or vomiting. Additional symptoms, including sore throat, headache, chills, confusion and loss of taste and/or smell sensation, were added in later versions. Efforts were devoted to reach underrepresented populations through several channels, including call centers, media appearance and promotion of the survey through Arabic-speaking TV stations to gain interest and compliance in all sectors of the population.

Responses from participants who did not meet reasonable criteria of age (0-120 years of age) and body temperature (35-43 degrees Celsius) were excluded (464 and 667, respectively). Another 164,799 responses recorded between March 22nd to March 26th were excluded due to infrastructure transition procedures held on these dates that resulted in faulty data being collected.

Symptoms Ratio

Data on the clinical characteristics of patients with COVID-19 is rapidly emerging. In order to measure the effect of the Israeli lockdown policy on a single measure which takes into account the prevalence of symptoms which were described as common in patients with COVID-19 infection to date, we used a single measure of symptoms, Symptoms Ratio (SR), defined as a weighted mean of symptoms that were described as prevalent in COVID-19 patients. Due to the fact that in many countries, only symptomatic individuals are being tested, the true prevalence of symptoms in individuals positive to COVID-19 remains unclear and to date was reported only in a small scale study (6). We therefore calculated this measure based on two different sets of weights. SR_t (targeted) was calculated by the overall prevalence of symptoms in confirmed patients (Zhao et al. 2020). In these patients, most diagnostic tests were most likely targeted. SR_s (screening) was based on the prevalence of symptoms in confirmed patients diagnosed by screening tests (Gudbjartsson et al. 2020) (see Section 2 in the Supplementary information). These unified measures were designed to be as informative as possible and to serve as the best possible indicator for reporting of coronavirus related symptoms. We included only symptoms that were reported to have a prevalence of more than 2% in patients with confirmed COVID-19 infection. Symptom weights were defined as their reported prevalence in these patients, divided by the sum of the total list of symptoms prevalence (see Section 2 in the Supplementary information). This measure aims to reflect the importance of each symptom with respect to its appearance in confirmed cases. The symptoms included for adults were fever, cough, fatigue, shortness of breath, muscle pain, sore throat, headache and diarrhea. Rhinorrhea was only included in the SRs.

Children experience a different clinical course of COVID-19 infection, with less severe clinical manifestations. Moreover, it has been reported that over 90% of all children are either asymptomatic, or experience mild or moderate disease (Dong et al. 2020). We thus defined Symptoms Ratio for children (SR_c) up to the age of 18 years old based on a recent systematic review (de Souza et al. 2020). The following symptoms were included: fever, cough, diarrhea, nausea and/or vomiting, rhinorrhea and/or nasal congestion (see Section 2 in the Supplementary information). We will refine these measures as more information will continue to accumulate on this topic.

Statistical analysis

To estimate the effect of the Israeli lockdown policy we analyze the prevalence of reported symptoms throughout the period of data collection. The analysis is done both on the complete study population, and also on subgroups of the population defined by age or residence city. In addition to the analysis of individual symptoms, we also analyze our constructed measures of SRt, SRs and SRc for the pediatric population. When analyzing individual symptoms we examined each symptom starting from the time it was included in our survey (see Section 1 in Supplementary appendix).

Results

Overall, 1,003,298 responses were collected during the study period of March 14th and April 22nd, 2020. Of these, 165,930 responses were excluded (Methods) and a total of 837,368 responses, 783,635 (93.583%) adults and 53,733 (6.417%) children were eventually included in the study. The characteristics of the responders are described in Table 1.

