Investigating Social Contact Patterns and their Role in Transmission Dynamics during the COVID-19 Pandemic in Japan

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Thesis submitted in accordance with the requirements for the joint degree of
Doctor of Philosophy
of the
University of London and Nagasaki University
January 2025

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Funded by Nagasaki University "Doctoral Program for World-leading Innovative and Smart Education" for Global Health, "Global Health Elite Programme for Building a Healthier World" (WISE)

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Declaration

Statement of Own Work

I, Tomoka Nakamura, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in my own thesis.

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January 2025

Abstract

The global pandemic of coronavirus disease 2019 (COVID-19), caused by the spread of the respiratory virus, SARS-CoV-2, challenged all countries in disease control. While many countries implemented lockdowns, Japan shortened business hours and issued non-binding public health recommendations without lockdowns. Although Japan has the second largest aging population in the world, the cumulative confirmed COVID-19 deaths per capita were reportedly 10 to 40 times lower than the United States and United Kingdom from 2021 to 2022.

Person-to-person interactions can impact the spread of respiratory infections. Social contact surveys provide crucial insights into these behaviors during epidemics.

This PhD thesis focused on two aims:

1. Collect data on contact patterns relevant to disease transmission using social contact surveys in Japan.
2. Explore the role of contact patterns and other factors in disease transmission through mathematical modeling.

In Japan, the mean number of contacts in 2021–2023 reduced by 50% compared to pre-pandemic times. Once governmental measures were relaxed, both frequency and duration of contacts increased gradually, but increased contacts were associated with longer hours of mask wearing, denoting a generalized cautiousness of the population without government mandates.

Mathematical models were developed to explore incidence as well as variation and synchronicity in the estimated transmission rates across all 47 prefectures in Japan. An age structured model was used to explore the impact of heterogeneity in contact patterns, vaccination, and demography, specifically focusing on Okinawa, the southernmost and westernmost prefecture of Japan, due to its unique epidemiological situation compared to other prefectures.

This PhD research spans the entire process, from designing and implementing social contact surveys to developing a mathematical model depicting COVID-19 dynamics in Japan. It underscores the critical role of social contacts in infectious disease transmission and highlights how cultural and country-specific factors influence human behavior during a pandemic.

Acknowledgements

First, I would like to wholeheartedly thank my supervisors, Dr. Kathleen O'Reilly, Prof Koya Ariyoshi, and Dr. Motoi Suzuki for all the support and guidance they have given me throughout my PhD. It was not an easy time to embark on this journey during the COVID-19 pandemic, but I thank Kath for believing in me even at times when I didn't believe in myself, Koya for the support and mentorship I received in Nagasaki, and Motoi for encouraging me to pursue my social contact study in Japan. I greatly appreciate Prof Hitoshi Oshitani for his continuous guidance since the day he reviewed my work as an examiner for my upgrading and Dr. Katie Atkins for her technical advice and connecting me to Prof Yoko Ibuka whose Japanese contact survey data has been instrumental for my research.

I would like to thank my friends and colleagues at Nagasaki University who welcomed me from the day I arrived in Nagasaki. To Dr. Toshihiko Sunahara who always made time to answer my questions on mathematical modeling, Dr. Lina Madaniyazi who has been my mentor in Nagasaki since the early days of my PhD, Dr. Chris Smith for his kind guidance during my time in Nagasaki, Dr. Akira Endo for his advice and support for my contact surveys, Dr. Kazuyo Machiyama, Rie Ogata and Fumiyo Tsujita for their generous support who made it possible for me to focus on my research.

I would also like to thank Dr. Melissa Jogie at University of Roehampton who invited me to take part in the collaborative research using qualitative methods. My thanks also extend to my mentors and supervisors at WHO—Marta Gacic-Dobo, Fatima Serhan, and Varja Grabovac—who continue to be my role models in public health and gave me courage to transition from my career at WHO to starting my PhD. I thank Prof Joanne Katz who gave me confidence in pursuing global health and epidemiology, Prof Akiko Shimamura who trained me to become a scientist, and Keiko Auckerman whose compassion to help those in need triggered my interest in a career in public health. My thanks go to Vanessa for helping me stay grounded and get through difficult times. I am grateful for my LSHTM and Nagasaki PhD classmates whose career trajectories have been inspiring and constantly reminding me that I wasn't alone throughout my PhD. It would have been much more isolating without you all as we faced work and life difficulties during the COVID-19 pandemic.

I would like to thank my parents, Masaya and Yumi Nakamura for letting me pursue my dreams. Without their support, I would not have been able to study and work abroad for more than half my life where I continued to live in countries that were many time zones away from Japan. Finally, I thank my husband, Luca Malatesta, for the endless emotional support, the countless days of cooking that you did for me, your help in coding and trying to disentangle infectious disease

epidemiology from a geologist's perspective, and fully believing in me that I could get to the finish line.

I dedicate this work for all the people who were impacted by the COVID-19 pandemic including those whose lives were lost, have had loved ones pass away, those who are still struggling to fully recover, and all the healthcare and public health workforce who fought the battle during the pandemic, both behind the scenes and at the frontline.

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Abbreviations

R_0	reproduction number
R_e	effective reproduction number
R_t	time-varying reproduction number
3C's	sanmitsu (in Japanese), stands for settings that are closed, crowded and close-contact
AIC	Akaike Information Criterion
CI	confidence interval
COVID-19	coronavirus disease 2019
CRR	Contact Rate Ratio
ED	Emergency Declaration
HER-SYS	Health Center Real-time Information-sharing Systems on COVID-19
MHLW	Ministry of Health, Labor and Welfare
NESID	National Epidemiological Surveillance of Infectious Diseases
NIID	National Institute of Infectious Diseases
PCR	polymerase chain reaction
PHSM	Public Health and Social Measures
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
SEIR	Susceptible-Exposed-Infectious-Recovered
VOC	Variant of Concern
WHO	World Health Organization

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Chapter 1 Overview

In this first chapter, I introduce the research context of my thesis, its rationale, general aims, and objectives. The last section provides a thesis structure to guide the reader how each chapter illustrates the stated aims of this research.

1.1 Introduction

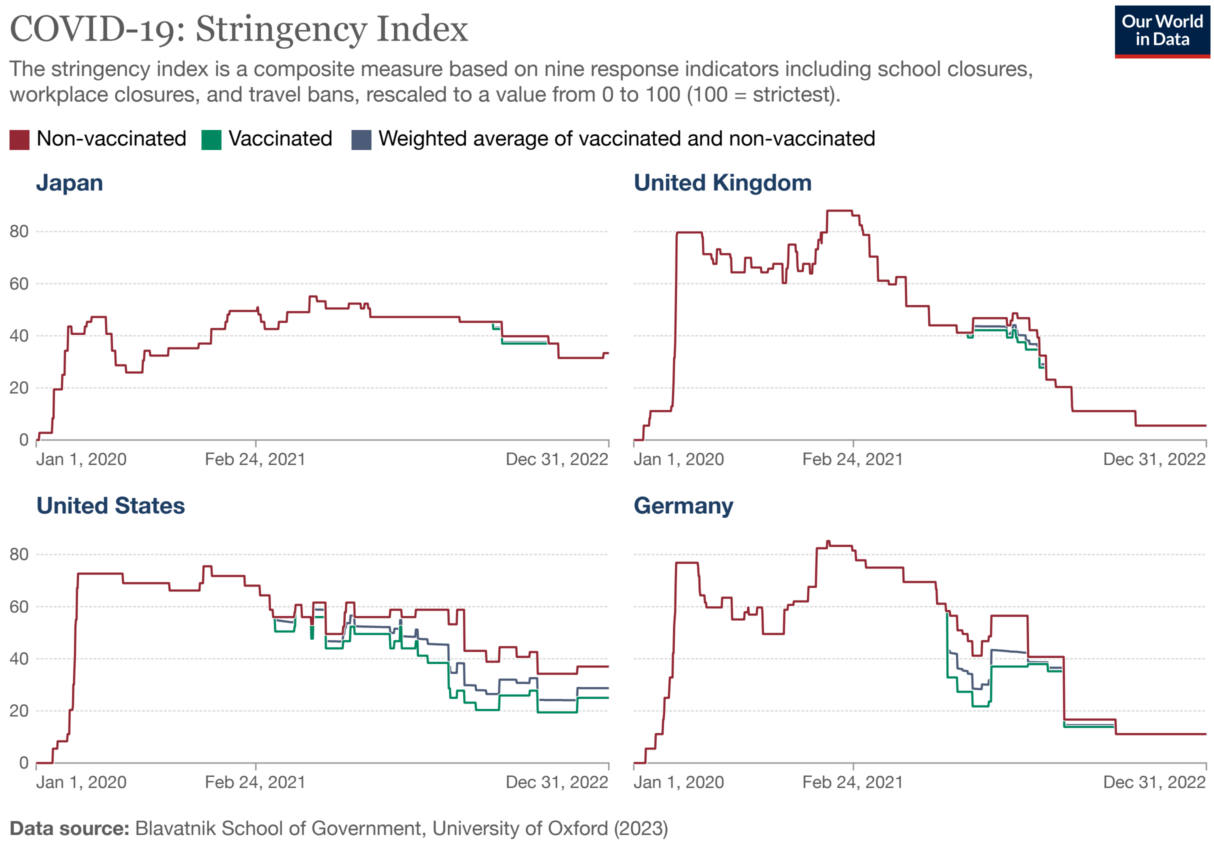
The global pandemic of coronavirus disease 2019 (COVID-19), caused by the spread of the respiratory virus named SARS-CoV-2, challenged all countries in disease control. As of September 2024, over 776 million cases of COVID-19 have been reported with more than 7 million deaths across the world (1), making it one of the most influential pandemics in history. A single case that was first identified in China in December 2019 soon became hundreds and thousands, spreading to almost every country in the world by March 2020. After the pandemic was categorized as a global health emergency, we started to grasp a better understanding of how SARS-CoV-2 spread which consisted mainly of airborne transmission. A prime example was the superspreading event that occurred at a church gathering in South Korea in February 2020 that sparked an outbreak in the next two months (2). Another important characteristic of the disease that we learned with time is how transmission not only occurred from individuals with symptoms but also from pre-symptomatic (infection before onset of symptoms) and asymptomatic (infection with no symptoms) individuals (3).

Without clear knowledge of the characteristics of the emerging pathogen and no vaccine or treatment yet for the disease, many countries took initial action by implementing strict lockdowns, school and business closures, and shutting country borders. China, New Zealand, South Africa, United States, and many western European countries including the United Kingdom, France, and Italy implemented lockdowns with stay-at-home orders. There were countries, such as Sweden, that relied primarily on herd immunity and did not implement any restrictions, except for shielding the older populations, to prevent the spread of COVID-19 (4).

In addition to lockdowns and stay-at-home orders in these countries, public health and social measures (PHSMs) were simultaneously implemented. PHSMs include non-pharmaceutical interventions such as physical distancing, handwashing, and mask wearing to prevent the spread of infectious disease transmission (5). Although these interventions have been understood to “flatten the curve” of an epidemic by buying time to develop new vaccines and medication, PHSMs were implemented in addition to lockdowns in these countries that makes evaluating the effectiveness of lockdowns difficult (6). In the US, after the first statewide PHSMs were implemented in 2020, a study showed difficulties in disentangling associations between changes in growth rate of COVID-19 cases and statewide restrictions on internal movement (i.e. lockdowns) (7). A mathematical model that utilized mortality data from 11 European countries from February 2020 to 4 March 2020 showed that PHSMs centered around lockdowns were effective in lowering the time-varying reproduction number (R_t) to less than 1 (8). On the contrary, a Bayesian model evaluated the impact of PHSMs in 34 European countries and 7 non-European countries (9). The results showed how stay-at-home orders implemented on top of PHSMs that were already in place had limited additional effect in lowering R_t (9).

Although Japan had strictly closed its country's borders throughout the pandemic, it did not implement any lockdowns and relied mostly on non-binding public health recommendations that were relatively less strict compared to other countries. Emergency Declarations (EDs) were issued in Japan that consisted of closure or shortening of hours among businesses (e.g. restaurants, bars), stay-at-home recommendations, and limiting movement between prefectures (10). Physical distancing measures were legally binding in countries such as France (11) and the UK (12) where individuals were fined when not abiding by the law. One of the factors that made Japan unique compared to other countries was its difficulty in assessing the strictness of the governmental recommendations that were not always legally binding. The Oxford Stringency Index was frequently used to characterize and compare COVID-19 related interventions across countries (13). However, its limitation was that it was based on governmental interventions, such as school and workplace closures, that took place in countries such as the UK, Germany, and the US but were minimal in Japan (**Fig 1.1**).

Fig 1.1 The trend of COVID-19 Oxford Stringency Index in the United Kingdom, United States, Germany, and Japan from 2020 to 2022.

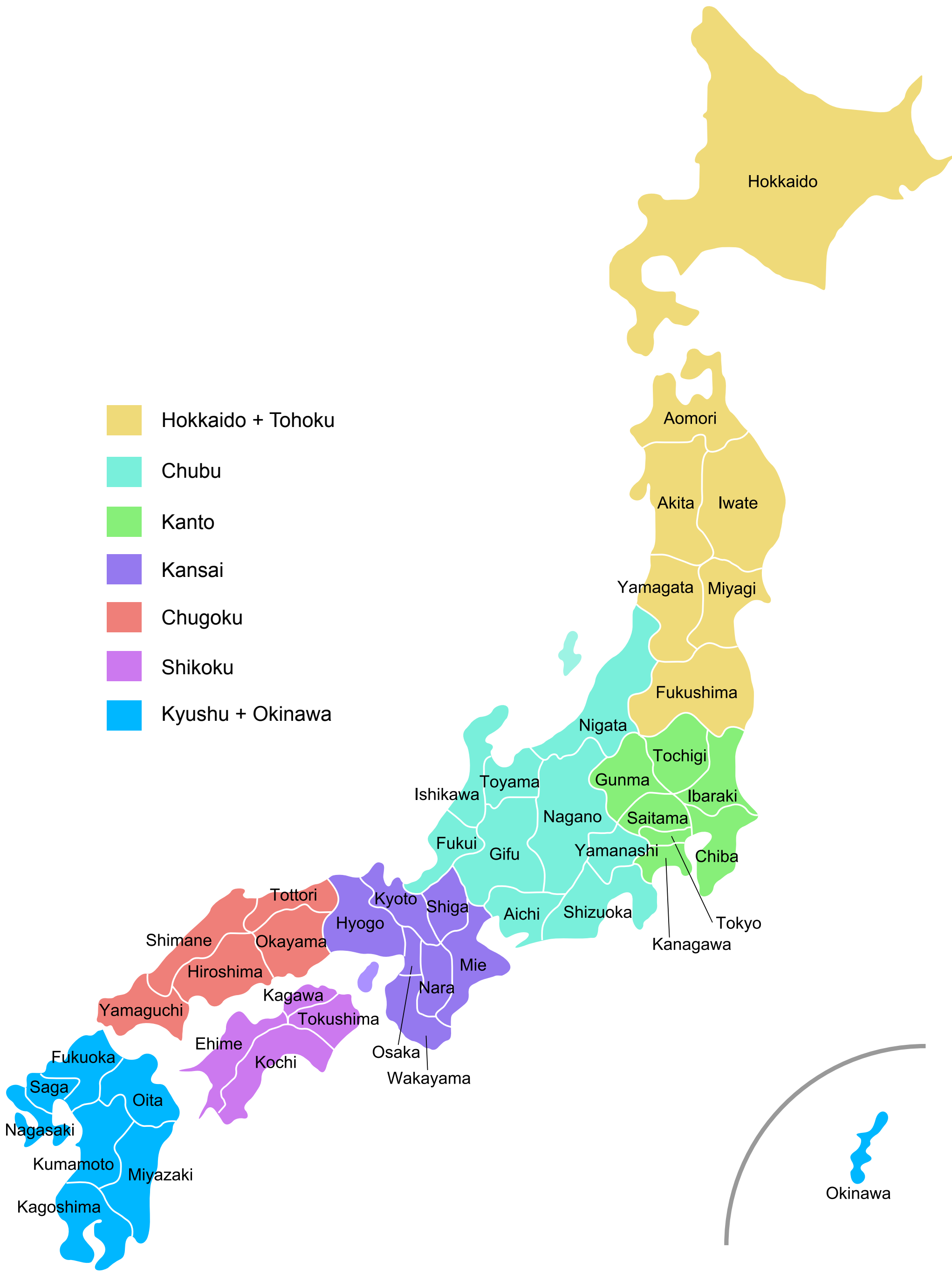


One of the stricter regulations was international border control that prohibited entry into Japan for tourists and business purposes (14). The level of strictness determined by the Oxford Stringency Index continued to hover between 40 and 50 from 2021 to 2022, showing the challenge of assigning a score on the various governmental recommendations that were often not legally binding. When EDs were lifted and transitioned to semi-EDs with less strict recommendations, these were implemented at the city/village/ward level depending on the incidence, so even within the prefecture, governmental policies can differ (15), making the Japanese context difficult to assign a numeric value on various COVID-19 related recommendations.

Although many of the COVID-19 policies were not legally binding, one of the key messages that was addressed to the public from early 2020 was to avoid the "**3Cs**" (***sanmitsu***) which stands for settings that are closed, crowded and close-contact (16). Backward contact tracing was also implemented early, an effective method in controlling SARS-CoV-2 by identifying not only the index case but also the upstream primary case that infected the index case (17). Patients with mild to moderate symptoms were isolated in hotels particularly during 2020-21 (18). Some prefectures, such as Tokyo, Osaka, and Fukuoka (**Map 1**) (adapted from (19)), that reported high COVID-19 incidence also enforced restaurants and bars to completely stop or limit the hours of serving alcohol and to reduce business hours as part of the ED. Osaka prefecture, located on the west of mainland Japan, has the third highest population next to Tokyo and Kanagawa prefectures (20). Fukuoka prefecture on Kyushu Island, which is south of mainland Japan, has the ninth highest population in Japan (20).

Map 1 Map of Japan with all 47 prefectures.

Each color indicates the specific region of Japan. Although Hokkaido and Okinawa are separate islands of Japan and considered to have their own separate geographical regions, Hokkaido is grouped together with the Tohoku region and Okinawa with the Kyushu region for analysis purposes.



This restriction was rooted from the policy to have people limit the 3C's as much as possible (21,22). Private testing for COVID-19 at hospitals began in early 2020 and focused on those with any cold or flu-like symptoms and close contact, but community testing was not a primary focus in Japan until much later in the pandemic. For instance, distribution of free rapid tests had started from February 2022 in Tokyo, the densest prefecture in Japan (20) with high COVID-19 incidence, after the start of the wave predominantly caused by the Omicron variant of SARS-CoV-2 (23).

Japan was also one of the countries that quickly gained attention by the global media due to one of the first major outbreaks of COVID-19 that occurred on the Diamond Princess cruise ship that was docked in Yokohama, Japan. Shortly after a former passenger had tested positive for SARS-CoV-2, the ship was placed under quarantine from 5 February 2020. After two weeks, a total of 634 people who were onboard tested positive for SARS-CoV-2 (24), eventually totaling to 712 people with confirmed cases (25). Among these confirmed cases, 328 (52.6%) were asymptomatic (24). Thus, the investigation of the Diamond Princess allowed researchers and public health experts to understand the clinical characteristics and severity of the disease as they discovered how asymptomatic cases can also lead to transmission (24). Additionally, they began to understand the transmission dynamics by investigating the contact between passengers, providing hints on the types of communal areas where human-to-human contact was common that could have led to the start of a transmission chain (26).

As the pandemic unraveled across the world with the introduction of SARS-CoV-2 variants, more countries began to actively test and conduct COVID-19 surveillance. Consequently, we began to see differences in cases and deaths due to the disease. Although Japan has the second largest aging population in the world after Monaco (27), the cumulative confirmed COVID-19 deaths per capita were reportedly 10 to 40 times lower than the United States and United Kingdom from 2021 to 2022 (28). This prompts us to ask what were the significant factors that led to lower incidence and mortality in Japan during a time when it became much more severe and harder to control in other parts of the world.

The global increase in incidence and mortality rates triggered the attention of governments and international organizations to accelerate the development and approval of vaccines. In December 2020, the UK was the first Western country that approved the use of any COVID-19 vaccine for mass vaccination (29). The first vaccine that was used in the UK was the mRNA vaccine developed by Pfizer-BioNTech, and many high-income countries followed with its introduction. Shortly after, another mRNA vaccine developed by Moderna, an adenovirus vector vaccine developed by Oxford-AstraZeneca and Janssen, and a recombinant vaccine developed by Novavax were prequalified by

WHO for emergency use (30). In Japan, mass vaccination started from February 2021, starting first with healthcare workers and then the older populations aged 65 and above and individuals with underlying diseases (31). By December 2021, 75% of the Japanese population completed the primary series (two doses) of the COVID-19 vaccine (32).

COVID-19 vaccines have been highly effective in reducing mortality and severe disease, but SARS-CoV-2 variants began to circulate globally from 2021, starting from the Alpha variant (B.1.1.7) that was first discovered in the UK (33). With increased transmissibility (34) and severity of disease (35), it became categorized as a Variant of Concern (VOC) by WHO which is a list of SARS-CoV-2 variants that potentially have serious implications on global health (36). The Beta variant (B.1.351) was discovered in South Africa which was also categorized as a VOC (36) with increased transmissibility and severity of disease (37). Later, the Delta variant (B.1.617.2), another VOC, was first discovered in India and became the predominant variant that circulated globally from May 2021 (38). Incidence in Japan had lowered significantly in the summer of 2021 until the Delta variant started to replace the Alpha variant in August 2021 (39), triggering the fifth wave of COVID-19 across the country. Shortly after in November 2021, the Omicron variant, starting from BA.1, was first detected in South Africa and Botswana (33), becoming the predominant strain globally throughout 2022 and 2023. Although the Omicron variant and its subvariants had increased transmissibility compared to earlier variants (40), they showed characteristics of lowered severity (41) especially among individuals who were vaccinated (42).

Although mass vaccination of the primary doses and boosters were under way, particularly among high-income countries, much of the concern was whether these variants evaded immunity after natural infection and vaccination. A meta-analysis of controlled trials and observational studies up until December 2022 showed that COVID-19 vaccines reduced infection, hospitalization, and mortality against any SARS-CoV-2 strain (43). This included also the Omicron variant, yet its vaccine effectiveness was lower than that of other variants (43). With evidence on evading immunity across the subvariants of Omicron (33), booster doses were newly developed that target Omicron.

Even though there is still a risk of new SARS-CoV-2 variants emerging today, WHO’s declaration of COVID-19 being a public health emergency came to an end in May 2023 (44). By the end of this declaration, more than 765 million COVID-19 cases were reported with nearly seven million deaths (44). Japan gradually reduced the strictness of public health emergencies; the last ED was issued in August 2021 and lifted in September 2021 (15). It transitioned to issuance of semi-EDs from 2022 in certain prefectures with high incidence; this constituted of lighter recommendations compared to an ED where there were no stay-at-home recommendations and entire closure of business policies but can still consist of shortening of business hours and limiting social contacts in 3C settings (15). The last semi-ED was lifted in March 2022 (15). As of 8th May 2023, COVID-19 was downgraded as an infectious disease from Category II to Category V (45). This included transitioning from daily active surveillance to sentinel site surveillance reporting at a weekly basis and ending the overall public recommendation to stay at home due to COVID-19 (45). However, COVID-19 vaccination continued to be recommended and free of charge for residents in Japan throughout 2023 (45).

One of the major difficulties of this pandemic was to decide how and when to relax some of the restrictions and strong public health recommendations that were in place. This was because there has not been clear scientific evidence on which PHSM was effective at what time point and where. One of the main objectives in implementing PHSM is to limit the person-to-person contact to reduce transmission. The challenge behind this is that person-to-person contact can be measured in various ways and the definition of a "contact" can vary depending on the method of measurement. Human mobility, as mentioned here in my PhD thesis, is defined as movement recorded from mobile phones. The definition of a contact recorded from contact surveys can slightly vary depending on the study design, but these contacts are based on a survey, diary, and/or phone interviews that directly ask an individual about the nature of their contacts. A study in Germany measured human mobility that showed a reduction in long-distance travel within the country, leading to flattening the curve of the epidemic in 2020 (46). On the other hand, in Denmark, weekday travel significantly reduced due to lockdowns, but mobility increased during the weekend (47). France also showed a 65% reduction in mobility, but the change in reduction varied by region and associated with socioeconomic disparities (48). A computer-assisted telephone interview survey conducted in Poland in 2020 showed that decreases in contacts depended on the type of occupation (49). In the UK, shortly after the first lockdown in March 2020, there was a 74% reduction in contacts per participant compared to pre-pandemic times based on contact surveys (50).

During the three years of the COVID-19 pandemic, a wide range of scientific studies was conducted globally that delved into understanding the disease better. Even after the end of the global public health emergency declaration, continuous studies were done to understand about the disease. There are studies that explore the mechanism behind long Covid which consists of symptoms such as fatigue and breathlessness that can continue to linger for months and years after being infected with the disease (51). Long-term impacts on mental health after lockdowns and isolation, such as due to school closures, are still being studied among individuals across all ages, highlighting the risks of these interventions (6). Studying the biological characteristics of SARS-CoV-2 gave rise to developing new vaccines that target the virus and its variants. Analyzing the epidemiological situations along with the appropriate PHSMs that were implemented throughout the pandemic led to a deeper understanding of COVID-19 transmission patterns.

For my PhD, I focused primarily on quantifying social contact patterns in Japan during the COVID-19 pandemic from 2021 to 2023. By designing and implementing social contact surveys at key time points with various governmental recommendations during the pandemic in Japan, I explored how certain aspects of human behavior stayed consistent throughout the pandemic while there were key elements of contact patterns that changed compared to pre-pandemic times. To elucidate the role of heterogeneities in contact patterns on COVID-19 transmission dynamics, I focused on developing a mathematical model that incorporated age-specific contact patterns, as well as vaccination coverage and demographic characteristics, specifically for Osaka, Fukuoka, and Okinawa prefectures.

1.2 Rationale for this Thesis

Having started my PhD studies during the COVID-19 pandemic from September 2020, it was an intense period when infectious disease epidemiologists and public health experts were in urgent need. As I had spent the first year of my PhD in Nagasaki from 2020 to 2021 and being a Japanese national, I was in a unique position where I experienced the Japanese pandemic response firsthand. It was a period with high level of uncertainty across the country. Prior to vaccine introduction, the primary concern of most hospitals was the lack of beds allocated for COVID-19 patients. The level of occupancy at hospitals that admitted COVID-19 patients was one of the measures of severity of the COVID-19 situation in Japan in 2020 and 2021 (15).

Fukuoka, which is the ninth most populated out of 47 prefectures in Japan (20) and approximately 100 km north of Nagasaki on Kyushu Island, had a rapidly growing incidence like Osaka and Tokyo. It was one of the first seven prefectures that entered in a state of emergency where an ED was issued by the national government in April 2020 due to high incidence (15). As the epidemic spread, there emerged a need to devise tailored policies and planning for each local setting. Many prefectural public health departments, including those of Nagasaki and Fukuoka, were initially forecasting incidence and necessary hospital beds based on a nationwide epidemic scenario modeling tool provided by the Ministry, of Health, Labor, and Welfare (MHLW). The model projections were being used to inform their policies, such as issuing prefecture-specific emergency declarations and broad recommendations to reduce contacts by 80% (52). Utilization of mathematical models to inform infectious disease control has been historically prevalent in a few countries including the UK, but it was only until the COVID-19 pandemic when it was formally integrated into national-level policymaking in Japan. However, the model used by MHLW had limited flexibility in reflecting local contexts. Since I was physically based in Nagasaki in 2020 and 2021, I often observed a gap between how national policies were addressing the epidemiological situations in urban vs. suburban and rural areas because incidence tended to be higher in urban cities. Although the definition of a “contact” was not clearly defined in this general recommendation, reducing 80% of contacts in Tokyo for a working individual in their 30’s who commutes to work within the city can look very different from an equivalent individual but based in Nagasaki that has a population 9% of Tokyo (20).

Nagasaki University was also the sole academic institution in Kyushu with an expertise in infectious diseases and integrating epidemiology and mathematical modeling in a public health context. These factors prompted the establishment of a task force in December 2020 called the COVID-19 Epidemiological Analysis Team led by Professor Koya Ariyoshi, Dr. Toshihiko Sunahara, Dr. Akira Endo, and me to focus on analyzing the epidemiological situations of the prefectures in Kyushu. As a team, we approached the Fukuoka prefectural office in November 2020 to see if we could join efforts in the COVID-19 response. We presented a mathematical model that forecasted COVID-19 infections and the hospital bed occupancy in Nagasaki. This triggered the attention of the Fukuoka policymakers as they wanted to see a similar model for Fukuoka city and the entire prefecture. In December 2020, I was invited back to their prefectural office to better understand their surveillance system and understand how the cities of Fukuoka prefecture were reporting case-based data to the prefectural office. This is described in more detail in **Chapter 2**.

The general recommendation to reduce contacts by 80% and limiting contacts in 3C settings were common public messages throughout the pandemic in Japan, but with existing data that was publicly available, it was difficult to quantify the level of change of contacts with respect to time and governmental recommendations. Mobility patterns in Japan have been explored using mobile phone data (53,54), and they are useful in assessing the aggregate changes in human movement across a wide geographical area. Social contact survey data, on the other hand, is unique because they provide highly resolved, individual data on contacts that are essential for understanding transmission. The first large-scale, repeated social contact survey that was implemented in the UK shortly after the first lockdown in March 2020 was the CoMix study led by LSHTM (50). As of 2020, Japan did not yet have a contact survey study done during the pandemic, and there were two studies that quantified Japanese contact patterns during pre-pandemic times (55,56). There was a research gap on the characteristics of contact patterns in Japan throughout the pandemic and to what extent they might have changed with time. To address this research gap, I designed and implemented social contact surveys in Japan—first in Fukuoka and Osaka prefectures and later also in Okinawa, the southernmost and westernmost prefecture of Japan, due to its unique epidemiological situation of COVID-19 compared to prefectures in mainland Japan. The results from the contact surveys are described in **Chapter 3** where it explores some of the specific changes and consistencies seen in contact patterns during the different phases of the pandemic in Fukuoka and Osaka. Individual characteristics and behavior associated with changes in contacts are also highlighted.

Another incentive for conducting these contact surveys was to establish a mathematical model that incorporates Japanese age-stratified contacts with an aim to further understand the role of contacts in disease transmission. The initial model that was developed to support Nagasaki and Fukuoka prefectures did not incorporate age-stratified contacts, but it went through multiple iterations to capture the COVID-19 transmission dynamics of the rest of Japan. This is illustrated in **Chapter 4**. In **Chapter 5**, the model was adapted to incorporate age-stratified contacts, vaccination coverage, and demographic characteristics of Fukuoka, Osaka, and Okinawa prefectures with an aim to uncover how each component is attributed to infections.

Additionally, I was invited by Dr. Melissa Jogie from University of Roehampton to apply for a COVID-19 grant funded by the British Academy. Along with other colleagues from University of Roehampton and Nagasaki University, we were successfully awarded with the grant, and I joined as a co-investigator on a comparative research project between Japan and the UK to explore the public's understanding of public measures and vaccination policies during COVID-19 (57). The results from this qualitative study have been published in BMC Public Health (May 2024) and included in **Chapter 6** as this contributes to having a more comprehensive understanding of the COVID-19 epidemic in Japan.

My PhD research spans the entire process, from designing and implementing social contact surveys to developing a mathematical model depicting COVID-19 dynamics in Japan. It was also possible to oversee how mathematical models were used in policymaking at the city and prefectural level. At the start of the pandemic, many of us did not foresee its level of severity and the extent of how long it could continue to circulate across the world. In fact, I had started my PhD with a completely different topic in mind which was to investigate the epidemiology of rotavirus and cost-effectiveness of the rotavirus vaccine in Japan that was introduced in its routine immunization program in 2020. As I had previous work experience in evaluating the effectiveness of the rotavirus vaccine in low- and middle-income countries, my original PhD topic would have been a natural transition. However, I had applied for the joint PhD program with LSHTM and Nagasaki University even before SARS-CoV-2 was detected across multiple continents. Consequently, from day one of my PhD, having regular face-to-face meetings with my supervisors, colleagues, and friends was impossible. During the first year of my PhD, I was fortunate to have been based in Nagasaki where the university remained opened, but it was early in the pandemic where COVID-19 cases were not openly discussed due to potential discrimination against those who became infected. All students and staff at Nagasaki University were obligated to monitor our health every day and record any presence or absence of respiratory symptoms on an online platform. There was also a school policy that discouraged students to travel to prefectures outside of Nagasaki, especially to prefectures with a higher incidence, so meeting my co-supervisor, Dr. Motoi Suzuki, at the National Institute of Infectious Diseases (NIID) in Tokyo was out of the question. Because of the strict international border control in Japan as well as a 14-day quarantine requirement after returning to Japan from abroad, it made traveling between London and Nagasaki very difficult. It was an unprecedented situation, but it was a unique moment to gain skills in infectious disease epidemiology and mathematical modeling.

By taking advantage of this joint PhD program with LSHTM and Nagasaki University that allowed working with colleagues both in Japan and the UK, I decided to shift the focus of my PhD project. With the CoMix study that was already well under way in the UK, it was a chance for me to learn how to design the contact survey to fit the Japanese context and implement it during a dynamic time when the epidemiological situation was constantly changing. Although the COVID-19 pandemic has come to a halt, many questions remain today—from the biological characteristics of the SARS-CoV-2 virus itself to the overall effectiveness of PHSMs. This pandemic has impacted all of us in a way that we did not foresee—from the individual level, such as our health and mental wellbeing, to the country and global level where the economy took a fall. As there are ongoing discussions on how countries can learn from how they responded or *could not* respond in a timely way, the pandemic has highlighted a vast range of challenges that are unique to each country. The aim of this research is *not* to pinpoint what Japan did right or wrong on their pandemic response or to find an answer, if any, on why Japan had a lower COVID-19 mortality rate compared to other countries. With hopes to positively impact future pandemic preparedness and response, the aim of my research is to underscore the critical role of social contacts in infectious disease transmission and to highlight how cultural and country-specific factors can influence human behavior during a pandemic.

1.3 Aims

There are two overarching aims of my research:

Aim 1: Collect data on contact patterns relevant to infectious disease transmission through the usage of social contact surveys in Japan

Aim 2: Explore how contact patterns and other factors play a role in infectious disease transmission by using mathematical modeling

1.4 Research Objectives

With these two aims in mind, there are six main objectives of my research:

Objective 1: To design a social contact survey in a Japanese context during the COVID-19 pandemic (**Chapter 2**)

Objective 2: To describe the changes in social contact patterns in Japan during the COVID-19 pandemic—how did people behave with respect to government recommendations and how did they change with time? (**Chapter 3**)

Objective 3: To elucidate the contact patterns relevant in the transmission of SARS-CoV-2 in Japan—what were some of the specific behavior, individual characteristics and attitude that were associated with the frequency of contacts? (**Chapter 3**)

Objective 4: To illustrate the COVID-19 epidemic waves across all 47 prefectures in Japan using a mathematical model. (**Chapter 4**)

Objective 5: To investigate the roles of heterogeneity in contact patterns, vaccination, and demography on transmission dynamics in Okinawa, Fukuoka, and Osaka prefectures. (**Chapter 5**)

Objective 6: To compare the public perspectives on COVID-19 public health and social measures between Japan and the UK through a qualitative study. (**Chapter 6**)

1.5 Thesis Structure

By adapting the survey used for the CoMix study in the UK, I designed and implemented ten cross-sectional surveys from 2021 to 2023 in Fukuoka, Osaka, and Okinawa prefectures as described in **Chapter 2**. This chapter also illustrates the surveillance system of COVID-19 in Japan and my field experience at the Fukuoka prefectural office as part of the COVID-19 pandemic response. The results from the contact surveys are described in my research paper of which I included as a manuscript form in **Chapter 3**. This chapter explores how contact patterns evolved with time from 2021 to 2023 and how they were associated with implementation of governmental measures in Fukuoka and Osaka prefectures. **Chapter 4** illustrates the COVID-19 epidemic in Japan using a mathematical model. By using this model, the variation and synchronicity in the estimated transmission rates are explored across all 47 prefectures in Japan. It also introduces the unique transmission patterns of Okinawa. **Chapter 5** is a continuation of Chapter 4 as it delves into Okinawa by assessing how its contact patterns, vaccination, and demography were attributed to COVID-19 incidence compared to Fukuoka and Osaka prefectures. **Chapter 6** includes a published study that used qualitative methods to compare the public perspectives on COVID-19 public health and social measures in Japan and the UK. Finally, my thesis concludes with an overall discussion in **Chapter 7**.

Chapter 2 Design and Implementation of Social Contact Surveys in Japan

The focus of this chapter explores the method of designing the social contact surveys and the process of implementation during the COVID-19 pandemic in Japan. Being involved in the pandemic response by working together with the Fukuoka prefecture office was one of the factors that prompted me in having a better understanding of the changes in contact patterns in Fukuoka and other prefectures. This chapter starts with a brief section that describes the overall surveillance system of COVID-19 in Japan as well as observations and lessons learned during my experience with the pandemic response team at the Fukuoka prefecture office.

2.1 Surveillance methods of COVID-19 during the pandemic in Japan

Infectious diseases have been actively detected in Japan through the National Epidemiological Surveillance of Infectious Diseases (NESID) program (58). It includes pathogen reporting, which is a laboratory-based surveillance, and patient reporting based on notifiable diseases that are detected at clinics and hospitals where some participate as sentinel sites for active surveillance (58). When a specific disease is detected, it is first notified to the public health center, which is the local government. The data is entered into an online database of NESID which gets reported to the prefectural health department and then to the Ministry of Health, Labor and Welfare (MHLW) and NIID where it provides feedback to local governments (58,59). Since the surveillance system became a statutory initiative after the Infectious Diseases Control Law came into effect in 1998, it continued to be dynamic with emerging pathogens, such as SARS and Ebola, when sharing information globally became even more critical than before (59).

During the beginning of the COVID-19 epidemic in Japan in early 2020, COVID-19 cases continued to be reported through NESID without major issues because the number of cases was low. However, at the end of January 2020, five charter planes arrived in Japan from Wuhan where everyone was PCR tested and quarantined (60), and shortly after, in early February, an outbreak occurred on the Diamond Princess cruise ship that was docked in Yokohama, Kanagawa (61). During this time, it was still unknown if SARS-CoV-2 had airborne transmissibility, and the frontline healthcare workers were frantically trying to figure out containment and treatment methods. Based on the traditional way of reporting, healthcare workers at hospitals and clinics have been faxing the patient information forms to public health centers (58). However, with this way of reporting, there is a time lag of at least one day until the case reaches MHLW and NIID. The time involved in filling out the case investigation form by the healthcare workers and the processing of the amount of paperwork at the public health centers started to become an immense burden, prompting the national government to establish a new digital reporting system called Health Center Real-time Information-sharing Systems on COVID-19 (HER-SYS) (62). With an aim to lessen the burden of public health centers and to improve timely reporting of COVID-19 cases, the new system was created to allow healthcare facilities and testing centers to directly report the confirmed COVID-19 cases along with patient information, contact information, disease severity, laboratory test results and clinical outcomes.

Another new component of HER-SYS was that it aimed for general usage by the public. The general protocol was for an individual to update the local public health center via phone if they were in close contact with a confirmed COVID-19 case or if they developed any respiratory symptoms that resemble COVID-19 (63). HER-SYS aimed to reduce this step of reporting by allowing the individuals to directly enter their information online. By consolidating all data from individuals, healthcare facilities, and public health centers in one platform, the government from local to national level can quickly retrieve the epidemiological situation, leading to timely response to outbreaks. HER-SYS was pilot tested in mid-May of 2020 and was nationally introduced from 29 May. By 10 September, MHLW announced that all 155 public health centers across Japan started using the new system (63).

Although NESID was supposed to be discontinued for entering COVID-19 data once HER-SYS was implemented, it took time for the new system to be fully in operation (59). A MHLW survey was conducted in September 2020 to evaluate the usage of HER-SYS at the local governments of each prefecture and healthcare facilities (63). Among the 113 out of 155 public health centers that responded, 60% were reporting via HER-SYS on behalf of the healthcare facilities that were sending their case investigation forms by paper (63). In the second half of 2020, MHLW and NIID faced the issue of not being able to retrieve the aggregated number of COVID-19 cases from both systems (59). Consequently, a national COVID-19 cluster taskforce, including governmental and academic experts in public health to support MHLW in the pandemic response, decided to develop a completely separate COVID-19 case database (64). Although this database eventually used a semi-automated process of data collection, it initially required manual extraction of case information that was publicly available and updated daily on each prefectural website as part of their press release (64). This database became a critical source of information to update the Japanese Government Advisory Panel on COVID-19 for decision-making on disease control policies and evaluating the epidemiological situation of each prefecture (59,64).

Two factors were raised by Suzuki et al. (59) that made implementation and utilization of HER-SYS difficult: one was due to the overall lack of digitalization across healthcare facilities in Japan where based on a MHLW investigation, 57% of general hospitals and 50% of general clinics across Japan had electronic health records as of 2020. Even among those that utilized a digitalized system, many were not connected to the internet due to data security reasons. Because HER-SYS required internet connection, the reporting methodology was not practical for frontline healthcare workers, requiring them to enter the data multiple times. As COVID-19 cases grew, it forced them to resort back to faxing the case investigation forms to the public health centers, adding more pressure to the local government in providing timely feedback to them and relaying the information to the prefecture level. The second factor was the overwhelming number of variables that was collected through HER-SYS. It aimed to serve as one platform that allowed outbreak investigation through contact tracing as well as analysis based on diagnosis, hospitalization, and treatment methods. Although the number of priority variables reduced by the start of 2022 due to having to respond to a surge of cases during the circulation of the Omicron variant, HER-SYS ended up not being fully utilized to its maximum capacity, leading to its complete closure in March 2024 (62).

2.2 Field experience at Fukuoka

December 2020 was the beginning of the third wave of the COVID-19 epidemic in Japan when I had the opportunity to be invited back at the prefectural office of Fukuoka to understand the surveillance methodology of COVID-19 within the prefecture. During this time at the end of the year, it was a period of high caution across the world when the pandemic coincided with Christmas and New Year holidays for the first time. Although Christmas is not a national holiday in Japan, the days leading up to New Year's Day and the few days after are national holidays when many people return home to see their families. This also meant there would be inter-generational contact of people and higher person-to-person contact than usual, potentially putting older populations at risk from COVID-19 transmission. Vaccination was not yet introduced at this time, and thus, there was a higher risk for an infected individual to deteriorate with more severe symptoms, leading to death in some circumstances. Especially with an aging population in Japan, where 28.9% of the entire population is 65 years old and above (20), this was a growing concern.

At the Fukuoka city hall where the local public health center was located, an entire floor as big as a gymnasium was transformed entirely for COVID-19 response. The local public health center was indeed the first responders where case investigation forms were being sent from healthcare facilities and contact tracing efforts were occurring. Especially during the beginning of the pandemic, their responsibility was to contact each confirmed COVID-19 case through face-to-face interviews, phone calls, and emails for contact tracing. Particularly in March-April 2020, contact tracing was a key component of Japan's pandemic response; public health centers conducted full investigations to trace the clusters and superspreading events occurring in nightlife businesses, such as night clubs, bars, and karaoke (65). Based on this evidence, many of the nightlife districts were priority areas where outbreaks were first detected, and thus triggering the government to implement policies such as closing of nightlife businesses by 8 pm and discouraging restaurants and bars to serve alcohol (65).

At the Fukuoka prefectural office, the COVID-19 response team was divided into several groups including a team that focused on data management and updating the epi curves and descriptive analyses of incidence and deaths. Aggregated data was reported on the website of the prefectural office as part of the daily press release. Although the case-based data was sent daily in Excel spreadsheets from the public health centers, cross-checking the data through multiple sources was done manually. Epidemiological analyses that were done daily, such as epi curves, were printed and checked by the various levels of hierarchy at the prefectural office before they were made publicly available. Every day, at approximately 6 pm, the chief medical officer of Fukuoka would give a press release to give an update on the day's confirmed COVID-19 cases, the current epidemiological situation, and any changes to the prefecture's public health recommendations. HER-SYS had been implemented by this time, but there was no indication of its usage by the government officials as the number of cases, deaths, hospital bed occupancy were constantly being updated on a big whiteboard.

Phones were continuously ringing throughout the day and night, and paperwork with the most updated information of COVID-19 cases detected in Fukuoka prefecture was circulated across various teams for verification. While one team was dedicated in directly communicating with the local public health center of Fukuoka city to verify the city's epidemiological situation, a separate team focused on the logistics of quarantine facilities, including specially designated hotels, where patients with mild or asymptomatic cases were isolated. This also applied to individuals who had difficulties in self-quarantine at their own homes. Isolation of confirmed cases was part of Japan's early pandemic response, and these cases were also constantly monitored by the city and prefectural office (66). Another team monitored the availability of beds and ICUs at designated hospitals that were assigned to admit COVID-19 patients. The government employees worked in shifts across the teams to be able to handle sudden changes in policies and epidemiological situations. Some of them were seconded from various departments for specific time periods to meet the needs of the pandemic response.

