Trend change of transmission route of COVID-19-related symptoms in Japan

Akifumi Eguchi, Ph.D., Daisuke Yoneoka, Ph.D., Shoi Shi, Ph.D., Yuta Tanoue, Ph.D., Takayuki Kawashima, Ph.D., Shuhei Nomura, Ph.D., Kentaro Matsuura, MSc., Koji Makiyama, MSc., Keisuke Ejima, Ph.D., Stuart Gilmour, Ph.D., Hiroshi Nishiura, M.D., Ph.D., Hiroaki Miyata, Ph.D.

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Short communication

Title

Trend change of transmission route of COVID-19-related symptoms in Japan

Authors

Akifumi Eguchi, Ph.D.*1, Daisuke Yoneoka, Ph.D.*2,4, Shoi Shi, Ph.D.*5,6, Yuta Tanoue, Ph.D.*7, Takayuki Kawashima, Ph.D.*8, Shuhei Nomura, Ph.D.*2,4, Kentaro Matsuura, MSc.9,10, Koji Makiyama, MSc.10,11, Keisuke Ejima, Ph.D.12, Stuart Gilmour, Ph.D.4, Hiroshi Nishiura, M.D., Ph.D.13, Hiroaki Miyata, Ph.D.†2

* Shared co-first authorship

Affiliations

- Department of Sustainable Health Science, Center for Preventive Medical Sciences, Chiba University, Chiba, Japan
- Department of Health Policy and Management, School of Medicine, Keio University, Tokyo, Japan
- 3. Graduate School of Public Health, St. Luke's International University, Tokyo, Japan
- 4. Department of Global Health Policy, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan
- 5. Department of Systems Pharmacology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan
- 6. Laboratory for Synthetic Biology, RIKEN Center for Biosystems Dynamics Research, Osaka, Japan
- 7. Institute for Business and Finance, Waseda University, Tokyo Japan
- 8. Department of Mathematical and Computing Science, Tokyo Institute of Technology, Tokyo, Japan
- Department of Management Science, Graduate School of Engineering, Tokyo University of Science, Tokyo, Japan
- 10. HOXO-M Inc., Tokyo, Japan
- 11. Yahoo Japan Corporation, Tokyo
- 12. Department of Epidemiology and Biostatistics, Indiana University School of Public Health-Bloomington, Bloomington, USA
- 13. Graduate School of Medicine, Hokkaido University, Hokkaido, Japan

Correspondence†

Prof. Hiroaki Miyata

Department of Health Policy and Management School of Medicine, Keio University, 35 Shinanomachi, Shinjuku-ku, Tokyo 160-8582, Japan

Tel: +81-35363-3774 | Fax: +81-33225-4828

1	Abstract		
2	Objectives		
3	The Japanese prime minister declared a state of emergency on April 7 to combat the outbreak of		
4	coronavirus disease 2019 (COVID-19). This declaration was unique in the sense that it was		
5	essentially driven by the voluntary restraint of the residents. We examined the change of infection		
6	route by investigating contact experiences with COVID-19-positive cases.		
7			
8	Study design		
9	This study is a population-level questionnaire-based study using a social networking service (SNS).		
10			
11	Methods		
12	To assess the impact of the declaration, this study used population-level questionnaire data		
13	collected from an SNS with 121,375 respondents (between March 27 and May 5) to assess the		
14	change in transmission routes over the study period, which was measured by investigating the		
15	association between COVID-19-related symptoms and (self-reported) contact with COVID-19-		
16	infected individuals.		
17			
18	Results		
19	The results of this study show that the declaration prevented infections in the workplace, but		
20	increased domestic infections as people stayed at home. However, after April 24, workplace		
21	infections started to increase again, driven by the increase in community-acquired infections.		
22			
23	Conclusions		
24	While careful interpretation is necessary because our data is self-reported from voluntary SNS		
25	users, these findings indicate the impact of the declaration on the change in transmission routes of		
26	COVID-19 over time in Japan.		
27			
28	Keywords		
29	Japan, COVID-19, Social network service, contact experience with COVID-19 cases		
30			