Table 1. Characteristics of study population			
Characteristic, mean (SD) or %	All responders (n = 837,368)	Adults (n = 783,635) (93.583%)	Children (up to 18 years old, n = 53,733) (6.417%)
Age (years)	48.703 (19.05)	51.25 (16.869)	11.55 (5.508)
Sex - Male	378,916 (45.251%)	351,358 (44.837%)	27,558 (51.287%)
Smoking (currently)	105,059 (12.546%)	103,635 (13.225%)	1,424 (2.65%)
Currently in Isolation	57,925 (6.918%)	55,566 (7.091%)	2,359 (4.39%)
Symptoms			
Body temperature (Celsius)	36.386 (0.472)	36.378 (0.46)	36.603 (0.676)
Fever (body temperature above 38 °C)	1,497 (0.179%)	1,061 (0.135%)	436 (0.811%)
Feel good	482,609 (94.267%)	438,316 (94.313%)	44,293 (93.817%)
Shortness of breath	8,741 (1.044%)	8,316 (1.061%)	425 (0.791%)
Rhinorrhea or nasal congestion	55,841 (6.669%)	52,087 (6.647%)	3,754 (6.986%)
Nausea and vomiting	4,712 (0.563%)	4,220 (0.539%)	492 (0.916%)
Muscle pains	11,703 (1.398%)	11,255 (1.436%)	448 (0.834%)
Sore throat	21,735 (2.855%)	20,731 (2.909%)	1,004 (2.058%)
Fatigue	23,633 (2.822%)	22,189 (2.832%)	1,444 (2.687%)
Diarrhea	9,412 (1.124%)	8,696 (1.11%)	716 (1.333%)
Loss of taste or smell	2,028 (0.266%)	1,910 (0.268%)	118 (0.242%)
Confusion	1,624 (0.213%)	1,472 (0.207%)	152 (0.312%)
Cough	53,993 (6.448%)	50,723 (6.473%)	3,270 (6.086%)
Dry cough	22,633 (2.973%)	21,335 (2.994%)	1,298 (2.66%)
Moist cough	23,728 (3.116%)	22,422 (3.146%)	1,306 (2.677%)
Headache	15,016 (1.972%)	14,390 (2.019%)	626 (1.283%)
Chills	3,526 (0.463%)	3,312 (0.465%)	214 (0.439%)
Symptoms ratio			
Symptoms Ratio (SRt)	0.027 (0.089)	0.027 (0.088)	0.028 (0.098)

Next, we calculated the prevalence of the various clinical symptoms reported by the responders throughout the study period, and analysed the effect of different policy changes implemented by the Ministry of Health (MOH) of Israel during this time period (Figure 1). Of note, data obtained from the Israeli MOH on Influenza like symptoms in Israel from previous years revealed a very low rate of influenza like illness in the time period which is parallel to the time in which our survey has been distributed, with less than 1 weekly clinic visit due to influenza like symptoms per 10,000 people, across all age groups (7). Our analysis revealed a significant reduction in the prevalence of nearly all symptoms (except nausea and vomiting) as physical distancing policies became more strict. The largest reduction was observed in confusion and muscle pain, which decreased by 85.36% and 84.58%, respectively, from March 15 to April 21. We also observed a reduction of 78.9% and 77.63% in our aggregated symptom measures SRt and SRs, respectively (Figure 1). Notably, the rate of responses to the survey changes over time (Figure 1), but at least 10,000 responses were received every day. Thus, the decrease in all reported symptoms is probably not a result of lacking reports, but of a true trend of symptoms reduction.

We also see a similar trend when separately analyzing the Symptoms Ratio in different cities in Israel (a few sample cities shown in Figure 2). Responses were associated with cities using the address respondents provided when answering the survey. The decrease in the Symptoms Ratio is evident in the majority of cities, despite significant population and geographic differences between them. For example in Jerusalem and Modi'in-Makkabbim-Re'ut we found a decrease of 76.91% and 87.51% percent of the SRt measure (accordingly).

The general trend of Symptoms Ratio decrease is also visible when subgrouping population by age (Figure 2). Unlike the cities subgroups, where the trend was relatively similar for most cities, we found notable differences between age groups, most distinct is the vast decrease of the Symptoms Ratio in children under the age of 18, which decreased by 86.27% from March 15 to April 21, as opposed to adults in the ages of 55-74, or 75 and older, for whom the SRt decreased by 76.57% and 62.42%, respectively.