One of the missions during my visit to the Fukuoka prefecture office was to convey the need to access the COVID-19 case-based data including information on the level of disease severity and whether each confirmed case required hospitalization. There was an increasing demand by the prefecture to forecast the number of hospital beds needed for severe cases as well as quarantine facilities needed for mild/asymptomatic cases. Hospital bed occupancy was one of the indicators that assessed the level of severity of the COVID-19 epidemiological situation, leading to changes in prefecture-specific policies such as recommending early closures of businesses. Especially during a period when it was leading up to the New Year holidays, the prefecture was calling out to the public to refrain from visiting families and moving outside of Fukuoka. During my visit, I was asked to meet in-person with the chief medical officer and the vice governor of Fukuoka with whom I explained the importance of active surveillance and the utility of a mathematical model in describing an epidemic that could help in decision making. I was reminded of the challenges in communicating science that could be understood by anyone including those who were unfamiliar with epidemiology and infectious disease control. Eventually, they understood the necessity of this work, granting the COVID-19 Epidemiological Analysis Team of Nagasaki University to access the case-based data that included the necessary variables for developing a mathematical model of Fukuoka prefecture.

2.3 Role of social contact surveys before and during COVID-19

During the third wave of COVID-19 in Japan when the cumulative number of cases in Fukuoka prefecture surpassed the peak of the previous wave, there were discussions at the prefecture office on issuing an Emergency Declaration (ED) within the prefecture. Even though an ED was not an equivalent to a lockdown, the national government continuously called for individuals to avoid the 3C's, to wear masks, and to handwash as part of PHSMs. This led me to ask how these practical recommendations relate to data that are used to inform transmission such as contact data.

When controlling respiratory infectious diseases, such as COVID-19 and influenza that are transmitted airborne, one of the aims of PHSMs is to isolate infections to curb transmission. Limiting person-to-person contacts is a key disease mitigation method since a "contact" is defined as the relationship between individuals that allows transmission of an infection (67). This is evident in the mathematical formula defined for the effective reproduction number shown below.

$$R_e = R_0 \times S = (c \times p \times D) \times S$$

First, in the above equation, the reproduction number, or R_0, appears which is the average number of secondary infectious individuals resulting from one infectious individual in a totally susceptible population. When R_0 > 1, the incidence of infectious individuals increases that can start an epidemic. When R_0 = 0, it reaches an endemic equilibrium when incidence remains stable in a population. When R_0 < 1, the incidence of infectious individuals decreases. The value of R_0 can vary depending on factors such as disease characteristics and transmissibility, contact patterns in the population, and duration of infectious periods. Depending on the availability of data on what we know about the disease and the population structure, R_0 can be estimated by using various equations. For instance, if individuals contact randomly and we know the proportion of individuals who are susceptible in getting infected, R_0 can be written as $\frac{1}{S}$ where S is the average proportion of the population that is susceptible. If we know the duration of infectiousness (D), the transmission rate (β), and the total population size (N), R_0 can also be written as βND assuming that individuals mix randomly (67).

As the number of infectious individuals increases with time, the proportion immune will also increase with time, leading to fewer transmissions from each infectious person. To appropriately describe this phenomenon, the effective reproduction number, or R_e, can be calculated where R_0 is multiplied with the proportion of individuals that is susceptible to the disease, indicated as S. R_e takes into account the changing proportions of susceptible individuals, and this can be due to those who have become immune from the disease through natural infection or vaccination. The number of contacts directly influences the transmission of a disease as R_0 can be written as the product of c, the number of effective contacts made by each person per unit time, p, the probability of resulting in an infection by an effective contact between two people, and D, the duration of infectiousness of the disease (67). It is the influence of these parameters on R_e that we use to frame how changes in contact patterns affect transmission in the context of COVID-19.

When we have data on age-specific contact patterns of a population, the number of secondary infections resulting from each infectious person depends on which subgroup (e.g. an age group) they belong. Based on these contact patterns across different age groups, a contact matrix can be developed which shows the average number of contacts between individuals in different age groups. Children, for instance, may have very different contact patterns compared to adults. Due to having different contact rates depending on age, individuals in different age groups will become infected at different rates. By using these age-specific contacts, the Next Generation Matrix can be calculated which is a matrix composed of the number of secondary infectious individuals caused by one infected individual in each specific age group. Here, R_0 can be calculated by taking the dominant eigenvalue of the Next Generation Matrix. To estimate R_e in a population that includes individuals who are immune, we can adapt the same methodology that was used for R_0, but instead of using the population size belonging to each age group, it can be replaced by the number of susceptible individuals (67). By incorporating age-specific contacts, this helps us model disease transmission that occurs across different age groups.

One of the common tools used to quantify and analyze contacts is a social contact survey. The first extensive social contact survey was the POLYMOD study conducted between 2005 and 2006 across eight European countries where individuals reported their physical and non-physical contacts on a single day (68). This study done by Mossong et al. showed that school-age children and young adults contacted the most with people of the same age. The study suggests that more than 80% of all reported contacts would be located either at home, school, workplace, and leisure settings. The social contact survey done in the UK during COVID-19, or the CoMix study, was adapted from POLYMOD where it defined a direct contact as "anyone who met the participant in person with whom at least a few words were changed or anyone with whom the participants had any sort of skin-to-skin contact" (50). This allowed a comparison possible with pre-pandemic contact patterns, demonstrating that contacts in the UK were reduced by 74% during the first lockdown (50). Although contacts increased shortly after the two lockdowns were lifted, contacts only reached about 50% of pre-pandemic levels based on CoMix results from March 2020 to March 2021 (69).

A systematic review was done by Liu et al. that comprised a total of 12 studies on social contact patterns from nine European countries, China, Kenya, South Africa, and the US in 2020 during the COVID-19 pandemic (70). All studies investigated contact patterns during and/or after national or regional lockdowns, showing marked reductions in contacts at work and community settings. In countries where schools and universities were closed, contacts among school-aged children and young adults (18 years or older) decreased to zero. Similar to the UK from what was found from the CoMix study, the mean contact rates among these countries did not reach pre-pandemic levels after PHSMs were relaxed. Because empirical studies on contact patterns have been limited to several countries before and during the pandemic, synthetic age-stratified contact matrices were developed for 177 geographical locations by combining empirical data from POLYMOD with country-specific survey data on household, school, and workplace settings (71).

Associations between contact patterns and COVID-19 infection can be investigated through contact surveys. A US study conducted by Nelson et al. had 3000-4000 participants complete two online surveys with questions adapted from the CoMix study and had them self-collect a dried blood specimen to test for their COVID-19 antibody level (72). Results showed that most of the contacts that were reported were at the workplace, and based on the comparison of two surveys that were done—once during the fall of 2020 and the second time in the spring of 2021—national contact rates were similar with one another. Nelson et al. found that individuals who tested positive for SARS-CoV-2 antibodies had a higher number of contacts than those who were seronegative. However, when the frequency of contacts was adjusted for age and race/ethnicity, it was not associated with serostatus, which suggests the importance of demographic characteristics on infection.

Another benefit of contact surveys is that the attitudinal questions can be asked, such as an individual's perception of risk in getting sick from COVID-19, as well as PHSMs on whether they wore masks, belonged to a high-risk category, and their COVID-19 vaccination status. Based on the CoMix study design, 21 European countries were compared between March 2020 and March 2022 that showed an association of higher contacts outside the home among individuals who wore masks, were vaccinated, and had concerns about getting infected (73). Another study based on CoMix that was conducted across 16 European countries between December 2020 and September 2021 showed an association between vaccination status and frequency of contacts where vaccinated individuals had 1.31 times higher number of contacts than those who were unvaccinated (74). This study also found that those who perceived COVID-19 with high severity had lower number of contacts than those who were neutral or perceived the disease with low levels of severity.

Keeping in mind of the type of questions that can be asked in a contact survey, one of the key questions that arose was where and when a contact survey can be conducted in Japan to detect a possible change in contacts. Secondly, I needed to know which survey results can be used as the baseline for comparing contact patterns during pre-pandemic levels. It was important to have a sample size with sufficient power needed to detect a difference in contacts as well as considering the realistic possibility for the internet survey company to reach the minimum sample size and have the individuals respond to the survey. Initially, there was only financial availability for two cross-sectional contact surveys, so it was critical to pinpoint two specific dates when we could predict to see a change in contact patterns.

There was a possibility of using mobile phone data to assess human mobility as it is useful in understanding how humans move from one place to another and identifying areas within the city that show aggregate changes in density across time. For instance, Google mobility data showed anonymized data from mobile phone apps, such as Google Maps, to detect changes in human movement. Compared to pre-pandemic times from January to February 2020, Japan showed pronounced decreases in mobility during the pandemic especially during periods when EDs were implemented in 2020 and 2021 (75). Until 2022, there were short, sudden decreases in human movement at workplaces and transit places while there were increases in residential areas during long weekends or long national holidays that spanned for consecutive days. This could indicate how individuals were reducing their contacts during this time when they may have more control over their behavior outside of work/school hours. These patterns are similar to what was observed in the contact surveys I implemented; contacts were reduced by approximately 50% compared to pre-pandemic times and they declined especially during periods with EDs. Contacts also declined during the weekends compared to weekdays. Detailed results from the contact surveys are discussed in the next chapter.

However, there are limitations to what we can conclude from analyzing mobile phone data. Although Google mobility data is publicly available, it lacks in granularity at the city or prefecture-level, so assessing the influence of region-specific contact patterns on incidence is difficult. It also does not provide individual-level data with covariates, such as age, occupation, vaccination status, and other factors that can be related to transmission. Mobile phone data serves as a proxy of an actual human-to-human contact and does not necessarily reflect an epidemiologically relevant contact. With a relatively high older population in Japan, they may not be using mobile phones as frequently as the younger populations and their mobility may be underrepresented when solely relying on mobile phone data. To analyze how individual factors were associated with changes in contact patterns with time, it would not be possible with mobile phone data, and a contact survey is one of the methods that can be used.

Since I hypothesized that contacts will be reduced the most during a period with highest restrictions, such as during an ED, I initially aimed to conduct one survey during an ED. I planned for the second survey to be implemented shortly after lifting of an ED, based on a hypothesis that contacts will increase again. It also made realistic sense to choose Fukuoka prefecture as one of the locations to conduct the survey since I was working closely with its prefectural office and had access to its COVID-19 case-based database. Broadening the sample population to include Osaka prefecture also made sense demographically, as it was the third most populated prefecture in Japan (20), and with its high COVID-19 incidence, a second ED was issued along with Fukuoka at the same time in 2021 (15). Osaka was also a prefecture where daily cases of COVID-19 and their epidemiological information were made publicly available.

The first two contact surveys took place in February 2021 during the middle of an ED and the second in March 2021 once the ED was lifted. Additional funding from Nagasaki University and NIID allowed me to conduct eight more subsequent surveys until 2023. The timing of each survey was semi-strategic as it was planned during expected changes in contact patterns and funding availability. For the last two contact surveys conducted in December 2022 and February 2023, Okinawa was added in addition to Fukuoka and Osaka. This was to address another research gap on what was driving higher incidence seen in Okinawa compared to the rest of Japan. Although the daily number of reported cases was reported for each prefecture on national news and through the MHLW, there was barely any study or report that investigated what was happening in Okinawa that set itself apart from other prefectures.

To compare contact patterns prior to the COVID-19 pandemic, there were two Japanese studies that could be referred as the baseline. One study was conducted by Munasinghe et al. in 2014 targeting all 47 prefectures from a total of 1476 households (2271 participants) including children (55). Another study was conducted by Ibuka et al. in 2011 that targeted a total of 3146 participants from all prefectures of Japan (56). Both studies conducted the surveys online (the survey done by Ibuka et al. was done also by mail targeting individuals above 65 years old). Both surveys asked the participants on the frequency, location, and age of the contacts. Munasinghe et al. asked the participants to record their contacts in a diary format, once during a weekday (one of the days between Monday and Friday) and the second time during a weekend (Saturday or Sunday). The study by Ibuka et al. asked the participants to record all contacts from the previous day. I adapted the design of my contact surveys by referring to the CoMix study and initially the Munasinghe et al. survey as I had contact with the researchers who were involved in both studies and thus had detailed information on the survey design. However, after further investigation on the age-stratified contact matrices published by Munasinghe et al., I found that the analysis was incomplete as it was limited to quantifying 0-10 contacts. Although their survey allowed participants to record over 10 contacts, they were not included in their overall calculation of age-stratified contacts which underestimated the total number of contacts reported per individual. This ultimately led me to choose the Ibuka et al. study as the baseline (i.e. pre-COVID-19 contacts) since their data was comprehensive and included all reported contacts per individual. Thanks to the support of Professor Yoko Ibuka, I had access to the detailed information of the Japanese age-stratified contact matrices from their study in 2011.

2.4 Design of the social contact survey questions in the Japanese context

During the process of designing the contact survey in Japanese, there were two key factors that were considered. One was to capture the essence of contact patterns of any individual living in Japan and second was to be able to compare the contact patterns in the UK by using the CoMix study. During the beginning of the pandemic and prior to the global circulation of the Omicron variant, there were stark differences in incidence and mortality due to COVID-19 between the two countries. As this sparked curiosity among many public health experts and researchers, I was eager to design my surveys that allowed comparison of contact patterns between Japan and the UK.

Firstly, the definition of a contact was important to clarify before the participants recorded their contacts. A direct contact from the CoMix study was defined as follows:

"Anyone who met the participant in person with whom at least a few words were exchanged or physical contact was made." (69)

For the Japanese contact surveys, a contact was defined similarly in Japanese but clarified that it can be either non-physical contact, which consists of face-to-face contact with at least three words in exchange during a conversation regardless of mask wearing or physical contact. Examples of physical contact were given including handshakes, hugs, kisses, playing contact sports, and sharing the same bed. It was important to give examples of physical contact because in Japanese culture, greetings and conversations with physical contact are rare in public settings. Also, in public transport such as on trains and buses, people can bump into each other and physically contact one another, but this was not included as an example of a contact. Contacts that we assumed were epidemiologically relevant to transmission were listed as examples.

Directions were given at least a week before the participants reported their contacts in the survey, so they could familiarize with the design of the survey and understand how they should report their contacts. In addition to these directions, a detailed description of the study and the motivation behind this research was explained in Japanese which also served as an informed consent. The participants were provided with this description, and if they agreed to proceed, they were given access to the online survey to fill in their response.

As part of the directions on how to participate in the survey, the participants were given beforehand the same table (as on the survey) with the questions on their daily contacts. Participants were asked of their contacts including their age, sex, type of contact (physical/non-physical), location of contact, duration of contact, and whether the contact was indoors, outdoors, or both. This information was for the first 10 contacts, and the participants can enter the name or initials of the contact for ease of memory and recording. If they did not know the exact age of the contact, they had the option to select an age category ranging from 0-9, 10's, 20's, 30's, 40's, 50's, 60's, and 70+. If they did not contact anyone during the day, zero reporting was also possible. These age categories were initially selected because these were used by the 2014 contact survey done by Munasinghe et al. and the initial plan was to utilize their data as baseline contacts. Only after the implementation and analysis of the first few contact surveys did I discover that the baseline contacts were from incomplete data, leading me to change plans and utilize the contacts from the 2011 Ibuka et al. study. Like the CoMix study, the age categorization could have been done differently with children divided into 0-4 and 5-17 years old to distinguish school-aged children. In my surveys, the exact age of the participants was reported, but when reporting the ages of contacts, I emphasized the importance of ease of reporting for the participants. If one did not know the exact age of their contacts, it is easier to distinguish age by decade instead of by school grade. The plan was to conduct repeat contact surveys with the same participants, so it was important to keep the survey simple and retain as many participants as possible. It was necessary to also be mindful about the minimum sample size that was necessary to detect a difference in contacts between each age category and thus needed to limit the number of age categories. When a statistical model was utilized to analyze how different factors were associated with change in contacts, age categorization of the participants was done to distinguish school-aged children based on the hypothesis that their contact rates would be higher.

For those who contacted more than 10 people, they could enter additional information on the next question in an aggregated way where they entered an approximate number of contacts categorized in three main locations including workplace, school/university, and other. For the age of the contacts, they could choose from three categories that ranged from 0-17, 18-59, to 60+ year olds (multiple selection possible). Although these age categories were not as granular as the 0-10 contacts, it allowed us to evaluate whether the contacts were among children (0-17), adults (18-59), and/or the elderly (60+). It was important for the participants to be able to report on the over 10 contacts because some professions, such as healthcare workers, school teachers, and store clerks can be in contact with many people during the day.

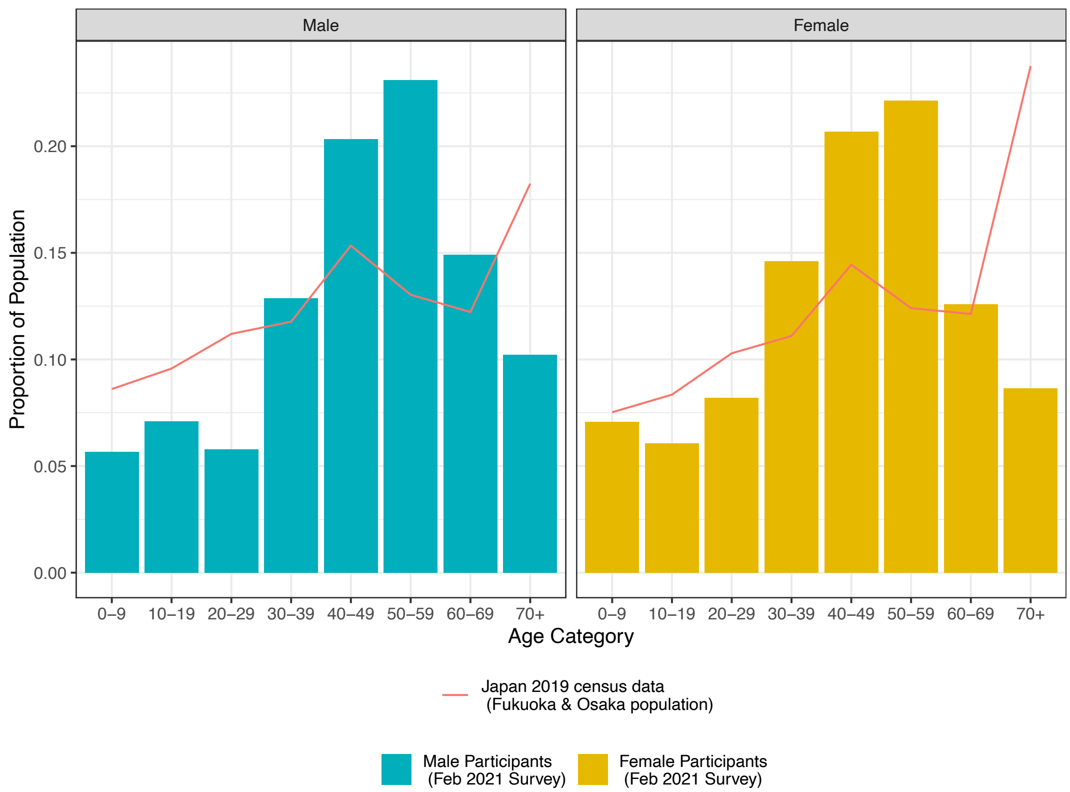
The location of contacts was adapted specifically to the COVID-19 context in Japan. Based on the governmental recommendations for people to avoid 3C settings at restaurants and bars, these locations were captured in the surveys. Izakaya (small bars where alcohol is often served), karaoke, and movie theaters were also included in the same category as these were often enclosed places that may not be well-ventilated. All these locations were included in the same category, but when it was decided that the survey was going to be implemented at multiple time points, it was important to re-assess the survey questions to align with the governmental recommendations. Location of “restaurants” was separated from “bars, izakaya, and karaoke” as the latter involved serving of alcohol. The motivation behind going to these locations often involved alcohol consumption. Movie theaters were also differentiated as a separate location based on an assumption that individuals would most likely be wearing a mask and not speaking at this setting. Based on the 10 contact surveys from February 2021 to February 2023, individuals were wearing masks between 3-4 hours per day, showing high compliance and consistency in mask wearing. Mask wearing has been reported to be common in East Asian countries such as Japan (16,76,77) where it was already a familiar disease mitigation method before COVID-19. For instance, an observational study of elementary school children conducted in 2015 at a suburban city in Nagano prefecture found that there was a 14.1% decrease in odds (odds ratio of 0.859, 95% CI: 0.778-0.949) in being infected with seasonal influenza among those who were wearing masks (78).

The sample size calculation was referred to the method used for the UK CoMix study (indicated in Supplementary Information) (50). A two-sample t-test calculation was done with a range of 700 and 800 participants per prefecture (total of approximately 1500 in Fukuoka and Osaka prefectures) across eight age categories. This would have a power of about 90% with a 5% Type 1 error, standard deviation beween 4.5 and 5, and 20% loss to follow-up to detect a mean difference of 2.5 contacts between two surveys across eight age categories. The recruited survey participants were from a pool of individuals who have been previously registered by the internet survey company. Based on the number of registered individuals per prefecture, the survey company can assess whether a specific sample size is feasible. Since Fukuoka and Osaka prefectures have a relatively large population, it was possible to have a sample size of approximately 750 from each prefecture. We proceeded with the sample size of our contact survey after assessing its power and consultation with the survey company of its feasibility and cost.

Survey participants included all ages, and children younger than 18 years old could have their parents or guardians to report on behalf of them. However, attitudinal questions, including their risk perception on COVID-19 and willingness to be vaccinated against COVID-19, were limited to adults aged 18 years and above. Participants in the same household were also permitted to participate as individuals, and among these participants, they were given a unique household ID in addition to a unique ID, so it was possible to link individuals from the same household. All participants were allowed to take part in the survey at multiple time points. The survey asked basic characteristics of the participants including their age and relation to their family if more than one person in the same household was participating in the survey. In the CoMix study, adult participants were asked about their salary range. This question was considered to be included for the Japanese study, but reporting annual incomes could be a personal and sensitive topic, so I limited to questions regarding their occupation and education level. The survey asked about the number of people in the same household which was defined as anyone who lived in the same address with a shared kitchen. This included individuals who lived in a shared house, apartment or dormitory that shared a kitchen.

Survey participants were compensated 300 Japanese Yen (equivalent of approximately 1.50 British Pounds) per survey which was provided as monetary credit that they could use online. The internet survey company regarded this as a higher end of compensation due to the relatively high level of detail of the survey questions. To check for representativeness among the survey participants, the first survey (February 2021) population characteristics were compared with the Japanese census data reported from 2019 (**Fig 2.1**). The younger populations under their 30's and the individuals aged 70 years or older were slightly underestimated.

Fig 2.1 The population distribution by age category among males and females residing in Fukuoka and Osaka prefectures based on the February 2021 contact survey**.**
The bar charts compare between the survey population and Japanese census data (red line) from 2019.



The gender balance of the survey participants reflected the overall Japanese population where 51.4% were female (2021 census) (20) and a range of 51.7% to 53.9% of the survey population were female (**Chapter 3 Table 3.1**). To account for these differences, the mean number of contacts was weighted by populational age and sex of Osaka and Fukuoka prefectures.

As previous contact survey studies have shown that there was a difference in the number of contacts comparing weekdays vs. weekends (55,56,68), my contact surveys asked the participants to report their contacts twice during a given week—once during the weekday and once during the weekend. Any day that was a national holiday between Monday and Friday was excluded as a "weekday" since such a day could be equivalent to a weekend. The change in status of an ED was one of the key factors in deciding when the survey was going to be implemented. Additionally, there were long holidays, such as Golden Week that consists of consecutive days of national holidays in early May. Days around these long holidays were considered as potential timepoints when changes in contacts might be observed. Surveys were implemented shortly after Golden Week (May 2021) and once during December 2021 and January 2022 with an assumption that there may be a surge in contacts during the New Year holidays.

When the survey questions were designed first in Japanese, I translated them into English (**Chapter 9 Appendix 1**) to receive feedback from English speakers at LSHTM. The Japanese version was also distributed among Nagasaki University's Department of Clinical Medicine and the administrative staff of the School of Tropical Medicine and Global Health. I received feedback from people with health and non-health backgrounds on the wording of the questions and answer choices, ease of understanding the questions, and length of the survey. Based on the trial entries of the survey as well as from their feedback, the qualitative questions on the risk of getting infected with COVID-19 and views on vaccination could be difficult to evaluate in the Japanese context. When these questions are asked to respond on a scale (e.g. range from zero to five or zero to ten), participants in Japan may not tend to answer at extreme ends of the spectrum. Even when the question is worded similarly with CoMix, the same answer on the same quantitative scale given in a Japanese context may have different meanings. This was important to keep in mind when attitudinal questions were going to be compared across countries.

2.5 Conclusion and Main Takeaway

When designing and implementing a contact survey during an epidemic, I conclude with the following four takeaway points:

1. *Assess the epidemiological situation when and where the survey is taking place.*
During the COVID-19 pandemic, governmental recommendations were constantly changing depending on the incidence level. If there are financial constraints that limit the number of contact surveys that can be conducted, it is important to find the "best" time points when contact patterns can be analyzed. The aim of my contact surveys was not to elucidate the contact patterns of the

entire population of Japan, which was why the sample population was not selected from all 47 prefectures. It was to capture the potential *changes* in contacts seen across different ages during the different phases of the pandemic. Assessing the association of governmental measures with changes in contact patterns was another objective of the study. Selecting the sample population and the time points will widely vary depending on the research question.

2. *Evaluate the necessity of each question and its role in answering the research question.* Balancing the length of the survey with potential response fatigue is key. It is easy to add more and more questions as we often value the opportunity to conduct a survey for research, but as the survey becomes longer, the more time the participants need to fill out the survey and less likely they would want to participate again if the cross-sectional survey is done at multiple time points. Recall bias can also happen when trying to recall the contacts that we had during the day (e.g. reporting as an approximate number for 10+ contacts), so adapting the survey questions is vital. The key questions, such as the basic characteristics (e.g. age, sex) of the participants and their contacts, should appear in the beginning of the survey and additional "nice to have" questions that complement the research, such as attitudinal questions and vaccination status, should follow.

3. *Be mindful of the dynamic epidemiological situation and adapt the survey questions if necessary.* In an epidemic, the epidemiological situation as well as governmental recommendations and policies may influence how individuals behave. In some instances, such as in the UK, individuals belonging to a "high risk" category shifted as government advice changed with time, which impacted how this particular question needed to be re-worded in the subsequent CoMix surveys (69). When the Japanese contact surveys were implemented at 10 time points from 2021 to 2023, the first survey was implemented during the time when individuals aged 65 years old and above were receiving their first dose of the COVID-19 vaccine. By the time the 10th survey was done, the fifth dose was already available for adults. The brand of the vaccine was asked in the beginning of the pandemic, but towards 2023 in the final few surveys that were conducted, what mattered more was whether the individual was fully protected with two doses and at least one booster. There was a continuous introduction of new variants, and with more research, we accumulated more knowledge about the level of protection gained from being fully vaccinated. This demonstrates the importance of being flexible in how the survey questions should be designed especially when the survey is done at multiple times points in a dynamic epidemiological situation. Simultaneously, it is worth keeping in mind how timely the survey results are needed especially if these results can be used in decision-making during an epidemic. A simple change in the survey design during the middle of a study requires more time and effort put into data cleaning before results can be fully analyzed.

4. *Evaluate the nuance of the language used for the survey.*

Designing the survey in the local language is key when reaching out to the target sample population. The nuance of the wording of the questions and answer choices can vaguely differ depending on the language. Some type of questions, such as asking for the annual income, can be too personal in some countries like Japan, and the same answer can be referred by complementing with other questions. Since English is a common language for scientific peer-reviewed journals, many of the publicly available resources, such as previously designed contact surveys, are in English. However, when these surveys are designed in a different language, it is advisable to ask for feedback from those who are fluent in that language to check for clarity and ease in understanding. In a time-sensitive situation like during an epidemic, one can tend to rush through the design of the survey without thinking too much on the details such as evaluating the nuance of some questions. However, it is important to foresee that the same survey may be used at multiple time points in the future, and taking the time in the beginning to carefully design the survey in the appropriate language will lead towards reliable, high-quality data.

Chapter 3 Continuing to be Cautious: Japanese Contact Patterns during COVID-19 and their Association with Public Health Recommendations

3.1 Introduction

This chapter includes a manuscript that is currently under peer review (as of September 2024) in *BMC Infectious Diseases* with the following title, authors, and their affiliations. References of this manuscript are at the end of this chapter and supplemental figures are included in **Chapter 9 Appendix 2**. Some of the results covered from this manuscript were also presented in Japan's daily COVID-19 Strategic Advisory Board meeting held on 8 June 2022 at the Ministry of Health, Labor and Welfare. The abridged report (in Japanese) is included in Chapter **9 Appendix 3**.

Continuing to be Cautious: Japanese Contact Patterns during the COVID-19 Pandemic and their Association with Public Health Recommendations

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I was the lead author in this manuscript and made the following author contributions: Conceptualization, Methodology, Data Collection, Data cleaning and curation, Formal Analysis, Writing – original draft, Writing – review and editing.

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SECTION A – Student Details

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LSHTM Student ID No	1804403		
First Name(s)	Tomoka		
Surname/Family Name	Nakamura		
Thesis Title	Investigating Social Contact Patterns and their Role in Transmission Dynamics during the COVID-19 Pandemic in Japan		
Nagasaki Supervisor(s)	Professor Koya Ariyoshi		
LSHTM Supervisor(s)	Dr Kathleen O'Reilly		

If the Research Paper has previously been published please complete Section B, if not please move to Section C.

SECTION B – Paper already published

Where was the work published?			
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Where is the work intended to be published?	BMC Infectious Diseases
Please list the paper's authors in the intended authorship order:	Tomoka Nakamura, Ryo Kinoshita, Akira Endo, Katherine E. Atkins, Hitoshi Oshitani, Yoko Ibuka, Motoi Suzuki, Koya Ariyoshi, Kathleen M. O'Reilly
Stage of publication	**Submitted**

SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	My role for this research was the following: Conceptualization, Methodology, Data Collection, Data cleaning and curation, Formal Analysis, Writing – original draft, Writing – review and editing

SECTION E – Names and affiliations of co-author(s)

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SECTION F

I confirm that all co-authors have agreed that the above paper will be included in my PhD thesis.

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3.2 Abstract

Background: Despite implementing no lockdowns and having a large elderly population, Japan had a low mortality rate due to COVID-19 compared to Europe and North America. The extent to which policies impacted person-to-person contact remains unclear. In this study, we examined changes in contact patterns and their association with behaviors and governmental recommendations in Japan during the pandemic.

Methods: Ten social contact surveys were conducted between 2021 and 2023 reaching over 1500 participants per survey in Osaka and Fukuoka prefectures where governmental recommendations were first implemented due to high COVID-19 incidence. Their contact patterns were assessed through their demographic characteristics, COVID-19 vaccination status, and individual disease mitigation measures. Generalized linear models were used to identify factors associated with increased contacts.

Results: The mean number of contacts during the pandemic declined by at least 49.8% (8.2 weekday contacts and 6.0 weekend contacts per individual, adjusted by age and sex) compared to a study conducted prior to 2020. Weekdays, occupation, larger household sizes, and mask wearing were associated with a higher number of contacts. The frequency and duration of contacts were negatively associated with the issuance of COVID-19 governmental measures, yet the relative change in contacts was not as prominent as pre- and post-lockdown situations in the United Kingdom.

Conclusions: There was a gradual increase in contacts with time and less strict public health recommendations. Yet, contacts that did not increase with uptake of COVID-19 vaccination and continuous mask wearing depict cautious behavior across the survey population during the pandemic and into 2023. These results are in contrast with European countries where contacts largely increased among vaccinated individuals compared to the non-vaccinated. Social contacts are country and context specific, highlighting the need for data collection across different communities.

Keywords: COVID-19, social contact survey, contact patterns, statistical model, behavioral changes

3.3 Background

The reported cases and deaths due to coronavirus disease 2019 (COVID-19) in Japan have been much lower compared to Western countries such as Europe and North America. For comparison, as of 28 June 2023, there were 74,694 cumulative deaths in Japan in a total population of 125.5 million

(59.5 deaths per 100,000) while there was a total of 227,524 deaths in the United Kingdom with a population approximately half of Japan (337.9 deaths per 100,000) (1). Japan is also unique having the second largest aging population in the world, after Monaco, (29.9% of the total population who are 65 years and above) (2) who are at a higher risk of COVID-19 mortality. Throughout the pandemic from 2020 to early 2022, cumulative confirmed COVID-19 cases (adjusted by population size) were reported 10 to 15 times higher in the United States and United Kingdom compared to Japan (1). Several factors, such as timing of government regulations and behavioral change interventions, have been discussed as potential determinants of a successful epidemic control (3).

Apart from strict international border control policies, Japan relatively has had less strict rules compared to many other countries. Though public health emergency declarations (EDs) with different levels of strictness were issued, neither lockdowns nor curfews were implemented. National school closure due to COVID-19 regulation spanned for at least three weeks in March 2020, but most schools reopened between April and May 2020 (4). Yet, there were key messages that continued to be addressed to the public, such as avoiding the “3Cs” which stands for settings that are closed, crowded and close contact (5). Reducing person-to-person contact has been one of the key tactics in epidemic control as it directly shapes the risk of transmission of respiratory viruses (6).

To quantify these contact patterns, mobile phone data (7) and synthetic contact matrices (8) have been used. During the COVID-19 pandemic in Japan, mobile device data was utilized to investigate how governmental interventions could have impacted mobility (9,10). Social contact survey data is another important input for epidemiological and mathematical models of infectious diseases. It has its advantages over mobile device data as it can capture changes in contact patterns with respect to age and sex of both survey participants and their contacts. Additionally, disease mitigation measures, such as vaccination and handwashing, can be linked with contact data. Social contact surveys have been well-utilized prior to the pandemic, such as POLYMOD in Europe (11) and in Japan (12,13). They showed that contact patterns are highly dependent on age, gender, household size and day of the week (14). These studies provide a baseline of contact patterns prior to any physical distancing or public health related measures.

To elucidate the changes in contact patterns relevant in the transmission of SARS-CoV-2 in Japan, we conducted 10 repeated cross-sectional surveys from 2021 to 2023 (**Fig 3.1**). In this paper, we aim to describe the changes in social contacts and other behaviors, such as hand hygiene and mask wearing, during the pandemic and into 2023. As different levels of EDs were issued and lifted with time, we evaluated the association of these governmental measures on social contacts. We also present a statistical model that explores individual characteristics and behavior that impact the frequency of contacts.

Fig 3.1 Number of daily and cumulative reported COVID-19 cases and deaths in Japan.

The dashed vertical lines indicate each time point when the contact surveys were conducted beginning from February 2021 to February 2023. The darker pink rectangles indicate the periods when emergency declarations were issued in Osaka and Fukuoka. The lighter pink rectangle indicates the period of semi-emergency declaration that was issued in Osaka and Fukuoka. In **Fig 3.1a,** the green arrows indicate the beginning of the transmission period when at least 50% of the genome sequenced COVID-19 cases was due to specific variants of SARS-CoV-2. In **Fig 3.1b,** the purple arrow indicates the start of the Tokyo Summer Olympics in 2021. Navy arrows indicate national holidays in Japan. Light green arrows indicate the dates of mass vaccination that occurred sequentially based on priority groups.

Fig 3.1a Number of daily and cumulative reported COVID-19 cases in Japan with the timing of the social contact surveys in this study and key events related to COVID-19.

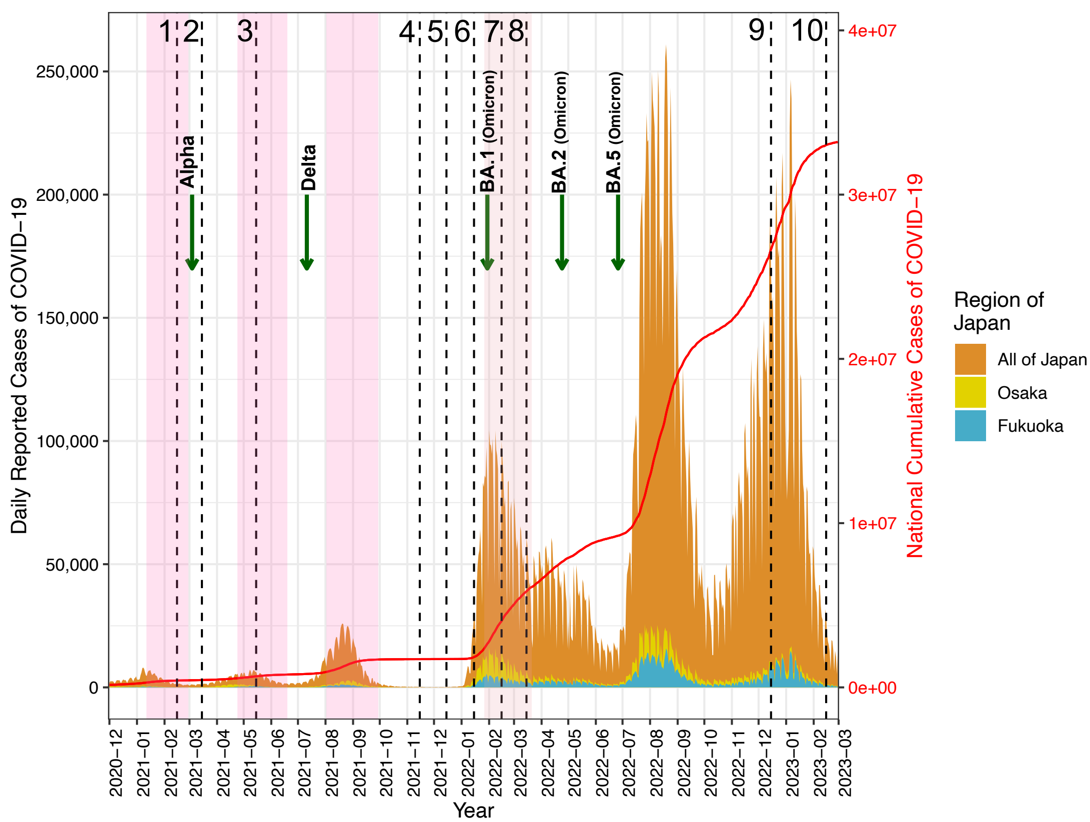
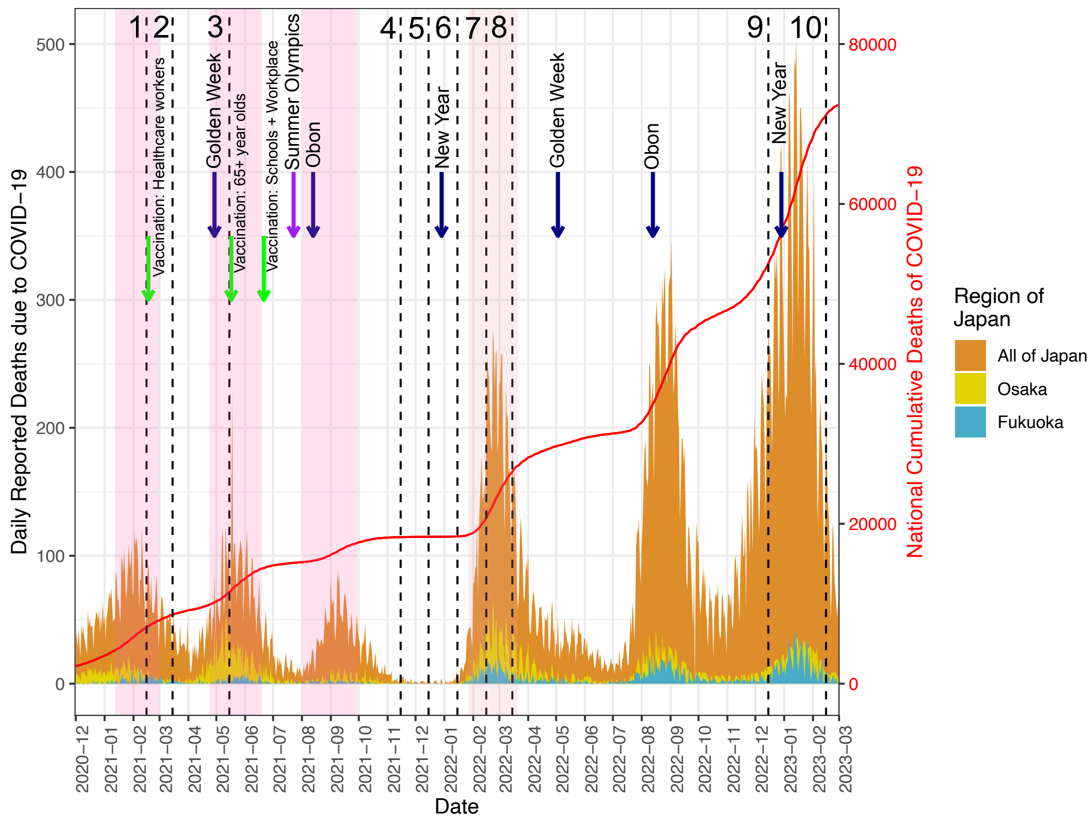


Fig 3.1b Number of daily and cumulative reported COVID-19 deaths in Japan with the timing of the social contact surveys in this study and key events related to COVID-19.



3.4 Methods

Survey design

Ten contact surveys, in which the participants were asked to report their individual characteristics and contact patterns, were conducted in Osaka and Fukuoka prefectures, Japan in 2021–2023 (**Fig 3.1**). Osaka prefecture is located on the west of mainland Japan and has the third highest population next to Tokyo and Kanagawa prefectures (15). Fukuoka prefecture is on Kyushu Island, which is south of mainland Japan, and has the ninth highest population (15). In 2021, three EDs were issued across Japan including Osaka and Fukuoka during which two surveys (#1 and 3, **Fig 3.1**) were conducted. During the height of the BA.1 (Omicron) transmission in 2022, a semi-ED was issued, which consisted of a less strict recommendation than an ED (Suppl. Table 1) (16). Two surveys (#7 and 8, **Fig 3.1**) were conducted during this time. Six surveys (#2, 4, 5, 6, 9, and 10, **Fig 3.1**) were conducted when ED was absent with the last survey in February 2023. The timing of the surveys was semi-strategic; they were planned during expected changes in contact patterns and funding availability.

Survey participants were recruited by a Japanese online survey company (F-press). Participants included anyone at least 18 years old residing in either Osaka or Fukuoka prefecture. Children under 18 years old participated with the consent of their guardians/parents who recorded their information on their behalf. Every individual in each household can fill out the survey as a participant, and all these individuals can be linked by household. The number of participants per survey was a minimum of 1,500, powered to detect a difference in contact numbers of 2.5 between pairs of observations with a 90% power and 5% Type I error and 20% loss to follow-up. The survey participants were compensated 300 Japanese yen per survey and were able to participate in as many surveys as they opted for between February 2021 and February 2023.

The survey was adapted from the UK CoMix study (17–19) in Japanese to capture the daily frequency and type of contacts. In each survey, they recorded their contacts during one weekday and one of the days during the weekend. A "contact" was defined as physical or non-physical: physical contact included handshakes, hugging, kissing, and playing a contact sport while non-physical contact was defined as facing another individual (with or without mask wearing) and exchanging at least three Japanese sentences to each other in a conversation. The participants were asked to record their contacts in a diary format with instructions a week prior to the day when the survey was implemented. They reported their contacts including their age, sex, type of contact (non-physical and/or physical), location of contact, approximate time of contact, and whether the contact was made indoors and/or outdoors (**Chapter 9 Appendix 2, Supp. Table 1**). These specified contacts were for the first 10 contacts. Those who reported more than 10 contacts were asked to approximate the number of contacts, location of contacts, and their age categories.

Participants were asked to report their individual characteristics as well as their individual preventive behavior such as frequency of mask wearing, handwashing, and teleworking (**Chapter 9 Appendix 2, Supp. Table 1**). They were asked COVID-19 related questions including their history of having tested PCR positive for COVID-19, their concern towards getting infected with COVID-19 (rank from one to five), and their vaccination status.

Statistical analysis

For each survey, we calculated the mean and median of contacts during the weekday and weekend, mean and median age, COVID-19 vaccine coverage, frequency of mask wearing, and the proportion of survey participants who tested COVID-19 positive. The population estimates of the mean contacts and vaccination coverage were adjusted by age and sex based on the 2021 October census (15).