Introduction

The World Health Organization (WHO) officially declared the outbreak of coronavirus disease 2019 (COVID-19) to be a pandemic on March 11, 2020. Since the first deaths were reported in early January [1], as of May 6, 215 countries and territories have confirmed COVID-19 cases, with 3,595,662 cases and 247,652 deaths reported worldwide [2, 3]. In response, the Japanese prime minister, Shinzo Abe, declared a state of emergency in 7 of the 47 prefectures on the evening of April 7 [4], and this was extended to become nationwide on April 16 [5] due to a gradual increase in polymerase chain reaction (PCR)-positive COVID-19 cases with an untraceable pathway of infection. The declaration had limited legally enforceable measures, which is different from the so-called 'lockdowns' (e.g. city blockades with penalties) that have been in place in the US, the UK, France, Germany, Italy and India, and it is essentially driven by the voluntary restraint of the residents in Japan [4]. In this sense, Japan has a unique Japanese-style lockdown policy based on the voluntary efforts of residents to weaken the spread of the infection, with no penalties for going out or commercial activities.

In infectious disease control, capturing the real-time epidemiological situation is a key factor to control the spread of the infection. To address this issue, COOPERA (COvid-19: Operation for Personalized Empowerment to Render smart prevention And care seeking), a new health care monitoring system, has recently been launched in a collaboration with the Kanagawa prefectural government and LINE Corporation as a way to monitor the spread of COVID-19 and associated societal factors [6]. LINE provides Japan's largest mobile messenger application with 83 million monthly active users (covering 65% of Japan's total population). COOPERA asks participants about their individual information, including medical and psychiatric conditions, and contact experiences with other individuals. In response to the given information, COOPERA provides personalised assistance, such as telephone consultation for participants who report serious symptoms [7]. Data collected by COOPERA have been used to monitor the real-time situation of COVID-19 and its usefulness for medical decision making has already been shown [8-10].

In this study, we focus on the change of association between COVID-19-related symptoms and (self-reported) contact experience with COVID-19-positive cases over time, including before and after the state of emergency. In particular, we investigate the time trend of (1) domestic infections (i.e., within-household infection) and (2) community-acquired infections with an unknown route of transmission. In addition, by examining the impact of the voluntary Japanese-style lockdown policy, this study provides a useful insight not only for Japan but also for other countries that are preparing to relax their lockdowns in the near future.

Methods

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COOPERA used LINE's chatbot system to request (1) basic characteristics of participants, including age, gender, occupation, medical history, preventive actions and postcode, and (2) health conditions, including current and past month's symptoms (presence or absence of fever, strong feeling of weariness or shortness of breath) and duration of these symptoms. In particular, we focused on fever in this study. Participants with any COVID-19-related symptoms were asked additional questions about their contact experiences with COVID-19-infected individuals, and, if yes, they were asked about their relationships with these individuals (e.g. if they were colleagues, classmates or family members). Participants with any COVID-19-related symptoms were followedup daily and those without any symptoms were followed-up once every 4 days. COOPERA recruited participants either via the QR code page on the prefecture's website or via the banner at the top of the screen. We used data from 1,386,330 participants who lived in the Tokyo metropolitan area, including Tokyo, Kanagawa and Saitama prefectures, between March 27 and May 5, 2020. In these prefectures, the declaration of emergency was in effect from April 7. In addition, the Governor of Tokyo, Yuriko Koike, requested cessation of nonessential or/and nonurgent travel from/to other prefectures and requested that individuals stayed at home from March 25 [11]. Due to the LINE Corporation's policy, users (and the COOPERA participants) are restricted to individuals aged ≥15 years old. Participants who reported contact with a COVID-19-infected individual when the relationship was with a family member who did not live in the same household or was with some other person (i.e. not a colleague or classmate) were excluded from the analysis. Proportions were plotted after taking a rolling 7-day-window average with confidence intervals (CIs) derived from 1000 bootstrap iterations. To examine the change points in the proportion, a piece-wise linear regression model was fitted with (at most) ten knots [12]. The difference in slopes before and after the estimated change point(s) was tested using the Davies test [13]. For those who had multiple answers, only the first answer was extracted. It should be noted that the populations of Tokyo, Kanagawa and Saitama prefectures were 13.9, 9.20, and 7.34 million, respectively, as of March 2020.

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Results

Characteristics of participants

Table S1 in the supplementary material shows the basic characteristics of the participants. In total, 121,375 of 1,386,330 respondents (8.76%) reported that they had a COVID-19-related symptom, and among them, 2937 (0.21%) reported having been in contact with a COVID-19-infected individual; these individuals were defined as the contact group. In addition, among the contact group, 2570 (93.1%) participants reported that the COVID-19-infected person with whom they had contact with was a colleague or classmate, while 207 (7.50%) reported that it was a family member in their household.