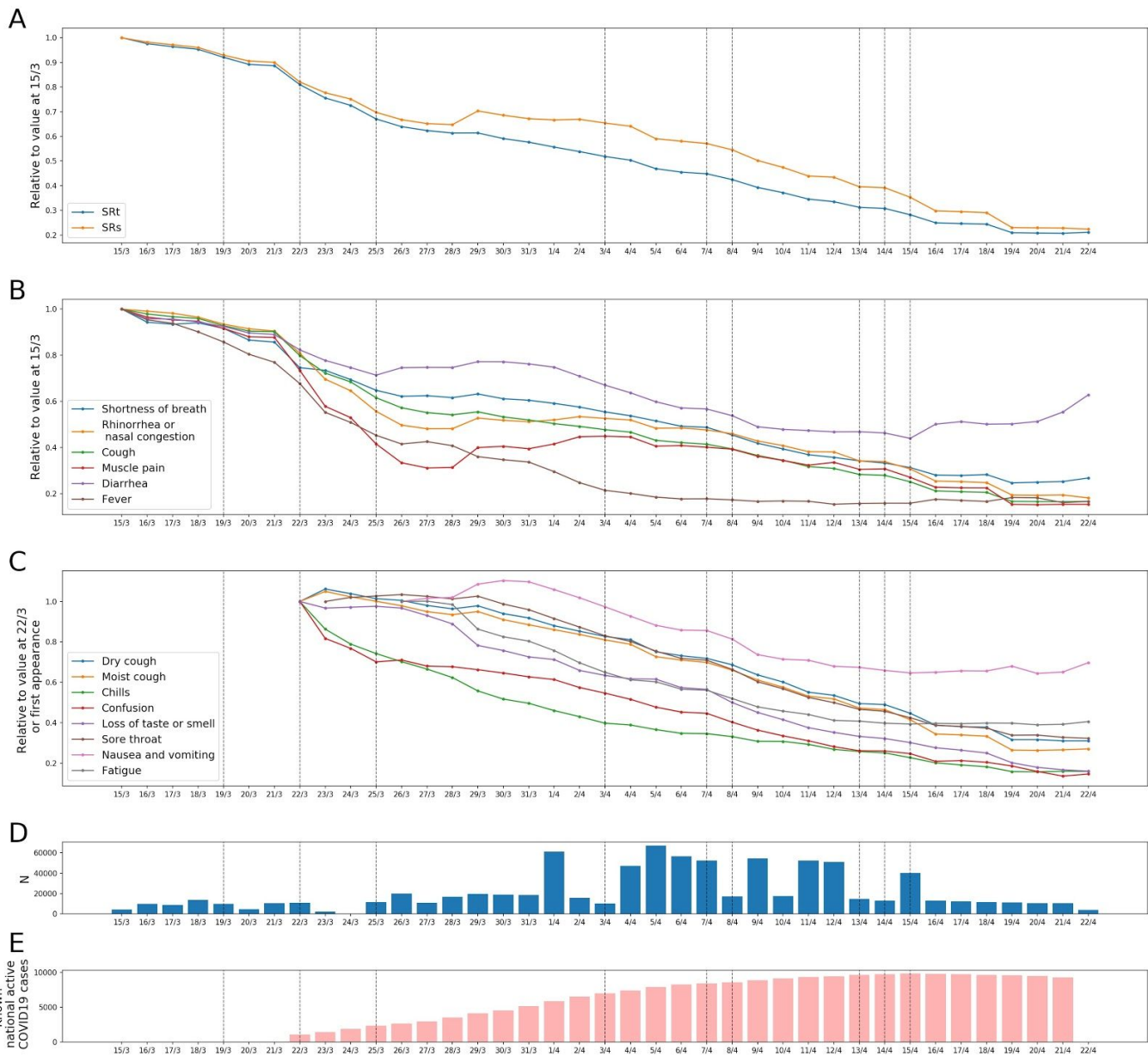
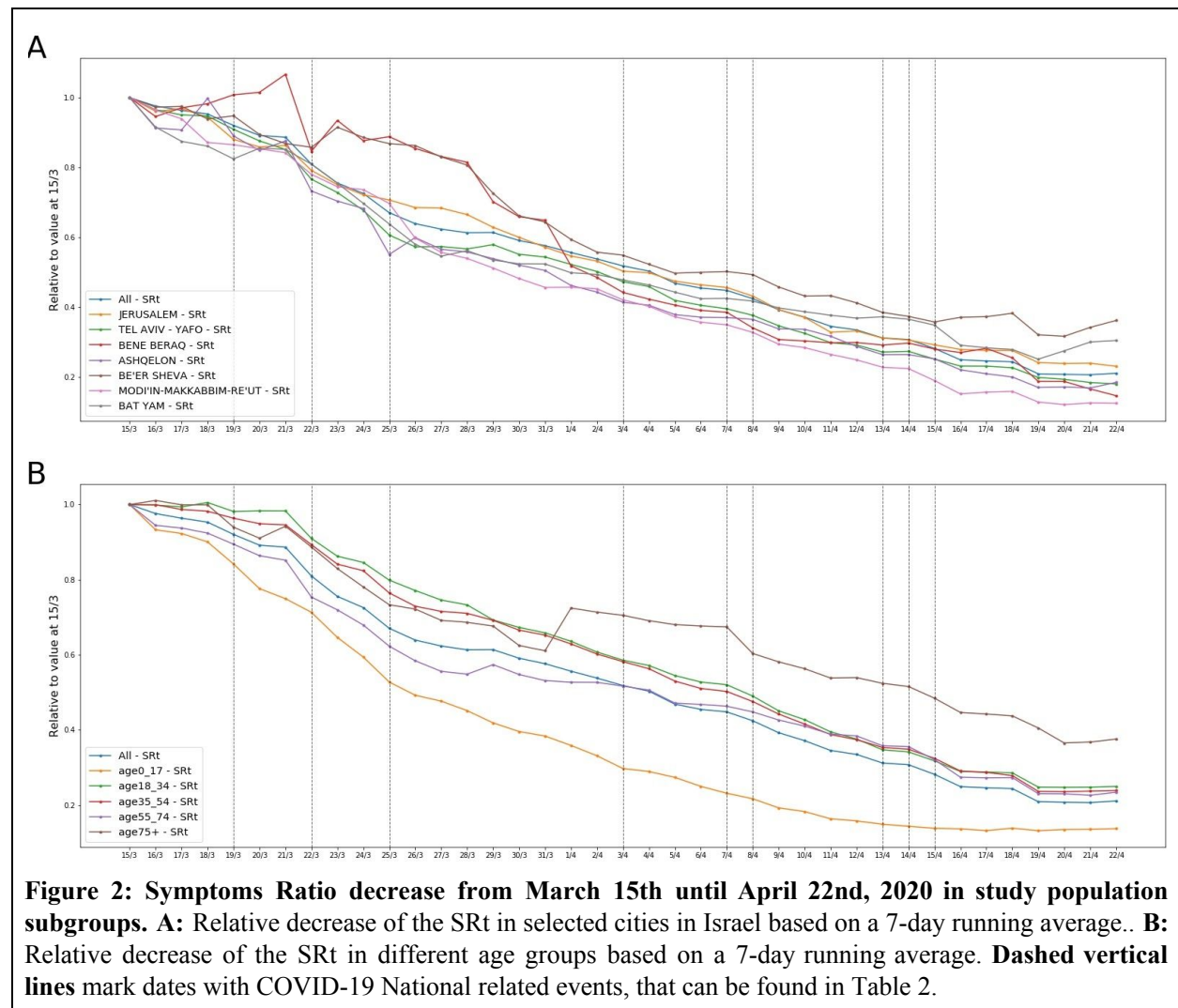