We compared our data to contact patterns analyzed by Ibuka et al. (12) as baseline data prior to the COVID-19 pandemic. Their survey methodology was similar to ours; the data included all reported contacts per individual during the week as well as the duration and location of contacts. Their contact surveys were also conducted with an objective to understand influenza-related behaviors which is relevant in the context of respiratory disease transmission. For our study, contact patterns were stratified by weekday and weekend and compared across eight age groups (0-9, 10-19, 20-29, 30-39, 40-49, 50-59, 60-69, and 70+) and across the study period.

Measures of uncertainty in age-specific contact numbers and duration were obtained using the bootstrap; the mean and 95% confidence intervals (CI) were obtained by sampling with replacement for 1000 times. Consistent with previous contact survey studies, we truncated the total number of contacts to avoid a few observations with hyperinflated contact numbers affecting age-specific summary statistics (11,19). We selected a truncation cutoff of 250 through a visual check by plotting the mean number of contacts with a range of cutoff points using a Weibull distribution. (**Chapter 9 Appendix 2, Supp. Fig 1**).

To investigate factors associated with the reported number of contacts (February 2023 survey only), we used a multivariable regression assuming a Weibull distribution with log link function. This distribution was selected to address the coefficient of variation in reported contacts and fit the right skewed distribution of contacts better than a negative binomial distribution. The dependent variable was the reported contacts, and 15 variables were selected from a list of variables (**Chapter 9 Appendix 2, Supp. Table 1**) as the model covariates based on a hypothesis-driven approach. The model was referenced on a 40-49 year old individual who lives with two others works as a company employee at their workplace, and fully vaccinated against COVID-19 with at least 3 or more doses. The participants' age was retained in the model as it could be a potential confounder. All other covariates that were selected in the multivariable model were associated ($p < 0.05$) with the number of contacts in an univariable model. The multivariable model was developed using both forward and backward stepwise selections until the Akaike Information Criterion (AIC) had no further improvement. The incidence rate ratios calculated from the regression model are referred here as contact rate ratios (CRR) where the relative mean number of contacts per day is compared to the reference of each covariate. Model fit was examined with residual plots and comparing predicted vs.

observed data. When analyzing summary statistics of contacts across the various time points and age categories, the Kruskal-Wallis test was used. When comparing two nested generalized linear models to test the significance of a variable, likelihood ratio test was used.

All statistical analyses were done in R version 4.0.3, using the packages “MASS”, “survival”, “tidyverse”, “dplyr”, “reshape2”, “scales”, “rstatix”, “ggplot2”, and “cowplot.”

3.5 Results

Comparison of contact survey participants with national data

A range of 1513 to 1721 participants recorded their contact patterns between February 2021 and February 2023 in Fukuoka and Osaka prefectures, Japan (**Table 3.1**). Depending on the survey, the mean age of the participants was between 45 and 48 years old. Between 52 to 54% of the participants were female. As of the 2021 national census, the mean age of the Japanese population was 48.4 and 51.3% being female (15). COVID-19 vaccine coverage among the survey participants increased with time. In Japan, healthcare workers were first vaccinated in February 2021, followed by the older population (≥65 years) from March 2021, and the rest of the population from June 2021 (20). Vaccine coverage reported in February 2023 was slightly higher among the survey participants compared to the national vaccine coverage as of February 2023 (21). Compared to national vaccine coverage reported in January 2023, vaccine coverage across all age groups were slightly higher among the survey participants in February 2023 (**Chapter 9 Appendix 2, Supp. Figure 6**). The percent of individuals and/or household members having tested COVID-19 positive increased from 0.3% (5/1721) in February 2021 to 8.7% (136/1569) in February 2023. A serosurvey (N = 5627) conducted between 3rd February and 4th March 2023 showed 35.8% of Osaka residents and 31.3% of Fukuoka residents tested positive with infection-induced antibodies (22). Our survey appropriately approximated the national statistics in terms of demographics but with a slightly higher vaccination coverage and lower percentage of people who tested COVID-19 positive.

Table 3.1 Characteristics of participants across all the contact surveys conducted in Fukuoka and Osaka prefectures from February 2021 to February 2023 compared to pre-pandemic (baseline) contact patterns and the Japanese national census data.

	Survey dates	N	Mean age (Median age)	% Female (N)	Mean weekday contacts* (Median contacts)	Mean weekend contacts* (Median contacts)	% vaccinated (reported at least 1 dose) (N/Total)	% vaccinated (reported at least 2 doses) (N/Total)	% vaccinated (reported at least 3 doses) (N/Total)	Mean hours of mask wearing in a day (Median hours)	% individuals and/or household members having tested COVID-19 positive
Ibuka et al (baseline)	2011	3146	N/A	50.6 (1593)	16.3 (14)	12.8 (8)	N/A	N/A	N/A	N/A	N/A
This study	Feb 2021	1721	45.2 (48)	51.7 (890)	7.78 (3)	3.79 (2)	N/A	N/A	N/A	4.16 (2.5)	0.3% (5/1721)
	Mar 2021	1513	45.7 (48)	53.4 (808)	7.84 (3)	4.53 (2)	N/A	N/A	N/A	4.18 (3.0)	0.5% (8/1513)
	May 2021	1640	46.5 (49)	53.9 (884)	8.00 (3)	4.23 (2)	N/A	N/A	N/A	3.88 (2.0)	0.7% (11/1640)
	Nov 2021	1699	47.3 (50)	52.4 (891)	7.92 (3)	12.76 (3)	78.10 (1327/1699)	77.46 (1316/1699)	N/A	4.58 (3.0)	1.4% (23/1699)
	Dec 2021	1642	47.5 (50)	52.4 (860)	9.51 (3)	6.82 (3)	79.72 (1309/1642)	79.11 (1299/1642)	N/A	4.11 (3.0)	1.0% (17/1642)
	Jan 2022	1635	47.5 (50)	52.4 (857)	7.15 (3)	4.50 (3)	79.08 (1293/1635)	78.47 (1283/1635)	3.24 (53/1635)	4.17 (3.0)	1.1% (18/1635)
	Feb 2022	1614	47.4 (50)	52.7 (851)	8.35 (3)	4.93 (3)	78.56 (1268/1614)	78.19 (1262/1614)	19.83 (320/1614)	4.19 (3.0)	1.5% (24/1614)
	Mar 2022	1612	47.6 (50)	52.5 (847)	8.55 (3)	6.98 (3)	79.28 (1278/1612)	78.91 (1272/1612)	38.40 (619/1612)	4.00 (3.0)	2.0% (33/1579)
	Dec 2022	1533	48.1 (51)	52.7 (808)	8.07 (3)	6.41 (3)	83.69 (1283/1533)	83.04 (1273/1533)	73.91 (1133/1533)	4.07 (3.0)	6.8% (105/1533)
	Feb 2023	1569	48.2 (51)	52.1 (818)	8.48 (3)	5.13 (3)	83.17 (1151/1569)	82.47 (1294/1569)	73.36 (1151/1569)	3.94 (2.5)	8.7% (136/1569)
National census of Japan		125.5† million	48.4‡	51.4†	N/A	N/A	77.93§	77.46§	68.26**	N/A	N/A

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* Mean weekday and weekend contacts were weighted by populational age and sex of Osaka and Fukuoka prefectures determined by the 2021 October Japanese census data (15)

† Source from 2021 October Japanese census data (15).

‡ Median age calculation done for 2020 from UN Population (39).

§ National COVID-19 vaccination coverage data as of 12 Feb 2023 from Japan's Digital Agency (21). The first and second dose coverage of the national data excludes vaccination coverage of healthcare workers.

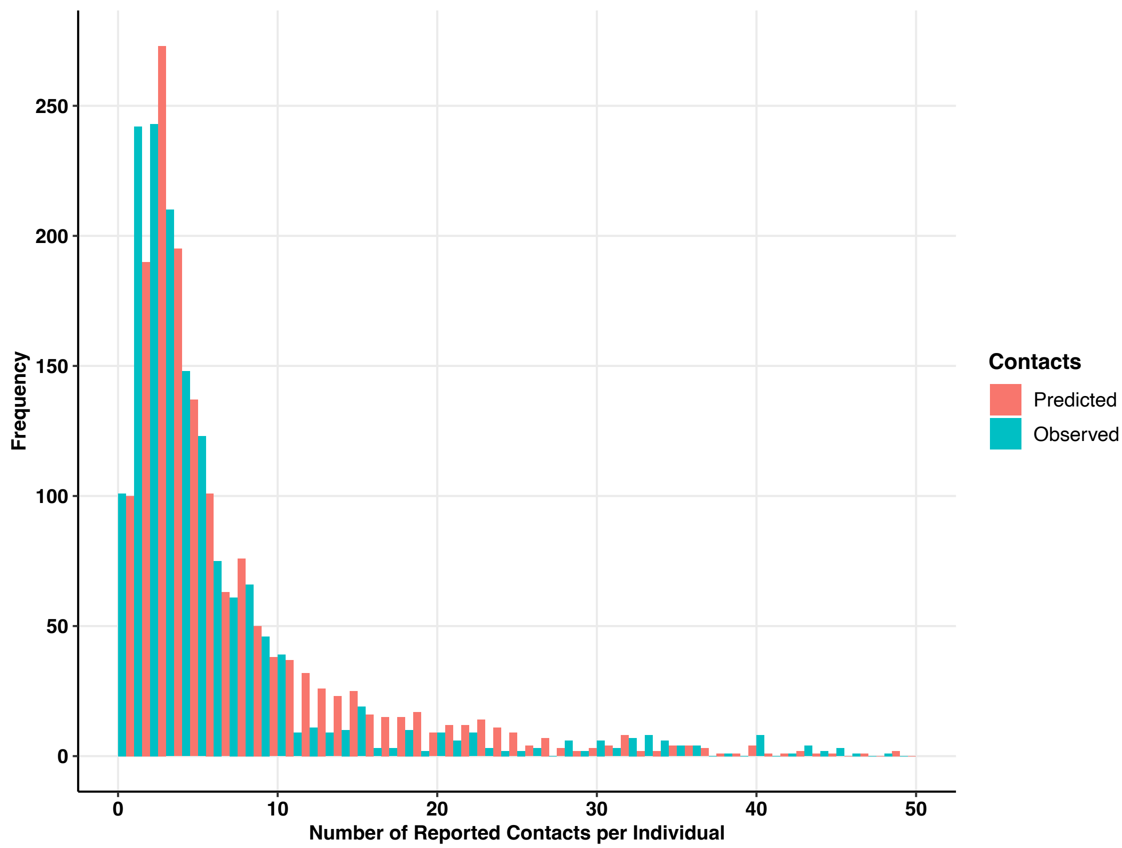
** 68.3% of the population only consists of those who received the 3rd dose and not the following additional booster doses.

Comparison with pre-pandemic contact patterns

The mean number of contacts during the pandemic reduced by 49.8% during the weekday and by 53.3% during the weekend when compared to pre-pandemic times (12); we report an average of 8.18 weekday contacts and 5.98 weekend contacts per individual. The sample distribution of contacts was right-skewed (**Fig 3.2**) where 60.2% of the participants contacted less than five individuals per day during the weekday (and 76.5% during the weekend) in February 2023. The sample distribution of contacts from the earlier surveys showed a similar distribution (**Chapter 9 Appendix 2, Supp. Fig 2**). Prior to the pandemic, the distribution of daily reported contacts (N=3146 participants) was also right-skewed and less than 2% of contacts reported zero contacts (12).

Fig 3.2 Distribution of contacts reported per individual during the weekday in Fukuoka and Osaka prefectures based on the contact survey conducted in February 2023.

There was a total of 1569 participants. The blue bars show the observed contacts reported from the contact survey. The pink bars show the predicted contacts based on the multivariable regression model using a Weibull distribution. Sixty participants (3.82%) recorded over 50 contacts.



Change in contact patterns across a typical week

To test whether there were substantial differences in frequency of contacts across a typical week, two generalized linear models with and without survey time were compared using a likelihood ratio test. Survey time point significantly explained the variability in the mean of contacts during the weekday (chi-squared = 29.33, p-value = 0.00057) (**Fig 3.3a**) and during the weekend (chi-squared = 98.79, p-value < 2.2×10^{-16}) (**Fig 3.3b**). Particularly among the 10's and 40's, the mean number of contacts increased in calendar time during the weekday and weekend.

Fig 3.3 Frequency (mean) of contacts by age category of participants during the weekday (Fig 3.3a) and the weekend (Fig 3.3b) for all surveys conducted (2021-2023) in Fukuoka and Osaka prefectures.

Each timepoint of the contact survey is indicated by color. The mean and 95% confidence intervals are obtained by bootstrapping.

Fig 3.3a: Weekday Contacts 2021-2023

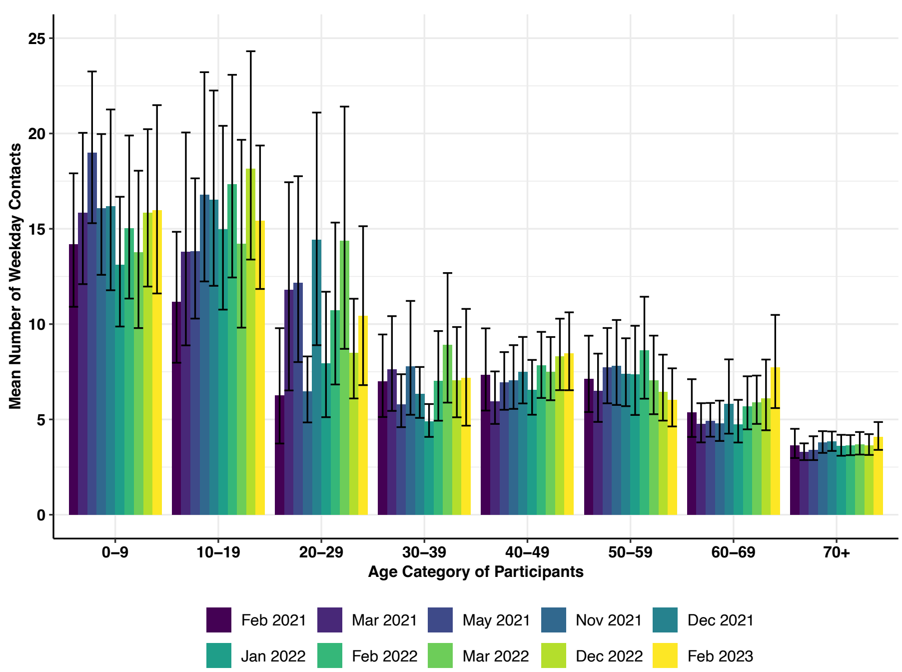
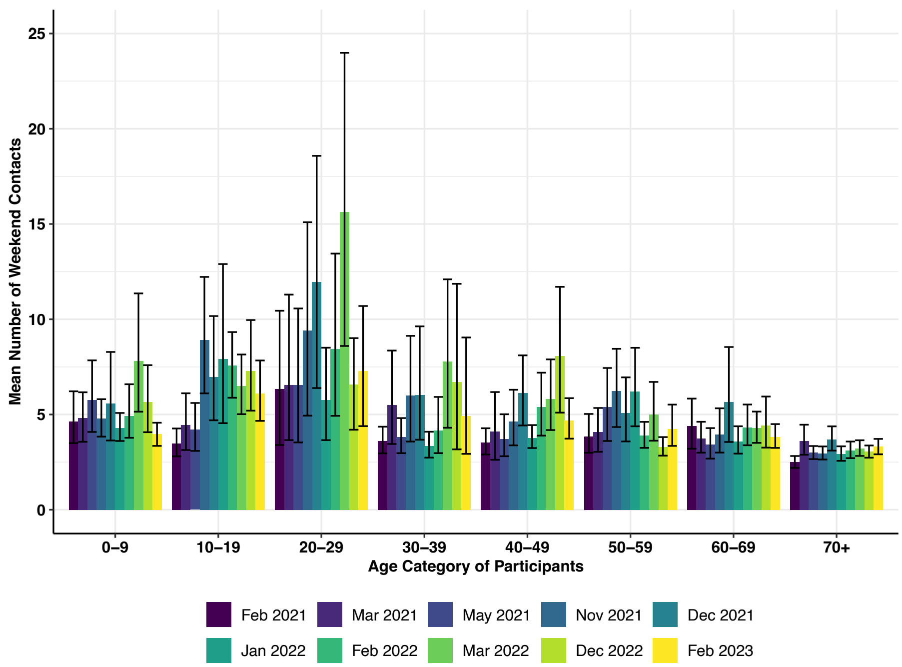


Fig 3.3b: Weekend Contacts 2021-2023



On the contrary, the older population (70+) consistently had low contacts during the weekday and weekend. Particularly during the weekdays, the mean number of contacts across all survey time points (February 2021-February 2023) was significantly lower amongst the 70+ year old compared to the 40's (chi-squared = 112.65, p-value < 2.2×10^{-16}). There were clear temporal changes in the duration of contacts in the 40's during the weekday (chi-squared = 49.47, p-value = 1.35×10^{-7}) (**Fig 3.4a**) and during the weekend (chi-squared = 54.04, p-value = 1.86×10^{-8}) (**Fig 3.4b**). For example, the mean duration of weekday contacts for the 40's increased from 6.10 hours (95% CI: 5.29-6.85) in February 2021 to 8.63 hours (95% CI: 7.75-9.48) in February 2023. There were similar temporal changes in the duration of contacts amongst the 70+ year old (chi-squared = 21.04, p-value = 0.012 for weekday; chi-squared = 25.51, p-value = 0.0025 for weekend).

Fig 3.4 Duration of contacts by age category of participants during the weekday (**Fig 3.4a**) and weekend (**Fig 3.4b**) for all surveys conducted (2021-2023) in Fukuoka and Osaka prefectures.

Each timepoint of the contact survey is indicated by color. The mean and 95% confidence intervals are obtained by bootstrapping.

Fig 3.4a. Weekday Contacts 2021-2023

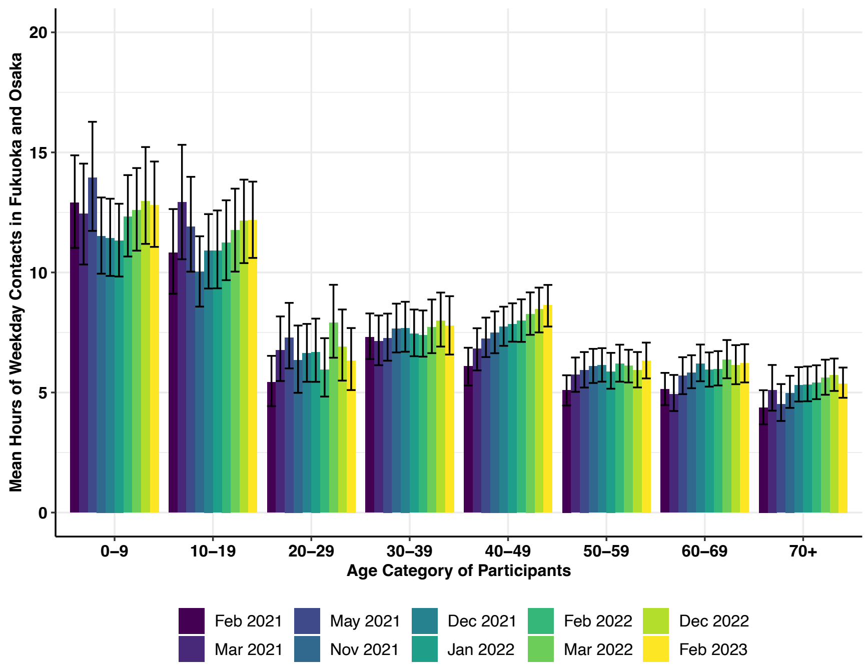
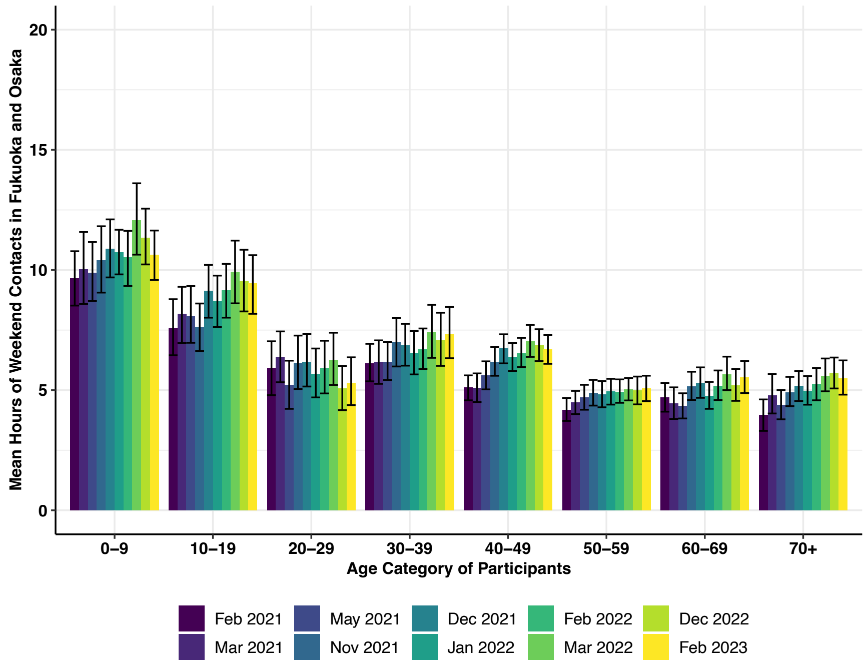


Fig 3.4b. Weekend Contacts 2021-2023



<u>Association of Emergency Declarations (ED) and Semi-ED</u>

We explored whether EDs (observed during surveys 1 and 3) were associated with reported contacts and their duration, and whether the strength of ED provided further granularity. After adjusting for age and sex in a generalized linear model, the issuance of an ED was negatively associated with the mean number of contacts during weekends (Adjusted CRR: 0.84 (95% CI: 0.79-0.88) compared with periods without any ED, yet there was no association during weekdays (Adjusted CRR: 0.96 (95% CI: 0.91-1.01). On the other hand, there was a slightly positive association between the issuance of a semi-ED (surveys 7 and 8) with contacts during weekends (Adjusted CRR: 1.06 (95% CI: 1.01-1.12)) and weekdays (Adjusted CRR: 1.05 (95% CI: 1.00-1.11)) compared with periods without any ED.

For example, a woman in her 40's would contact an average of 3.32 individuals (95% CI: 3.09-3.56) during weekends when an ED was issued, but she would contact an average of 3.97 individuals (95% CI: 3.74-4.20) during periods when any level of ED was absent (**Table 3.2**). Since surveys 9 and 10 were conducted two years after the initial survey and could have significantly different contact patterns due to "pandemic fatigue," the same analysis was conducted by excluding these two surveys, but the negative association between ED and contacts remained the same.

When surveys 1 and 3 (ED issued) were compared with survey 2 (ED absent) after adjusting for age and sex, there was no evidence of an association between the frequency of contacts and the issuance of an ED during the weekday (Adjusted CRR: 1.03 (95% CI: 0.95-1.12) or the weekend (Adjusted CRR: 0.95 (95% CI: 0.88-1.04).

The issuance of an ED was negatively associated with the duration of contacts during both weekdays (Adjusted CRR: 0.90 (95% CI: 0.86-0.95)) and weekends (Adjusted CRR: 0.87 (95% CI: 0.82-0.91)) after adjusting for age and sex. Following the same example given previously, a woman in her 40's would have an average contact duration of 5.09 hours (95% CI: 4.76-5.43) with other individuals during weekends when an ED was issued and 5.86 hours (95%CI: 5.55-6.18 during periods without any ED.

Because one of the key restrictions during ED was either complete closure or shortening of restaurant/bar hours with restricted hours of serving alcohol (**Chapter 9 Appendix 2, Supp. Table 2**), we investigated the number of individuals who reported contacts at restaurants/bars[††]. After adjusting for age and sex, these contacts were negatively associated with the issuance of ED during weekdays (Adjusted CRR: 0.77 (95% CI: 0.72-0.83)) and weekends (Adjusted CRR: 0.68 (95% CI: 0.63-0.74)) compared to periods when ED was absent.

Table 3.2 Predicted frequency and duration of contacts for a woman in her 40's during the weekday or weekend.

Each row is based on a multivariable regression model that included age, sex, and the level of Emergency Declaration (ED) that was either absent, semi-ED or full ED. Each model includes all 10 survey time points from February 2021 to February 2023 (N=16,178 individuals).

	Scenario: Emergency Declaration (ED) absent (Surveys 2,4,5,6,9, and 10)	Scenario: Period with Semi-ED (Surveys 7 and 8)	Scenario: Period with ED (Surveys 1 and 3)
Outcome 1: Predicted Frequency of Contacts per individual (95% CI)			
a) Weekday	5.79 (5.46-6.12)	6.08 (5.68-6.52)	5.53 (5.17-5.92)
b) Weekend	3.97 (3.74-4.20)	4.22 (3.93-4.52)	3.32 (3.09-3.56)
Outcome 2: Predicted Duration of Contacts (hours) per individual (95% CI)			
a) Weekday	6.91 (6.55-7.28)	7.13 (6.69-7.60)	6.24 (5.86-6.65)
b) Weekend	5.86 (5.55-6.18)	6.20 (5.80-6.62)	5.09 (4.76-5.43)
Outcome 3: Predicted Contacts at Restaurants and Bars per individual (95% CI)			

[††] For this analysis, the contact location of restaurants and bars were combined which included izakaya (informal Japanese bars where alcohol and food are served), karaoke, and movie theaters.

a) Weekday	0.022 (0.021-0.024)	0.020 (0.019-0.022)	0.017 (0.016-0.019)
b) Weekend	0.035 (0.032-0.038)	0.034 (0.031-0.037)	0.024 (0.022-0.026)

<u>Factors associated with contact patterns</u>

Based on our multivariable regression model, an individual with the reference characteristics had an expected 2.35 contacts (95% CI: 1.70-3.23) during the weekday. Each variable was compared to this reference, and we reported on characteristics that were statistically different to this value (**Table 3.3**). To check the model fit, the predicted values of weekday contacts were plotted against the observed values reported from the February 2023 contact survey (**Fig 3.2**).

Residual plots were also evaluated (**Chapter 9 Appendix 2**, **Supp. Fig 5**). Heteroscedasticity was evident (**Chapter 9 Appendix 2**, **Supp. Fig 5 a-b**) which was expected due to the sample distribution showing overdispersion. The majority of deviance residuals (in absolute value) was shown between 0 and 2 and randomly distributed across all categories (**Chapter 9 Appendix 2**, **Supp. Fig 5 c-f**).

Contact patterns varied by location (**Table 3.3**). Participants who reported contacts at home, school, restaurants, and bar settings had higher contacts than those who did not report any contacts at these locations. Those who lived in a household of four or five people had higher contacts than those who lived in a household of three people. The association between contacts and occupation differed depending on the occupation type where healthcare professionals and government employees, including public school teachers, had significantly higher contacts. Different work conditions were associated with contact patterns. While those who teleworked had lower contacts, those who moved to a different prefecture at least six times in the past month for work/school purposes had higher contacts. As of February 2023, among those who reported as employed or attending school, 73.2% (818/1118) reported they have never teleworked from home. Disease mitigation measures, such as mask wearing frequency increased significantly with higher number of contacts, but there was no increasing trend of handwashing frequency with more contacts. There was no evidence of association between contacts and vaccination status and their level of concern in getting infected with COVID-19.

Table 3.3 Characteristics of participants and their reported number of weekday contacts from the February 2023 contact survey conducted in Fukuoka and Osaka prefectures compared to the reference category.

The relative mean number of contacts per day is indicated as the contact rate ratio (CRR). The crude CRR is from a univariate regression model and the adjusted CRR is from a multivariable regression model. Rows highlighted in yellow are the variables that were associated ($p<0.05$) with the mean number of contacts in the multivariable regression model.

Category	Number of Participants	% of Participants	Mean Number of Contacts	Median Number of Contacts	Lower IQR (Contacts)	Upper IQR (Contacts)	Crude Contact Rate Ratio	Lower 95% CI (Crude)	Upper 95% CI (Crude)	Adjusted Contact Rate Ratio	Lower 95% CI (Adjusted)	Upper 95% CI (Adjusted)
Participant Age (years)												
0-5	45	2.87	13.27	5.00	2.00	14.00	1.56	1.01	2.40	1.46	0.37	5.78
6-17	136	8.67	17.01	9.00	4.00	24.00	2.17	1.64	2.89	1.25	0.49	3.16
18-29	120	7.65	10.53	4.00	2.00	8.00	1.20	0.90	1.62	1.00	0.74	1.36
30-39	162	10.33	7.19	3.00	2.00	6.00	0.82	0.63	1.07	0.81	0.65	1.02
40-49 (reference)	275	17.53	8.46	4.00	2.00	7.00	NA	NA	NA	NA	NA	NA
50-59	331	21.10	6.03	3.00	1.00	6.00	0.70	0.56	0.87	0.88	0.74	1.06
60+	500	31.87	6.05	3.00	1.00	5.00	0.70	0.57	0.86	1.07	0.88	1.29
Number in Household												
1 person	154	9.82	3.45	2.00	0.00	3.00	0.51	0.40	0.66	1.36	1.03	1.82
2 people	378	24.09	5.88	2.00	1.00	5.00	0.90	0.74	1.09	1.09	0.92	1.28
3 people (reference)	408	26.00	6.00	3.00	2.00	6.00	NA	NA	NA	NA	NA	NA
4 people	368	23.45	10.88	5.00	3.00	8.00	1.77	1.46	2.14	1.46	1.24	1.73
5+ people	261	16.63	13.34	5.00	3.00	10.00	2.03	1.64	2.51	1.68	1.40	2.02
Occupation												
Company Director/Executive Manager	17	1.08	5.00	3.00	1.00	6.00	0.68	0.36	1.29	0.95	0.54	1.65
Company employee (reference)	445	28.36	7.77	4.00	2.00	8.00	NA	NA	NA	NA	NA	NA
Temporary contractor	81	5.16	9.46	3.00	1.00	6.00	1.05	0.77	1.43	0.79	0.60	1.03
Government employee	45	2.87	17.02	5.00	3.00	15.00	2.17	1.45	3.26	1.50	1.05	2.13
Commerce industry/independent business	59	3.76	4.36	3.00	2.00	4.00	0.60	0.42	0.87	0.72	0.53	0.98
Non-healthcare professional (e.g. lawyer, accountan	12	0.76	11.00	4.00	2.00	10.00	1.45	0.68	3.08	1.16	0.61	2.22
Healthcare professional	19	1.21	16.21	8.00	6.00	16.00	2.22	1.21	4.08	2.27	1.35	3.80
Social work service (e.g. long-term care facility)	3	0.19	15.33	14.00	13.00	17.00	2.42	0.54	10.84	2.45	0.70	8.59
Part-time job (non-homemaker)	106	6.76	8.92	4.00	1.00	8.00	1.13	0.85	1.50	1.15	0.90	1.47
Homemaker (with part-time job)	57	3.63	6.18	4.00	3.00	6.00	0.87	0.61	1.26	0.80	0.58	1.10
Homemaker (without part-time job)	200	12.75	4.40	3.00	1.00	4.00	0.59	0.47	0.73	0.80	0.55	1.15
Freelancer	36	2.29	8.08	3.00	1.00	4.00	0.91	0.58	1.43	1.49	1.00	2.23
Infant (pre-school)	24	1.53	6.21	4.00	2.00	6.00	0.85	0.50	1.47	1.05	0.27	4.13
Kindergartner	26	1.66	21.58	16.00	4.00	30.00	2.93	1.74	4.95	1.31	0.33	5.15
Primary school student	60	3.82	18.02	10.00	4.00	33.00	2.58	1.80	3.68	0.83	0.32	2.17
Middle school student	45	2.87	17.51	8.00	4.00	15.00	2.30	1.53	3.45	0.70	0.27	1.84
High school student	30	1.91	12.40	5.50	2.00	18.00	1.68	1.03	2.74	0.60	0.25	1.41
Post high school prep student	1	0.06	4.00	4.00	4.00	4.00	0.64	0.05	8.50	0.65	0.07	5.80
College student	46	2.93	11.11	3.50	2.00	8.00	1.35	0.91	2.02	0.84	0.50	1.42
Unemployed/helps at the house	72	4.59	3.01	2.00	1.00	3.00	0.40	0.28	0.55	0.55	0.36	0.85
Pension retiree	179	11.41	3.78	2.00	1.00	4.00	0.51	0.41	0.64	0.56	0.38	0.83
Other	6	0.38	6.67	3.50	0.00	5.00	0.83	0.29	2.40	0.74	0.29	1.88

Category	Number of Participants	% of Participants	Mean Number of Contacts	Median Number of Contacts	Lower IQR (Contacts)	Upper IQR (Contacts)	Crude Contact Rate Ratio	Lower 95% CI (Crude)	Upper 95% CI (Crude)	Adjusted Contact Rate Ratio	Lower 95% CI (Adjusted)	Upper 95% CI (Adjusted)
Moving Prefectures for Work/School during the Month												
Less than 6 times (reference)	1465	93.37	7.54	3.00	2.00	7.00	NA	NA	NA	NA	NA	NA
More than 6 times	104	6.63	15.81	5.00	3.00	10.00	1.99	1.51	2.63	1.44	1.14	1.82
Location of Work												
Telework at home	320	20.40	3.56	2.00	1.00	4.00	0.37	0.31	0.44	0.57	0.46	0.71
Workplace (reference)	610	38.88	10.38	5.00	3.00	9.00	NA	NA	NA	NA	NA	NA
School	188	11.98	17.70	8.00	3.00	24.00	1.79	1.45	2.21	0.81	0.52	1.26
Not Employed	451	28.74	4.20	2.00	1.00	4.00	0.42	0.36	0.49	0.70	0.49	0.99
Frequency of Teleworking												
Never (reference)	818	52.14	11.28	5.00	2.00	9.00	NA	NA	NA	NA	NA	NA
Few times per month	85	5.42	6.96	5.00	3.00	8.00	0.69	0.51	0.93	0.76	0.59	0.98
2-3 times per week	96	6.12	6.96	3.00	2.00	6.00	0.59	0.45	0.78	0.81	0.62	1.06
4-5 times per week	119	7.58	2.58	2.00	1.00	3.00	0.26	0.20	0.33	0.66	0.50	0.87
Reported Location of Contact												
No Contact at Home (reference)	279	17.78	3.99	1.00	0.00	3.00	NA	NA	NA	NA	NA	NA
Home	1290	82.22	8.97	4.00	2.00	8.00	2.86	2.38	3.44	2.65	2.16	3.26
No Contact at Others' Home (reference)	1517	96.69	7.96	3.00	2.00	7.00	NA	NA	NA	NA	NA	NA
Others' Home	52	3.31	11.83	6.00	3.00	8.00	1.57	1.06	2.33	1.30	0.95	1.79
No Contact at School (reference)	1400	89.23	6.42	3.00	2.00	6.00	NA	NA	NA	NA	NA	NA
School	169	10.77	21.92	10.00	6.00	30.00	3.70	2.99	4.59	3.51	2.50	4.93
No Contact at Restaurant (reference)	1479	94.26	7.81	3.00	2.00	7.00	NA	NA	NA	NA	NA	NA
Restaurant	90	5.74	12.57	6.00	4.00	10.00	1.72	1.28	2.33	1.34	1.03	1.75
No Contact at Bar (reference)	1536	97.90	7.89	3.00	2.00	7.00	NA	NA	NA	NA	NA	NA
Bar	33	2.10	17.00	9.00	4.00	22.00	2.38	1.46	3.88	2.18	1.42	3.36
Frequency of Mask Wearing during the Day												
<3 hrs (reference)	798	50.86	4.40	3.00	1.00	5.00	NA	NA	NA	NA	NA	NA
3-6 hrs	273	17.40	7.48	3.00	2.00	7.00	1.61	1.35	1.92	1.18	1.00	1.39
6-9 hrs	258	16.44	8.77	5.00	2.00	9.00	2.01	1.68	2.40	1.27	1.07	1.51
9-12 hrs	149	9.50	18.64	7.00	4.00	20.00	4.06	3.25	5.08	2.14	1.71	2.68
12+ hrs	91	5.80	22.97	6.00	3.00	22.00	4.69	3.55	6.19	2.53	1.92	3.34
Frequency of Handwashing during the Past 3 hrs												
None	258	16.44	6.24	3.00	1.00	7.00	0.72	0.58	0.89	0.74	0.62	0.88
1 time (reference)	532	33.91	8.70	4.00	2.00	8.00	NA	NA	NA	NA	NA	NA
2 times	311	19.82	9.14	3.00	2.00	7.00	1.03	0.84	1.26	0.98	0.83	1.15
3 times	213	13.58	7.20	3.00	2.00	6.00	0.85	0.68	1.06	0.74	0.62	0.89
4 times	76	4.84	8.53	4.00	2.00	8.00	1.00	0.71	1.40	0.77	0.59	1.02
5 times	92	5.86	9.04	3.00	1.00	8.00	1.00	0.73	1.37	1.04	0.81	1.34
6+ times	87	5.54	6.85	3.00	1.00	6.00	0.80	0.58	1.10	0.67	0.52	0.87
Number of Times Vaccinated against COVID-19												
Never Vaccinated	264	16.83	11.69	3.00	2.00	9.00	1.54	1.27	1.86	1.06	0.88	1.28
1 dose	11	0.70	4.00	4.00	2.00	6.00	0.63	0.27	1.45	0.59	0.31	1.16
2 doses	143	9.11	7.05	4.00	2.00	7.00	1.01	0.79	1.29	0.88	0.71	1.08
3+ doses (reference)	1136	72.40	7.42	3.00	2.00	7.00	NA	NA	NA	NA	NA	NA

Category	Number of Participants	% of Participants	Mean Number of Contacts	Median Number of Contacts	Lower IQR (Contacts)	Upper IQR (Contacts)	Crude Contact Rate Ratio	Lower 95% CI (Crude)	Upper 95% CI (Crude)	Adjusted Contact Rate Ratio	Lower 95% CI (Adjusted)	Upper 95% CI (Adjusted)
Perspective on COVID-19												
1 - Most concerned (reference)	344	21.92	8.06	3.00	2.00	6.00	NA	NA	NA	NA	NA	NA
2 - Concerned	562	35.82	6.87	3.00	2.00	6.00	0.90	0.74	1.08	1.05	0.90	1.23
3 - Neutral	186	11.85	7.17	3.00	1.00	7.00	0.94	0.73	1.20	0.99	0.80	1.22
4 - Not concerned	183	11.66	6.67	3.00	2.00	6.00	0.93	0.72	1.19	1.08	0.88	1.34
5 - Least concerned	71	4.53	4.89	2.00	1.00	4.00	0.65	0.45	0.93	0.73	0.54	1.00
6 - Do not know	223	14.21	14.14	6.00	3.00	18.00	1.97	1.55	2.49	0.60	0.39	0.92

‡‡, §§***

‡‡ Among those who reported their frequency of teleworking, there were 451 people (28.71%) who reported not employed (not shown on Table 3).

§§ There were 15 people (0.96%) who reported NA on their vaccination status (not shown on Table 3).

*** Variables related to contact location (including home, others' home, school, restaurant, and bar) were based on questions asked about contacts related specifically during the weekday only.

3.6 Discussion

Our study is one of the few that have characterized social contact patterns in Japan during the COVID-19 pandemic through repeated cross-sectional surveys. Contact surveys were conducted in Japan during and after the Tokyo Olympics in August 2021 that resulted in having a median of three contacts per day (mean of 8.92) (23), similar to our results from the March 2022 survey. Although our surveys did not capture contact patterns in 2020, a study using mobility data has shown that there was a 70% reduction in daily total contacts in April 2020 after there were government recommendations to telework and close the public schools (24). This is comparable to countries such as Norway (67-73% decrease) (25), France (70% decrease) (26), Germany (73% decrease) (27), United Kingdom (74% decrease) (17), Belgium (80% decrease) (28) and United States (82% decrease) (29) where strict lockdowns were implemented. Many contact patterns remained subdued even after post-lockdowns (e.g. China, 21 European countries) (30,31).

Although Japan never implemented lockdowns, our results suggest that the objective of ED issuance was met as it was associated with changes in frequency and duration of contacts. Particularly during the weekend, there were fewer contacts and shorter duration of contacts. This suggests that individuals may have changed their behavior during the days they have more control over compared to the weekdays when they either commute to school or work. Even as of February 2023, two years after the second ED, the majority (73.2%) of those who were employed or attending school had never worked from home. This corresponds to a survey that showed among approximately 20,000 employed individuals, 70.3% were not teleworking during the first ED in April 2020 when stay-at-home and teleworking recommendations were issued for the first time during the pandemic (32). Prior to the pandemic, teleworking was a practice rarely implemented in Japanese society; a national survey in September 2019 showed 20.2% of 2,118 companies had implemented teleworking strategies for their employees (33).

The duration of contacts increased with time particularly among children, teenagers, and adults in their 40s. This is correlated with governmental restrictions that were gradually lifted, such as having less stringent measures during semi-EDs compared to EDs. However, the mean number of contacts remained subdued across the first three surveys in 2021, including March when ED was absent, showing that the lifting of ED was not what may have influenced the increase in contact patterns per se. These can be signs of pandemic fatigue where there may be a gradual shift towards behavior more like pre-pandemic times. It is also worth noting that there were other factors that also increased with time, such as vaccination and circulation of omicron, a less virulent strain of SARS-CoV-2. It is, however, important to note that even after ED was lifted in March 2021 before mass vaccination started, the frequency and duration of contacts did not change. This contrasts with periods when the first and second lockdowns were lifted in the UK, also prior to vaccine rollout to the entire public, adults (18 years and above) increased their contacts from 29 to 59% compared to during the first lockdown (19). These empirical data illustrate how contact patterns can vary from country to country during a pandemic. Understanding how individuals behave, especially during periods prior to vaccine rollout, may provide hints on the level of necessity, timing, and severity of governmental recommendations in future epidemics.

The Japanese population that had consistently low number of contacts was those over 70, which consist of 22.6% of the national population (15). They not only met with fewer than five contacts during the week, but each contact remained short (average of one hour of contact per day) with very limited physical contact throughout the pandemic (Supp. Fig 3a). Their contact patterns also did not change after mass vaccination started from May 2021 for 65 years and above. With the combination of shielding the older populations in long-term care facilities (34), this may have helped in preventing a surge of COVID-19 outbreaks and deaths amongst this population during the beginning of the pandemic—an issue that was apparent in the US (35) and the UK (35,36).

"Prosocial behavior," such as physical distancing, mask wearing, and getting tested as described by Sachs JD et al., (3), is critical in pandemic control, and countries in WHO's Western Pacific region were quick in encouraging it as part of their "suppression strategy" (3). Our results in Japan reflect this. In addition to EDs, the 3C policy was implemented from early 2020 which was especially relevant in the Japanese context as our results showed that indoor contacts were more frequent than outdoor contacts (Supp. Fig 4a and 4b). Individuals who went to restaurants and bars had higher contacts compared to those who did not. The close contact that is likely in these settings highlight the importance of mitigation approaches such as improved ventilation for disease control (37).

In our surveys there were increased hours of mask wearing with higher number of contacts, demonstrating prosocial behavior. Frequency of mask wearing continued to be stable throughout 2021 to 2023 which contrasts with the UK where mask wearing was strongly associated with changes in government policy (19). On the other hand, handwashing was not associated with the frequency of contacts. This may be due to the public message of 3C where avoiding crowded conditions and close-contact settings were highlighted in Japan more than handwashing and disinfection—another key difference compared to other countries (5). Contacts were not associated with vaccination status, opposite from the European countries where vaccinated individuals reported higher contacts (38). This could be due to Japan not implementing any restrictions in accessing public or indoor areas due to vaccination status, unlike in Europe where vaccine certificates were issued. Such differences suggest behavioral patterns that are triggered by risk perception vs. governmental intervention. The number of deaths increased after the introduction of the omicron variant, but the suppression strategy in Japan from 2020-2021 – a combination of reduced contacts, prosocial behavior, and high vaccination coverage – may have helped in keeping a low cumulative mortality like other Western Pacific countries where the suppression strategy was implemented early (3).

There are limitations of our study. Our surveys were limited to Osaka and Fukuoka prefectures, where incidence has been typically higher than the remaining 45 prefectures in Japan. Extrapolating our findings to other prefectures in Japan should be done with caution, as contact rates may be lower. However, Japanese contact survey studies prior to the COVID-19 pandemic by Ibuka et al. (12) and Munasinghe et al. (13) did not report any differences in contact rates across prefectures, while Tsuzuki et al. (23) examined contact rates between rural and urban areas and did not find any meaningful differences. We can therefore have moderate confidence in the relevance of our findings for the rest of the country. Selection bias could have been introduced as the surveys captured a sample population that had a slightly higher vaccination coverage than the national average. Recording contacts retrospectively may result in recall bias, leading to an underestimation of contacts.