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104	Comparisons	of fever rate
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Figure 1 shows the proportion of participants reporting a fever at each study timepoint, stratified by contact experience (left) and relationship with the COVID-19-infected individual (right). The daily proportion of participants experiencing fever was higher in the contact group than in the noncontact group throughout the study period. Between April 17 and 24, there was a significant change (p < 0.001), with no upward trend in the contact group; however, after April 24, the proportion with fever in the contact group started increasing again and was parallel to the noncontact group. In terms of the proportion of individuals experiencing fever, stratified by the relationship with the infected persons, this remained higher in the group with infected family members living together than in the group having contact with infected colleagues or classmates throughout the study period. The difference between the group having contact with infected family members living together and the group having contact with infected colleagues or classmates has widened since March 30 (1.71 times higher in the former group) and peaked at April 27 (2.56 times higher in the former group).

(Figure 1 here)

Discussion

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This is the first study to examine the real-time COVID-19 epidemic in Japan stratified by contact experience and relationship with COVID-19-infected persons by using a surrogate indicator (i.e. fever). The proportion of those who had a fever showed an increasing trend in the contact group, followed by a stable trend between April 17 and 24 (10-17 days after the declaration of the state of the emergency on April 7 among the prefectures in this study). However, the proportion of individuals with fever in the in the non-contact group, which corresponds to infections of unknown transmission route, steadily increased throughout the study period. In addition, the proportion of those experiencing fever among the group who had contact with infected family members living together and the group who had contact with infected colleagues or classmates continually increased; the gap between these two groups was greatest at around April 27. There were no special events around April 27 that would have impacted the time trend other than the declaration of emergency that was issued on April 7. This evidence implies that the declaration may have reduced the number of contacts mainly at workplaces and classrooms, with an approximate 2week time-lag and the epidemic was moved to the domestic transmission phase because most people were staying in their homes. This impact of the declaration was effective during the initial stage, but approximately 2 weeks after the declaration, workers staying home were exposed to the risk of the infection (measured by a fever) as the number of community-acquired infections with an unknown route of transmission started to grow.

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This study has several limitations. First, fever is one symptom, although not an absolute indicator, of COVID-19 infection. Second, the number of participants who reported having contact with an infected individual and with an infected family member living in the same household was approximately 1/50 and 1/500, respectively, of the total number of participants who reported no contact with infected individuals (see Figure S1 in the supplementary material). Therefore, it should be noted that the proportion may not be stable on some days due to a small number of respondents. Third, the difference in available information about the symptoms of family members and those of colleagues and classmates might be a source of bias (e.g. information on family members was easy to obtain, but that of classmates and colleagues was relatively difficult). Other limitations are discussed extensively elsewhere [10, 14].

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In conclusion, given that Japan has a unique and weak lockdown policy with limited legally enforceable measures, the results of this study provide a useful insight for preparing for second or third waves of COVID-19 without enforcing a strong lockdown in other countries, such as Europe, the US and in low- and middle-income countries.

155	Figure legends
156	Figure 1: Plot of the rolling 7-day-window average of the proportion of participants who had a
157	fever with bootstrap confidence intervals. The left pane is a comparison between contact/non-
158	contact groups and the right pane is a comparison between the relationship status of the
159	participant with the COVID-19-infected persons.
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161	Supplemental Figure 1: Number of respondents at each time period, stratified by contact
162	experience and relationship with the COVID-19-infected individual. The left and right panes are the
163	denominator and numerator for the plotted proportion in Figure 1, respectively.
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166	Author statements
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173	information provided to the participants from professional perspectives.
174	
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176	Ethical approval was granted by the ethics committee of Keio University School of Medicine, under
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178	
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183	manuscript; or decision to submit the manuscript for publication.
184	
185	Competing interests
186	Hiroaki Miyata reports a grant from the Ministry of Health, Labour and Welfare of Japan, and
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188	Johnson, outside the submitted work. All other authors declare no competing interests.
189	
190	Author contributions
191	All authors took responsibility for the integrity of the data and the accuracy of the data analysis. All
192	the authors made critical revisions to the manuscript for important intellectual content and gave