Figure 1: Symptoms sharply decrease from March 15th until April 22nd, 2020 in full study population. A: Relative decrease of the aggregated symptom measures SRt (blue) and SRs (orange) based on a 7-day running average. **B:** Relative decrease of symptoms reported since March 15th based on a 7-day running average **C:** Relative decrease of symptoms reported since March 22nd based on a 7-day running average. **D:** Number of responses per day. **E:** Cumulative number of confirmed COVID-19 patients in Israel per day. **Dashed vertical lines** mark dates with COVID-19 National related events, that can be found in Table 2.



Date	COVID-19 National related event
12/03/20	Israel limits gatherings to 100 people. Closure of educational facilities including schools, and universities, two days later all other educational facilities were also closed.
14/03/20	Israel limits gatherings to 10 people with a distance of 2 m (6 ft) between one another. Closure of all leisure venues including restaurants, malls, gyms and movies.
16/03/20	Only 30% of employees are allowed to go to work apart from essential workers, resulting in hundreds of thousands of employees in a state of unpaid leave.
19/03/20	National state of emergency declared - citizens not allowed to leave their homes unless absolutely necessary.
25/03/20	New MOH regulations forbid citizens to leave their home for a distance of more than 100 meters apart from essential workers, or under special circumstances such as medical care and buying groceries. No more than 2 people in a car. Non-essential shops are ordered to be closed, public transport reduced to 25%.
03/04/20	Bnei Brak, the biggest ultra- orthodox city in Israel is closed for coming and going apart for special clearance due to high infection rates.
07/04/20	Masks become a mandatory requirement.
08/04/20	Passover dinner in Israel - all shops are closed at 18pm, national quarantine from 18pm until 7am on 09/04 to prevent joint dinners.
13/04/20	No public transportation from 8pm until the 16th of April at 5am
14/04/20	City quarantine from 5pm until 16th of April at 5am - citizens are required to stay in their city.
19/04/20	Workers from Essential industries are allowed to go back to work under physical distancing rules. Limited social events allowed

Table 2: COVID-19 related national events by date. Each event is marked with a vertical dashed line in figures 1 and 2.