Lastly, there are limitations of the multivariable regression model. The Weibull distribution that was selected for the model fits the higher number of contacts but there was a sharper difference in the predicted contacts compared to observed contacts that had a frequency of one and two contacts. This indicates that the Weibull distribution puts more emphasis on the heavy tail, and the model may better explain the factors associated with individuals who reported higher contacts. The drop seen in the observed contacts after 10 contacts may also be due to the design of the survey where participants are asked to enter additional information on over 10 contacts. Due to the limited number of questions that could be asked in each survey, our model could have included covariates that were not included in the model, leading to residual bias. Some of these variables could have impacted contact patterns with time.

This was an initial exploration of our data, and future work is planned such as investigating factors that could have influenced the change in contacts during the pandemic by analyzing the same individuals across multiple time points. Interaction can also be explored between time points and age as well as ED to further assess their relationships with contacts. Data on households can be incorporated by utilizing a mixed-effects model to account for the clustering of contacts within households. Based on the assumption that individuals within the same household are likely to have similar contact patterns from shared living conditions, the model can incorporate households as a random effect (i.e. random intercept) while considering other covariates, such as occupation, mask wearing, and vaccination, as fixed effects. The number of people in each household would most likely vary across households, so this variable can also be included as a random slope and hence incorporates its effect to differ between households.

Compared to other countries, Japan has been unique in tackling the COVID-19 pandemic without implementing lockdowns and long school closures; it mostly relied on recommendations that were not legal enforcements. Prosocial behavior, such as limiting contacts especially during the weekend in 2021 and continued mask wearing until 2023 were evident. Although issuance of EDs occurred as the pandemic progressed in waves, contacts remained subdued compared to pre-pandemic times. By recognizing some of the key factors that influence contact patterns in Japan, it can contextualize mathematical models of SARS-CoV-2 that are developed to understand the transmission dynamics and disease. Behavior can be difficult to predict and contact patterns may differ in a future pandemic. The age-specific contacts from our study can be utilized in mathematical modelling, for example to characterize infectious disease spread and support pandemic planning. Most importantly, identifying these country-specific factors that influence human behavior provides further support for policies in controlling disease transmission that are context specific, not only for COVID-19 but also for other infectious diseases that may emerge in the future.

3.7 Conclusions

We conducted repeated surveys in Japan to understand how the population modified its behavior and contact patterns during the pandemic. Our results showed that daily contacts dropped by approximately 50% during the pandemic, rebounding only slowly after the government recommendations were relaxed. People proceeded with caution as they wore masks longer if they had more contacts and consistently wore masks until 2023, even after a full year since the last governmental recommendation was lifted. The frequency of contacts did not increase after individuals received the COVID-19 vaccine which is in contrast with European countries where the opposite trend was reported. Our findings provide evidence on the importance of reduced contacts, careful behavior, and high vaccination coverage that potentially limited disease transmission and mortality in Japan.

List of abbreviations

AIC: Akaike Information Criterion

CI: confidence interval

COVID-19: coronavirus disease 2019

CRR: Contact Rate Ratio

ED: Emergency Declaration

Ethics

Participation in the survey was voluntary and all analyses were performed on anonymized data. The study design including the survey questions and informed consent were approved by the ethics committee of Nagasaki University School of Tropical Medicine and Global Health (approval number: NU_TMGH_2022_162_4). Informed consent was obtained from all participants who provided data from the surveys.

Data availability

Aggregated datasets are available to reproduce all the figures in the main manuscript. A processed dataset with the selected covariates in the multivariable generalized linear model is available to reproduce Table 3. Due to potentially sensitive and identifiable information included, the original dataset of the contact surveys is not made public and is available from the corresponding author upon reasonable request.

Code availability

All accompanying code to generate all the figures in the main manuscript is available on GitHub: https://github.com/tomokanakamura/jp_contactsurvey.git

Acknowledgements

We would like to acknowledge F-press that implemented the social contact surveys online and the study population in Osaka and Fukuoka prefectures who kindly participated in our surveys. We thank John Edmunds and our colleagues within the Centre for Mathematical Modelling of Infectious Diseases at LSHTM, the National Institute for Infectious Diseases in Japan, and Nagasaki University's School of Tropical Medicine and Global Health and the Department of Clinical Medicine for input during the development of this study.

Author Contributions

TN, KA, KMO, RK, and AE contributed to designing the contact surveys. TN and RK collected the contact survey data. TN processed and analyzed the contact survey data. TN and KMO designed the statistical analysis. KA, KMO, KEA, MS, AE, YI, and HO provided feedback on the study design and analysis plan. All authors contributed to the interpretation of the study results, writing and critical revision of the manuscript.

Competing Interest Statement

The authors have declared that no competing interests exist.

3.8 References

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3.9 Main Takeaway

Based on the ten social contact surveys conducted in Fukuoka and Osaka prefectures in Japan from 2021 to 2023 during the COVID-19 pandemic, there were four main takeaway points. First, the mean frequency of contacts during the pandemic declined by at least 49.8% (8.2 weekday contacts and 6.0 weekend contacts per individual, adjusted by age and sex) compared to pre-pandemic times based on a similar survey conducted in Japan in 2011. This was comparable to other countries, such as the UK, US and France, that conducted contact surveys during the pandemic where strict lockdowns and school closures were implemented.

Second, Japan never implemented lockdowns and long school closures during the COVID-19 pandemic. Apart from strict international border control policies, it implemented less strict rules compared to other countries and depended mostly through emergency declarations (EDs) that consisted of soft recommendations to stay at home and to avoid the “3Cs” which indicate settings that are closed, crowded, and close contact. The objective of ED issuance was met as it was associated with reductions in frequency and duration of contacts. However, we observed careful behavior particularly during the beginning of 2021 when the frequency of contacts remained low even after ED was lifted. This demonstrates that the absence of ED may not have been the only factor that influenced an increase in contacts; it could have included factors such as pandemic fatigue and circulation of less virulent strains of SARS-CoV-2.

Third, there was strong evidence of fewer contacts and shorter duration of contacts during the weekend compared to the weekday. Over 70% of the survey participants who were employed or attending school reported that they never worked remotely even as of February 2023. This suggests behavioral change may have been more likely to occur during weekends when they have more personal flexibility than weekdays dominated by work or school commutes.

Lastly, our study showed contact patterns that reflected prosocial behavior through reduced contacts and mask wearing. Individuals who reported higher number of contacts had increased hours of mask wearing, and such behavior continued until 2023. There was no association between contacts and COVID-19 vaccine uptake, whereas vaccinated individuals reported higher contacts in European countries shortly after the start of mass vaccination. While Japan did not implement any legal restrictions in accessing public places due to vaccination status, vaccine certificates in Europe were utilized. Such differences highlight behavioral patterns that may have been influenced by risk perception in Japan compared to policy-driven measures in Europe.

Although human behavior is difficult to predict, a social contact survey is a tool that allows us to identify how key factors, such as governmental recommendations and public health and social measures, can influence how individuals contact one another. Understanding country-specific contact patterns reinforces the importance of context-specific policies for controlling disease transmission, not only for COVID-19 but also for other emerging infectious diseases.

Chapter 4 Illustrating the COVID-19 Epidemic in Japan using Mathematical Modeling

4.1 Introduction

This chapter explores two research aims. The first aim is to illustrate the COVID-19 epidemic in Japan starting from 2020 using a mathematical model which is explored in Part 1 of Chapter 4. The second aim is to understand the roles of heterogeneity in contact patterns, vaccination, and demography on COVID-19 transmission dynamics. This will be illustrated in Chapter 5. Both chapters complement one another to illustrate the epidemiological situation of COVID-19 in Japan and to utilize the contact study data in a mathematical model to better understand the role of person-to-person contacts in SARS-CoV-2 transmission. Chapter 4, in addition to contact survey results shown on Chapter 3, gave way to further research questions that will be explored in Chapter 5.

As I was one of the members of the COVID-19 Epidemiological Analysis Team of Nagasaki University from late 2020, shortly after I started my PhD program, I was involved in the co-development of the Fukuoka model from an early stage. The model was first initiated by one of our team members, Dr. Toshihiko Sunahara (Assistant Professor at Nagasaki University), while Professor Koya Ariyoshi (Nagasaki University), Dr. Akira Endo (currently Assistant Professor at the National University of Singapore), and I provided feedback. The original motivation behind the model development was to forecast hospital bed capacity. Particularly in late 2020, Fukuoka prefecture was heavily relying on the hospital bed occupancy percentage to determine the level of severity of how the prefecture was being impacted from COVID-19. In this chapter, I used the same model framework to estimate weekly transmission rates and explore what might influence observed variation across all 47 prefectures in Japan.

As the pandemic progressed, mathematical modeling studies were continuously being published globally that described the characteristics of COVID-19. One of the initial studies calculated early transmission dynamics in Wuhan from January to February 2020 by estimating the reproduction number through a model with four compartments, including susceptible, exposed, infectious, and removed (or isolated, recovered or no longer infectious) (79). Other modeling studies explored the mitigating effect on transmission rates due to PHSMs in 11 European countries by estimating the time varying reproduction number (R_t) (8) and how tiered restrictions in late 2020 would reduce COVID-19 deaths and hospitalizations in the UK (80).

There was considerable geographic variation in COVID-19 incidence and mortality across Europe (81) and also within the same country in the US (82) and the UK (83), but the reason behind this variability has not been well explained. In the UK, for example, regional disparities in COVID-19 mortality were reported during the first wave of the epidemic in April 2020, and age-standardized mortality rate was highest among individuals living in the most deprived regions (83). A cross-sectional prefecture-level ecological study was done in Japan that evaluated the associations of COVID-19 cases and deaths (reported up to February 2021) with socioeconomic and prefecture-specific characteristics (84). This study showed that similar to Western countries, prefectures with lower socioeconomic status indicated by factors such as unemployment rate, education level, and proportion of the population receiving public assistance had higher incidence and mortality rates from COVID-19 (84).

Throughout the pandemic, the role of naturally acquired immunity on the dynamics of SARS-CoV-2 infection were not well quantified, and after COVID-19 became widespread after the circulation of the Omicron variant, understanding immunity from prior infection along with multiple doses of the COVID-19 vaccine became more complicated. Having new variants with different transmissible characteristics along with various types of vaccines being introduced, there were many changing variables to consider. A large, prospective cohort study called the SARS-CoV-2 immunity and reinfection evaluation (SIREN) enrolled and followed up almost 45,000 UK healthcare workers to evaluate immunity from prior infection and vaccination (85). Based on this analysis that included 9560 participants who were recruited between June 2020 and March 2021, immunity was longer lasting for those who had both been infected and vaccinated with three doses compared to those who were just vaccinated.

With these remaining questions on COVID-19 transmission dynamics, I analyzed the incidence and transmission rates of COVID-19 at a spatial aggregated level by prefecture of Japan. The data of reported cases was fit to a mathematical model of SARS-CoV-2 infection to estimate time varying rates of transmission. This chapter focuses on the development of the mathematical model, describing the geographical variation in transmission patterns, and presenting hypotheses on how some factors may be associated with the differences seen in transmission dynamics across prefectures.

4.2 Methods

Development of the mathematical model

We developed a compartmental, deterministic SEIR (Susceptible-Exposed-Infectious-Recovered) model with added compartments that incorporate multiple doses of vaccination. A compartmental deterministic model describes what happens "on average" in a given population that is stratified in subgroups, or compartments, that include individuals who are susceptible, exposed (or pre-infectious), infectious, and recovered from an infection. Through the usage of such a model, it can describe the transmission of an infection, such as during an epidemic, by using the total number of individuals that are allocated in each of these compartments. In our model, we used difference equations to describe the transitions from one compartment to another using discrete time steps, which was by day. These equations show the number of individuals at a given day, $t+1$, which would indicate tomorrow if we referred to the earlier time point t as today. It was sensible to use difference equations in our model because one of our aims was to estimate the transmission rate, or β, on a weekly basis, and thus, it was not necessary to have a finer time step. The data that we used to fit our model was also based on daily confirmed COVID-19 cases reported per prefecture, so it was reasonable to have our time step defined by day. When difference equations are used, the size of the time step should be less than the shortest average duration that an individual spends in one compartment (67). This was met because the shortest duration of a potential individual infected with an Omicron variant in our model was 1.11 days that can be spent in the exposed compartment (i.e. latent period or $\frac{1}{\varepsilon}$) or in the infected compartment (i.e. infectious period or $\frac{1}{\gamma}$).

Before setting up the model, we made assumptions used in our model listed below.

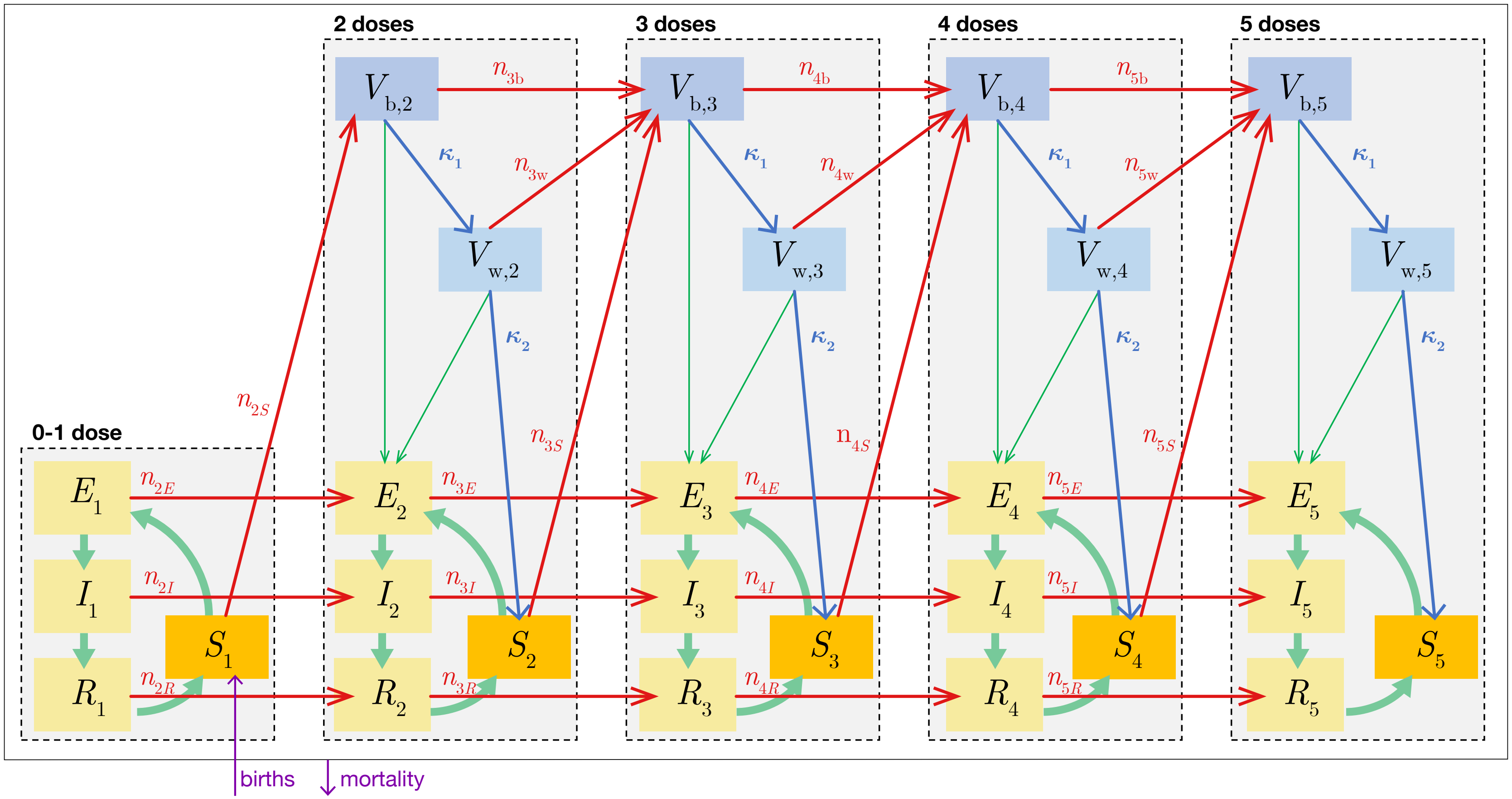
1. Birth and death rates are constant (by prefecture).
2. Contact between individuals is random. No age structure and age-specific contacts are assumed.
3. Individuals who were unvaccinated or partially vaccinated were considered in the same criteria. The first dose of vaccination was assumed to be priming and provides no immediate protection against infection, so we assumed they would be as equally susceptible to getting infected as those who were unvaccinated.
4. Because the highest COVID-19 incidence occurred after the introduction of the Delta variant during the period between 2020-2021, the model reflected its serial interval and reduction in protection from vaccination while between 2022-2023, it reflected the characteristics of the Omicron variant.
5. Due to the possibility of individuals having acquired the infection but being asymptomatic they can become vaccinated while still remaining in the Exposed, Infectious, and Recovered compartments (i.e. one can shift from E_1 to E_2 or I_1 to I_2).

Since we had initially developed this model before the first COVID-19 mass vaccination started, the model was a simple SEIR model without any vaccination compartment. As the first two doses were introduced and subsequent boosters afterwards, we added the subsequent vaccination compartments into the model up to the 5^{th} dose. There was another layer of complication to retrieve this data because it was not initially consolidated in one online platform. There were different levels of publicly available information on vaccination coverage by prefecture. While some prefectures publicized their vaccine coverage by age, some only showed the proportion of the population that received a specific dose. Especially as incidence became higher, there was less granularity in the data that was made publicly available. However, data on the number of people receiving the vaccine by day continued to be available for all prefectures, so this was utilized for the model.

The final model that we developed incorporated up to five doses of the vaccine (**Fig 4.1**).

Fig 4.1 An SEIR model with vaccination compartments from unvaccinated/partially vaccinated (<2 doses) up to 5 doses.

The red arrows indicate individuals who are vaccinated with subsequent doses. The blue arrows indicate individuals with waning immunity after being vaccinated. The green arrows indicate individuals getting exposed to SARS-CoV-2 after being vaccinated. Births enter the first susceptible compartment (S_1) by a constant birth rate and people are removed from all compartments by a constant death rate.



All the compartments shown on **Fig 4.1** and in **Chapter 9 Appendix 4** with the difference equations are summarized below.

- S_i (Susceptible group) (i = 1,2,3,4,5): The compartments for susceptible individuals are defined as anyone who is fully at risk of infection. When they are exposed to an infected individual, they transition into the exposed group. For the individuals who are in these compartments after being vaccinated with two doses or more, the susceptible individuals include those who are again at risk of getting infected after having had natural immunity and/or vaccine immunity.

- E_i (Exposed group) (i = 1,2,3,4,5): The compartments for exposed individuals are defined as those who have been exposed to SARS-CoV-2. They are not yet infectious as they are in the latent or pre-infectious period.

- I_i (Infectious group) (i = 1,2,3,4,5): The compartments for infectious individuals are defined as those who are infected with SARS-CoV-2 and at an infectious state, meaning they can transmit the disease to others.

- R_i (Recovered group) (i = 1,2,3,4,5): The compartments for recovered individuals are defined as those who recovered from their infection and acquired immunity from natural infection. Almost all who are infected recover except for those who die or a few individuals who transition directly from being infected with vaccine dose n to continuously being infected with vaccine dose $n + 1$.

- $V_{b,i}$ (Vaccine group with booster) (i = 2,3,4,5): The compartments for individuals in these compartments are defined as those who received more than one vaccine dose. These individuals remain susceptible to infection but at a reduced rate compared to the susceptible classes. The reduced transmission rate is modelled using the parameter ν. These individuals may receive the next dose of vaccine before they are exposed to the virus, their immunity wanes, or they die.

- $V_{w,i}$ (Vaccine group with waning) (i = 2,3,4,5): The compartments for individuals in these compartments are defined as those who received more than one vaccine dose but with waning immunity. These individuals may receive the next dose of vaccine before they are exposed to the virus, their immunity wanes to return to being fully susceptible for infection, or they die.

The dynamic nature of the model stems from how the force of infection, as defined as the rate at which susceptible individuals are infected per unit time, changes with time (67). All the parameters used in the model are constant (**Table 4.1**) except for the transmission rate that is dynamic. As individuals get vaccinated, they gain vaccine immunity and they are protected (though not fully) against infection, and thus, reduces the transmission rates.

Table 4.1 Parameters used for the SEIR model with vaccination.

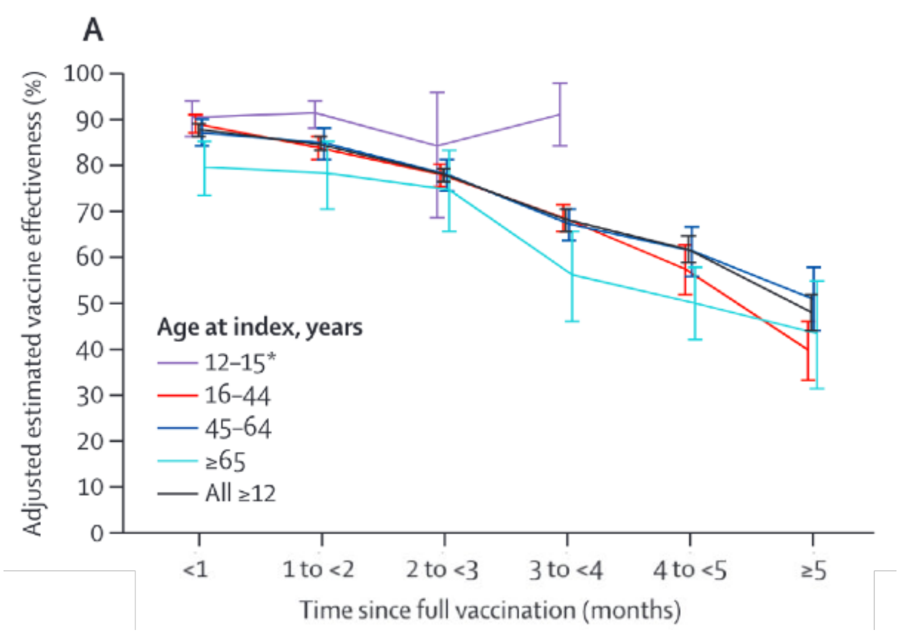
Parameter	**Model 1 (2020-01-16 to 2021-12-31) Delta-like variant**	**Model 2 (2022-01-1 to 2023-07-26) Omicron-like variant**	**Description**	**Source**
ε	0.4	0.9	Rate from E to I	**(86,87)**
γ	0.4	0.9	Rate from I to R	**(86,87)**
ρ	$\frac{1}{365 \cdot \frac{9}{12}} = 0.00365$	$\frac{1}{365 \cdot \frac{9}{12}} = 0.00365$	Rate from R to S (waning immunity after natural infection)	**(88)**
κ_1	$\frac{1}{30} = 0.0333$	$\frac{1}{30} = 0.0333$	Rate from Vb1 to Vw1 (waning immunity after vaccination)	**(89,90)**
$\kappa_2 2$	$\frac{1}{200} = 0.005$	$\frac{1}{142} = 0.007$	Rate from Vw1 to S1	**(89,90)**
ν	0.85	0.7	Reduction in transmission due to vaccination (partial immunity)	**(89,90)**
Birth rate b	Prefecture-specific		Constant birth rate per prefecture	**(91)**

		based on 2022 census	
Death rate m	Prefecture-specific	Constant death rate per prefecture based on 2022 census	**(92)**

Parameter ν was inferred from two studies. When ν is 0.85 in Model 1 reflecting the circulation of the Delta variant, this was referred from a retrospective cohort study that was conducted in the US during the circulation of the Delta variant (89). Tartof et al. evaluated vaccine effectiveness (VE), defined here as providing protection against SARS-CoV-2 (Delta variant) infections and COVID-19 related hospital admissions. As shown on **Fig 4.2**, the initial VE at <1 month since full vaccination was approximately 85%.

Fig 4.2 COVID-19 vaccine effectiveness evaluated from a retrospective cohort study conducted in the United States using Pfizer-BioNTech mRNA vaccine against SARS-CoV-2 infections.

Vaccine effectiveness is defined here as providing protection against SARS-CoV-2 (Delta variant) infections and COVID-19 related hospital admissions. Full vaccination indicated here shows two doses (89).

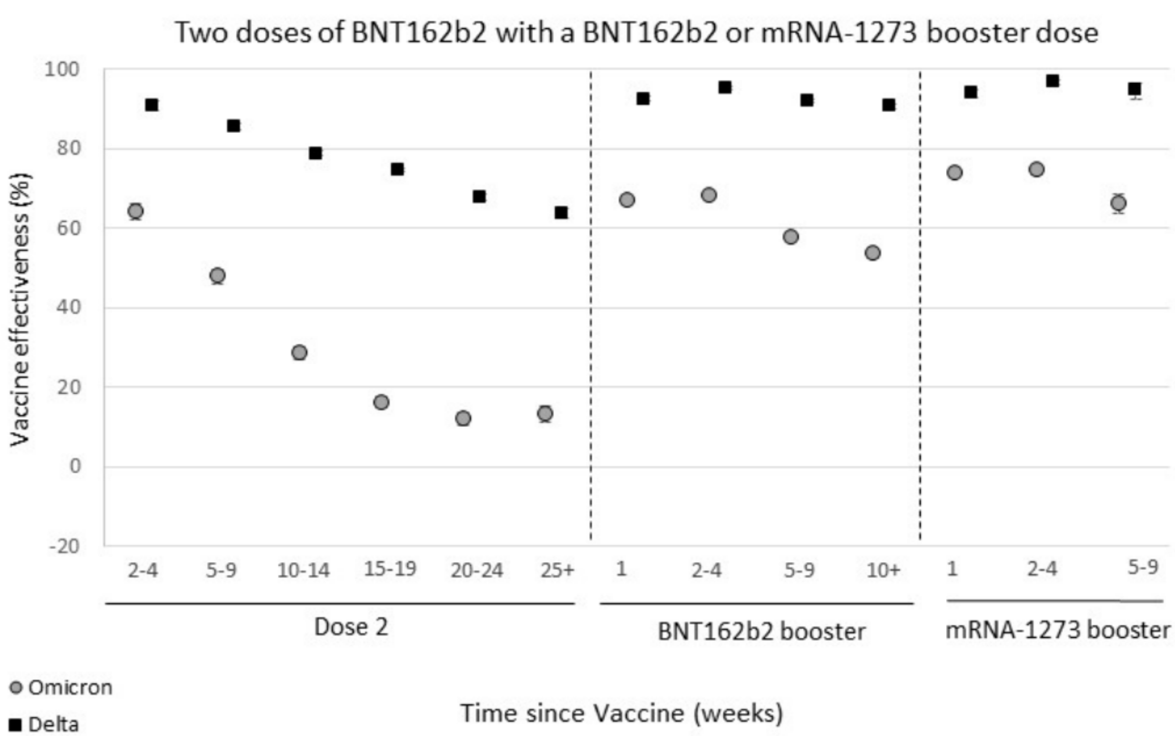


When ν is 0.7 in Model 2 reflecting the circulation of the Omicron variant, this was referred from a test negative case control study in the UK (90). Vaccine effectiveness was defined here as providing protection against symptomatic infections caused by the Omicron variant. As shown on **Fig 4.3**, the initial VE was approximately 70% at 2-4 weeks since being vaccinated with the second dose.

Fig 4.3 COVID-19 vaccine effectiveness evaluated from a test negative case control study in the UK comparing recipients of two doses of Pfizer (BNT162b2) vaccine as the primary course and Pfizer or Moderna as a booster (90).

Vaccine effectiveness is defined here as protection against symptomatic infections caused by the Omicron variant of SARS-CoV-2.

(b)



The model incorporates waning immunity due to vaccination. Individuals transition from $V_{b,i}$ to $V_{w,i}$ at a rate of κ_1, or in other words, the inverse of the number of days the individual spends in the $V_{b,i}$ compartment. When the vaccinated individual transitions to the $V_{w,i}$ compartment, immunity continues to wane for the next 200 days (approximately six months) (89) during 2021 (**Fig 4.2**). Immunity was set to wane more rapidly in the next 142 days (approximately 4.67 months) from 2022 to 2023 when the Omicron variant was predominantly circulating (90) (**Fig 4.3**). These rates of waning are indicated as $\kappa_2$in the model.

Rate of onset of infectiousness (or the inverse of the average number of days during the pre-infectious period) and the rate of recovery (or the inverse of the average number of days during the infectious period) were determined by the serial interval—the period that includes the incubation period and the infectious period—reported by multiple studies. The serial interval can be written as $\frac{1}{\varepsilon}+\frac{1}{\gamma}$. We estimated the parameters of ε and γ based on the serial intervals reported from studies. For our model based on 2020-2021 that reflected Delta circulation, the serial interval was set as five days ($\varepsilon = \gamma = 0.4$, **Table 4.1**) and two days ($\varepsilon = \gamma = 0.9$, **Table 4.1**) during 2022-2023 that reflected Omicron circulation. During the beginning of the pandemic, the mean serial interval was estimated to be 4.7 days (95% credible interval (CrI): 3.7, 6.0 days) with a standard deviation of 2.9 days (95% CrI: 1.9, 4.9 days) based on a model using a log normal distribution on publicly available data from outbreak investigations (86). Once the Omicron variant was predominantly circulating, multiple studies reported having a shorter serial interval compared to earlier variants, ranging from 2 to 4 days (87,90).

Difference equations of the mathematical model

Our mathematical model was developed using Microsoft Excel. Difference equations were used to represent individuals transitioning from one compartment to the next within the SEIR compartments and shifting from one vaccination dose to another as they get vaccinated with each subsequent dose. The daily birth rate of each prefecture was incorporated by adding the number of individuals born per day into the S_1 compartment. This was calculated by multiplying the prefecture's total population with the birth rate per 1000 per 365 days. The daily death rate of each prefecture was calculated similarly from the prefecture-specific death rate, and this death rate was incorporated in all compartments in the model as an individual at any state can die. The red arrows indicated on **Fig 4.1** show the number of people receiving subsequent doses of the vaccine. These numbers are retrieved from the publicly available data of each prefecture showing the aggregate number of vaccinated individuals per dose. Details on all the difference equations that were used for the model are covered in **Chapter 9 Appendix 4**.

Running the model in Excel

The initial conditions of the model are all the parameters covered in **Table 4.1** with one infected individual in the infected compartment of the 0-1 vaccine dose bucket. The rest of the population reflected by the prefecture-specific total population is in the susceptible compartment of the 0-1 vaccine dose bucket.

Automation of the simulation performed for each of the 47 prefectures was done using Visual Basic in Excel. Some snapshots of the model are shown below (**Fig 4.4**, **Fig 4.5**). As shown on **Fig 4.4**, the parameters shown on two columns on the left remain constant with each simulation done for each prefecture. The parameter estimates used for the model are explained in **Table 4.1**. “Pref_No” shows the prefecture that is numbered from 1 to 47 and simulations are run for all 47 prefectures. “Population” indicates the total population of each prefecture reported on Japanese census data.

Fig 4.4 Snapshot of the SEIR model with the parameters set for simulating Okinawa prefecture starting from 16 January 2020.

Vaccination compartments are not shown here as vaccination had not yet started during this time.

Pref_No	1		Date	Count	Row	Cell	beta	S1	E1	I1	R1
Pref	北海道		2020/01/16	1	22	B22	0.496	5182999	0	0.9908813	0
Population	5183000		2020/01/17	2	22	B22	0.496	5182865	0.4914364	0.5944892	0.3963525
			2020/01/18	3	22	B22	0.496	5182731.3	0.5896768	0.5532443	0.6327003
epsilon	0.4		2020/01/19	4	22	B22	0.496	5182597.5	0.6281547	0.5677951	0.8516868
gamma	0.4		2020/01/20	5	22	B22	0.496	5182463.8	0.658449	0.5919163	1.0756937
birth	73.84		2020/01/21	6	22	B22	0.496	5182330	0.6885789	0.6185057	1.3085307
death	0.00004		2020/01/22	7	22	B22	0.496	5182196.3	0.7198336	0.6465102	1.551153
rho	0.003652968		2020/01/23	1	23	B23	0.496	5182062.5	0.7524642	0.6758137	1.8040907
kappa	0.033333333		2020/01/24	2	23	B23	0.496	5181928.7	0.7866401	0.7064469	2.0678259
lambda	0.005		2020/01/25	3	23	B23	0.496	5181795	0.8223287	0.7384959	2.342851
nu	0.85		2020/01/26	4	23	B23	0.496	5181661.2	0.8596263	0.7719995	2.629691

Each SEIR compartment is shown on each column indicated as “S1,” “E1,” “I1,” and “R1.” The numbers indicated for each column show the unvaccinated (i.e. have never had been vaccinated against COVID-19) or partially vaccinated individuals (i.e. received just one dose) who are in these compartments. For simplicity, the 0-1 dose individuals are combined as one category of individuals because to gain protection from the vaccine, they must receive at least two doses.

As soon as mass vaccination starts for the general population in Japan, individuals can flow to the subsequent “bucket” that includes the next set of SEIR compartments along with the vaccinated compartments ($V_{b,i}$ and $V_{w,i}$). Individuals in the susceptible compartment who are vaccinated will transition to the V_b compartment, and with waning immunity of the vaccine, they will then eventually move to the V_w compartment. Although not shown in **Fig 4.5**, columns are added onto the right (e.g.

S_2, E_2, I_2, R_2, $V_{b,2}$, $V_{w,2}$) to represent the individuals that transition to SEIR compartments within the specific vaccine dosage that they received. As shown on **Fig 4.1**, the model allows individuals to receive up to five doses of vaccination.

Relating model-simulated infections to COVID-19 case data

The total number of infections per time step is the sum of all the compartments, indicated on the column labeled as "Total" (**Fig 4.5**). Another key component of the model is taking into account the parameter of individuals seeking healthcare and the proportion of individuals being detected as a positive COVID-19 case. The column labeled as "seek_healthcare" is the proportion of individuals who seek a healthcare facility or a governmental office when they presented with symptoms. Keeping in mind that especially during the early phases of the pandemic in 2020-2021, there was no mass testing that was publicly available and rapid tests were not yet readily available for home-use in Japan. Severe cases were often hospitalized so they were detected and reported by designated hospitals that accepted severe COVID-19 patients. The mild and less severe cases that did not require hospitalization were also detected and reported. Across Japan, many clinics and small healthcare facilities exist in each city, and they have been readily accessible throughout the pandemic. Especially during the beginning of the pandemic, mild cases were continuously being reported to the local public health center which was responsible for monitoring these cases and providing guidance on how to quarantine. Although the details of reporting obligations of confirmed COVID-19 cases varied by prefecture, prefectures such as Tokyo with high incidence had a call center available at the prefectural office which served as a first contact point for potentially infected individuals (93). This guided them with specific healthcare facilities that they should seek when necessary.

Fig 4.5 Continued snapshot of the SEIR model with the parameters set for simulating Okinawa prefecture starting from 16 January 2020.

seek_healthcare	pos_detected	reported_cases	log_likelihood	Total	est_cases_weekly	reported_cases_weekly
0	0	0		5183000		
0.158940186	0	0		5182867		
0.222509903	0.031788037	0	-0.031788037	5182733		
0.266887678	0.044501981	0	-0.044501981	5182600	0.258467324	0
0.304834118	0.053377536	0	-0.053377536	5182466	0.332668083	0
0.339164737	0.060966824	0	-0.060966824	5182333	0.412885095	0
0.371003792	0.067832947	0	-0.067832947	5182199	0.467092687	0
0.401085063	0.074200758	0	-0.074200758	5182066	0.514219588	0
0.429978144	0.080217013	0	-0.080217013	5181932	0.558034028	0
0.458144406	0.085995629	0	-0.085995629	5181799	0.599814819	1
0.48595988	0.091628881	0	-0.091628881	5181665	0.640330129	1
0.51373807	0.097191976	0	-0.097191976	5181532	0.680167604	1
0.54174129	0.102747614	1	-2.378227261	5181399	0.719806044	1
0.570191165	0.108348258	0	-0.108348258	5181265	0.759643229	1
0.599277264	0.114038233	0	-0.114038233	5181132	0.800013666	1
0.629164071	0.119855453	0	-0.119855453	5180998	0.841218955	1

Based on a serosurvey that was conducted in Kobe, Japan among 2000 participants (1000 from August 2021 and 1000 from December 2021), it showed the number of COVID-19 infections would have been approximately 2.5 times higher than what was detected and reported (94). In other words, 40% of the infections were the individuals who accessed a healthcare facility and being detected as positive cases. All who seek a healthcare facility in Japan with any kind of respiratory symptoms, particularly during the pandemic, are regularly tested for COVID-19. The 40% of the total infections are reflected in the column labeled "seek_healthcare" in **Fig 4.5**. We also incorporated a delay in reporting among this proportion of infected individuals. We estimated for a confirmed case to take approximately five days (i.e. rate of $0.2 = \frac{1}{\#\, of\ days\ to\ report\ a\ positive\ case} = \frac{1}{5}$) after an infected individual seeks a healthcare facility, getting tested by PCR, and reporting of the confirmed case to the local government. This is reflected in the column labeled "pos_detected" that is calculated as 20% of the individuals in "seek_healthcare."

<u>Fitting the model to incidence data</u>

The model is fit to data using the daily reported number of cases indicated in red on the column labeled as "reported_cases" (weekly reported cases, or the sum of seven days of "reported_cases", is also indicated on the column labeled as "reported_cases_weekly") (**Fig 4.5**). When developing this model specifically for Nagasaki and Fukuoka prefectures, the incidence data was manually retrieved from the websites of the respective prefectural offices on a daily basis (95,96) and then later for all prefectures in a consolidated database provided by the Ministry of Health, Labor and Welfare (97).

To estimate transmission, I compared the model to the data using maximum likelihood estimation. The data are counts of reported cases, and this corresponds to Poisson distributed (count) data. The corresponding log likelihood of the model estimate, shown as θ, given the COVID-19 case data, defined here as x, is shown as the following equation:

$$\ln L(\theta|x_1, x_2, \dots, x_n) = -n\theta + \left(\sum_{i=1}^{n} x_i\right)\ln\theta - \ln\left(\prod_{i=1}^{n} x_i!\right).$$

n is corresponds to the time step where in our model corresponds to day i. For each day of data (i), we have reported cases (x_i) and we compare this to the modelled estimate of cases (θ_i). Since we calculate the log likelihood for each day, n is equal to 1. Since $\ln\left(\prod_{i=1}^{n} x_i!\right)$ is a constant in the calculations, we have omitted this. In the column labeled "log_likelihood" in **Fig 4.5**, it is calculated as follows:

$$-(model\ estimates)_i + (reported\ cases\ from\ data)_i \cdot \ln(model\ estimates)_i$$

Since we have multiple timepoints, we calculate the total likelihood of the model given the data. As each likelihood for each day is on the log scale, we can simply sum together to obtain the joint likelihood as the following:

$$\ln L(\theta\,|x_i, \dots, x_n) = \sum \ln L(\theta\,|x_i, \dots, x_n)$$

To find the best fitting estimate of beta, we used the Solver function in Excel. For each iteration of the model for all 47 prefectures, the simulation took approximately eight to nine hours.

Statistical analysis

To evaluate transmission patterns in a spatially aggregated way, weekly beta, or the transmission rate per week, from the mathematical model was fit to case data and plotted as an output per prefecture for all 47 prefectures of Japan from 2020 to 2023. This was to explore whether transmission rates were more similar among the adjacent prefectures or prefectures in the same region (as described in **Chapter 1 Map 1**) compared to prefectures outside the region. In the Kanto and Kansai regions, where two of the biggest cities, Tokyo and Osaka, are located, many children and adults commute for school and work across these prefectures within the same region. Many of these prefectures within the same region are connected by public transportation. As also seen from **Chapter 3,** 73.2% (818/1118) of the survey participants who were employed or attending school had never worked from home as of February 2023. Based on this, I hypothesized that people would still be contacting with one another at work or school settings, and transmission patterns would be similar among the prefectures in the same region. To test this hypothesis, a paired t-test was done to compare the mean beta of one prefecture with the mean beta of another prefecture across all time points, and this was repeated for all 47 prefectures so each prefecture's mean beta would be compared with one another from 2020 to 2023. A paired t-test was the appropriate statistical test as the data met its conditions: 1. data was quantitative, 2. distribution of the mean differences was normal and 3. the mean differences were independent of each other. When multiple paired t-tests were carried out to compare the mean beta across the 47 prefectures, q-value was utilized to determine the false discovery rate.

In the statistical analysis where certain hypotheses were tested, results with p-values were indicated which measure the strength of the evidence against the null hypothesis. The smaller the p-values, the stronger the evidence against the null hypothesis (98). As a reference, p-value between 1.0 and 0.1 showed weak evidence against the null hypothesis, p-value between 0.1 and 0.001 showed increasing evidence against the null hypothesis with decreasing p-values, and p-value less than 0.001 showed strong evidence against the null hypothesis.

When Japanese census data of 2020 (99) was used to assess the relationship between COVID-19 incidence, potential factors were chosen with an underlying hypothesis that they may be positively or negatively correlated with incidence. Six characteristics were analyzed including population density (per km^2), households with a married couple, households with a 65-year-old and above living alone or as a couple, institutional households (e.g. non-private households including student dormitories, inpatients of hospitals), households including non-relatives, and households with three generations. (for more detailed descriptions of the categorization of the census, refer to (100)). For the multivariable linear regression model used for exploratory analysis purposes, a generalized linear model was used where the outcome was incidence of COVID-19 and the covariates included the periods when the predominant variant was circulating (including pre-Alpha, Alpha, Delta, Omicron, BA.5, and sub-lineages of Omicron variants) and these six demographic characteristics.

Proportions of these characteristics were calculated by dividing by the number of reported households per prefecture. COVID-19 incidence reported by the MHLW (97) was stratified by one of the six pre-dominant variants that marked each period. The start and end dates were determined by the period when each variant was predominantly circulating as detected by genomic surveillance by NIID (101). Since each period varied in duration and incidence needed to be normalized by population, incidence was calculated as the (number of reported cases per 1000 per person-year). A smoothed line was added using a generalized linear model to visualize the trend of the relationship and to compare the correlation across prefectures.

4.3 Results

Description of incidence and estimation of transmission in Japan

Each wave of COVID-19 in Japan was marked by the different variants (**Fig 4.6**). The predominant variant that was circulating during each wave ranged from Alpha, Delta, Omicron, BA.5 of the Omicron variant, and the sub-lineages of Omicron. The total number of COVID-19 cases surged after the introduction of the Omicron variant. When COVID-19 incidence was stratified by each of the SARS-CoV-2 variant that was predominantly circulating, it showed how incidence grew progressively as new variants began to circulate in Japan (**Fig 4.7**). It also showed how incidence became increasingly similar across all regions of Japan from Omicron onwards.

Fig 4.6 Epidemic curve of the total COVID-19 cases reported in Japan from 2020 to 2023 marked by the predominant variant of SARS-CoV-2 that was circulating across Japan.

All detected variants were reported through genomic surveillance by the National Institute of Infectious Diseases.