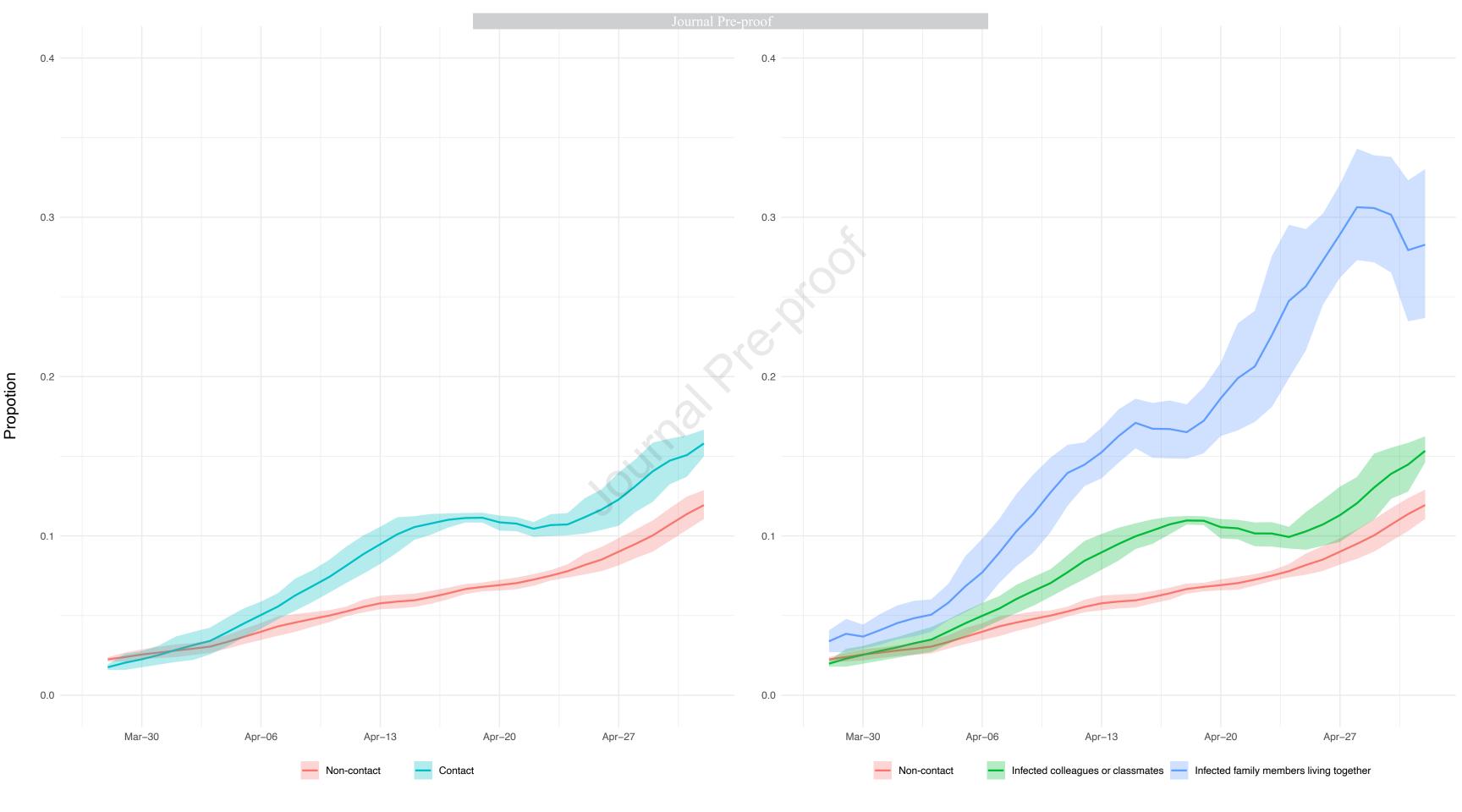
- final approval of the manuscript. The opinions, results, and conclusions reported in this paper are those of the authors and are independent from the funding bodies.
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Highlights

Following a weak lockdown, the transmission route of COVID-19-related symptoms changed.

COVID-19 monitoring responses from over 120,000 social networking service users in Japan were used for analysis.

The emergency declaration prevented infections in the workplace and increased domestic infections.

Even lockdown with limited enforcement may prevent the spread of infection.