Discussion

Here, to the best of our knowledge we quantify for the first time the effect of lockdown policies on the prevalence of self-reported clinical symptoms in the population. We show that implementation of various measures of physical distancing throughout time results in a dramatic decrease in the prevalence of different clinical symptoms, both in adults and in children. This knowledge is crucial for assessing the impact of these policies, and for devising effective control measures both in the current COVID-19 pandemic and in future pandemics.

Previous studies during the current COVID-19 pandemic have estimated the effects of lockdown policies on clinical variables that are more specific to COVID-19 infection, such as the effect of the lockdown on the virus doubling time (I). We believe that our study provides a more global view on the overall reduction in the prevalence of infectious diseases during the lockdown, including, but not limited to, COVID-19 infection. Since

the symptoms included in our survey are not specific to COVID-19 infection, the prevalence of other infectious diseases are most likely reflected by them. This is supported by the fact that the decrease in the prevalence of symptoms is global, and is not limited to specific symptoms which were described as common in individuals with COVID-19 infection. In addition, while the number of confirmed patients with COVID-19 infection in the Israeli population is increasing (14,326 on April 22nd), it still represents a small fraction (0.16%) of the Israeli population (8) and is unlikely to be the sole contributor to the large decrease in symptoms visible in our data. Many infectious diseases other than COVID-19 are transmitted by Aerosol transmission (9) or physical contact (10), which are greatly reduced when implementing physical distance measures, and will be therefore affected by these measures as well. For example, a previous study found a decrease of 42% in the overall diagnoses of respiratory infections in children during school closure as part of an organized labor dispute during a previous influenza outbreak (11).

One may argue that the reduction in symptoms viewed in our data is due to other factors, which are not related to the lockdown policies, such as the normal seasonal variation of Influenza infection. We believe that this is not the case, since we started distributing our survey in the middle of March, when according to the Israeli Ministry of Health, the levels of infection caused by Influenza were already extremely low. Furthermore, data on Influenza like symptoms in Israel from previous years suggest a very low rate of influenza like illness in the time of year in which our survey was distributed (with less than 1 weekly clinic visit due to influenza like symptoms per 10,000 people) (7).

Our study has several limitations. First, we ask participants to fill the survey anonymously since we are obligated to ensure the privacy of our participants. As such, we cannot link daily surveys of the same responder, which could have provided symptoms trends at the individual level and insights on the progression of symptoms and the disease over time, and the influence of lockdown policies on the progression of symptoms at the individual level. At the time of writing, we are deploying newer versions of our survey that will be distributed nationally in Israel, allowing us not only to collect data which will be more representative but also to link responses of an individual over time, while protecting the anonymity and privacy of the responders.

Second, our surveys were deployed as a voluntary tool, and thus the population of the study, which was defined by the responders to the survey, is prone to selection bias, and may not represent the entire Israeli population across all geographic locations. In an attempt to reduce this bias, the survey was distributed in six different languages to reflect the most common languages spoken in Israel and substantial efforts were made to reach disadvantaged populations by engaging leaders in local religious communities, and promoting the survey through both Hebrew and Arabic-speaking media channels. Ongoing work is done to reduce the effect of this selection bias utilizing several statistical analysis tools such as Multilevel Regression and Poststratification models (12). Of note, even if selection bias exists, it will most likely be present throughout the entire study period, and is therefore less likely to lead to the relative changes that are seen in the symptoms prevalence during the study period.

Despite the preliminary nature of our results, we believe that it is important to publish them now, as time is crucial. In the past few weeks, an international Coronavirus Census Collective, the CCC, has been established among several additional initiatives across the globe who have surfaced to use daily self-reported symptoms as a means to track disease spread and predict outbreak locations (Segal et al. 2020). Overall, our study quantifies the effect of lockdown policy on the prevalence of several clinical symptoms, which are related to both

COVID-19 and other infectious diseases. Such information is critical at this time, and may inform decision-makers worldwide as they consider actions to prevent the ongoing spread of coronavirus.

Data availability statement

Tables of de-identified, aggregated data are available at <https://github.com/hrossman/Covid19-Survey>.

Code availability statement

Analysis source code is available at <https://github.com/hrossman/Covid19-Survey>. Source code for the questionnaires is available at <https://github.com/hasadna/avid-covider> as an open source project, and can be readily adapted to use in other countries.