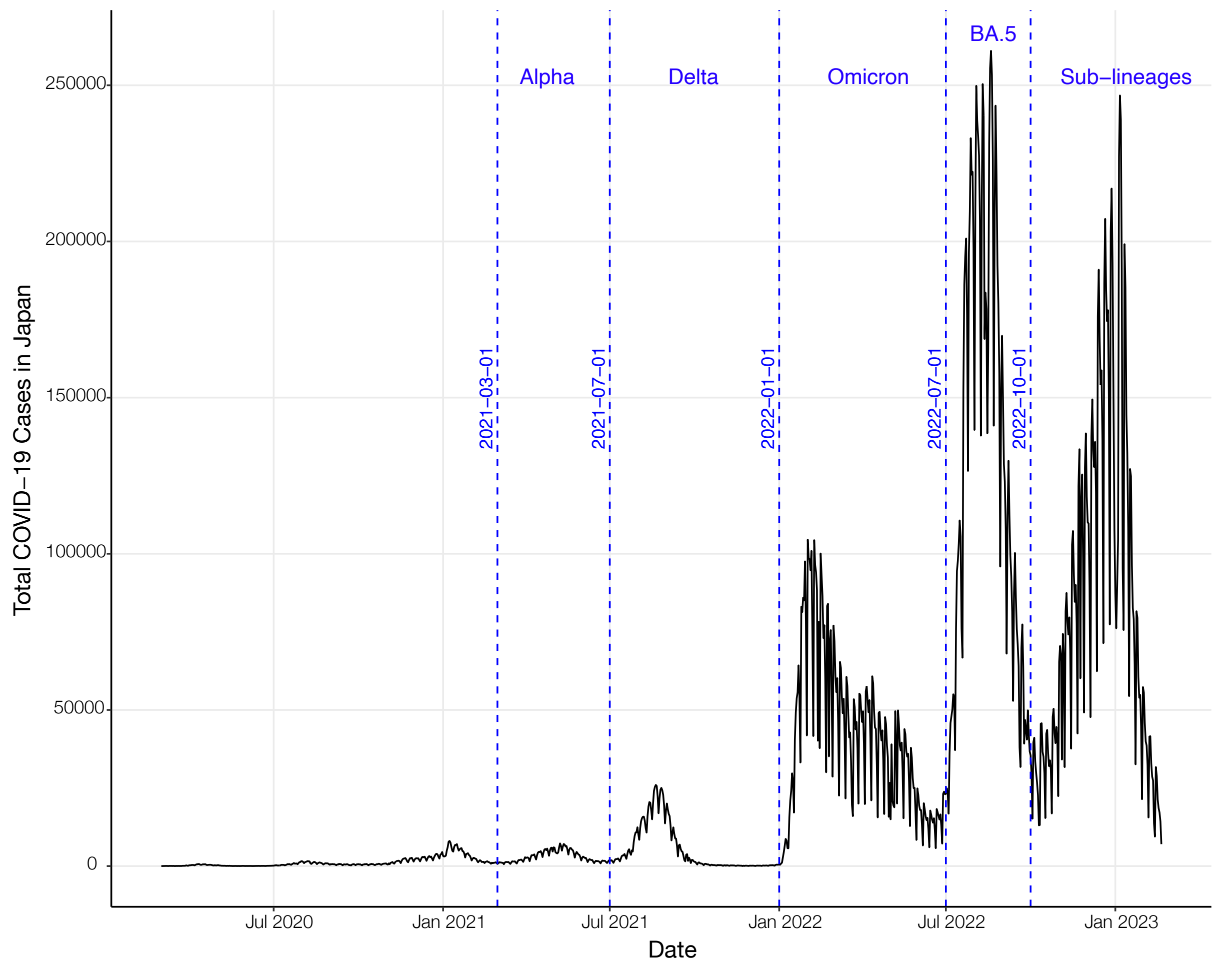
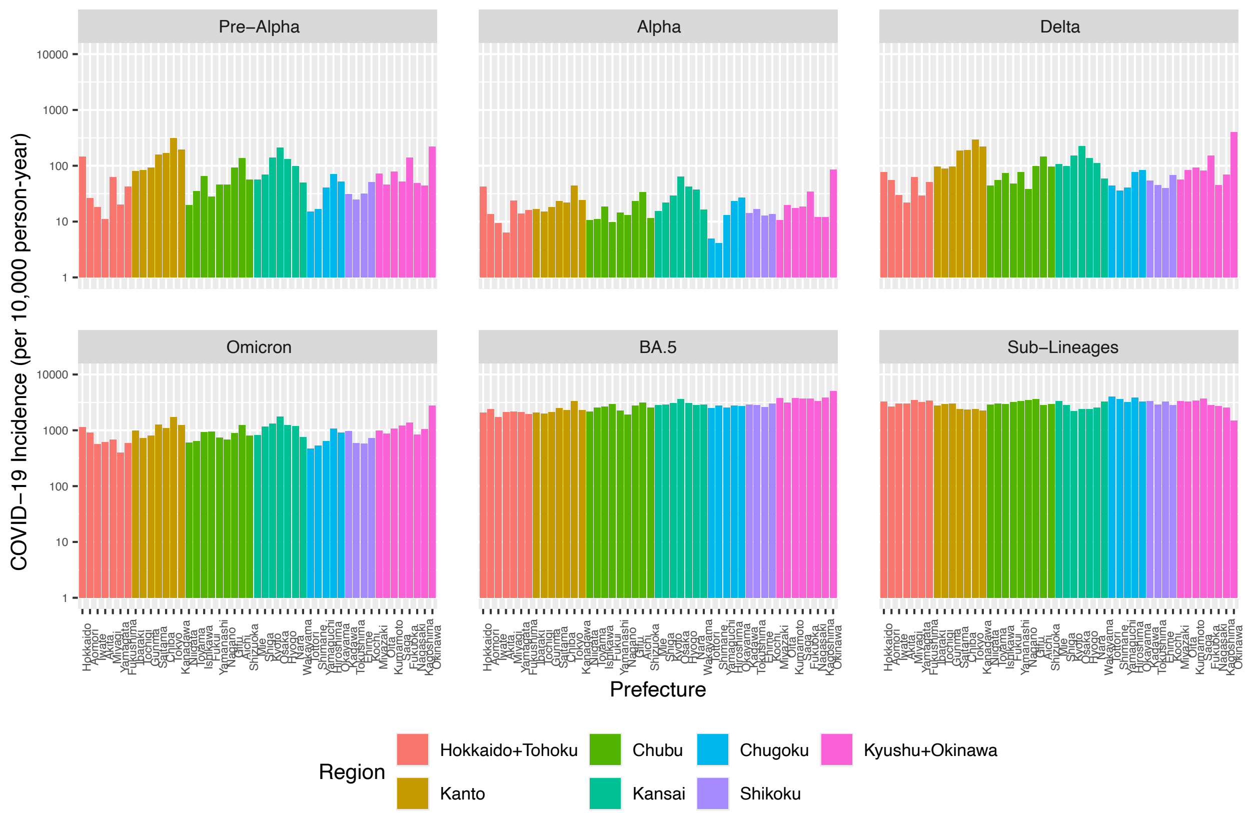


Fig 4.7 COVID-19 incidence by region of Japan and stratified by type of SARS-CoV-2 variant that was predominantly circulating.



To compare COVID-19 incidence from 2020 to 2023 across the prefectures in the same region, three prefectures were chosen per region and plotted (**Fig 4.8**). It was apparent that there were more similarities across the prefectures in the same region (by row) compared to prefectures in a different region (by column). The Kansai and Kanto regions showed three distinct peaks from the circulation of Omicron, BA.5, and Omicron sub-lineages. Okinawa was showing additional peaks of incidence prior to the BA.5 circulation.

Fig 4.8 COVID-19 weekly incidence across prefectures in Japan by region from 2020 to 2023.

When each prefecture's model was fit to the COVID-19 cases reported per prefecture, it was apparent how each wave of the epidemic evolved. In Okinawa prefecture, for example, each successive wave particularly from January 2021 to September 2022 became higher than the previous wave (**Fig 4.9** and **Fig 4.10**, note the different scales of the y-axes). As shown from **Fig 4.6**, the beginning of the Alpha variant circulation was from March 2021 that was followed by the Delta variant introduced after July 2021. COVID-19 cases in Okinawa decreased to zero in November and December 2022. Yet, from 2022 onwards, the Omicron variant was introduced with the BA.5 subvariant circulating after July 2022 when more than 6000 cases were reported in Okinawa during that summer. After the circulation of Omicron, COVID-19 cases persisted and did not decrease to zero like after the end of the Delta wave in November and December 2022.

Fig 4.9 Okinawa model fit to reported COVID-19 cases in Okinawa prefecture from 2020 to 2021.

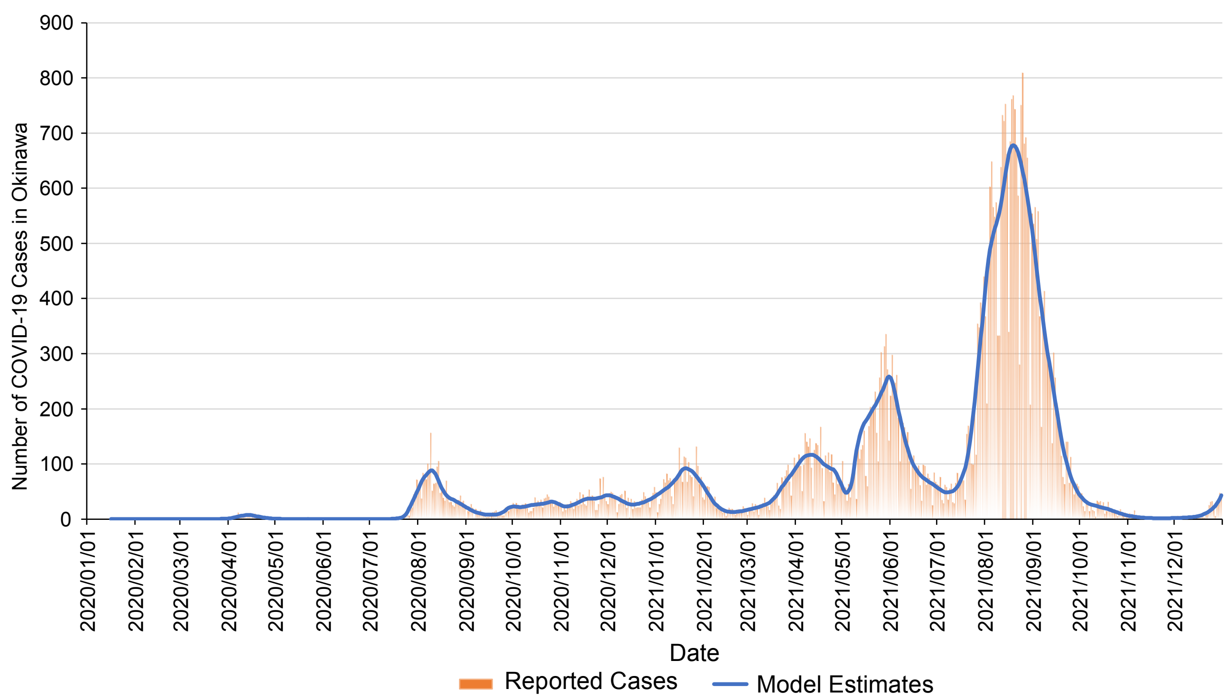
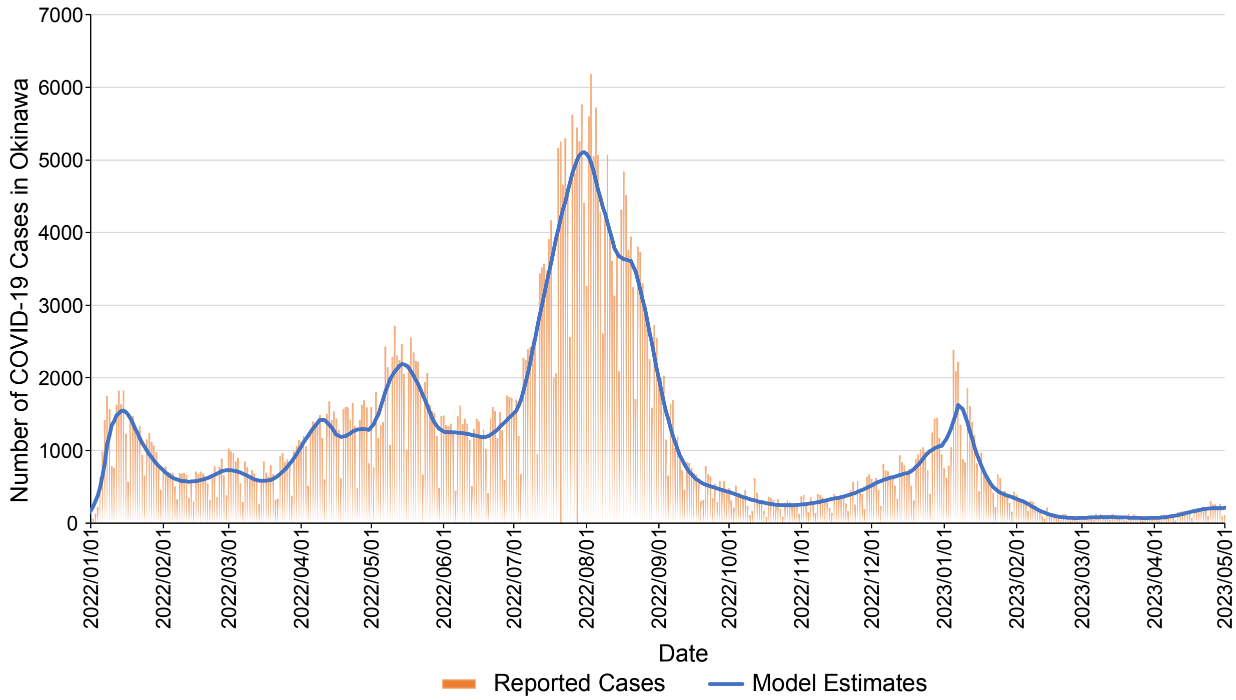


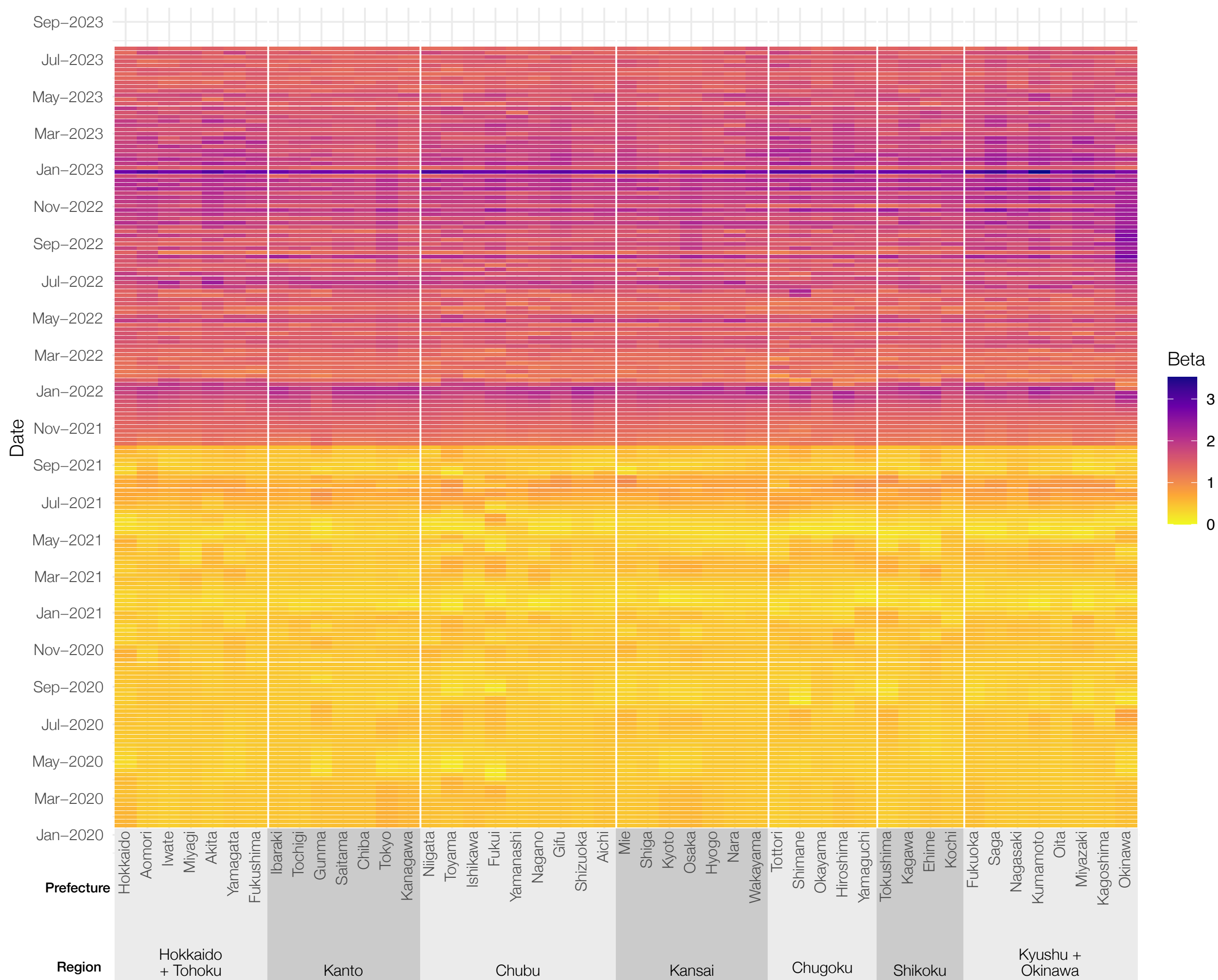
Fig 4.10 Okinawa model fit to reported COVID-19 cases in Okinawa prefecture from 2022 to 2023 (Note the different scale on the y-axis compared to **Fig 4.9**).



Exploration of transmission rates

To evaluate how transmission rates evolved across Japan, weekly beta (transmission rates) that was fitted to the reported COVID-19 cases per prefecture was extracted from January 2020 to August 2023 and plotted as a heat map of all 47 prefectures (**Fig 4.11**). Higher the transmission rate, the increase in color of the heatmap from yellow to purple in a gradient. The order of the prefecture is shown from north (Hokkaido, left of x-axis) to south (Okinawa, right of x-axis). Note the two different sets of parameters being used to reflect the most predominant variant that was circulating; January 2020 to October 2021 followed Delta variant characteristics (Model 1, **Table 4.1**) and October 2021 onwards reflected Omicron variant characteristics (Model 2, **Table 4.1**). The artifact of the sudden increase shown in transmission rates from October 2021 is due to this date being selected as the cutoff point to plot the transmission rates together from the two models.

Fig 4.11 Heatmap of beta, or in other words the transmission rate, from the mathematical model fitted to the reported COVID-19 cases per prefecture from January 2020 to August 2023. The x-axis shows all 47 prefectures of Japan from north (Hokkaido) to south (Okinawa).



Shortly after September 2021, there was a shift in transmission across all prefectures as it increased compared to 2020 and early 2021. Synchronicity, defined here as similarity of transmission rates across prefectures in Japan, seemed to become more evident from late 2021 onwards as there was a visual increase in transmission particularly in January 2022 and January 2023. This time period coincides with the New Year holidays when more people tend to have social and family gatherings. There was also another slight increase in May 2021 and 2022 as well as August 2021 and 2022 that correlate with the Golden Week and Obon holidays respectively, which are consecutive national holidays that span for about a week each. One outlier that stood out visually was Okinawa where transmission continued to be especially elevated from May 2022 to January 2023.

Especially in prefectures with urban cities with high density, such as Tokyo, Osaka, and Fukuoka, many of them are interconnected with the surrounding area by public transportation (e.g. bullet trains). To test the hypothesis of transmission rates being more similar to adjacent prefectures and within the same region from having higher interconnectivity (i.e. more individuals traveling across prefectures and thus more contacts with one another at work or school settings), the transmission rates of all prefectures were analyzed statistically for 2020-2021 and 2022-2023 (**Fig 4.12**). In the first two years (**Fig 4.12a**), there was no strong evidence ($p \geq 0.1$) in the transmission rates differing across prefectures, showing synchronicity in transmission across Japan. Okinawa also did not show strong evidence ($p \geq 0.1$) of its transmission rates being different from the rest of Japan. There was no observation with a q-value < 0.05, indicating there was no evidence for a false positive among the 1081 paired comparisons.

Fig 4.12 Heatmap of p-values calculated from a paired t-test comparing the mean transmission rates of prefectures from the mathematical model fitted to the reported COVID-19 cases per prefecture.

Fig 4.12a shows the transmission rates from 2020-2021 and **Fig 4.12b** shows the transmission rates from 2022-2023.

Fig 4.12a

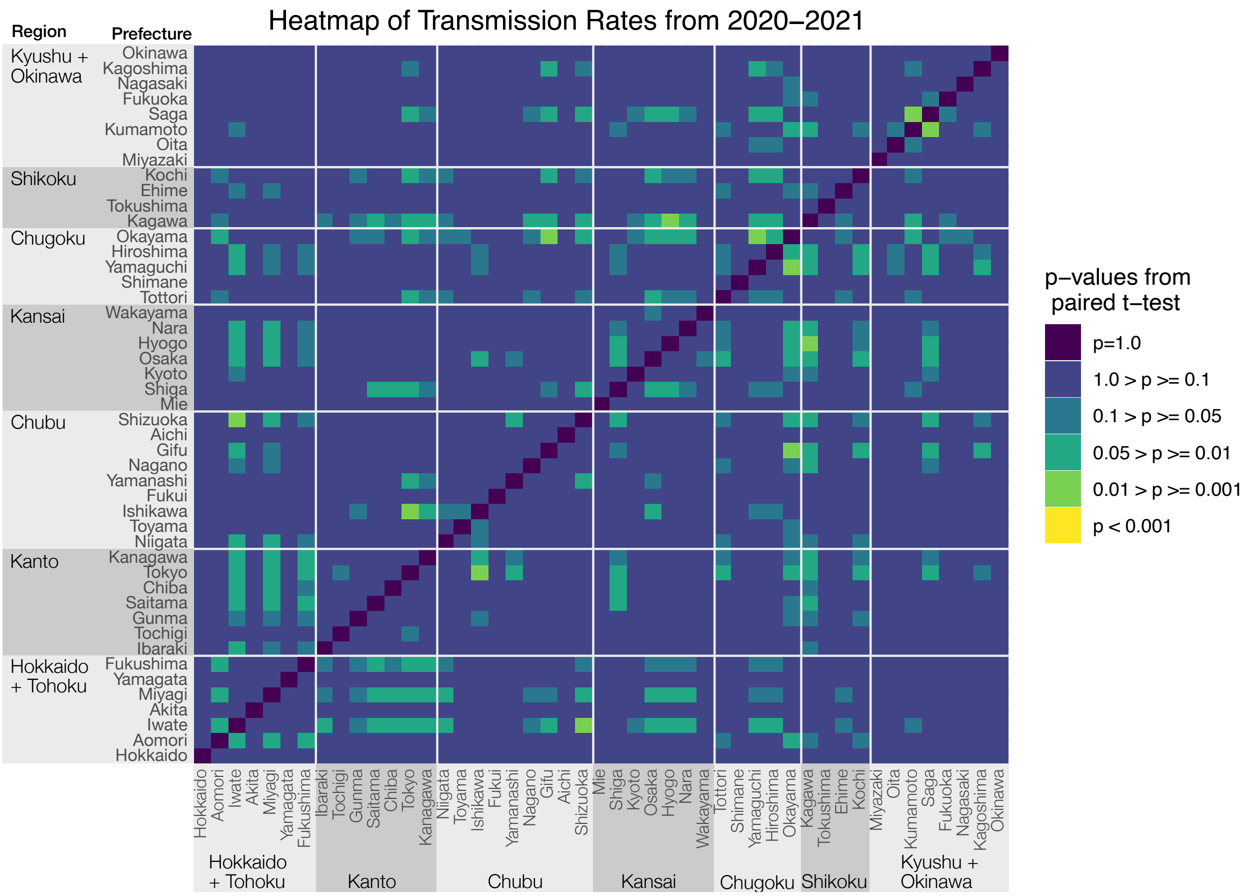
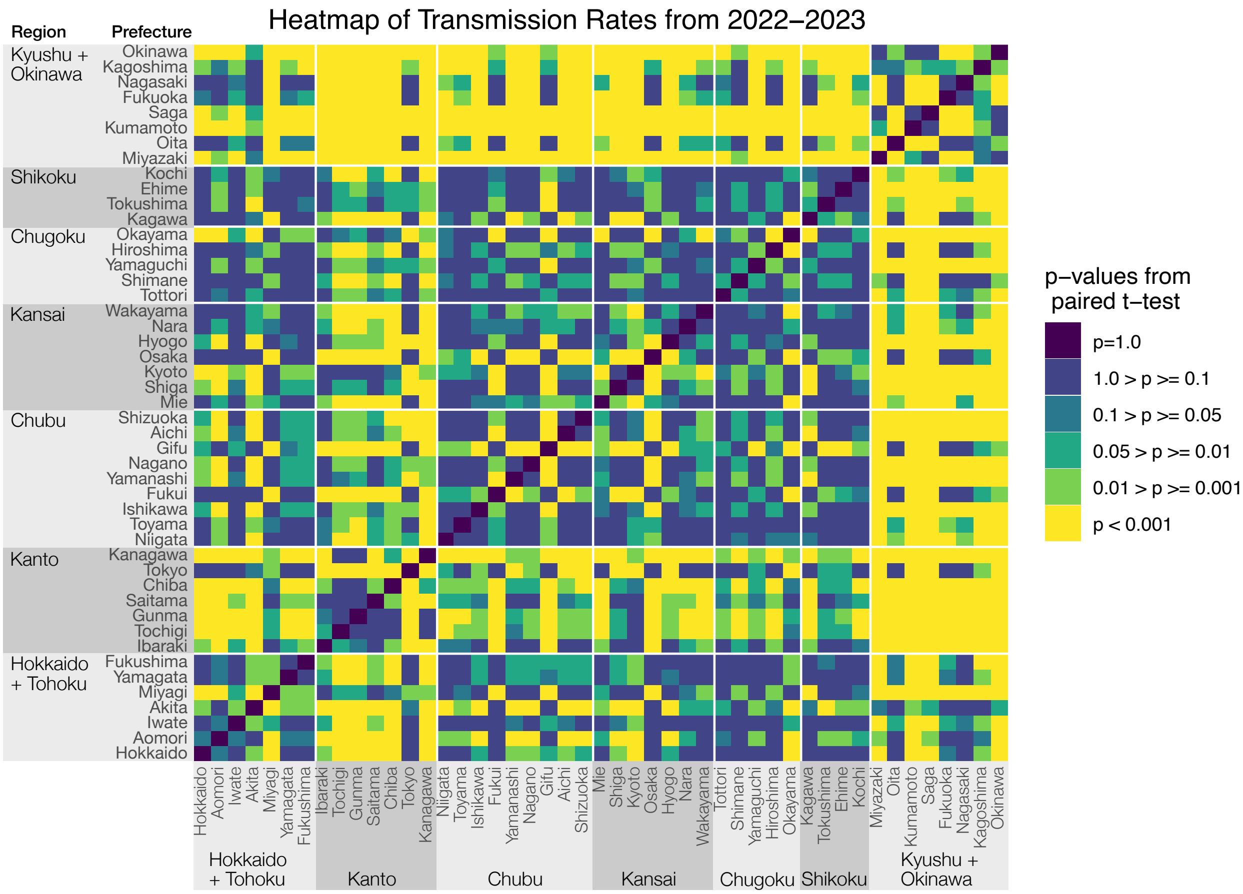


Fig 4.12b



Although there was more variability in the transmission rates across Japan in 2022-2023 compared to 2020-2021, there were three distinct patterns (**Fig 4.12b**). One was that when observing the transmission rates amongst the prefectures in the same region, there was a tendency of having more similar transmission rates ($p \geq 0.05$ indicated in darker green and purple colors). Secondly, there was a cluster of synchronized transmission rates among the Chubu, Kansai, Chugoku, and Shikoku regions as shown by the blue and purple cluster in the center. Lastly, there was strong evidence in different transmission rates ($p < 0.001$ indicated in yellow) when comparing the prefectures in Kyushu (Miyazaki, Oita, Kumamoto, Saga, Fukuoka, and Nagasaki prefectures) and Okinawa to the rest of Japan. Among the 1081 paired comparisons, 775 observations had a q-value < 0.05 (i.e. 39 observations expected to be false positive) indicating a false discovery rate of approximately 3.6%.

When these transmission patterns were plotted by the mean difference of transmission rates, the trend became more apparent by region and highlighted prefectures that tended to have lower or higher transmission rates compared to other prefectures (**Fig 4.13** and **Fig 4.14**, note the different scales on y-axes). In 2020-2021, prefectures in the Kanto and Kansai regions, especially Tokyo and Osaka, had higher mean transmission rates than other regions (**Fig 4.13**). Okinawa also showed a higher mean transmission rate compared to prefectures in Kyushu. In 2022-2023, there was a clearer difference in transmission rates when comparing northern vs. southern prefectures (**Fig 4.14**). Okinawa had a higher mean transmission rate compared to the rest of Japan, and the transmission patterns of the prefectures on Kyushu were clustered together that appeared separate from the other regions.

Fig 4.13 Boxplot showing the mean difference of beta from the mathematical model fit to reported COVID-19 case data per prefecture from 2020 to 2021.

The x-axis shows all 47 prefectures of Japan from north (Hokkaido) to south (Okinawa). Mean difference = mean beta across all time points of the prefecture in comparison – prefecture indicated on the x-axis.

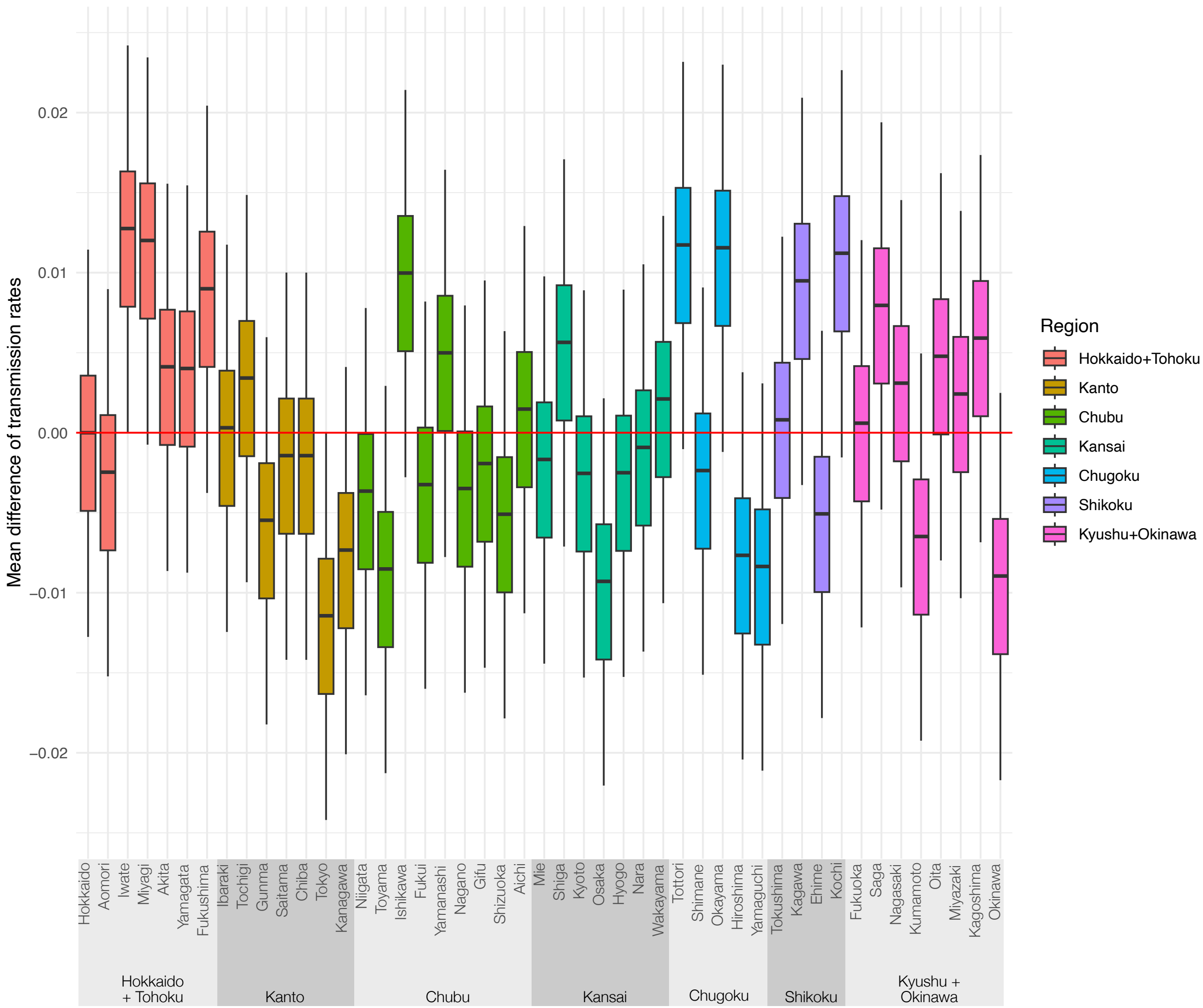
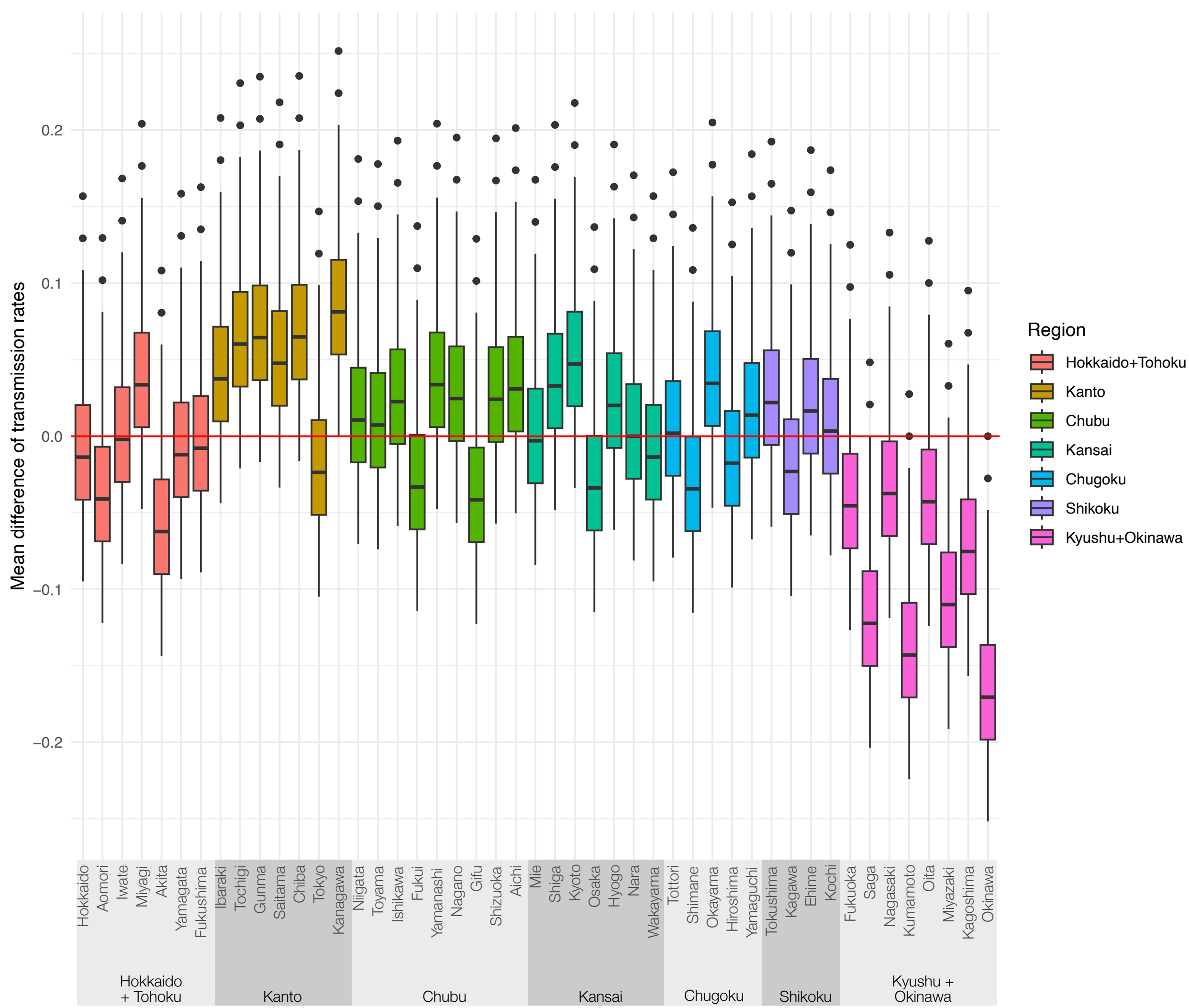


Fig 4.14 Boxplot showing the mean difference of beta from the mathematical model fit to reported COVID-19 case data per prefecture from 2022 to 2023.

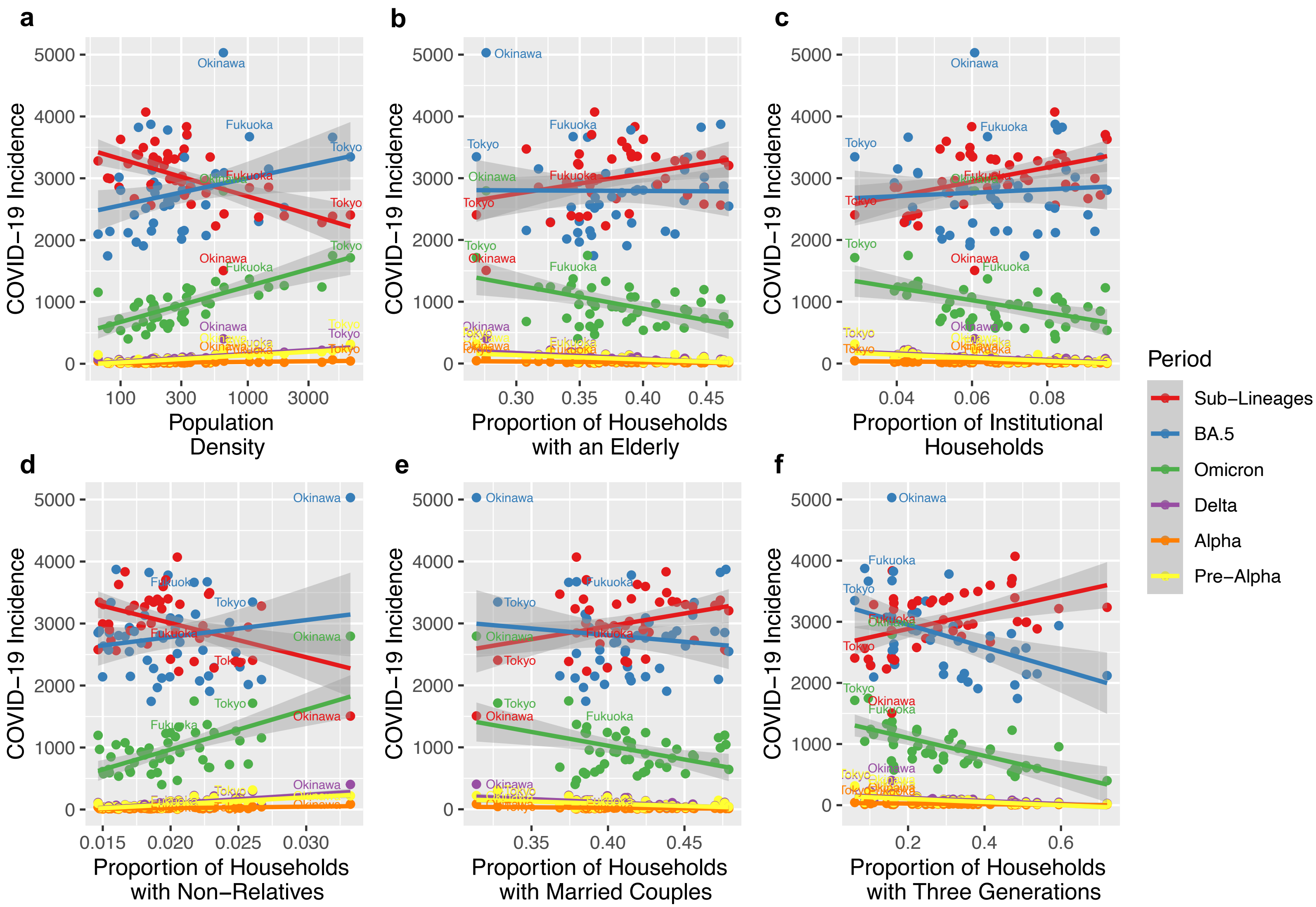
The x-axis shows all 47 prefectures of Japan from north (Hokkaido) to south (Okinawa). Mean difference = mean beta across all time points of the prefecture in comparison – prefecture indicated on the x-axis.



Keeping in mind of the uniqueness of transmission patterns in Okinawa, normalized COVID-19 incidence of each prefecture was plotted against prefecture characteristics based on a hypothesis of having a positive relationship of prefectures with higher population densities and COVID-19 incidence (**Fig 4.15**). Another hypothesis was having a higher COVID-19 incidence in prefectures with a higher proportion of households with three generations, based on an assumption that there would tend to be more outbreaks linked to household transmissions. A generalized linear model was used to examine the correlation between COVID-19 incidence and demographic characteristics across all prefectures. No potential confounders were adjusted. COVID-19 incidence was stratified by the type of SARS-CoV-2 that was circulating, ranging from pre-Alpha to Omicron's sub-lineage variants. As a result, there were three main characteristics. First, there was a strong positive correlation between population density and COVID-19 incidence from when pre-Alpha was circulating up to BA.5 variant. Once Omicron's sub-lineages emerged, the correlation switched directions and showed a negative correlation. Second, prefectures with lower proportions of households with three generations had a negative correlation with incidence until during the period of sub-lineages, the correlation switched to positive. The other household characteristics, such as proportion of institutional households, non-relatives, elderly individuals, and married couples, did not show a strong correlation with incidence as the trends seemed to be mostly influenced by outliers. Third, these outliers were identified as Tokyo and Okinawa. Incidence in Okinawa was especially high during the circulation of BA.5 despite its mid-level population density. While Okinawa's proportion of households with non-relatives was highest in Japan, it had a smaller proportion of households with individuals ages 65 years and above, married couples, and those with three generations.

Fig 4.15 Scatterplots showing the correlation between COVID-19 incidence (reported number of COVID-19 cases per 10000 per person-year) and prefectural demographic characteristics.

a. population density per km^2 (in log scale) **b.** households with an elderly (65 year old and above) living alone or as a couple, **c.** institutional households, **d.** households including non-relatives, **e.** households with married couples, and **f.** households with three generations. Each dot represents a prefecture and each color signifies the predominant SARS-Cov-2 variant that was circulating between 2020 and 2023.



For exploratory analysis purposes (and not for prediction), six of these demographic characteristics explored from **Fig 4.15** were included in a multivariable linear regression using a generalized linear model. The outcome was COVID-19 incidence and the model based incidence during the Delta variant period as the reference. The results of the coefficients are summarized in **Table 4.2**.

Table 4.2 Coefficient estimates with 95% confidence intervals (CI) of the multivariable linear regression using a generalized linear model with covariates including the period when each variant was circulating (Delta variant as the reference) and demographic characterstics of Japan.

	Estimate	**Lower 95% CI**	**Upper 95% CI**
Period with predominant variant circulating			
Pre-Alpha	0.76	0.64	0.89
Alpha	0.23	0.19	0.27
Omicron	11.55	9.81	13.58
BA.5	35.01	29.76	41.19
Sub-lineages	38.09	32.38	44.81
Demographic characteristics of Japan			
Population density (log10)	1.27	1.01	1.59
Households with an elderly living alone or as a couple	5.26E-01	9.14E-03	30.23
Institutional households	1.79E-01	1.42E-03	22.56
Households with non-relatives	4.27E+10	46.78	3.90E+19
Households with married couples	6.07E-01	1.45E-02	25.42
Households with three generations	3.23E-01	1.71E-01	0.61

There was very strong evidence of higher incidence during the circulation of Omicron, BA.5, and sub-lineages compared to during the Delta variant period. After adjusting for the variant period, there was strong evidence of incidence increasing with population density and decreasing with with higher proportions of households with three generations. Note the high estimate of the households with non-relatives. These estimates should be interpretated with caution as we identified Okinawa as an outlier from **Fig 4.15**. When Okinawa was excluded in the analysis, the proportion of households with non-relatives did not show strong evidence (p-value: 0.074) in having an association with incidence.

4.4 Discussion

Throughout the COVID-19 pandemic, countries utilized mathematical modeling for various purposes such as forecasting the next epidemic and evaluating the effect of governmental regulations and PHSMs on incidence. As the pandemic progressed, we gained more scientific evidence on the characteristics of SARS-CoV-2 and human behavioral characteristics, such as contact patterns. This made possible the development of more sophisticated models with higher-precision parameters. Although the mathematical model presented in this chapter does not capture all the characteristics of SARS-CoV-2 that we understand as of today, our findings were built upon a model that initially had a specific focus on Fukuoka prefecture and its projections on the occupancy of hospital beds for COVID-19 patients. The objective of expanding the model to the rest of Japan was to describe the COVID-19 epidemic waves across all 47 prefectures. The model was first developed using Microsoft Excel because this was the software that was commonly used by the Japanese government officials including the Ministry of Health, Labor, and Welfare. It was important to make the model simple and useable by a wide audience including policymakers who did not necessarily have a public health background. We maintained this simplicity as the model was fit to prefectural incidence data without incorporating infectious contacts and networks within and across prefectures. Although we now know that these factors have been critical in disease transmission of COVID-19, the modeling approach that we took regards each prefecture as separate epidemics. This was because we had developed this model during an emergency situation with no expected end date of the pandemic. The epidemiological situation was constantly changing, so having a quick turnaround of results to characterize the epidemic was prioritized.