Ethics Declarations

The study protocol was approved by the institutional review board (IRB) of the Weizmann institute of science. Informed consent was waived by the IRB, as all identifying details of the participants were removed before the computational analysis. Participants were made fully aware of the way in which the data will be stored, handled and shared, which was provided to them and is in accord with the privacy and data-protection policy of the Weizmann Institute of Science (<https://weizmann.ac.il/pages/privacy-policy>).

Competing Interests Statement

The authors declare no competing interests.

Authors contribution

A.K., A.G., H.R., S.S. & T.M. conceived the project, designed and conducted the analyses, interpreted the results and wrote the manuscript. T.K., A.L., D.K., I.K., S.S., & N.G. designed and conducted the analyses, interpreted the results and wrote the manuscript. O.C. directed the organizational and logistic effort and interpreted the results. A.A.Z & A.I. provided and interpreted data. B.G, Y.D., R.B., V.S. & E.S. conceived and directed the project and analyses, designed the analyses, interpreted the results, wrote the manuscript, and supervised the project.

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Supplementary appendix

1. COVID-19 daily questionnaire
2. Symptoms ratio weights
3. Absolute symptom changes

1. COVID-19 daily questionnaire

COVID-19 Daily questionnaire

This questionnaire was designed to detect potential geographic areas in which the coronavirus is spreading in Israel. You will be asked about potential symptoms of the virus. A better estimation of the number of infected people in each area will help to identify locations in which the number of infected people is particularly high. Please fill the questionnaire every day for each family member separately. Please fill it also in cases you and your family are feeling well and do not experience any symptoms.

Of note, this questionnaire can not diagnose a coronavirus infection. It is anonymized and all the data will be used solely for epidemiologic purposes. We are taking every measure to keep the privacy of the responders.

We thank you for your participation

 &*Age

&*Gender:

- ☐ Male
☐ Female

&*City, Street

#House number

#*I am:

- ☐ Feeling well
☐ Not feeling well

*Are you experiencing any of the following symptoms?

- ☐ Cough :
 ☐ #Dry cough (no sputum)
 ☐ #Wet cough (with sputum)
- ☐ Fatigue
☐ Muscle pain
☐ Shortness of breath
☐ Rhinorrhea (Runny nose) and/ or Nasal congestion
☐ Diarrhea
☐ Nausea and /or vomiting
☐ #Sore throat

- ☐ #Headache
- ☐ #Chills
- ☐ #Confusion
- ☐ #Experiencing loss of taste and/or smell sensation

&*Have you been diagnosed with any of the following conditions:

- ☐ Diabetes mellitus
- ☐ Hypertension
- ☐ Cardiovascular disease or stroke
- ☐ Chronic lung disease including Asthma (with the exception of childhood Asthma)
- ☐ Chronic kidney disease
- ☐ #Malignancy (cancer)
- ☐ #Immunodeficiency (including consumption of drugs which cause immunodeficiency)

*I am currently:

- ☐ Not in isolation
- ☐ In isolation (including from family members, staying in a separate room) from the date of _____ - due to :
 - ☐ A recent international travel
 - ☐ A contact with an individual who was infected with coronavirus or an individual who recently returned from any destination abroad
 - ☐ #Experiencing disease symptoms
 - ☐ #Voluntary isolation
- ☐ #I have a confirmed infection with COVID-19 (by a lab test) and currently:
 - ☐ In home isolation
 - ☐ Staying in a hotel
 - ☐ Hospitalized in a hospital
 - ☐ I recovered from COVID-19 infection and staying at home

&*Cigarette smoking habits

- ☐ I currently smoke
- ☐ I used to smoke and stopped more than 5 years ago
- ☐ I used to smoke and stopped less than 5 years ago
- ☐ I have never smoked

What is your current body temperature?

- ☐ I did not measure my temperature in the last 24 hours
- ☐ I measured my temperature and it was _____

With how many individuals have you been in contact in the last 24 hours? (within approximately 2 meters (6 ft 7 in) for more than 15 minutes)

Adults (age above 18 years old _____)

Children (age below 18 years old _____)

Supplementary Figure 1: COVID-19 Daily questionnaire *Questions that the responder is required to answer, & Questions that should be filled only once #Questions that were added in newer versions of the questionnaire

Integration time of different symptoms to our survey:

- Symptoms reported from March 15th: Shortness of breath, Rhinorrhea or nasal congestion, Cough, Fatigue, Nausea and vomiting, Muscle pain, Fever, Diarrhea
- Symptoms reported from March 22nd: Dry cough, Moist cough, Chills, Confusion, Loss of taste or smell
- Symptoms reported from March 23rd: Sore throat

2. Symptoms ratio weights

For adults, the symptoms were weighted by this table:

Symptom prevalence	SRt	SRs
Fever	79%	19.5%
Shortness of breath	3.5%	N/A
Cough	58%	36.8%
Fatigue	29.3%	N/A
muscle pain	3.8%	21.8%
sore throat	3.2%	29.9%
Headache	6%	20.7%
Diarrhea	5.7%	N/A
Rhinorrhea	<2%	27.6%

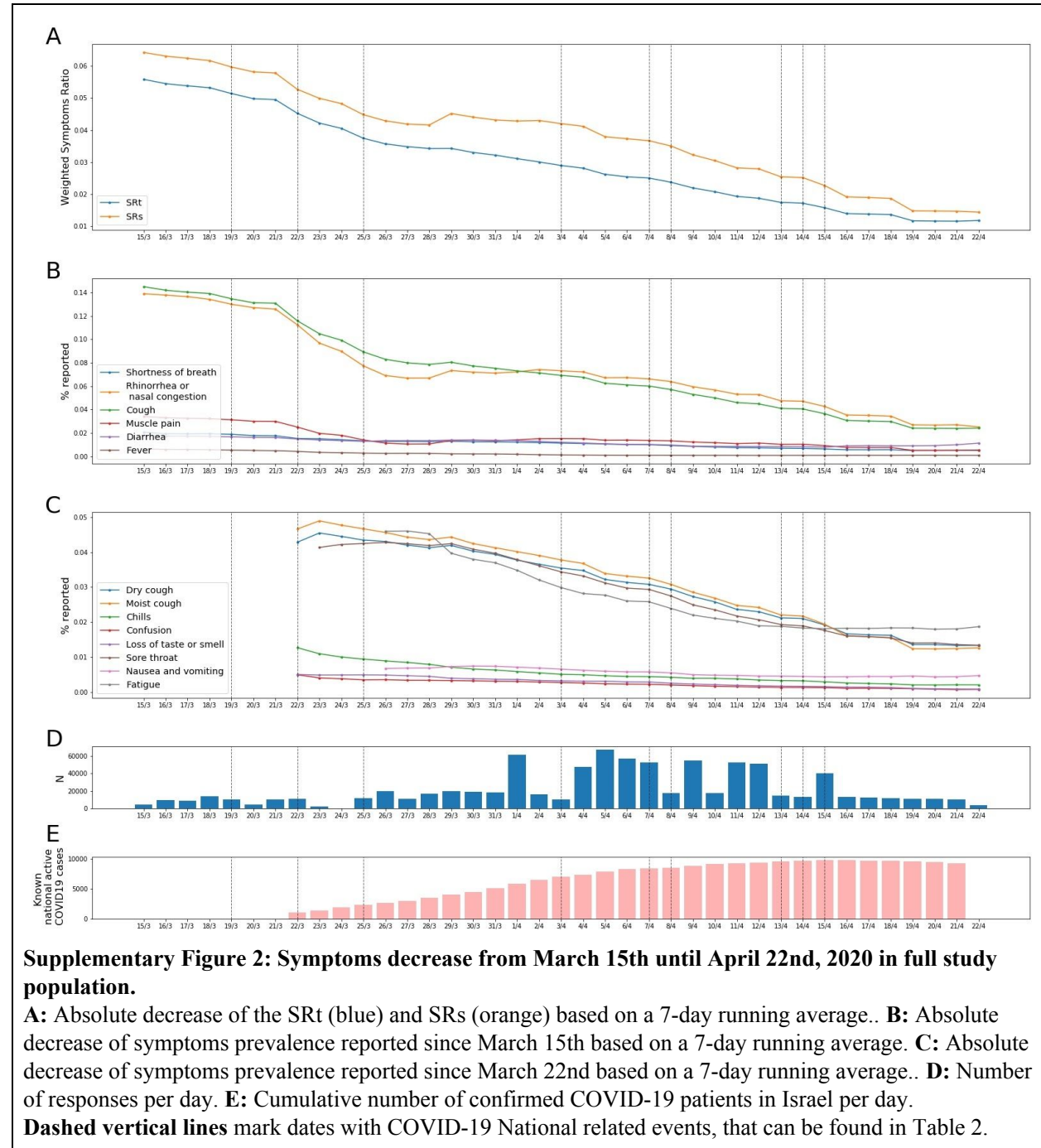
Supplementary table 1: The prevalence of different symptoms which were used to defined Symptoms ratio in targeted population (SRt) and Symptoms ratio in screening population (SRs) (6)