There are limitations of the model. One is the assumption that contacts were assumed to be random, and age-stratified contacts were not incorporated when this model was developed. As demonstrated in **Chapter 3** from the contact surveys conducted in Fukuoka and Osaka prefectures, contacts vary by age as most individuals have the highest contacts among individuals in the same age category, and younger populations contact with one another especially among school-aged children. Vaccinated populations were also not age-stratified which is a limitation as there are reported differences in vaccine coverage by age in Japan. In addition, the model used discrete time with difference equations, assuming individuals move between different categories (e.g. transitioning from infected to recovered) in discrete time intervals. The next chapter will address these limitations by incorporating age-stratified contacts in the model and using differential equations that allow the number of susceptible, infectious, etc. to change continuously. Another limitation of the model covered in this chapter is how hybrid immunity, developed from both natural infection and vaccination, was not incorporated in this model. As recent studies have shown that hybrid immunity can reduce infectiousness of SARS-CoV-2 and provide increased protection against infection

(102,103), the model may not accurately capture the transmission dynamics of these individuals and thus, it may have overestimated the number of infections from not considering the added protection.

4.5 Main Takeaway

There were four main takeaway points. First, the model demonstrated how each wave of COVID-19 was marked by each variant, demonstrating the sharp increase in transmission rate and incidence after the Omicron variant was introduced. Although by the time BA.5 of the Omicron variant was circulating, Japan was well into the process of providing booster shots of the COVID-19 vaccine with 77% of the national population having received two doses by February 2023 (104). This showed the variant's increased transmissibility compared to previous variants.

Second, the trend of transmission rates was more homogeneous geospatially in 2020-2021 compared to 2022-2023. Since contact rates drive transmission, contact patterns may had been more uniform across all of Japan during the first two years of the pandemic. EDs were implemented nationally during this time whereas during 2022-2023 when governmental regulations became more relaxed depending on the prefecture's incidence, differences in contact patterns may had started to show. These first two points reaffirm the importance of two key factors—virus characteristics and contact patterns—that can influence transmission patterns.

Third, by analyzing the transmission rates and normalized incidence rates across all 47 prefectures, outliers such as Okinawa became apparent. Based on prefecture characteristics assessed by census data, Okinawa was unique with fewer households with married couples, fewer elderly individuals and couples living in a household, and fewer households with three generations. Based on 2022 census data, Okinawa was reported as the prefecture that has the highest proportion of the population below 15 years old and the only prefecture that has a higher proportion of individuals aged below 15 than the 75 years old and above (105). With Okinawa having a generally younger population, it led us to question whether this would affect the contact patterns such as by increasing more frequent contacts and thus more infections. Such findings led to the exploration of Okinawa in the next chapter to disentangle contact patterns and demographic characteristics that may affect SARS-CoV-2 transmission.

Finally, Okinawa has a populational density average of 640 people per km^2 and was inconsistent with the reported high incidence compared to the rest of the prefectures where there was a positive correlation between incidence and population density. During the Omicron sub-lineage circulation, this correlation switched; Okinawa dropped to having the lowest incidence out of all prefectures in

2023. This could possibly be a build-up of herd immunity; the more rural, less densely populated prefectures that did not initially go through an intense epidemic may have had a more susceptible population and thus were more likely to get infected during the later years of the pandemic as they may not have had protection from natural immunity. When the variant period and demographic characteristics were adjusted in a multivariable linear regression, incidence decreased with higher proportion of households with three generations. This was the opposite trend from what we had initially predicted. Compared to individuals who live alone or as a couple, there may be unique contact patterns among individuals who live in households with three generations, which often include older individuals. These changes observed in relationship after the emergence of sub-lineages suggest the need to incorporate interaction between the period when each SARS-CoV-2 variant was circulating with demographic characteristics such as population density and households with three generations. This can be explored in the future by incorporating an interaction term in the multivariable linear regression model to further assess the relationship of demographic patterns with COVID-19 incidence.

The next chapter dives deeper into the aspect of how heterogeneities in age-stratified contact patterns, demography, and vaccination coverage impact SARS-CoV-2 transmission. It revisits Fukuoka and Osaka prefectures by utilizing their contact patterns but also those of Okinawa prefecture as it was shown to be an outlier based on high incidence rates and some of their unique demographic characteristics. Despite the gaps in the current model, it provided a broad overview of how the epidemic progressed throughout Japan during the three years of the pandemic and identified Okinawa to be explored further for its uniqueness in transmission and demographic patterns.

Chapter 5 Elucidating the Roles of Heterogeneity in Contact Patterns, Vaccination, and Demography on COVID-19 Transmission Dynamics

While **Chapter 4** described the subsequent waves of the COVID-19 epidemic across Japan from 2020 to 2023, it also highlighted some prefectures that showed as outliers when comparing their transmission patterns. One of them was Okinawa, a prefecture that is unique in its geographical location as it is the southernmost and westernmost prefecture of Japan, but also distinctive in its demographic characteristics and COVID-19 transmission patterns. This chapter is a continuation of the previous chapter and one of the research aims of this chapter is to explore Okinawa more in detail by comparing their age-specific contact patterns with Fukuoka and Osaka prefectures. The second aim of this chapter is to investigate the roles of heterogeneity in contact patterns, vaccination, and demography on transmission dynamics in Okinawa, Fukuoka, and Osaka prefectures.

5.1 Methods

Data from social contact survey, vaccination coverage and demography

An age-structured model was developed by incorporating age-stratified contacts from Fukuoka, Osaka, and Okinawa prefectures based on. the contact surveys that were conducted in December 2022. There was a total of 738 participants in Fukuoka, 795 participants in Osaka, and 172 participants in Okinawa. The contact survey design was done in the same way as described in **Chapter 2 section 2.4** as well as the method of collection of participants that was described in **Chapter 3 section 3.4**. Okinawa was added as a new prefecture with an initial aim to detect differences in contacts between two time points—once in December 2022 and the second in February 2023. This was based on a hypothesis that there would be a difference in contacts during and after a new surge of COVID-19 cases that started from November 2022. By taking into account the smaller population in Okinawa and the feasibility of gathering participants by the survey company, the most realistic sample size was approximately 200 participants at one time point. By using a two-sample t-test calculation, a total sample size of 200 across eight age categories (assuming 200/8 = 25 individuals per age category) would have a power of 41% with a 5% Type 1 error to detect a mean difference of 2.5 contacts between two surveys. For the model simulations, the December 2022 contact survey was utilized as the date was closer to the age-stratified, prefecture-specific COVID19 vaccination coverage that was publicly available on 10 January 2023 on the website of the Prime Minister's Office of Japan (now available as aggregate data on the website of the MHLW (106) and with the assistance of access through Dr. Motoi Suzuki at NIID). This age-stratified, prefecture-specific vaccination coverage data was used for the model simulations. The demographic characteristics of each prefecture (i.e. proportion of the population by age category) utilized for the model were derived from the 2022 Japanese census data (99).

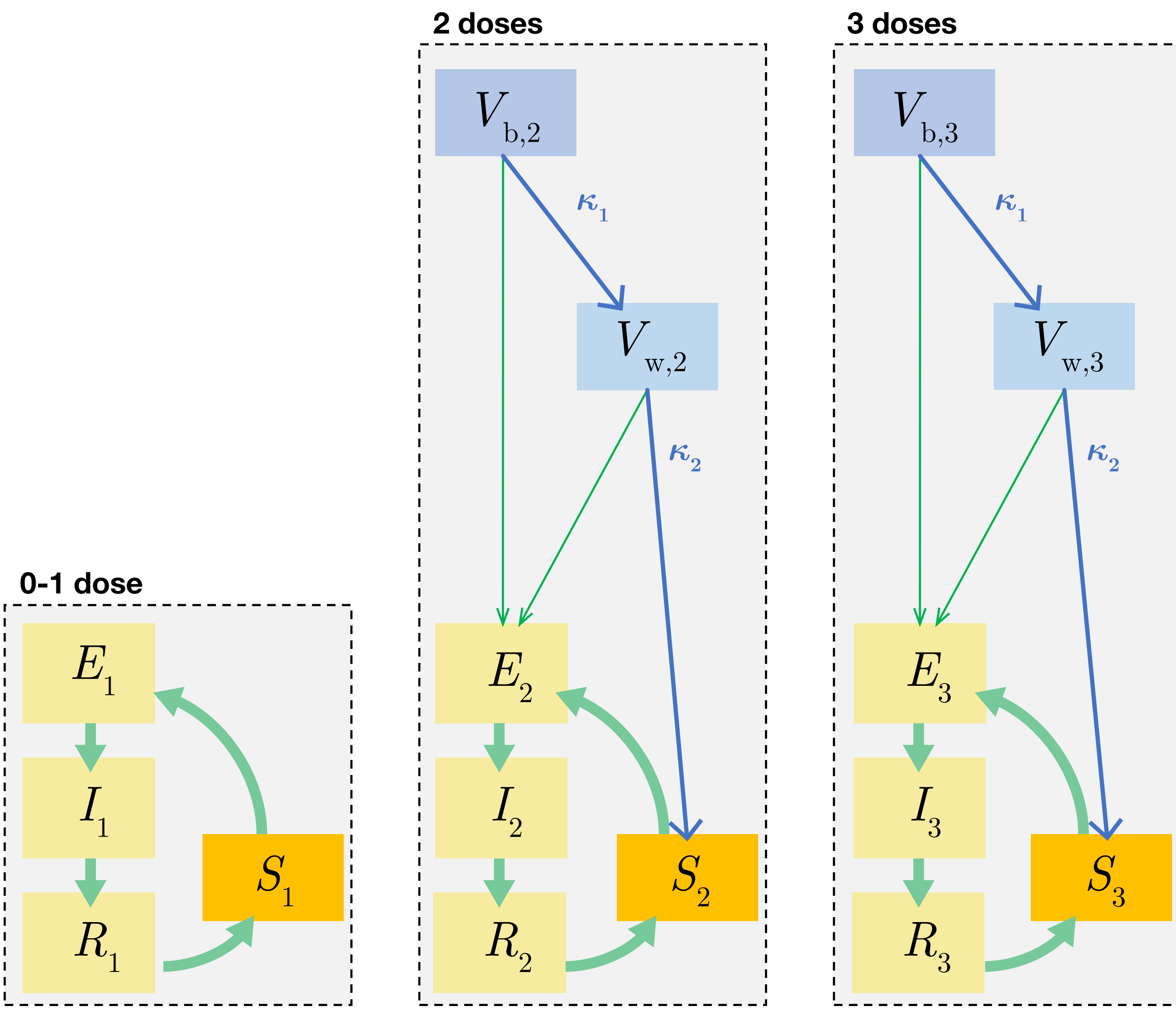
Adaptation of the mathematical model

The SEIR model that was presented in **Chapter 4** was simplified (**Fig 5.1**) but incorporated an age structure along with vaccination and demographic characteristics. To capture the potential difference in simulated incidence among those who were unvaccinated or partially vaccinated (1 dose) vs. those with full doses (2 doses) and a booster (3 doses), the model simulated individuals who were in one of these three vaccination categories. Based on national COVID-19 incidence data, each wave (i.e. from the beginning of a surge to the end after a reported "peak") lasted approximately two months, so the model was simulated for 60 days with each time step defined per day. The total simulated population consisted of 100,000 individuals. All other parameters used for this were the same as Model 2 parameters indicated on **Table 4.1**. Births and deaths were not incorporated in this model as the simulation was for 60 days, a short period that would have minimal changes due to populational birth and death rates. Additionally, the individuals moving from one dose of vaccine to the next were not included in this model as we assumed that this would be minimal within the time span of 60 days. The initial conditions included having one infected individual per age category. Among the individuals in the unvaccinated or partially vaccinated (1 dose) category, the rest of the population started in the susceptible compartment. For those with full doses (2 doses) and a booster (3 doses), the rest of the population started in the V_b compartments as newly vaccinated.

All work was done using R version 4.2.2 using packages including *deSolve (107), dplyr (108), tidyr (109), reshape2 (110), ggplot2 (111) , scico (112),* and *readxl (113)*.

Fig 5.1 An SEIR model with vaccination compartments including individuals who are unvaccinated/partially vaccinated (0-1 dose), those with two doses, and those with three doses.

The blue arrows indicate individuals with waning immunity after being vaccinated. The green arrows indicate individuals getting exposed to SARS-CoV-2 after being vaccinated.



Model equations

The model was developed using the package *deSolve* with the help of examples of age structured models developed by King and Wearing (114) and Soetaert et al (115). The method to calculate R_e, the effective reproduction number, was referred to the method using the Next Generation Matrix derived by Diekmann et al (116). Fundamental concepts of developing a mathematical model using age-stratified contacts, including calculating the effective reproduction number for a population that gained immunity from natural infection and vaccination, was referred to methods covered by Vynnycky and White (67) and Keeling and Rohani (117). The reproduction number of SARS-CoV-2 that was referred to in the calculation of the effective contact was derived from the estimate made by Kucharski et al. that was based on the initial outbreak in Wuhan (118). Each prefecture's model was simulated until it reached its endemic state (>35 years). The reproduction number at the endemic state from the model simulations was calculated by the inverse of the total number of susceptible individuals (including all vaccine status).

The ordinary differential equations used for the model as well as the calculation of R_e using the Diekmann et al. method, and calculation of the probability of an effective contact are all explained in detail in **Chapter 9 Appendix 5**. The notations used in the ordinary differential equations are the same as those shown on **Fig 5.1**. The R scripts for the model simulations are attached in **Appendix 6** and **Appendix 7**.

Statistical analysis

Contact patterns were analyzed similarly to the statistical method explained in **Chapter 3**. Contacts were truncated at a cutoff of 250 to avoid a few observations with hyperinflated contact numbers. Measures of uncertainty in age-specific contact numbers and duration of contact were obtained using the bootstrap; the mean and 95% confidence intervals were obtained by sampling with replacement for 1000 times. When the frequency and duration of contacts were compared across prefectures, age and prefecture were adjusted in a generalized linear model using a Weibull distribution. This distribution was selected to fit the right-skewed distribution of contacts. An interaction term between age and prefecture was also included in the model to assess the possible interaction between the two variables associated with frequency and duration of contacts.

5.2 Results

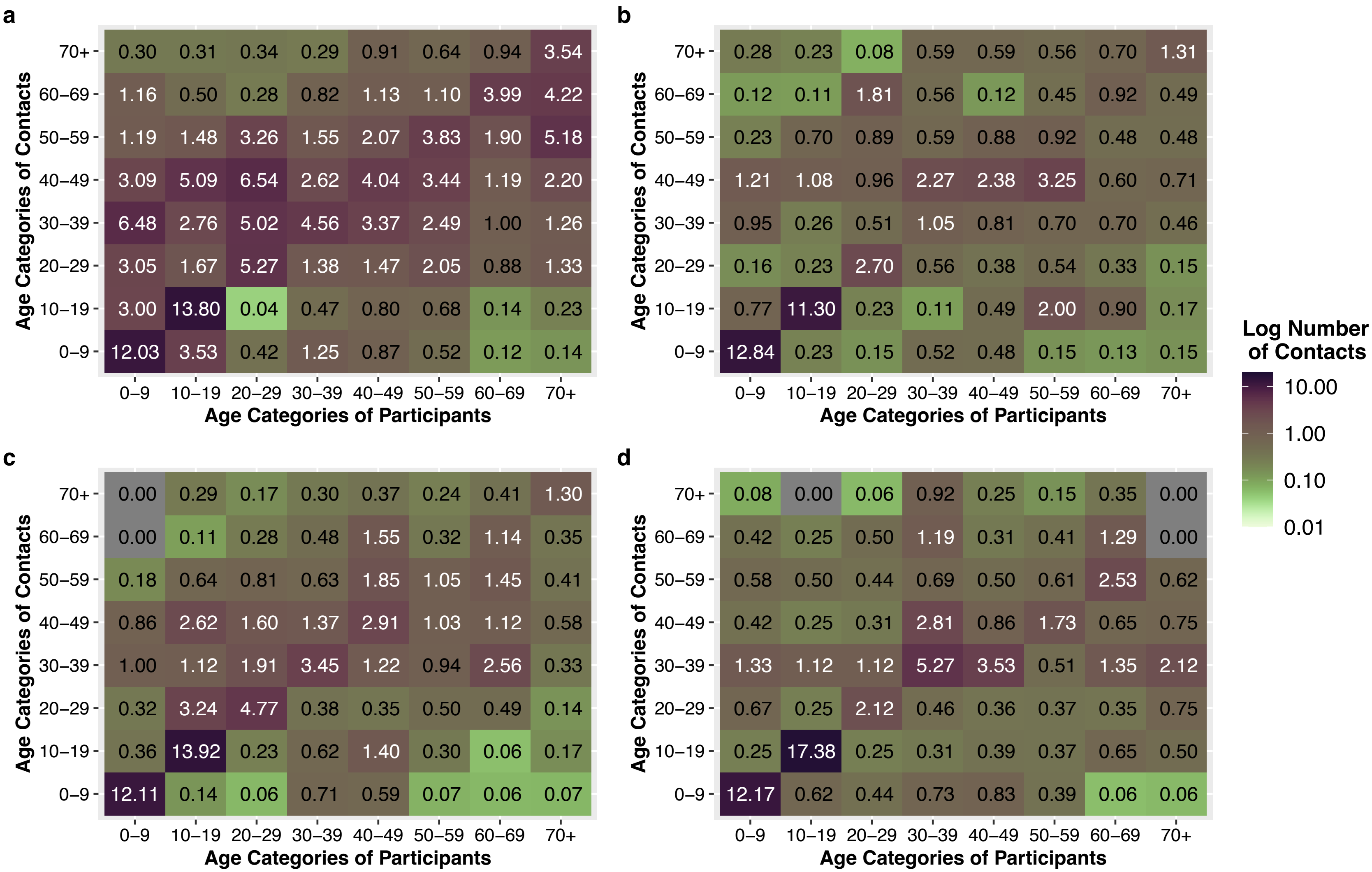
Contact patterns, demographic characteristics, and vaccination coverage across Okinawa, Fukuoka, and Osaka prefectures were analyzed prior to incorporating these parameters in a mathematical model to understand each role in transmission.

Contact patterns

Similar to Fukuoka and Osaka prefectures, contacts in Okinawa prefecture had the highest frequency of contacts among the younger population, especially among the 0-9 year olds and 10-19 year olds based on the contact survey conducted during the weekday in December 2022 (**Fig 5.2**).

Fig 5.2 Age-stratified contact matrices from social contact surveys conducted in Japan. Each cell represents the average number of contacts reported by the survey participants in their respective age categories.

a. Weekday contact patterns of all prefectures in Japan from 2011 (Ibuka et al.) **b.** Weekday contact patterns of Fukuoka prefecture in December 2022 **c.** Weekday contact patterns of Osaka prefecture in December 2022 **d.** Weekday contact patterns of Okinawa prefecture in December 2022.



As shown on the contact matrices, individuals reported the most contacts who were in the same age categories in Okinawa. Compared to baseline 2011 contacts from the Ibuka et al. study (56) (**Fig 5.2a**), the average number of reported contacts for all other ages had mostly decreased to less than one during the COVID-19 pandemic. Individuals older than 70 years old had lower reported contacts across the three prefectures compared to the younger population with an exception of individuals in their 70s in Okinawa contacted with those in their 30s at an average of 2.12 contacts per person.

As described in **Chapter 4**, Okinawa had a higher incidence than other prefectures, leading to a hypothesis that their contact rates may be higher that could lead to more infections. To test this hypothesis, Okinawa's frequency of contacts was compared against Fukuoka and Osaka based on the contact surveys that were conducted during the weekday and weekend in December 2022 (**Fig 5.3**). Younger populations in the 0-9 age category had an average of 15.75 (95% CI: 8.25-23.25) weekday contacts and 12.91 (95% CI: 3.67-30.10) weekend contacts in Okinawa compared to 16.51 (95% CI: 11.42-22.42) weekday contacts and 5.90 (95% CI: 4.00-8.81) weekend contacts in Fukuoka.

In a generalized linear model including age and prefecture, the predicted weekend contacts were reduced across the three prefectures compared to weekday contacts (**Table 5.1**) and as seen from the weighted mean contacts during the weekend (**Table 5.2**). An interaction term between age and prefecture was also explored for weekday and weekend contacts. For all age categories across the three prefectures, the p-value was > 0.05, showing low evidence of having an interaction between the two variables on frequency of contacts.

In a generalized linear model including age and prefecture, an individual in Okinawa would have 1.36 (95% CI: 1.08-1.72) times higher contacts than an individual in Fukuoka during the weekend. In other words, an individual in their 40's in Okinawa would have an average of 6.47 contacts (95% CI: 4.99-8.41) during the weekend where a same-aged individual in Fukuoka would have an average of 4.76 contacts (95% CI: 3.98-5.70) and an average of 5.22 contacts (95% CI: 4.40-6.21) in Osaka (**Table 5.1**). Older populations aged 70 and above had lower contacts; an individual in Okinawa would have an average of 3.51 contacts (95% CI: 2.66-4.63) whereas a same-aged individual in Fukuoka would have an average of 2.58 (95% CI: 2.13-3.12) contacts and 2.83 contacts (95% CI: 2.33-3.43) in Osaka during the weekend. There was no strong evidence in the frequency of Okinawa's weekday contacts being different from Osaka and Fukuoka.

The duration of contacts was also compared across the three prefectures (**Fig 5.4**). Using a similar method with age and prefecture adjusted in a generalized linear model, there was a tendency of longer duration of contacts among the 0-9 year olds compared to 40-49 year olds and 70+ year olds during the weekday and weekend (**Table 5.1**). However, overall, there was no strong evidence in the duration of weekday and weekend contacts being different across the three prefectures. Similar to the frequency of contacts, there was also no strong evidence of an interaction between age and prefecture on the duration of contacts.

Table 5.1 Predicted frequency and duration of weekday and weekend contacts for an individual in their respective age ranges in Osaka, Fukuoka, and Okinawa prefectures based on a generalized linear model including prefecture and age. The contact data was retrieved from the social contact survey conducted in December 2022.

	0-9 year olds		**40-49 year olds**		**70+ year olds**	
Frequency of contacts						
	Weekday	**Weekend**	**Weekday**	**Weekend**	**Weekday**	**Weekend**
Osaka	14.36 (10.59-19.47)	5.57 (4.06-7.64)	6.64 (5.63-7.83)	5.22 (4.40-6.21)	3.39 (2.81-4.09)	2.83 (2.33-3.43)
Fukuoka	13.43 (9.97-18.07)	5.08 (3.74-6.91)	6.21 (5.21-7.40)	4.76 (3.98-5.70)	3.17 (2.63-3.82)	2.58 (2.13-3.12)
Okinawa	13.96 (9.89-19.69)	6.90 (4.86-9.81)	6.45 (5.04-8.26)	6.47 (4.99-8.41)	3.30 (2.53-4.29)	3.51 (2.66-4.63)
Duration of contacts (hrs)						
Osaka	14.51 (11.35-18.55)	12.23 (9.46-15.81)	9.35 (8.17-10.70)	8.40 (7.29-9.68)	7.22 (6.22-8.38)	7.10 (6.08-8.28)
Fukuoka	14.00 (11.01-17.82)	11.76 (9.16-15.10)	9.03 (7.86-10.36)	8.08 (7.00-9.32)	6.97 (5.98-8.12)	6.82 (5.82-8.00)
Okinawa	16.89 (12.79-22.28)	13.44 (10.06-17.96)	10.88 (8.90-13.30)	9.23 (7.51-11.36)	8.40 (6.76-10.43)	7.80 (6.22-9.77)

Table 5.2 Comparison of incidence, demography, and mean weekday contacts per person based on the contact survey conducted in December 2022 across Osaka, Fukuoka, and Okinawa prefectures.

	Osaka	**Fukuoka**	**Okinawa**
Incidence per 100,000 reported 2022-07-31 (BA.5 circulation)	1563.26	1617.19	2459.67
Incidence per 100,000 reported 2022-11-06 (Omicron sub-lineages circulation)	280.39	254.45	148.59
Incidence per 100,000 reported 2022-12-25 (Omicron sub-lineages circulation)	781.26	1162.09	512.22
Demography (<20 years old)	17% (Total N: 5.1 million)	18% (Total N: 8.8 million)	22% (Total N: 1.5 million)
Vaccine coverage as of 1 Dec 2022 (3 doses)	60.6%	63.5%	50.1%
Mean weekday contacts per person (weighted by age and sex) in Dec 2022	8.54	7.47	8.99
Mean weekend contacts per person (weighted by age and sex) in Dec 2022	6.21	6.85	7.26

Fig 5.3 Frequency of contacts reported from the social contact surveys conducted in Okinawa, Osaka, and Fukuoka prefectures in December 2022 during the weekday (top) and weekend (bottom). The 95% confidence intervals were bootstrapped with contacts truncated at 250 contacts.

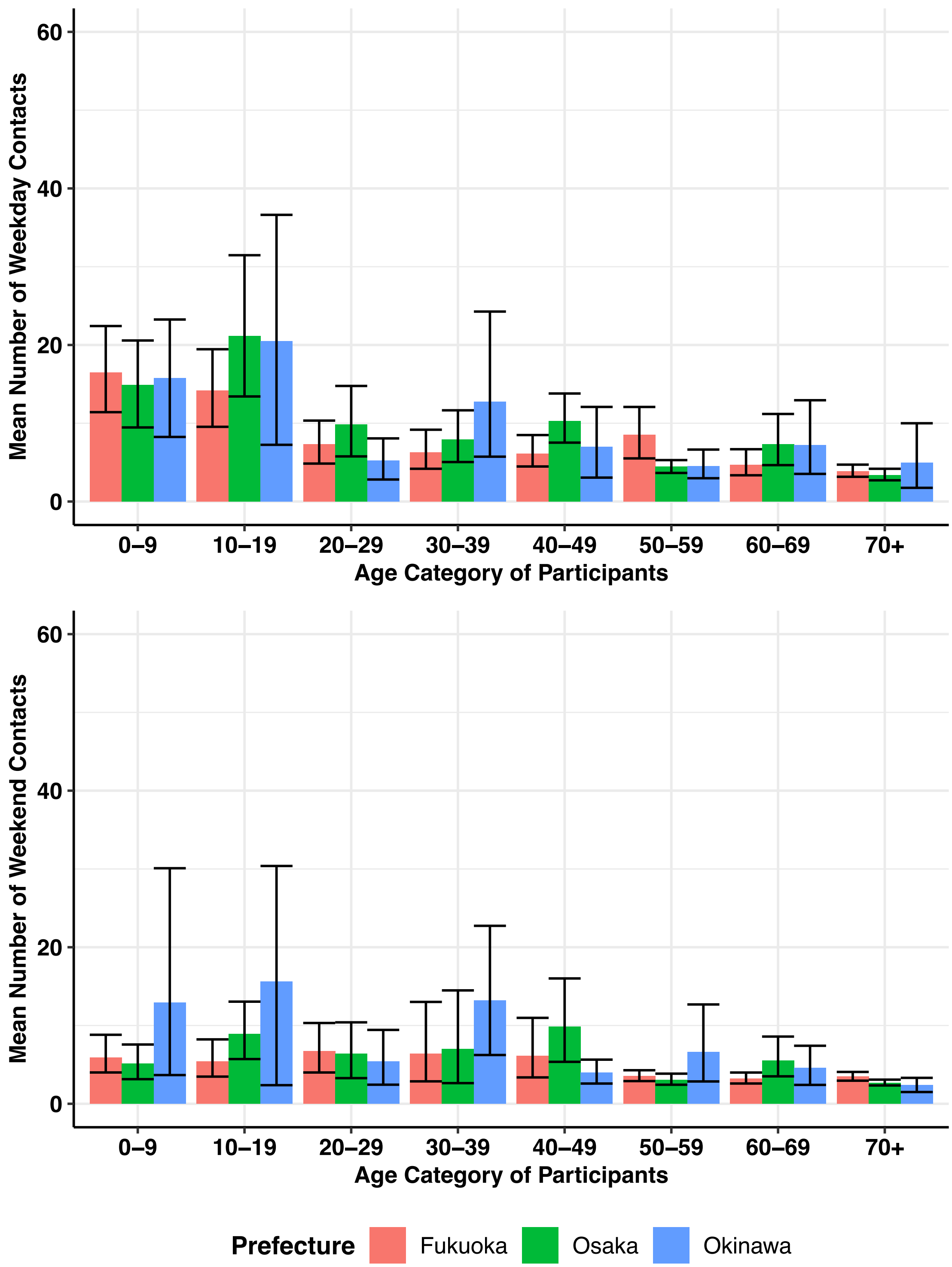
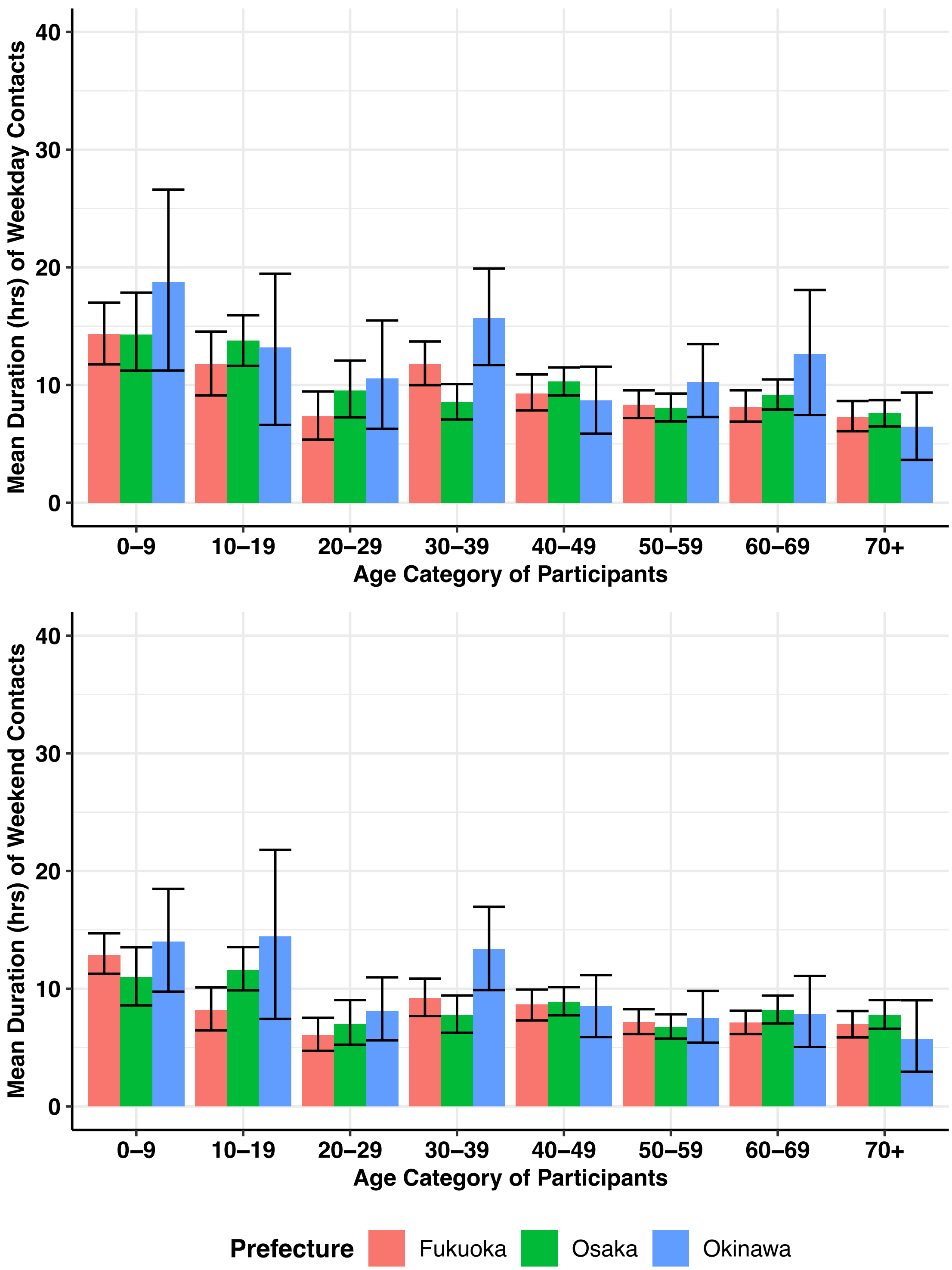


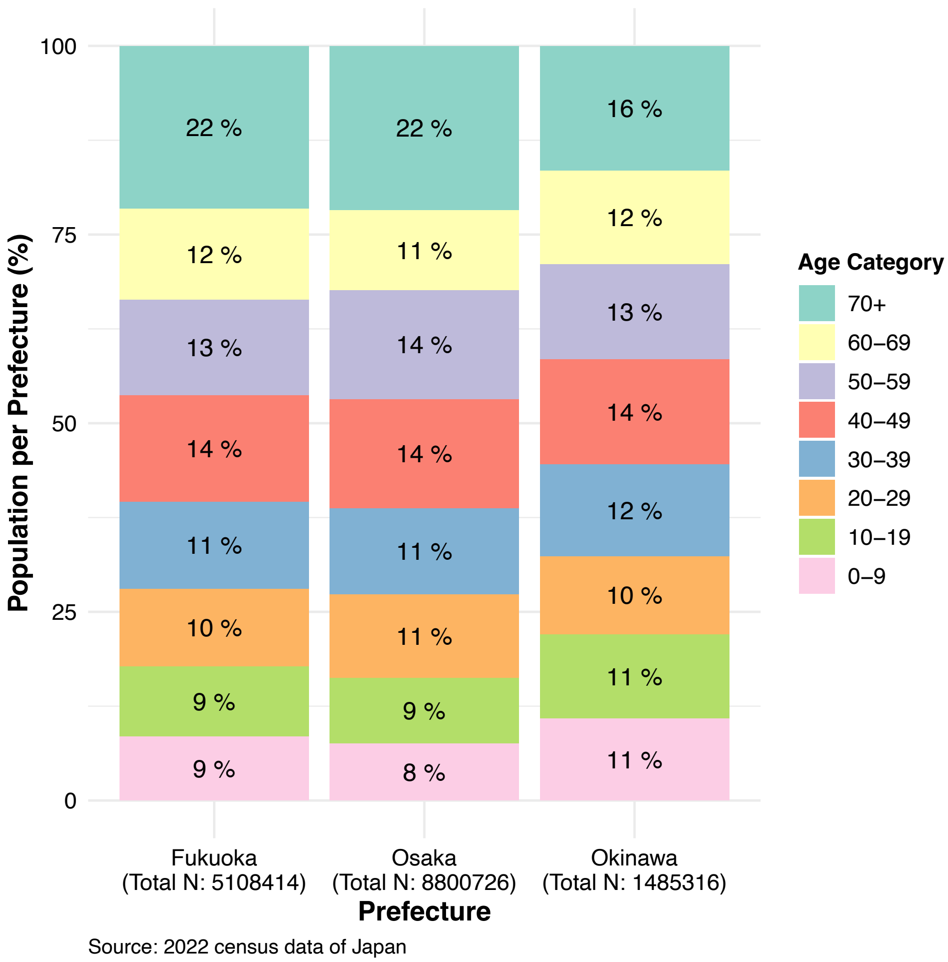
Fig 5.4 Duration of contacts reported from the social contact surveys conducted in Okinawa, Osaka, and Fukuoka prefectures in December 2022 during the weekday (top) and weekend (bottom). The 95% confidence intervals were bootstrapped with contacts truncated at 250 contacts.



Demography

Based on the Japanese census data from 2022, demographic characteristics were analyzed for the three prefectures (105). Individuals younger than 20 consisted of 22% of the population in Okinawa while it was 18% in Fukuoka and 17% in Osaka. For the older populations, 28% of the population was aged over 60 while it was 34% in Fukuoka and 33% in Osaka (**Fig 5.5**).

Fig 5.5 Demographic characteristics in Fukuoka, Osaka, and Okinawa prefectures based on Japanese census of 2022. These proportions per age category were utilized in the mathematical model.



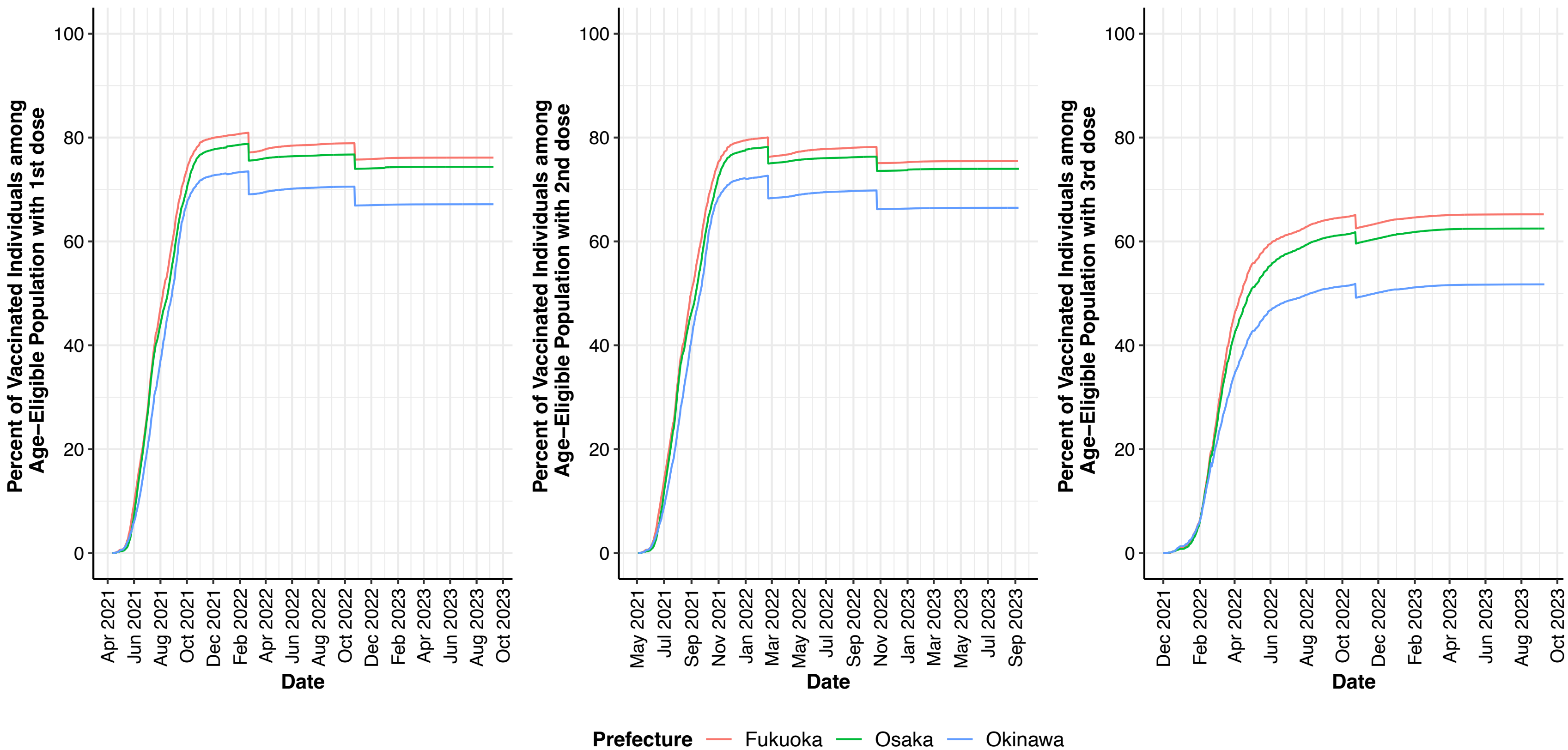
Vaccination coverage

Since COVID-19 vaccination was made available nationally to children at a later stage during the pandemic, it was important to assess vaccine coverage among the age-eligible population. From 17

February 2021, 12-year-olds and above were eligible to receive the first dose of the COVID-19 vaccine, and from 21 February 2021, 5-year-olds and above were eligible. Children aged above 6 months became eligible from October 2022. Because the age-eligible population (i.e. denominator) varied based on this national schedule, there were sudden drops in coverage at these time points (**Fig 5.6**) (104). As of September 2023, Osaka had 73.9% of their population vaccinated with two doses while Fukuoka prefecture had a coverage of 75.5%, but Okinawa's coverage of two doses was 66.5%. For the third dose, coverage was lower across all three prefectures, but Okinawa had the lowest (51.7%) as of September 2023 compared to Osaka (62.5%) and Fukuoka (65.2%).

Fig 5.6 COVID-19 vaccination coverage shown in percent of vaccinated individuals among age-eligible population across Fukuoka, Osaka, and Okinawa prefectures from 2021 to 2023.

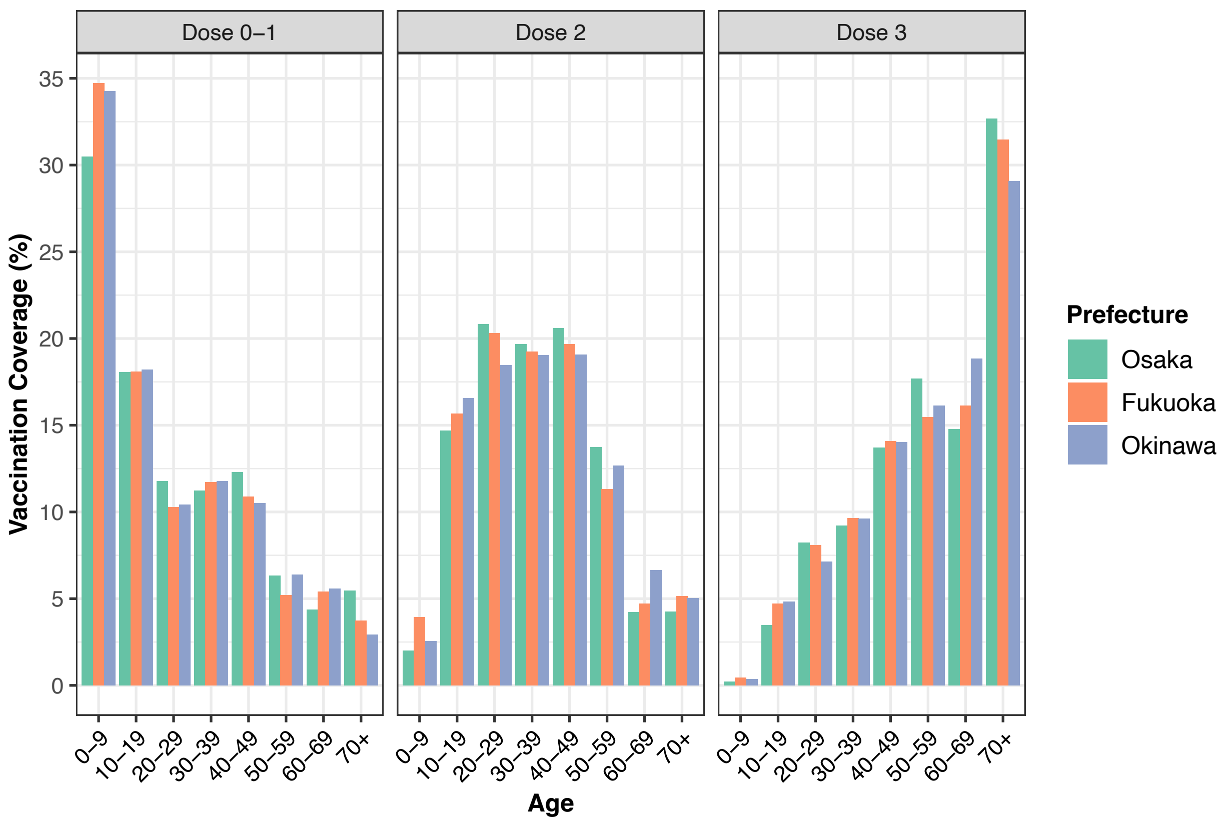
Vaccination coverages are shown for individuals who received their first dose (left), second dose (center), and third dose (right).



The differences seen in vaccine coverages across the three prefectures was taken into account in the model simulations (**Fig 5.7**). Since the model incorporated age-stratified contacts and demographic characteristics, vaccination coverage was also analyzed by age. As of January 2023, those aged 70 and above had been vaccinated the most with three doses of the vaccine across the three prefectures whereas those aged 0-9 were vaccinated the least (0-1 dose). The majority of those who received two doses across the three prefectures was aged between 20 and 40 years old.

Fig 5.7 Vaccination coverages of Fukuoka, Osaka, and Okinawa prefectures that were used for model simulations.

Dose 0-1 includes individuals who did not receive any dose and those who received just one dose. Doses 2 and 3 include individuals who received exactly two doses and three doses respectively. Vaccination coverage is calculated as the individuals in each respective dose per age category divided by the total number of individuals receiving this dose.



Source: COVID–19 vaccination coverage data reported on 10 Jan 2023
by the Prime Minister's Office of Japan

By referring to the proportion of individuals getting vaccinated per age category for each prefecture based on the vaccine coverage data reported on 10 January 2023 (**Table 5.3**), the biggest difference in coverage across the three prefectures was those who received the third dose. Between the ages of 10 and 59, Okinawa consistently had a range of 10.6% to 15.1% lower coverage in the third dose compared to Fukuoka. On the other hand, a range of 76.1% to 92.7% of those who were aged 60 and above had received three doses across all three prefectures.

Table 5.3 Vaccination coverage as of 10 January 2023 for Osaka, Fukuoka, and Okinawa prefectures.

Percentages indicate the proportion of individuals who received each dosage of the COVID-19 vaccine per the total population in each age category of its prefecture. Population number per age category of each prefecture was retrieved from the 2022 Japanese census data.

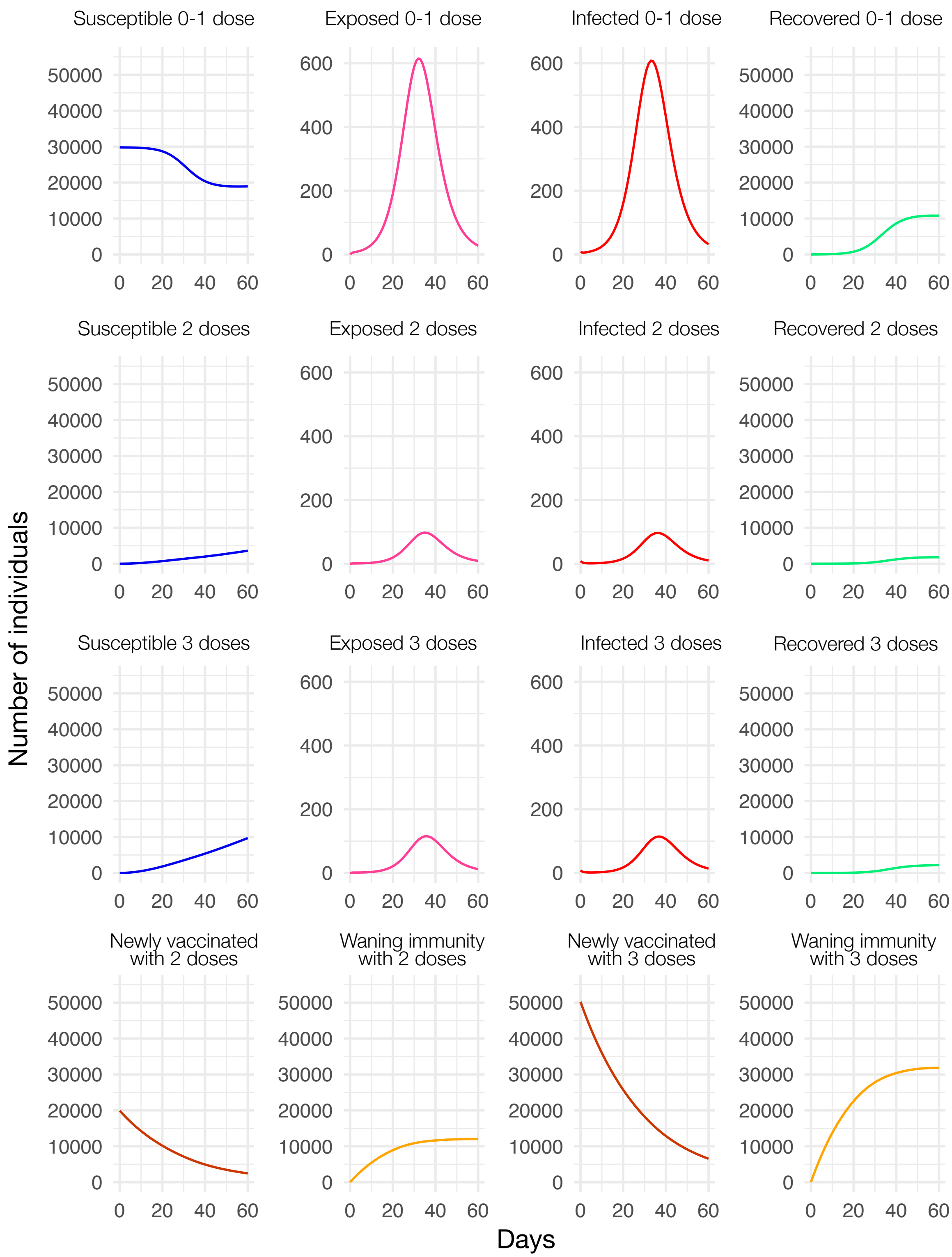
Prefecture and COVID-19 vaccine dose received	Age Category							
	0-9	10-19	20-29	30-39	40-49	50-59	60-69	70+
Osaka 1 dose	6.28%	52.07%	75.78%	77.41%	80.53%	89.99%	90.61%	94.35%
Osaka 2 doses	6.02%	51.48%	75.19%	76.96%	80.19%	89.73%	90.43%	94.12%
Osaka 3 doses	1.73%	24.23%	44.89%	49.04%	57.27%	74.33%	84.02%	90.97%
Fukuoka 1 dose	10.85%	57.92%	79.45%	78.45%	83.66%	91.27%	90.36%	96.44%
Fukuoka 2 doses	10.07%	56.79%	78.02%	77.49%	83.05%	90.88%	90.15%	96.18%
Fukuoka 3 doses	3.42%	32.33%	49.65%	53.30%	63.02%	77.91%	84.54%	92.72%
Okinawa 1 dose	6.77%	52.38%	71.36%	72.01%	78.27%	85.32%	87.03%	95.05%
Okinawa 2 doses	6.26%	51.37%	70.05%	71.09%	77.59%	84.83%	86.67%	94.69%
Okinawa 3 doses	1.62%	21.78%	34.53%	39.83%	50.41%	64.70%	76.06%	88.61%

Model simulations

With age-stratified contacts, demography, and vaccination characteristics incorporated in the mathematical model, the simulated incidence (i.e. number of infections per 100,000) was compared across the in silico experiments as well as across the different doses of the COVID-19 vaccine. Because Fukuoka and Osaka prefectures showed similar contact patterns and they both had similar demographic and vaccination coverages (**Table 5.2**), the model simulation results presented here compare Fukuoka and Okinawa. As shown on the table, Okinawa had the highest incidence during the circulation of BA.5 variant in July 2022. The weighted mean weekday and weekend contacts per person was also the highest in Okinawa compared to Fukuoka and Osaka prefectures. An example of the model simulations of Okinawa is shown on **Fig 5.8** where it was evident that the highest incidence occurred among the unvaccinated and partially vaccinated (0-1 dose). These results also showed a growing increase in the susceptible population among those who were vaccinated with two and three doses.

Fig 5.8 Transmission dynamics of Okinawa prefecture based on model simulations with Okinawa's vaccination coverage, demographic characteristics, and contact patterns.

Note the different y-axis scale for the exposed and infected compartments.



To elucidate each role of contact patterns, demography, and vaccination on transmission, the percent increase and arithmetic difference in incidence were compared between each in silico experiment (**Table 5.4**). First, simulated incidence attributed to weekday contact patterns was analyzed by comparing Fukuoka and Okinawa. When we assigned the Fukuoka model (i.e. all three parameters of contacts, vaccination coverage, and demography from Fukuoka data) as our default model, there would be a total of 363.1 infections compared to a total of 819.0 infections from the Okinawa model which would be a 125.6% increase. In scenario H1, where just the contacts are replaced with Okinawa's but vaccination coverage and demography remain as Fukuoka's, there would be a 46.7% increase in total infections compared to the default Fukuoka model. The next simulations would be to understand how close the total infections would be to the Okinawa model by changing the vaccination coverage or demography to Okinawa's patterns by keeping the contacts as Okinawa's. When comparing scenario H4 (Okinawa contacts and vaccination) and H6 (Okinawa contacts and demography), there was an 80.3% and 84.7% increase respectively.

When we observed the difference between H1 (Okinawa contacts) and H0 (default Fukuoka model), there was an arithmetic difference of 169 infections. The arithmetic difference between H2 (Okinawa vaccination) and H0 was 60 infections. When we took the sum of these differences, it totaled as 229 infections, which was less than H4 (Okinawa contacts and vaccination) that had an arithmetic difference of 291 infections compared to the default Fukuoka model. This was indicative of a mechanistic interaction between contacts and vaccination coverage. When we observed the difference between H3 (Okinawa demography) and H0 (default Fukuoka model), there was an arithmetic difference of 101 infections. When adding this with 60 infections, the arithmetic difference shown in H2 (Okinawa vaccination), the sum equaled to 161 infections, which was less than H5 (Okinawa vaccination and demography) that had an arithmetic difference of 178 infections. This showed that demography and vaccination coverage also had an interaction with incidence. These calculations showed that there was a multiplicative effect of contacts, demography, and vaccination on incidence.

When we explored the simulated incidence attributed to vaccination, there was a 16.6% increase in incidence (scenario H2) when only vaccination data was switched from Fukuoka's to Okinawa's. When combined with Okinawa's demographic characteristics (scenario H5), there was a 50.0% increase in incidence and an 80.3% increase when the model incorporated Okinawa's contact patterns and vaccination data (scenario H4). Lastly, the level of demographic patterns attributed to Okinawa's incidence was analyzed. When only the demographic characteristics were switched from Fukuoka's to Okinawa's (scenario H3), there was a 27.9% increase in incidence and when combined with Okinawa's contacts (scenario H6), there was an 84.7% increase in incidence.

Table 5.4 Simulated incidence attributed to Okinawa prefecture's age-specific contact patterns. The percent increase and arithmetic difference of the total infections indicated on H1 to H7 scenarios are calculated by referring H0 (all Fukuoka) as the reference.

In silico Experiment	Age-stratified Contacts	Vaccination coverage	Demography	Incidence 0-1 dose (out of Total N: 100,000)	Incidence 2 doses (out of Total N: 100,000)	Incidence 3 doses (out of Total N: 100,000)	Total infections (out of Total N: 100,000)	% increase	Arithmetic difference
H0 default Fukuoka	Fukuoka	Fukuoka	Fukuoka	296.940	22.772	43.365	363.077	0	0
H1 Okinawa contacts	Okinawa	Fukuoka	Fukuoka	374.918	54.944	102.639	532.501	46.663	169.424
H2 Okinawa vaccination	Fukuoka	Okinawa	Fukuoka	355.294	29.131	38.828	423.253	16.574	60.176
H3 Okinawa demography	Fukuoka	Fukuoka	Okinawa	379.134	29.368	55.972	464.474	27.927	101.397
H4 Okinawa contacts and vaccination	Okinawa	Okinawa	Fukuoka	485.138	77.757	91.731	654.626	80.299	291.549
H5 Okinawa vaccination and demography	Fukuoka	Okinawa	Okinawa	453.577	37.448	49.906	540.931	49.985	177.854
H6 Okinawa contacts and demography	Okinawa	Fukuoka	Okinawa	472.890	68.825	128.735	670.450	84.658	307.373
H7 Okinawa	Okinawa	Okinawa	Okinawa	608.173	96.554	114.268	818.995	125.571	455.918

Across these scenarios, incidence was also compared across the different vaccine doses. Incidence was highest among the unvaccinated and partially vaccinated (0-1 dose) individuals, and the next highest was those with three doses and lastly those with two doses. Using the prefecture's respective contact patterns, vaccination coverage, and demography, R_0 was calculated at its endemic state for Fukuoka (R_0: 1.154), Osaka (R_0: 1.246), and Okinawa (R_0: 1.293). When weekend contact patterns were used with the same parameters used from the previous simulations that used weekday contacts, an epidemic did not start for all three prefectures.

To have a clearer picture on how incidence differed by an individual's age and their vaccine status, simulated incidence was compared across the three prefectures by different ages and dosage of the vaccine (**Table 5.5**). When comparing the adults in their 20's and 40's with those aged 70 and above across all three prefectures, it was clear that incidence was higher among the younger generations. There was a starker difference among those who were unvaccinated or partially vaccinated (0-1 dose) compared to those who had received two or three doses.

Table 5.5 Comparison of simulated incidence across Osaka, Fukuoka, and Okinawa prefectures by different ages and vaccine status.

Prefecture	**0-1 Dose Incidence**			**2 Doses Incidence**			**3 Doses Incidence**			**Overall Incidence**		
	20s	40s	70+	20s	40s	70+	20s	40s	70+	20s	40s	70+
Osaka	334.21	334.88	15.10	161.94	151.92	4.44	239.18	377.08	81.21	735.33	863.88	100.75
Fukuoka	66.18	167.51	12.61	32.52	74.38	5.30	55.65	230.46	98.83	154.35	472.35	116.74
Okinawa	318.72	354.67	36.59	142.87	163.62	16.61	138.95	302.08	219.19	600.55	820.37	272.38

5.3 Discussion

Both Chapters 4 and 5 explored COVID-19 transmission dynamics of Japan with the usage of a mathematical model, first by broadly depicting the trajectory of the epidemic across all 47 prefectures that allowed us to explore a specific prefecture, such as Okinawa, that showed unique epidemic patterns. This led us to examine how transmission patterns of Okinawa differed from other prefectures due to their contact patterns, vaccination coverage, or demographic characteristics. When the frequency of weekday contacts was analyzed after age and prefecture were adjusted, there was no strong evidence of differences across Okinawa, Fukuoka, and Osaka prefectures, but when these age-stratified contacts were incorporated in the mathematical model with vaccination and demographic characteristics, Okinawa's simulated incidence was 1.26 times higher than Fukuoka's and 1.09 times higher than Osaka's. When comparing the proportions of populational demographics, Okinawa has a 5% bigger population aged younger than 40 compared to Osaka and Fukuoka. There was no difference in the frequency of weekday contacts across the three prefectures when analyzed in a generalized linear model, but the age-stratified contact matrices showed a higher trend of weekday contacts amongst school-aged children (10-19 years old) and young adults in their 30's in Okinawa. Additionally, the biggest difference in vaccination coverage was individuals in their 30's where in Okinawa, coverage of the third dose was 15% and 10% lower than in Fukuoka and Osaka, respectively. The bigger proportion of individuals younger than 40, combined with a lower vaccination coverage and higher contacts may have been the driving factors of higher incidence and R_0 at the endemic state in Okinawa.

Although the power for the Okinawa contact survey was relatively low, there was no other contact survey that investigated specifically Okinawa's contact patterns, both before and during the COVID-19 pandemic. Based on its unique epidemiological situation compared to other prefectures in Japan, we hypothesized Okinawa's contact patterns to be different as we observed the contextual background to hold considerable importance in transmission dynamics. Recognizing the limitation of a smaller sample size, we proceeded with the contact survey in Okinawa, with an aim to address this research gap in understanding the prefecture's epidemic patterns.

The in silico experiments demonstrated how contacts were heavily attributed to the number of infections across all three prefectures. When comparing the simulated incidence across these prefectures, the age-stratified contact patterns, demography, and vaccination coverages had a multiplicative effect on incidence with a pronounced effect seen in Okinawa. The interaction seen across these factors demonstrated its importance on incidence, and analyzing each factor independently would not fully capture the transmission dynamics. Analyzing simply the frequency and duration of contacts was a preliminary approach in understanding how individuals contact one another at one point in time. Although analyzing the overall frequency and duration of contacts by age provided a broad overview of contact patterns, it was difficult to assess how these contacts were attributed to incidence. Using a mathematical model made it possible to approach the question on how some of these differences (though not always showing strong statistical evidence in being different) in frequency of contacts across various ages and prefectures can affect transmission dynamics, resulting in differences in the number of infections. The simulated incidence also demonstrated the critical point on how mixing of the population within and across the different age categories, as seen in the age-stratified contact matrices, can impact transmission.

In addition, the number of infections resulting from each simulated scenario differed by vaccine dose. Since the individuals in the 0-1 dose category never have the chance to be protected by belonging in the vaccinated compartments (i.e. $V_{b,i}$ and $V_{w,i}$ compartments), they do not have a delayed effect in returning to become a susceptible individual (i.e. at risk of infection) except after they become infected and gain natural immunity that wanes in nine months, as indicated by the inverse of ρ. This leads to having more individuals being infected in the 0-1 dose category. Among the individuals categorized in the two-dose or three-dose, incidence was higher amongst the individuals who received three doses. It is important to keep in mind of the population already vaccinated with three doses was the largest proportion (60.0% of the Fukuoka population and 50.3% of the Okinawa population based on 10 January 2023 vaccine coverage data) as the starting condition of the simulation.

In contrast to weekday contact patterns, the frequency of weekend contacts across all three prefectures was reduced. When age-stratified weekend contacts were solely used for the model simulations while maintaining the same parameters as the weekday model, an epidemic did not start. These simulations showed that if an individual followed weekend-like contact patterns throughout the week, contacts were reduced enough to prevent an epidemic. One of the limitations of this model is that these reduced weekend contacts were not incorporated together with the weekday contacts, so the simulated incidence from these model outputs may be overestimated. This limitation can be addressed by utilizing time-varying contact patterns. Instead of incorporating weekday or weekend contacts per se, combining the two different sets of contact patterns can address the variation we observe in contact patterns throughout the week. If each time step is one day, weekday contacts can be repeated five times consecutively followed by weekend contacts repeated twice and then back to weekday contacts until the end of the simulation.

Another limitation is the initial conditions of the model simulations. Each epidemic started by having one infected person in each age category per vaccination category. Among the individuals who were placed in the two-dose and three-dose categories, the one infected individual was in the infected compartment (I_2 or I_3) while the rest of the individuals were in the $V_{b,i}$ compartment. This does not necessarily reflect the exact trajectory of transmission in these three prefectures at this specific moment in time; the pandemic was well into the third year as many people across Japan had acquired immunity through natural infection or vaccination. In reality, there would have already been individuals in each compartment, including those in the $V_{w,2}$ or $V_{w,3}$ compartments where their vaccine immunity would have already started waning. Since the starting condition assumed that all the vaccinated individuals (except for the one infected individual per age category) were freshly vaccinated either with the second or third dose, this may have underestimated the overall incidence. However, the objective of these simulations was not to reflect incidence in absolute numbers—the goal was to illustrate how heterogeneities in contact patterns, vaccination, and demography can impact COVID-19 incidence by comparing Okinawa with Fukuoka and Osaka prefectures.
These model simulations provide a starting ground in improving our understanding of how reductions in contacts can play a role in "flattening the curve" of an epidemic. Especially throughout an epidemic when there continues to be a mixture of individuals who acquired immunity from natural infection and vaccination, an overall blanket statement of "reducing contacts" regardless of age may not be the most effective way in curbing transmission. By recognizing how the various levels of vaccine coverage by age as well as the demographic proportion and contact patterns lead to changes in incidence, these insights can inform decision makers when implementing targeted interventions. Demographic characteristics cannot be changed immediately in the timescale of an epidemic. Reducing contacts to the weekend level every day would be unrealistic in Japan where a lockdown was not implemented, and most individuals continued to go to work or school. In contrast, vaccination coverage is one factor that can most likely be changed. For instance, in Okinawa, considering its young population with a relatively lower vaccination coverage among the young adults in their 20's and 30's compared to other prefectures, it could be effective for the prefecture to strategize ways in reaching out to this population to increase vaccine uptake. Changing the vaccination coverage by a specific percentage in the model can project the number of infections that can be reduced.

In addition to vaccination, PHSMs have been encouraged throughout the pandemic to dampen transmission. However, there is a lack of consistency across scientific studies that assess the effectiveness of PHSMs. There is difficulty in conducting randomized controlled trials that evaluate the effect of each PHSM, such as mask wearing, during an epidemic. Such challenges make it difficult to hypothesize the effect of PHSMs in reducing the percentage of transmission per effective contact. Yet, evaluating simulations of a mathematical model with context-specific parameters can lead to a better understanding of the role of each variable. Although behavior, such as person-to-person contact, is difficult to predict particularly during the time of a pandemic, a contact survey is an important tool that provides us with a snapshot of contact patterns at one point in time that can then be utilized to simulate incidence in a mathematical model. The future dynamics of SARS-CoV-2 and other emerging respiratory viruses may also have different transmission characteristics than what were used in this model, so these parameters would need to be modified accordingly for improved projections. Yet, the model simulations explored in this chapter demonstrated that higher incidence reported in Okinawa was attributed to its pronounced interaction of contact patterns, vaccination coverage, and demographic characteristics. These insights shed light on the importance of time- and context-specific contacts on infectious disease transmission as well as their interaction with demographic characteristics and vaccination coverages that can drive the direction of incidence during an epidemic.

5.4 Main Takeaway

Age-stratified contact patterns, demographic characteristics, and vaccination coverages were explored across Okinawa, Fukuoka, and Osaka prefectures. Across all three prefectures, individuals reported the highest contacts who were in the same age categories with the older population (aged 70 and above) reporting lower contacts compared to the younger population. Although there was no strong evidence in the frequency of Okinawa's weekday contacts being different from Osaka and Fukuoka, Okinawa showed higher weekend contacts than an individual in Fukuoka and Osaka. While 22% percent of Okinawa's population is 20 years old and younger, it consists of 17% and 18% of the population in Osaka and Fukuoka prefectures respectively. As of 1 Dec 2022, 50.1% of the vaccine-eligible population was vaccinated with three doses of the COVID-19 vaccine while the coverage was 60.6% in Osaka and 63.5% in Fukuoka. COVID-19 incidence grew progressively as the sub-variants of Omicron circulated in 2022; it rose to at least 2400 cases per 100,000 in Okinawa and up to 1600 cases per 100,000 in Osaka and Fukuoka when BA.5 was the main circulating variant.

The variations observed in contact patterns, demography, and vaccination were incorporated in a mathematical model to understand each role in disease transmission. The SEIR model was developed that included an age structure as well as the prefecture-specific demographic patterns and vaccination coverages. The in silico experiments showed that contacts were heavily attributed to the number of infections across Okinawa, Fukuoka, and Osaka prefectures. Simulated incidence was higher among adults in their 20's and 40's compared to those aged 70 and above. There was also evidence of higher simulated incidence among those who were unvaccinated or partially vaccinated compared to those who had received two or three doses. These simulations demonstrated that particularly in Okinawa, having a bigger demographic of individuals younger than 40 combined with a lower vaccination coverage and higher contacts could have led to higher incidence and R_0 at its endemic state. These results showed how the interaction of contact patterns, vaccination, and demographic patterns were attributed to COVID-19 incidence.

Simulations from a mathematical model can provide insights on how varying vaccination coverage, contact patterns, and demographic characteristics can lead to changes in incidence and provide evidence for targeted interventions. Behavior is difficult to predict, and public health interventions are not always translatable from one pandemic to another. However, a contact survey is an important tool to quantify contact rates that can be used in a mathematical model that is context- and country-specific, which is key when designing effective public health interventions.

Chapter 6 Public Perspectives on COVID-19 Public Health and Social Measures in Japan and the United Kingdom: A Qualitative Study

6.1 Introduction

This chapter includes a manuscript that was published in *BMC Public Health*. The full article is included in **Chapter 9 Appendix 8**. The abstract and summary of our findings are below.

Public Perspectives on COVID-19 Public Health and Social Measures in Japan and the United Kingdom: A Qualitative Study

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Abstract

Background *The COVID-19 pandemic, caused by SARS-CoV-2, was one of the greatest modern public health crises that the world has faced. Countries undertook sweeping public health and social measures (PHSM); including environmental actions such as disinfection and ventilation; surveillance and response, such as contact tracing and quarantine; physical, such as crowd control; and restrictions on travel. This study focuses on the public perceptions of PHSM in two countries, Japan and the United Kingdom (UK) as examples of high-income countries that adopted different measures over the course of the pandemic.*

Methods *This study was conducted between November 2021 and February 2022, a period in which the Omicron variant of SARS-CoV-2 was predominant. Fourteen online focus group discussions were conducted in each country. Overall, 106 total participants (50 from the UK and 56 from Japan)*

participated in 23 focus groups (11 in the UK and 12 in Japan) with an average of three to six participants per group. Both countries were compared using a thematic analysis method.

Results *Both countries' participants agreed that vaccination was an effective measure. However, they did not favor mandatory vaccination policies. Working from home was well accepted by both sides, but they reported that schools should have continued to be opened as before COVID-19. Both sides of participants expressed that temperature testing alone in indoor facilities was ineffective as a COVID-19 control measure. There were contrasting views on face covering rules in public spaces, international and domestic movement restrictions. High acceptance of mask-wearing was reflective of Japanese customs, while it was accepted as a strong recommendation for participants in the UK. Japanese participants favored quarantine for international travel, while the UK participants supported banning non-essential travel.*

Conclusion *Similar and contrasting views on PHSM against COVID-19 between Japan and the UK demonstrated how policies in controlling an epidemic should be tailored by country with respect to its norms, cultures, economic and disease burden. Our findings may guide how policy makers can engage with the public through effective health communication and consider regulations that are aligned with the public's views and capacities in changing their behavior for future pandemic preparedness.*

I was a co-author in this manuscript and made the following author contributions: Study design and conceptualization, Data Collection, Data interpretation and translation, Writing review and editing. This research was part of a bigger qualitative study of which I was a co-investigator with my colleagues from University of Roehampton, LSHTM, and Nagasaki University. This collaborative research was funded by the British Academy in 2021 that funded research on vaccine engagement across G7 countries (119). Our research was titled, "Adapting to the 'New Normal': Implications for the Post-COVID-19 Health Communication and Education."

The study covered in this manuscript is a comparative analysis between Japan and the UK to evaluate the public perceptions of PHSMs by using a mixed methods design that included a discrete choice experiment through a survey followed by focus groups. The study consisted of a total of 106 participants (56 from Japan in the Kansai region including Osaka and 50 from the UK in the Greater London area) through 23 focus groups that were conducted between November 2021 and February 2022, a period when the Omicron variant of SARS-CoV-2 was widely circulating in both countries. I was involved in the data collection including preparing Japanese material for collecting study participants, communicating with the study participants to inform them about the objective and methodology of the study, and co-facilitating the focus groups that took place in Japan. All the video and audio recordings from the focus groups were transcribed and translated by the research assistants (Saki Kawamitsu and Tin Zar Win). During the analysis phase, I checked the nuances of the responses of the study participants to capture them accurately, keeping in mind of the cultural context of Japan. I was involved in the thematic analysis which is a method used to categorize common themes that emerge from focus groups.

6.2 Main Takeaway

Based on the 23 focus groups (12 in Japan and 11 in the United Kingdom) that were conducted between November 2021 and February 2022, participants from Japan and the UK shared commonalities and expressed different views on various public health and social measures (PHSMs) against COVID-19. Participants from both countries did not agree on having COVID-19 vaccination as compulsory for everyone and preferred either being strongly advised to be vaccinated or having a general vaccination campaign without having penalties if unvaccinated. Both countries agreed on limiting contacts such as through teleworking and virtual learning for school children, but the participants in Japan noted the importance of schools to remain opened to ensure continued education.

There were differences in views on other PHSMs such as mask wearing; while the UK participants agreed on having mandatory fines for those who do not abide by the regulation of mask wearing, the participants in Japan were aware of the high proportion of people wearing masks in the society and thus only a recommendation would suffice. In general, the UK participants responded to COVID-19 preventive measures and made their decisions based on the reported number of hospitalizations and deaths while the participants in Japan emphasized more on the reported number of cases and hospitalizations.

In summary, these findings on public perceptions across the two countries suggested how PHSMs were communicated by the government, providing evidence on how policies may or may not align with the public's views and their capacities in following them. Such similarities and differences highlighted the importance of tailoring disease control policies; what works in one country may not work in another country due to social norms, culture, trust, and expectations one might have on the government.

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First Name(s)	Tomoka		
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Thesis Title	Investigating Social Contact Patterns and their Role in Transmission Dynamics during the COVID-19 Pandemic in Japan		
Nagasaki Supervisor(s)	Professor Koya Ariyoshi		
LSHTM Supervisor(s)	Dr Kathleen O'Reilly		

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SECTION E – Names and affiliations of co-author(s)

Please list all the co-authors' names and their affiliations.

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SECTION F

I confirm that all co-authors have agreed that the above paper will be included in my PhD thesis.

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Chapter 7 Discussion

As of August 2024, four and a half years have passed since the first circulation of SARS-CoV-2 was detected in Wuhan, China as it progressed to a pandemic that disrupted the health and livelihood of many individuals globally. There were many unknowns of the respiratory virus itself at the beginning of the COVID-19 pandemic when the mode of circulation was yet unclear. One of the immediate responses taken by countries was to implement a lockdown with a broad goal to limit person-to-person contact. Japan followed a different approach and instead of implementing lockdowns and long school closures, it heavily relied on non-binding public health recommendations such as by limiting contacts, discouraging travel between prefectures, and encouraging mask wearing. Especially prior to the rollout of COVID-19 vaccination, these were behavioral changes that were encouraged at the individual level but needed to be done collectively as a society to "flatten the curve." As the pandemic progressed, more scientific evidence revealed how the virus spread and evolved. We acquired different lines of defense, through natural and vaccine immunity, and by adopting PHSMs to reduce the risk of transmission. Simultaneously, we began to observe stark differences in COVID-19 deaths across countries; as of 18 August 2024, the cumulative COVID-19 deaths reported to WHO in the UK was 342 per 100,000 while in Japan, it was 59 per 100,000 (1). My PhD research focused on describing the COVID-19 epidemic in Japan and examining how contact patterns and other factors played a role in infectious disease transmission in the Japanese context.

Key research contributions

Through my involvement of the pandemic response with the Fukuoka prefectural office, I identified gaps in the Japanese approach of surveillance. While COVID-19 reminded us of the importance of flexibility in surveillance methodologies, it highlighted the lack of digitalization of surveillance data in Japan. Not having a centralized system of reporting infectious diseases prior to the pandemic made it almost impossible for the local governments, hospitals, and clinics to fully adapt to a new digital reporting system (i.e. HER-SYS, or the Health Center Real-time Information-sharing Systems on COVID-19). This overwhelmed the amount of workload for frontline workers, and during the midst of the pandemic, there was no time—from the healthcare facility to the national level—to adapt to a completely different surveillance system, let alone a fully digitized system.

Having real-time surveillance data, such as cases and deaths, is critical during the acute phase of an outbreak to strategize effective ways in controlling the spread of the disease. Yet, as an outbreak turns into an epidemic and eventually transitions towards the recovery phase, having access to longitudinal data, such as temporal trends of vaccination coverage by age and prefecture, becomes critical to have a more comprehensive view of the disease characteristics and transmission patterns after implementation of disease control interventions. When there is a clear objective, such as responding to an epidemic, data should not be collected for the sake of collecting. Key variables must be selected with a clear outcome in mind. This outcome can differ by prefecture as each prefecture has its own policies on when to declare the status of a public health emergency and what restrictions that entails.

A similar concept was applied when designing and implementing social contact surveys in Japan during the COVID-19 pandemic. For these surveys, the objective was clear; it was to capture the change of contact patterns during the various stages of the epidemic determined by the governmental measures that were put into place. Unlike COVID-19 surveillance, these contact surveys were implemented for research purposes, so the objective was not for outbreak investigation purposes. However, similar to deciding which key variables to be collected as part of surveillance, the designing of such a survey during a time-sensitive situation in a pandemic was done carefully by balancing the necessity of each question and respondent fatigue. Implementing a survey requires time and cost, and even though these contacts surveys were implemented for research purposes, results can be utilized as evidence for policymakers during and after the pandemic.

The design of these surveys allowed us to assess the change in contact patterns and its association with factors such as governmental interventions, individual characteristics including occupation, household sizes, and behavioral aspects like mask wearing. The contact surveys showed that there was a gradual increase in contacts with time and implementation of less strict public health recommendations. However, we observed careful behavior from 2021 to 2023. For example, the duration of mask wearing increased with higher frequency of contacts. This was in contrast to some European countries, including the UK, where contacts increased after lockdowns were lifted. Contacts also increased among vaccinated individuals in European countries whereas our contact surveys in Japan showed no change in frequency of contacts based on vaccination status. Our findings here showed how cautious behavior with reduced contacts may have played an important role in limiting disease transmission and ultimately maintaining a lower mortality from COVID-19 compared to other countries. Our study provided evidence on how a society can continue to function during a pandemic—not through lockdowns and long school closures but through collective behavior, such as by reducing contacts, wearing masks, and being vaccinated.

Japan still experienced a multitude of COVID-19 waves from 2020 to 2023 as incidence grew with introduction of new SARS-CoV-2 variants. When observing the national incidence of Japan, each peak was defined by each variant ranging from Alpha, Delta, Omicron, BA.5, to Omicron's sub-lineages. With the usage of a mathematical model, weekly transmission rates were estimated from 2020 to 2023 that allowed us to explore how transmission evolved with time and by region. Transmission patterns were more homogeneous geospatially across Japan in 2020-2021 compared to 2022-2023. This could indicate an interplay of different levels of transmissibility due to each variant, reduced contacts during the beginning of the pandemic, and a mix of natural and vaccine immunity during the latter half of the pandemic. Amongst the 47 prefectures, Okinawa showed as an outlier when its transmission rates and normalized incidence rates were compared with the rest of Japan. Although Okinawa does not have the highest populational density in Japan, it had the highest incidence of the country during BA.5 circulation.

To explore this further, we compared contact patterns, vaccination coverage, and demographic characteristics of Fukuoka, Osaka, and Okinawa prefectures. Contact surveys were conducted in Okinawa in December 2022 and February 2023. Like Fukuoka and Osaka, Okinawa showed the highest frequency of contacts among the individuals in the same age categories especially among those who were aged 0-9 and 10-19. Although Okinawa showed strong evidence of its weekend contacts being higher than Fukuoka and Osaka, there was no difference in weekday contacts across the three prefectures. When the mean frequency of contacts was weighted by prefecture-specific age and sex, the mean weekend contacts was less than the weekday contacts cross all three prefectures.

Vaccination coverage differed across the three prefectures. In Okinawa, the biggest gap in vaccination coverage was among those who received the third dose (as of January 2023); individuals aged between 10 and 59 showed a range of 10.6% to 15.1% lower coverage compared to those in Fukuoka. On the other hand, the older populations aged 60 and above who received the third dose had a range of 76.1% to 92.7% vaccine coverage. As for demographic characteristics, Okinawa generally had a younger demographic; 22% of the population in Okinawa were younger than 20 years old while it was 18% of the population in Fukuoka and 17% in Osaka.

The prefecture-specific contact patterns, vaccination coverage, and demographic characteristics were incorporated into the mathematical model to examine how each factor was attributed to incidence. Even though there was no strong evidence of differences in weekday contact patterns across Okinawa, Fukuoka, and Osaka prefectures, Okinawa's simulated incidence was 1.26 times higher than Fukuoka's and 1.09 times higher than Osaka's. The in silico experiments showed that there was a multiplicative effect of contacts, vaccination coverage, and demographics on incidence. These results particularly highlighted the role of high vaccine uptake across all eligible ages and provided inputs on why incidence could vary in prefectures. Okinawa, for instance, had a relatively lower vaccination coverage compared to Fukuoka and Osaka. Combined with its relatively large proportion of the younger population under 40 years old and higher weighted weekday contacts, the model simulations showed that these factors may had been the main driving factors of Okinawa's higher incidence.

Lastly, I explored the behavioral aspect of the COVID-19 pandemic through a qualitative study by comparing the public perceptions of public health and social measures (PHSMs) in Japan and the UK. Through focus groups, perceptions on COVID-19 vaccination, mask wearing, and other PHSMs were discussed. While both countries' participants agreed that vaccination should not be mandatory, there were contrasting views on policies for mask wearing and restrictions made on domestic and international travel. This was also indicative of how public perceptions on PHSMs did not always align with how governmental policies are implemented and communicated. Analyzing the socio-behavioral impact of COVID-19 through qualitative studies like this one provides more depth to the existing evidence we have about the disease and provides a framework on how the public's opinions can be incorporated when new policies are being implemented and communicated across the country.

Future directions and conclusion

What must be done now, especially during "peace time" after a pandemic has subsided, is to review what we have learned and identify action points that can prepare us for the next pandemic. First, in Japan, the structure of its surveillance system must be revisited. If a new surveillance methodology is implemented, it needs to be reviewed together with the healthcare workers, epidemiologists, data managers, public health nurses at local governments, and all stakeholders who were involved in the COVID-19 response. The Diamond Princess outbreak was a clear reminder that even with a strong surveillance system that was well-functioning in Japan that actively detected infectious diseases across all prefectures, not having a digitalized, multi-tier surveillance system that link hospitals, local governments, and the Ministry of Health, Welfare and Labor was detrimental during an outbreak caused by an emerging pathogen.

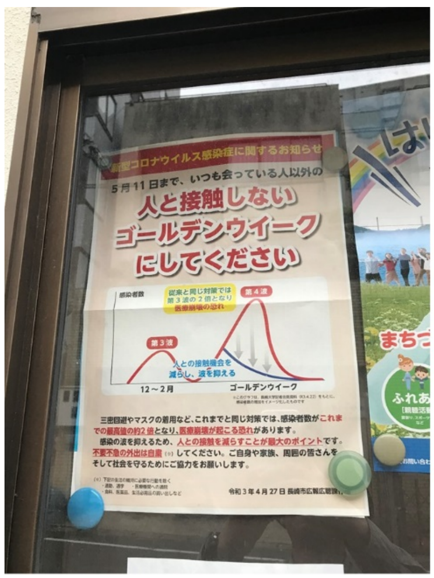
Health data continues to be fragmented in Japan due to the lack of digitalization across all platforms used in the health system. Although all residents in Japan are covered by national health insurance, each individual health record is not linked across hospitals and clinics, making it difficult to conduct large-scale, retrospective epidemiological studies using health data records. If individual health records were linked digitally across all platforms, COVID-19 status, vaccination history, and treatment methodologies can be analyzed longitudinally, allowing us to have a more comprehensive view of the disease characteristics and transmission patterns. Data accessibility was also an issue. While age-stratified vaccine coverage per prefecture was made publicly available, the previous data (i.e. vaccination coverage reported on past dates) was not archived publicly, so accessing data across multiple time points was difficult. Although the National Institute of Infectious Diseases is a national government agency, it does not automatically grant them access to these data due to its sole ownership belonging to the local municipalities.

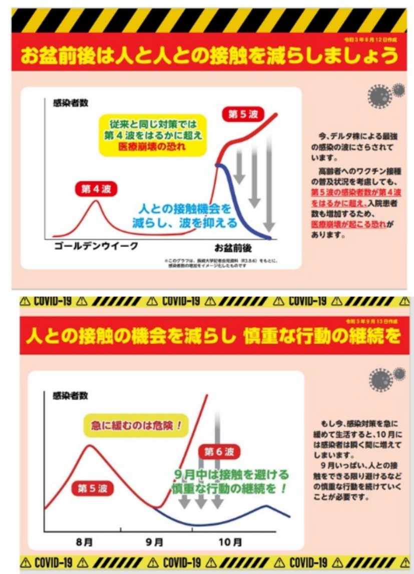
Data digitalization in public health can be one key strategy for pandemic preparedness in Japan. Another type of surveillance, such as wastewater surveillance for COVID-19, was integrated from 2024 (120), and with different tools emerging to detect various pathogens, it becomes critical to consolidate all the available data digitally to prevent from having parallel systems. This issue must also be addressed with data accessibility and reassessing the “how” and the “what” in terms of the surveillance data that can be used as evidence to support policies.

The use of social contact surveys, epidemiology and mathematical modeling made it possible to assess the epidemic in Japan, providing evidence to support some of the disease mitigation methods and policies that were put in place at the time. As these retrospective data are analyzed further, these provide resources for the next pandemic. Hitoshi Oshitani, whose work was instrumental for the COVID-19 response in Japan, commented how PHSMs that were suggested to be effective for an influenza pandemic were not effective during the COVID-19 pandemic (6). This demonstrates that PHSMs that were effective against COVID-19 would not necessarily mean that they would be equally effective in the next pandemic. What is needed now is to utilize the existing data to fill in the remaining gaps on socio-behavioral aspects of how people change or maintain their behavior during a pandemic. There are remaining variables in the contact surveys that have yet to be analyzed; for instance, a longitudinal analysis can be done by linking the same individuals or households across the ten contact surveys that were conducted in Fukuoka and Osaka prefectures. Frequency of contacts, perceptions on getting infected with COVID-19, and views on the COVID-19 vaccine can be analyzed temporally. Although this is specific to the COVID-19 context, it can provide perspectives on how individuals react to an emerging pathogen and a new vaccine. It can also provide insights on how the public may or may not readily accept disease control policies in the emergence of a new or more dangerous pathogen.

As demonstrated by the model simulations using Okinawa data, its higher incidence was attributed to heterogeneities in the prefecture’s contact patterns, vaccination coverage, and demographic characteristics. Simulated incidence that differed by age also highlighted how the approach of having a blanket statement to "reduce contacts" may not be the most effective way of communicating to the public. Our contact surveys showed a constantly low number of contacts among the older populations (70+ year olds) while the younger populations (30 years old and less) had a tendency of having higher contacts with lower vaccination coverage. In the future, strategizing on the best public health message would be necessary to reach the targeted population to reduce contacts and to be vaccinated, especially when a pandemic can be prolonged for multiple years.

Health communication was a key element as part of the pandemic response in Japan. In addition to press conferences, newspaper articles, and online updates from the prefecture's mayor in Nagasaki, posters were disseminated across Nagasaki city (121). These posters (right) showed the simplified version of our model outputs, so the public can visually understand how reduction in contacts can flatten the curve. The left photo was titled "Please Refrain from Contacting with Others during the Golden Week National Holidays" and was taken at the Nagasaki Public Library in May 2021. Such public announcements aimed to inform citizens, not only about the dynamic epidemiological situation but also the reasoning behind the recommendation of reducing contacts and local restrictions that were put in place.





This narrative on how modeling was utilized to inform policy was accepted to be included as one of the case studies in the *Lancet Commission* paper on "Strengthening the Use of Epidemiological Modeling of Emerging and Pandemic Infectious Diseases" that will be published in the coming months in 2024.

With emerging SARS-CoV-2 variants that could have different transmission characteristics, the mathematical model introduced in this thesis can be adapted accordingly. For example, if the transmission rate was higher among children compared to adults, this could be incorporated in the model to understand how much higher the number of infections would be given that infants and school-aged children have the highest contact rates. A comparative study between Japan and the

UK may be done by interchanging Japanese contacts with British contacts using the CoMix study to evaluate the differences in simulated incidence. Since the epidemic progressed differently in the two countries with very different COVID-19 government policies, the challenge here would be to identify time points that would be comparable. Since contact patterns are time and country-specific, new contact surveys should be conducted during the next pandemic to accurately illustrate how individuals contact one another. Contact patterns may have shifted to a “new normal” after the COVID-19 pandemic, so age-specific contacts may not be the same today as how our contact survey results showed between 2021 and 2023. It will also be important when developing future models with contact patterns and parameters that reflect the country context and are epidemiologically sound.

After the COVID-19 pandemic subsided, it is easier today to assess its evolution especially with the wealth of knowledge that was uncovered about the disease, thanks to the countless research studies and outbreak investigations that were done globally. Now, stakes are low when evaluating governmental policies and recommendations that were put in place during the pandemic since the countries are not under pressure to strike the balance between controlling transmission and preventing economic downfall. What needs to happen now is not to simply reflect on what was done in the past but to utilize the lessons learned from the COVID-19 pandemic. My thesis covered a wide range of topics from designing a contact survey to overseeing how mathematical model outputs can be communicated to the public to reduce contacts. The complexity behind a pandemic remains, yet the research presented here shed light on the interlinkage of contact patterns, immunity acquired from natural infection and vaccination, demography, and perceptions on PHSMs that are shaped by personal experience, culture, legal architecture, and ways of communicating that can impact disease transmission.

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Chapter 9 Appendix

Appendix 1. English translation of the social contact surveys that were conducted in Fukuoka and Osaka prefectures in December 2021.

As part of the research protocol, here is the questionnaire for the social contact survey that will be given online for the participants. The formatting may change due to the design of the online platform, but the context of the questions will remain the same. The Japanese version that follows the English version will be given to the participants.

After the screen with informed consent:
C1. Will you participate in this survey?

1. Yes, I will participate as well as my family members (also applies to same household members) after receiving consent.
2. I will not participate in the survey.

C2. If you are also recording data for your family members/same household members, what are their relationships to you? For the following questions, please record their social contact pattern information as well as their occupation and age.

*By household, we mean anyone living at the same address as you, that you share a kitchen with.
*For those who live in student dormitories or apartments for singles, please only record your own data.

1. Grandfather
2. Grandmother
3. Father
4. Mother
5. Husband
6. Wife
7. Older brother
8. Older sister
9. Younger brother
10. Younger sister
11. Grandchild
12. Uncle
13. Aunt
14. Niece
15. Nephew
16. Partner
17. Other (indicate)

Social Contact Survey Questions (from Q1 to Q12)

Q1. What is your main type of occupation?

1. Firm/Corporate executive
2. Company/Organization employee
3. Temporary staff/contract worker

4. Government employee
5. Commerce and industry/independent contractor
6. Agriculture/Fishery
7. Professional (excluding healthcare; e.g. lawyer, accountant, certified tax accountant)
8. Healthcare professional (e.g. doctors, nurses, dentists, physician assistant)
9. Social care worker
10. Part-time job (excluding homemaker)
11. Homemaker with part-time job
12. Homemaker without part-time job
13. Freelance
14. Infant (pre-school child)
15. Child in kindergarten
16. Elementary school student
17. Middle school student
18. High school student
19. Preparatory school student
20. University/2-year college/professional school student
21. Non-employed/assist house chores
22. Pension recipient
23. Other (indicate)

Q2. What is your highest level of education?