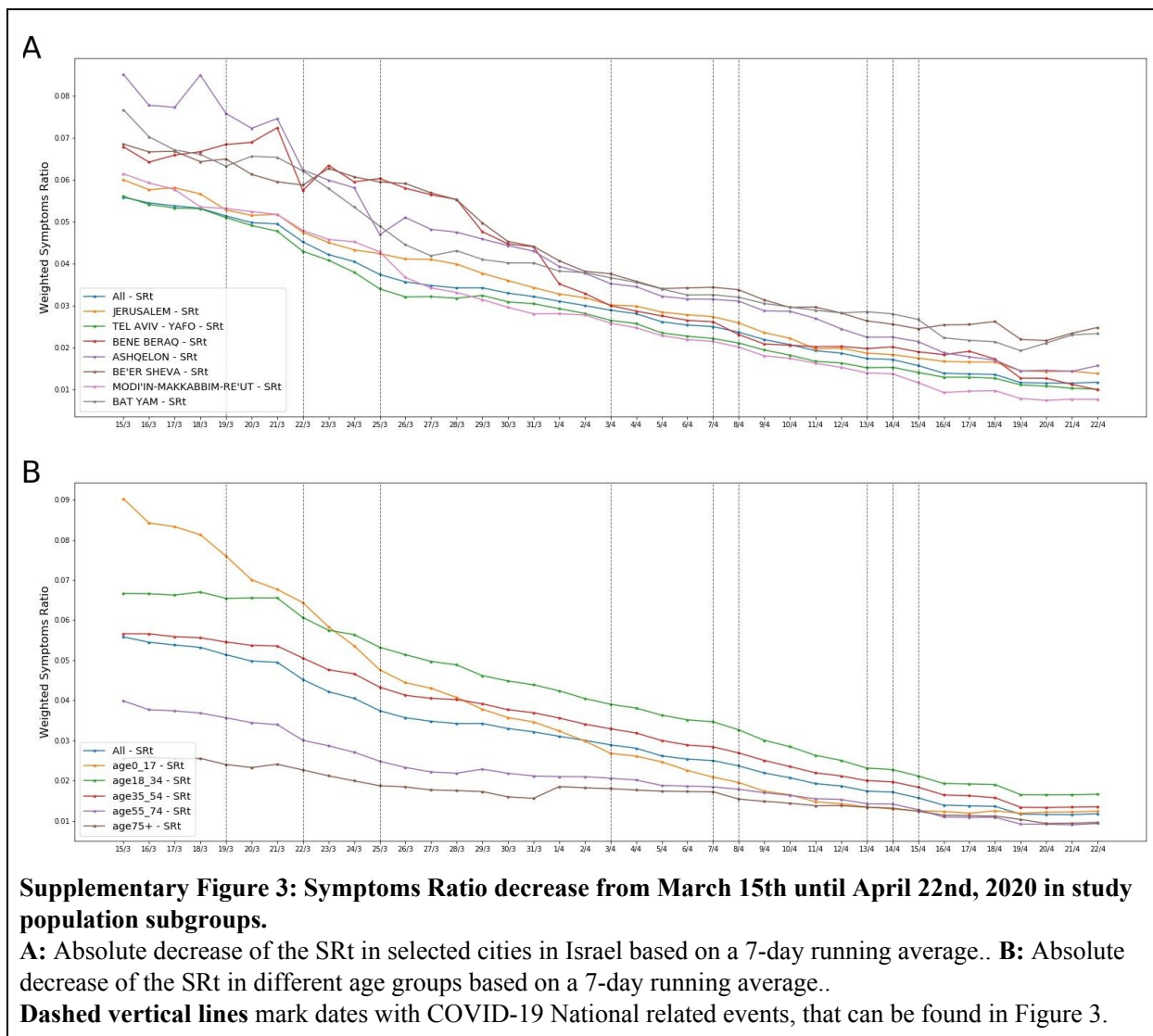
For children up to the age of 18 years old, symptoms ratio was calculated by the following prevelances,

Symptom prevalence	SRc
Cough	14.4%
Fever	16.3%
Diarrhea	2.7%
Nausea and vomiting	2.5%
Rhinorrhoea and Nasal congestion	3.6%

Supplementary table 2: The prevalence of different symptoms which were used to define Symptoms ratio in children (SRc) based on a recent systematic review (13).

3. Absolute symptom changes





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