1. Not graduated from middle school (e.g. currently in pre-school, kindergarten, elementary school or middle school)
2. Middle school graduate
3. High school graduate
4. Professional school graduate
5. 2-year college graduate
6. University graduate
7. Graduate school graduate
8. Other (indicate)

Q3. **Not including yourself,** how many people are living in the same house? Include any family members or any partners. By household, we mean anyone living at the same address as you, that you share a kitchen with.

*For those living in student dormitories or dormitories for singles, include anyone who shares the same kitchen.
*Do not include any pets.

1. Myself only
2. 1 person
3. 2 people
4. 3 people
5. 4 people
6. 5 people
7. 6 people
8. 7 people
9. 8 people
10. 9 people
11. 10 people
12. 11+ people

Q4. Do you or any other household member mentioned in Q3. have health conditions or chronic diseases that hinder your/his/her everyday life?

Chronic diseases include the following: chronic respiratory disease, chronic heart disease, chronic kidney disease, chronic liver disease, and chronic neurological disease

Conditions include the following: diabetes (all types), immunosuppression (due to disease or treatment), obesity (BMI >= 40), and pregnant women.

0. Yourself
1. Grandfather
2. Grandmother
3. Father
4. Mother
5. Husband
6. Wife
7. Older brother
8. Older sister
9. Younger brother
10. Younger sister
11. Grandchild
12. Uncle
13. Aunt
14. Niece
15. Nephew
16. Partner
17. Other (indicate)

Columns:

1. Yes
2. No
3. Do not know
4. Prefer not to answer

Q5. Please fill out the below questions based on the diary you recorded during the week/weekend

Please note that there are 2 types of direct contact:

- Physical contact
- Non-physical contact

Examples shown below:

Non-physical contact	Physical contact
- Face-to-face with another individual and having a conversation of at least 3 sentences (regardless of wearing a mask or not)	- Handshake - Hug/Embracing - Kissing - Playing contact sports - Sleeping in the same futon

1	2	3	4	5	7	8	9
Nickname	Age group of person	Sex of person	Type of contact	Location of contact	Length of time at point of contact	Indoor or Outdoor at point of contact	Household or non-household contact
Please indicate the name or nickname of the person you had contact with (e.g. parent, grandparent, child, sibling, housemate, partner)	Enter the age of the person or if specific age is unknown, use dropdown option for age range	Is the person male or female?	Was your contact with this person physical or non-physical?	Where did you meet the person? (able to tick off more than one)	About how long did you spend time with this person today?	Did you spend the time with this person indoors or outdoors? If both, indicate one where you spent the **most time.**	Did this contact involve a person who lives in the same household?

Enter name/nickname	____ years old Or dropdown options: 0= 0-9 years 1= 10s 2= 20s 3= 30s 4= 40s 5= 50s 6= 60s 7= 70+	1 = Male 2= Female	1=physical 2=non-physical	1. At home 2. At someone else's house 3. At work 4. At a place of worship 5. On public transport 6. At school, pre-school, or nursery 7. At a supermarket, grocery store, or market 8. At a shop 9. At a place of entertainment such as a restaurant, bar, cinema 10. At a place for sports such as a gym or sports club/match 11. Outside, for example in a park, on the street or in the countryside 12. Somewhere else (please specify)	1= <5 min 2= 5-15 min 3=15-59 min 4=1-4 hrs 5=>4 hrs	1=Indoors 2=Outdoors	1 = Yes 2= No
#1							
#2							
#3							
#4							
#5							
#6							
#7							
#8							

#9							
#10							

Q6. Until this question, we have asked you a maximum of 10 people with whom you had direct contact. However, have you had physical contact with more than 10 people?

a. I have already reported on all of the people I made direct contact
b. I have not reported on all of the people I made direct contact

If answered yes on b, please indicate how many people you made physical contact with the below:

I made direct physical contact with >10 people at (multiple selection possible):

- Workplace
- School
- Other

Indicate the approximate number of people with physical contact: ###

Indicate the age categories of the people with physical contact (multiple selection possible):

- 0-17 years old
- 18-59 years old
- 60+ years old

I made non-physical contact with >10 people at (multiple selection possible):

- Workplace
- School
- Other

Indicate the approximate number of people with non-physical contact: ###

Indicate the age categories of the people with non-physical contact (multiple selection possible):

- 0-17 years old
- 18-59 years old
- 60+ years old

Current individual preventive measures

Q7. Please fill out the below questions based on your preventive measures, including wearing a face mask, handwashing and teleworking, that you may have done currently.

	Face mask		Handwashing	Teleworking		Traveling	
	For how long did you wear a face mask in total?	Where did you use your face mask?	How many times did you wash your hands with soap in the last 3 hours?	During the indicated time period, where was your main work location?	How frequently did you telework or attend school classes at home?	During the past month, how many times did you travel to a prefecture outside your home prefecture for work?	During the past month, how many times did you travel to a prefecture outside your home prefecture for leisure/personal reasons?
Current (2021)	Insert number of hours and minutes	1. Everywhere outside my house 2. When walking on the street 3. When cycling 4. On public transport 5. In supermarkets/shops 6. In cinema/bar/restaurant 7. At home 8. At work/school/college/university 9. Other (please specify) Columns: Yes/No/Not applicable	Insert number of times (range from 0-25)	1: Home 2: Workplace 3: School 4: Not employed	0: Never or not possible to telework/attend classes 1: A few times per month 2: 2-3 times per week 3: 4-5 times per week	Insert number of times (range from 0-100+)	Insert number of times (range from 0-100+)

Individual preventive measures taken in the past
The Japanese government declared a national emergency on 16th April 2020 due to COVID-19. Then, on 13th January 2021, another national emergency declaration was announced in 7 prefectures including Fukuoka and Osaka prefectures.
Q8.* Please fill out the below questions based on your preventive measures you may have taken in 2020 (July through December), 2020 (March through June), and 2019.
*Ask Q8. only **once**, either during the week or weekend:

	Face mask		Handwashing	Teleworking	
	How frequently did you wear a face mask?	Where did you use your face mask?	How frequently did you wash your hands with soap? (Can select more than one)	During the indicated time period, where was your main work location?	How frequently did you telework or attend school classes at home?
July 2021 to September 2021	0: Never 1: Only when I felt ill or had cold-like symptoms or allergies 2: Same frequency as now 3: Less frequently than today 4: More frequently than today 5: I do not remember	1. Everywhere outside my house 2. When walking on the street 3. When cycling 4. On public transport 5. In supermarkets/shops 6. In cinema/bar/restaurant 7. At home 8. At work/school/college/university 9. Other (please specify) Columns: Yes/No/Not applicable	0: Never 1: Only when I felt ill or had cold-like symptoms or allergies 2: Same frequency as today 3: Less frequently than today 4: More frequently than today 5: I do not remember	1: Home 2:Workplace 3: School 4: Not employed	0: Never or not possible to telework/attend classes 1: A few times per month 2: 2-3 times per week 3: 4-5 times per week
2019 (pre-COVID 19)	0: Never 1: Only when I felt ill or had cold-like symptoms or allergies 2: Same frequency as today 3: Less frequently than today 4: More frequently than today 5: I do not remember	1. Everywhere outside my house 2. When walking on the street 3. When cycling 4. On public transport 5. In supermarkets/shops 6. In cinema/bar/restaurant 7. At home 8. At work/school/college/university 9. Other (please specify) Columns: Yes/No/Not applicable	0: Never 1: Only when I felt ill or had cold-like symptoms or allergies 2: Same frequency as today 3: Less frequently than today 4: More frequently than today 5: I do not remember	1: Home 2: Workplace 3: School 4: Not employed	0: Never or not possible to telework 1: A few times per month 2: 2-3 times per week 3: 4-5 times per week

Questions related to COVID-19
Q8. How willing are you to receive the COVID-19 vaccine? (Scale of 0 to 10)

0 1 2 3 4 5 6 7 8 9
10

0: Very unlikely to get vaccinated 5: Uncertain about getting vaccinated 10: Very likely to get vaccinated

Q9. If answered “7” or less on Q8, please select the primary reason why (tick only 1)
1. Only people who are at risk of serious illness from COVID-19 need to be vaccinated
2. Unsure of the effectiveness in preventing COVID-19
3. Concerned about potential side effects and safety of the vaccine
4. Afraid of needles
5. Do not think vaccines are effective in preventing infectious disease
6. The government is not requiring me to be vaccinated
7. Specify other reason

Q10. Have you or any other household member been tested for coronavirus (COVID-19)? (Rows should appear based on what was answered on Q3

1. Yourself
2. Grandfather
3. Grandmother
4. Father
5. Mother
6. Husband
7. Wife
8. Older brother
9. Older sister
10. Younger brother
11. Younger sister
12. Grandchild
13. Uncle
14. Aunt
15. Niece
16. Nephew
17. Partner
18. Other (indicate)

Columns:

1. Tested and the test showed I/they have coronavirus
2. Tested and the test showed I/they DO NOT have coronavirus
3. Tested and still waiting to hear the result
4. Not tested
5. Do not know
6. Prefer not to answer

Q11. Coronavirus would be a serious illness for me
1. Strongly agree
2. Tend to agree
3. Neither agree nor disagree

4. Tend to disagree
5. Strongly disagree
6. Do not know

Q12. Based on your answer on Q11., please write the reason why:
____

Q13. If you have been vaccinated against COVID-19, which month did you receive the first dose?

Month of first dose	Type of COVID-19 vaccine (first dose)
• Indicate month (Jan – Dec): • Did not receive first dose (if this is selected, option of type of vaccine will not be selectable) • Do not know	• Pfizer • Moderna • AstraZeneca • Other • Do not know

Q14. If you have been vaccinated against COVID-19, which month did you receive the second dose?

Month of second dose	Type of COVID-19 vaccine (second dose)
• Indicate month (Jan – Dec): • Did not receive second dose (if this is selected, option of type of vaccine will not be selectable) • Do not know	• Pfizer • Moderna • AstraZeneca • Do not know

At the end of survey, the participant will fill out the below before submitting the entire survey:
Sex:

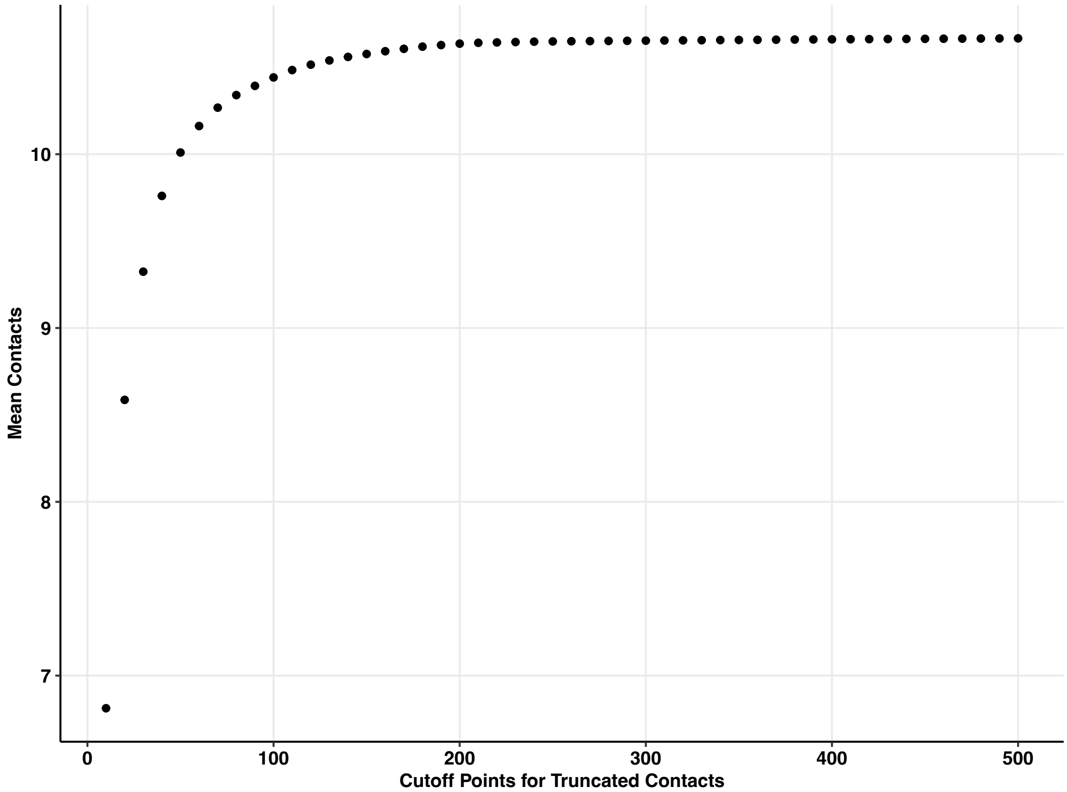
- Male
- Female

Indicate age: ________ years old

Place of resident: by postal code (first three digits that will tell you the prefecture and city)

Appendix 2. Supplementary figures of the manuscript covered in Chapter 3 titled “Continuing to be Cautious: Japanese Contact Patterns during the COVID-19 Pandemic and their Association with Public Health Recommendations.”

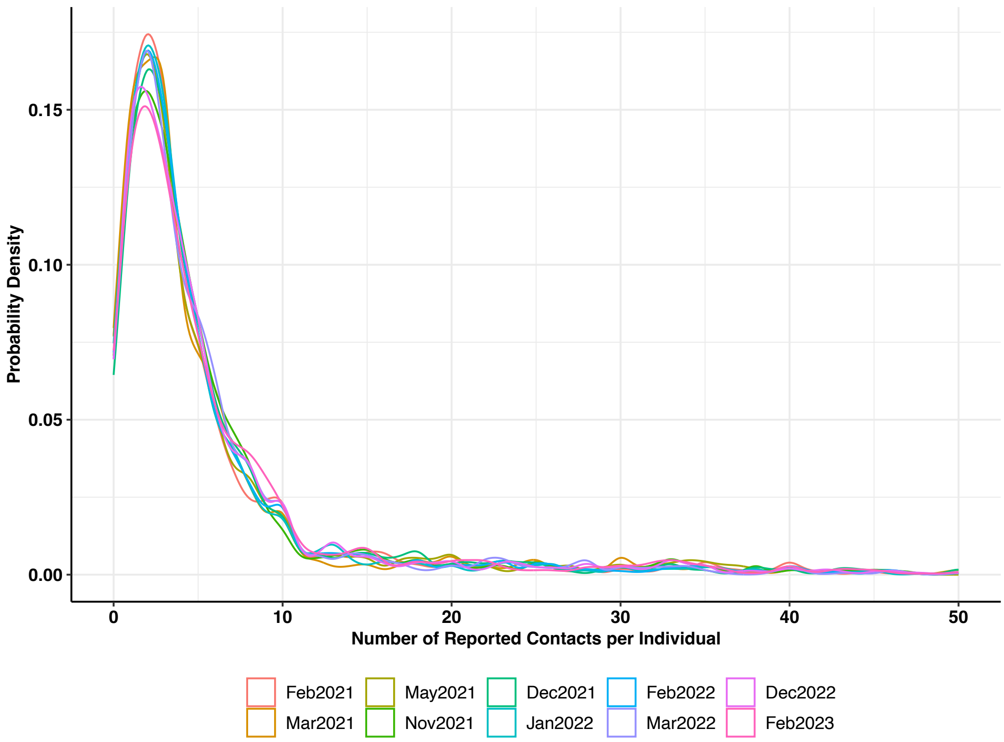
Supplementary Figure 1: Plot showing the overall mean contacts based on various cutoff points for truncated contacts ranging from 10 to 500 contacts. A Weibull distribution was used to describe the mean contacts reported throughout the week from the February 2023 contact survey.



Supplementary Table 1: List of variables that were included in the social contact survey and analyzed when developing the multivariable regression model using Weibull distribution.

Variable	Response reported in contact survey
Individual and household characteristics	
Age	Numerical value
Sex	Male/Female
Prefecture of residence	Osaka/Fukuoka
Do you or any of your household members belong to a high risk category with health conditions or chronic diseases that hinder your/their everyday life? (e.g. chronic respiratory disease, chronic heart disease, chronic kidney disease, chronic liver disease, and chronic neurological disease	List the person who meets this category
Occupation	List given as shown on Table 2
Number of people in the same household	Numerical value
Health mitigation and COVID-19 related characteristics	
How concerned are you of getting infected with COVID-19?	1: Mostly concerned, 2: Somewhat concerned, 3: Neither concerned nor unconcerned, 4: Somewhat unconcerned, 5: Mostly unconcerned, 6: Don't know, 7: Do not want to answer
Have you or any other household member been tested positive by PCR for coronavirus (COVID-19)?	List the person who meets this category
How long did you wear a mask today?	Numerical value
How many times did you wash your hands with soap in the last 3 hours?	Numerical value
How many times have you been vaccinated against COVID-19?	Numerical value
Work-related characteristics	
Where was your main work location?	Home, Workplace, School, Not employed
How frequently did you telework or attend school classes at home?	0: Never/not possible, 1: A few times per month, 2: 2-3 times per week, 3: 4-5 times per week
During the past month, how many times did you travel to a prefecture outside your home prefecture for work?	Numerical value
Possible locations of contact	
Home	Yes/No
Other person's home	Yes/No
Work	Yes/No
School	Yes/No
Restaurant	Yes/No
Bar/karaoke	Yes/No
Shop	Yes/No
Place of worship	Yes/No
Public transportation	Yes/No
Gym	Yes/No
Movie	Yes/No
Market/Supermarket/Convenience store	Yes/No
Other place	Yes/No

Supplementary Figure 2: Distribution of contacts reported per individual during the weekday in Fukuoka and Osaka prefectures from February 2021 to February 2023.



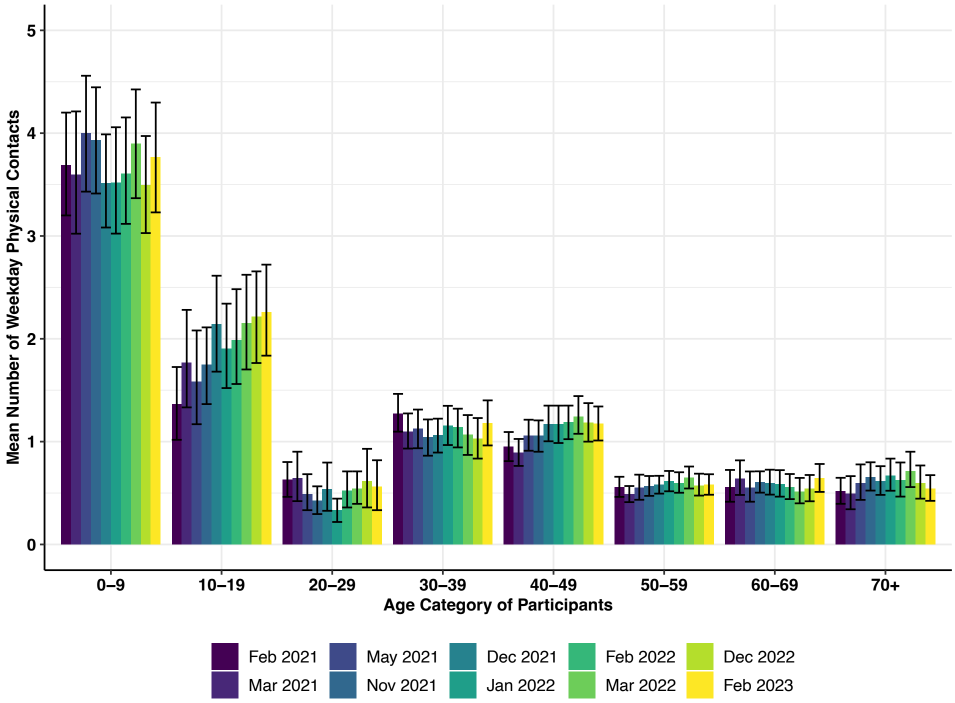
Supplementary Table 2: Timetable of Japan's restrictions, including public health emergency declarations and governmental recommendations, implemented to curb COVID-19 transmission from 2020 to 2023.

Start Date	End Date	Place	Regulation Type/Event	Description
2020-03-02	2020-05 (varied by city/town/village)	National	School closure	All primary, middle and high schools to be closed at least until spring break that starts end of March.
2020-03-21	2022-10-11	National	Border control	Forbidden entry to Japan from abroad (all tourists, business) except for Japanese citizens, permanent residents
2020-04-07	2020-05-14 (Fukuoka) 2020-05-21 (Osaka)	Prefectures including Osaka, Fukuoka	State of emergency	Recommendation include (but not limited to): • Stay at home • Limit social contacts in 3C settings • Discourage moving between prefectures for non-essential travel • Complete closure or shortening of restaurant/bar hours • Restricted hours of serving alcohol
2020-04-16	2020-05-25 (last prefecture)	National	State of emergency	Same as above
2021-01-14	2021-02-28	Prefectures including Osaka, Fukuoka	State of emergency	Same as previous state of emergency
2021-02-17	Ongoing	National	Vaccination	First COVID-19 vaccination to start for healthcare workers
2021-05-17	Ongoing	Tokyo, Osaka	Vaccination	Mass COVID-19 vaccination to start for 65-year-old and above
2021-06-21	Ongoing	National	Vaccination	Mass COVID-19 vaccination for the public to start at universities and workplace
2021-04-24	2021-06-19	Tokyo, Osaka, Hyogo, Kyoto	State of emergency	Same as previous state of emergency
2021-05-11	2021-06-19	Prefectures including Fukuoka	State of emergency	Same as previous state of emergency
2021-07-11	2021-09-30	Tokyo	State of emergency	Same as previous state of emergency
2021-07-23	2021-08-08	Tokyo	Summer Olympics	No general audience during the Olympics
2021-08-02	2021-09-30	Prefectures including Osaka	State of emergency	Same as previous state of emergency
2021-08-20	2021-09-30	Prefectures including Fukuoka	State of emergency	Same as previous state of emergency
2022-01-27	2022-03-21	Prefectures including Osaka, Fukuoka	State of semi-emergency	Soft recommendation to limit social contacts in 3C settings, shortening of restaurant/bar hours. No stay-at-home and closure of business policies.

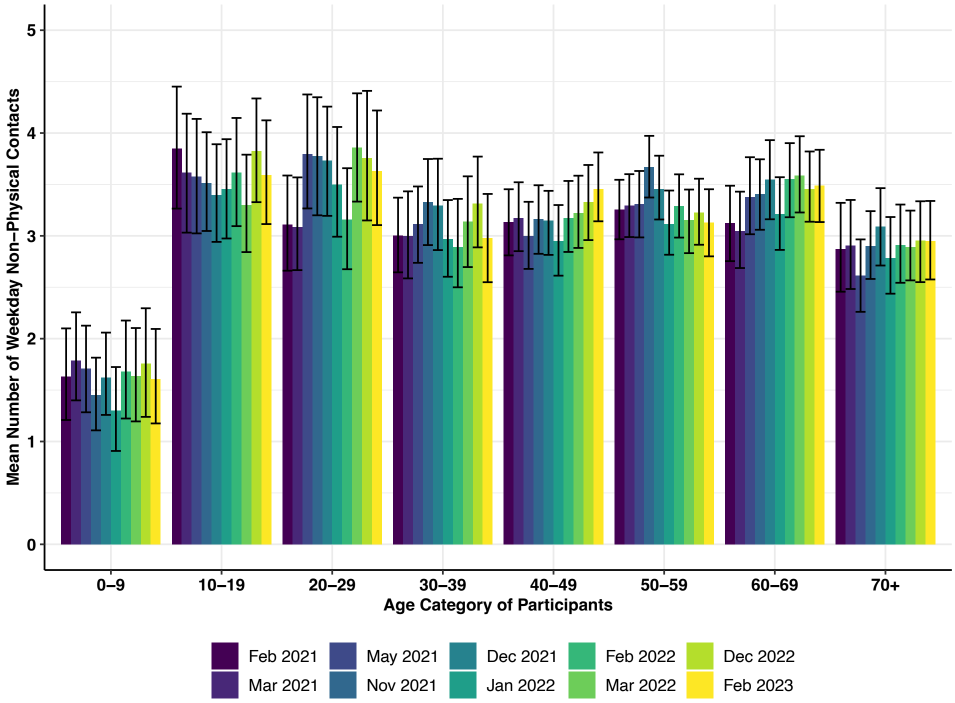
Supplementary Figure 3: Mean Number of Physical and Non-Physical Contacts during the Weekday

The mean number of weekday contacts was calculated based on the first ten contacts that were reported by the study participants in Fukuoka and Osaka prefectures from February 2021 to February 2023 for physical contacts (3a) and non-physical contacts (3b). A contact is defined here as any contact that occurred at an indoor setting (includes contacts that could have happened both indoor AND outdoor). The mean and 95% confidence intervals are obtained by bootstrapping.

Supplementary Figure 3a: Mean Number of Physical Contacts during the Weekday

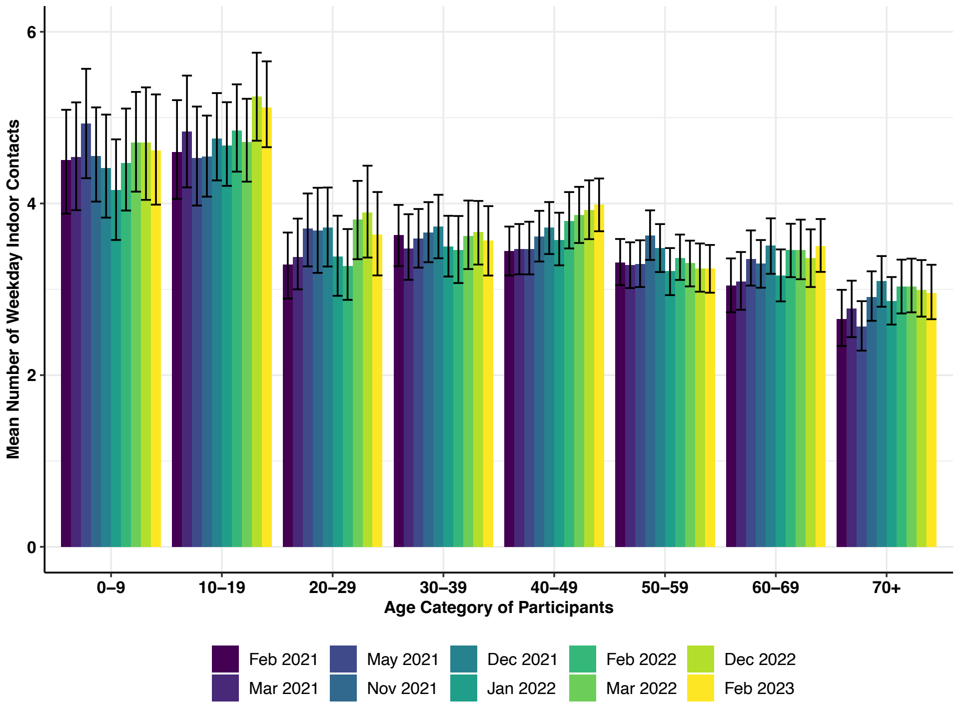


Supplementary Figure 3b: Mean Number of Non-Physical Contacts during the Weekday

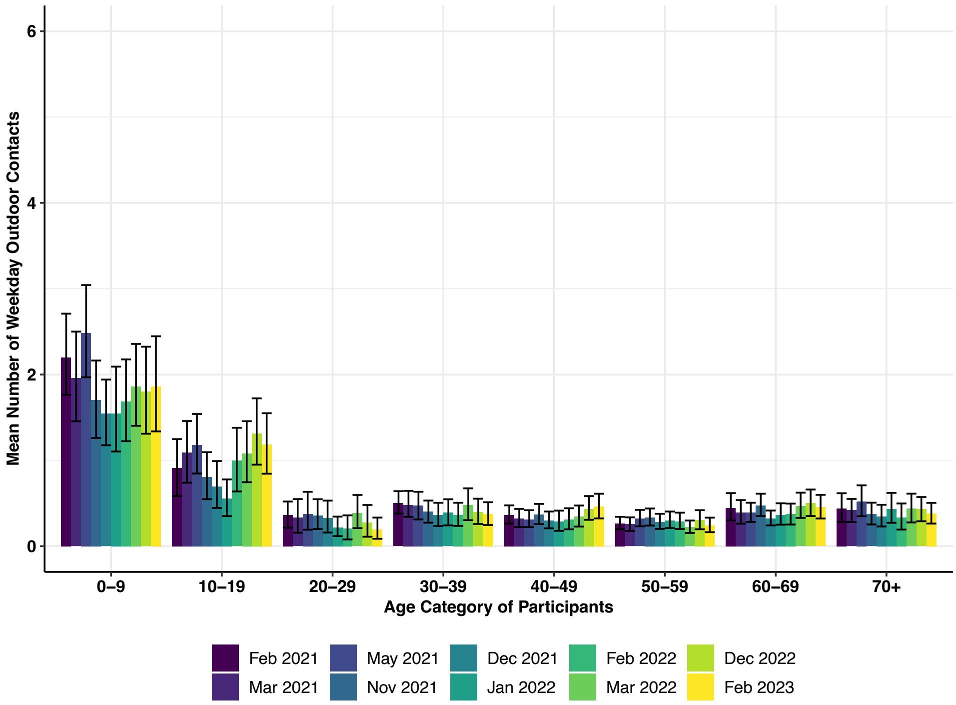


Supplementary Figure 4: Mean Number of Weekday Indoor and Outdoor Contacts
The mean number of weekday contacts was calculated based on the first ten contacts that were reported by the study participants in Fukuoka and Osaka prefectures from February 2021 to February 2023 that took place indoors (4a) and outdoors (4b). A contact is defined here as any contact that occurred at an indoor setting (includes contacts that could have happened both indoor AND outdoor). The mean and 95% confidence intervals are obtained by bootstrapping.

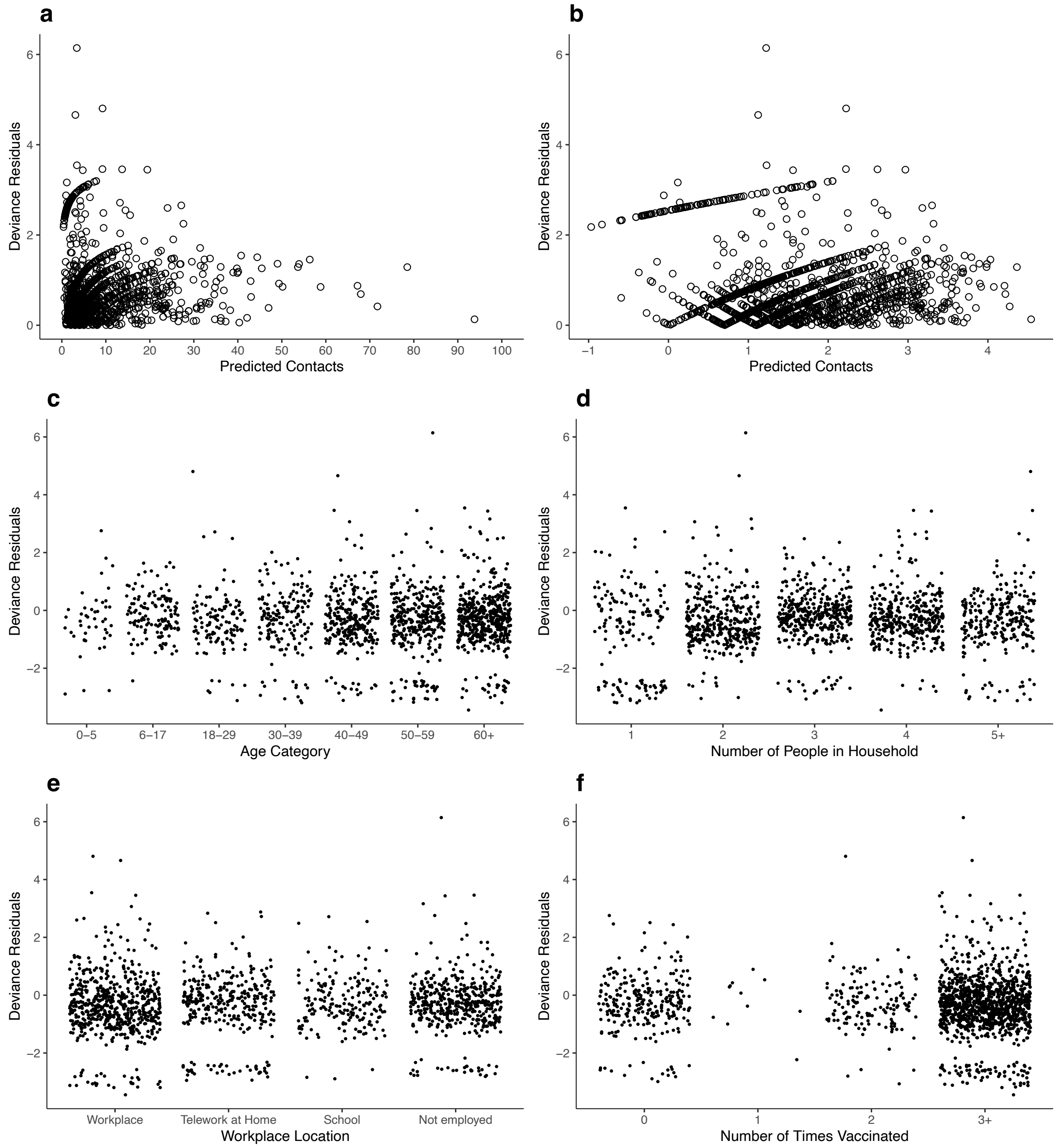
Supplementary Figure 4a: Mean Number of Weekday Indoor Contacts



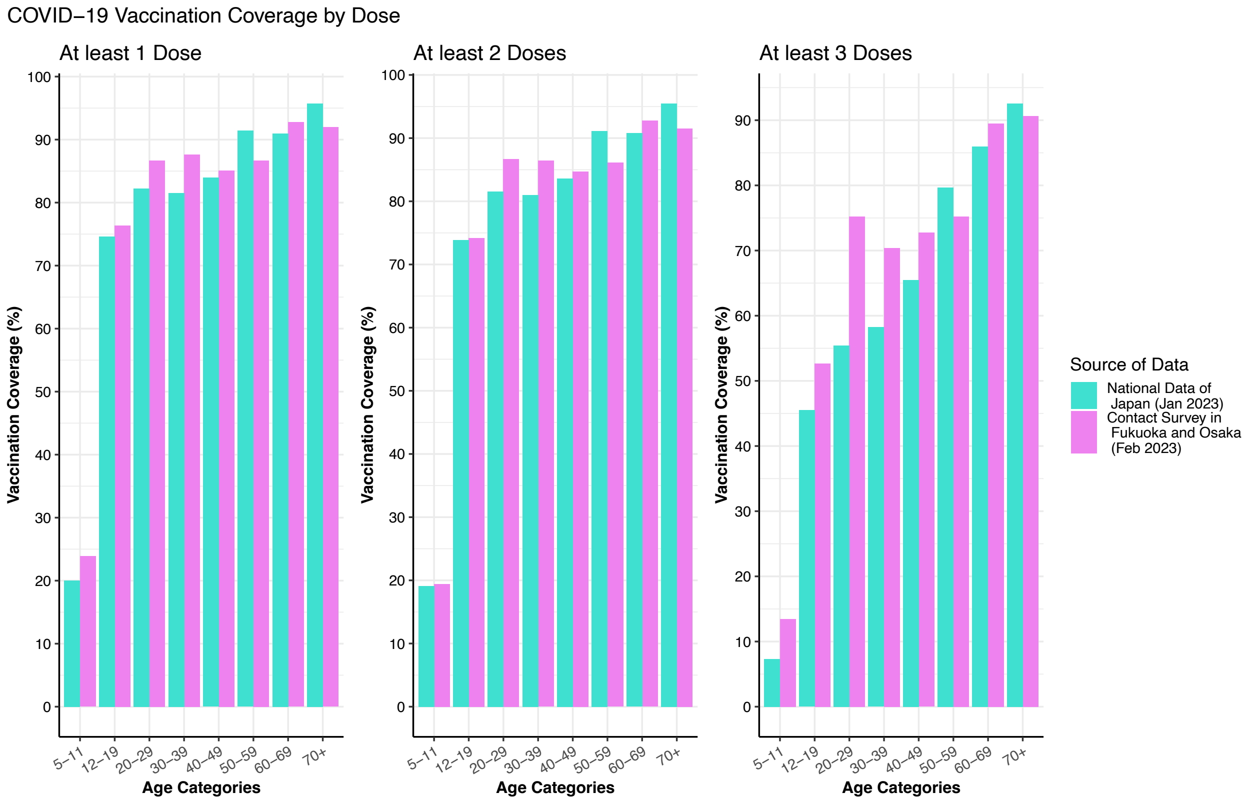
Supplementary Figure 4b: Mean Number of Weekday Outdoor Contacts



Supplementary Figure 5: A series of residual plots from the multivariable regression model using a Weibull distribution based on weekday contacts in Feb 2023. a) Residual plot showing predicted contacts in natural scale. b) Residual plot showing predicted contacts in a log link function. Plots a and b are shown with absolute values of the residuals. c) through f) show residuals against each of the selected predictors in the multivariable regression model.



Supplementary Figure 6: A comparison of national data of individuals who received the COVID-19 vaccination as of January 2023 with the individuals who reported their doses of vaccination from the social contact surveys conducted in February 2023.[10]



[10] Not all national vaccination coverage data of Japan has been publicly available. However, data from January 2023 collected by the Prime Minister's Office of Japan was the time point that was most comparable with the social contact survey and was shared with permission by the National Institute of Infectious Diseases (Japan).

Appendix 3. Preliminary results from the social contact surveys conducted in Fukuoka and Osaka prefectures that were presented during Japan's daily COVID-19 Strategic Advisory Board meeting held on 8 June 2022 at the Ministry of Health, Labor and Welfare.

The abridged report (in Japanese) is shown here as slides that were presented by Dr. Motoi Suzuki of the National Institute of Infectious Diseases.

資料の要点：2022年6月8日時点

- 全国の実効再生産数はわずかに低下傾向にあり、概ね値が確定した5月22日時点で**0.91**であった。全都道府県で同様に低下傾向がみられる。ただし地域によっては検査の遅れや入力の遅れが発生していることから、値の解釈には注意を要する（P2-6）。
- 年代別の新規症例数の推移（P7-15）、地域別の流行状況を図示した（P16-44）。
- 東京都、大阪府、北海道、沖縄県の流行状況をまとめた（P45-56）。
- 東京都、大阪府、北海道、沖縄県の新規症例数のリアルタイム予測を行った（P57-60）。
- 小児における流行状況をまとめた（P61-63）。
- 学校保健会が運用する学校等欠席者・感染症情報システムのデータを更新した（P64-72)。
- 民間検査機関の検体を用いたゲノムサーベイランスのデータを用いて、BA.2検出割合の推定を更新した。また、検出割合を基に各株・系統の患者数を推定した（P73-79)。
- 2021年2月から2022年3月の期間に大阪府と福岡県の住民を対象として実施した社会的接触調査（コンタクトサーベイ）の結果を報告する（P80-82)。
- 2022年2月までのデータを用いた超過死亡の分析結果を報告する（P83-97)。超過死亡数の推定おける、2020年以降のデータの取り扱いに関する論点を提示。またパンデミック前後の日本における日本人と在日外国人の年齢標準化死亡率の比較結果を報告する。
- 新型コロナワクチンの有効性の評価を目的とする多施設共同研究の結果について報告する（P98-106）。

国立感染症研究所　感染症疫学センター　サーベイランスグループ、疫学研究グループ
病原体ゲノム解析研究センター、研究企画調整センター
協力：新潟大学　菖蒲川由郷（GIS）、日本学校保健会、森本浩之輔（長崎大学）、有吉紅也（長崎大学）、中村友香（LSHTM）
超過死亡分析チーム

社会的接触調査（コンタクトサーベイ）の結果について

厚生労働省研究班「新型コロナウイルス感染症等の感染症サーベイランス体制の抜本的拡充に向けた人材育成と感染症疫学的手法の開発研究」

日本における新型コロナウイルス感染症流行時の社会的接触パターンについて

- 2021年2月から2022年3月の期間に大阪府と福岡県の住民を対象として社会的接触調査（コンタクトサーベイ）を実施し、1人あたりの接触人数（1日平均）の推移を検討した。

- 新型コロナウイルス感染症（COVID-19）流行後（2021年と2022年）は、1人あたりの接触人数は8.1人（平日）、5.9人（週末）であった。これは流行前（2011年）に実施された同様の調査の16.3人（平日）、12.8人（週末）と比べて減少していた。この減少傾向は、平日、週末を問わず、すべての年齢層で見られた。

- 流行期間中、20代における接触人数については他世代よりも大きな変動が観察され、2021年12月に明らかな増加が見られた。

- 2022年3月時点の接触人数は流行前の水準には戻っていないが、比較的若い世代（10代から30代）の接触人数については平日、週末ともに1年前の2021年3月と比較して増加傾向が見られる。

＊詳細は別添報告書を参照のこと

中村友香（London School of Hygiene and Tropical Medicine・長崎大学）、鈴木基（国立感染症研究所）、有吉紅也（長崎大学）

「新型コロナウイルス感染症等の感染症サーベイランス体制の抜本的拡充に向けた人材育成と感染症疫学的手法の開発研究」（厚生労働科学研究）分担研究

[1] Ibuka Y, et al. 2016, doi: 10.1136/jech-2015-205777.

新型コロナウイルス感染症流行前(2011年)と流行時（2021年2月ー2022年3月）を比較した平日と週末における年齢区別の1日平均接触人数

図１　平日における平均接触人数

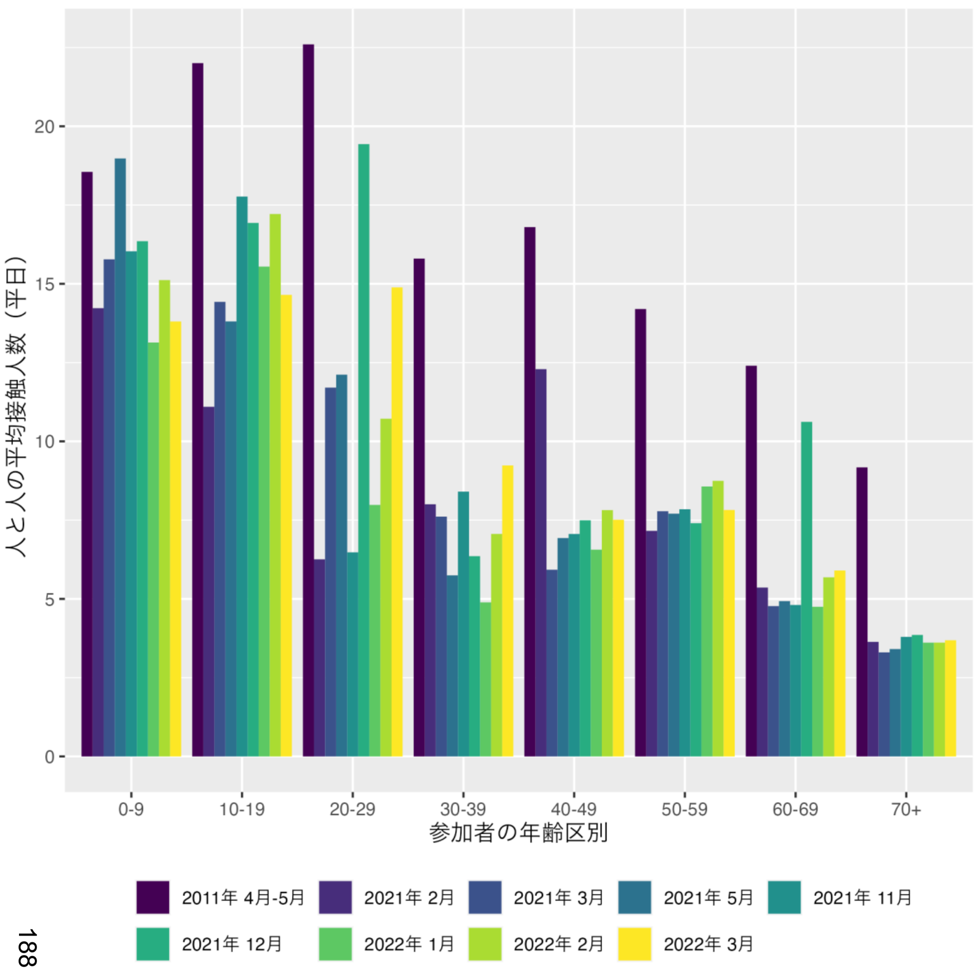
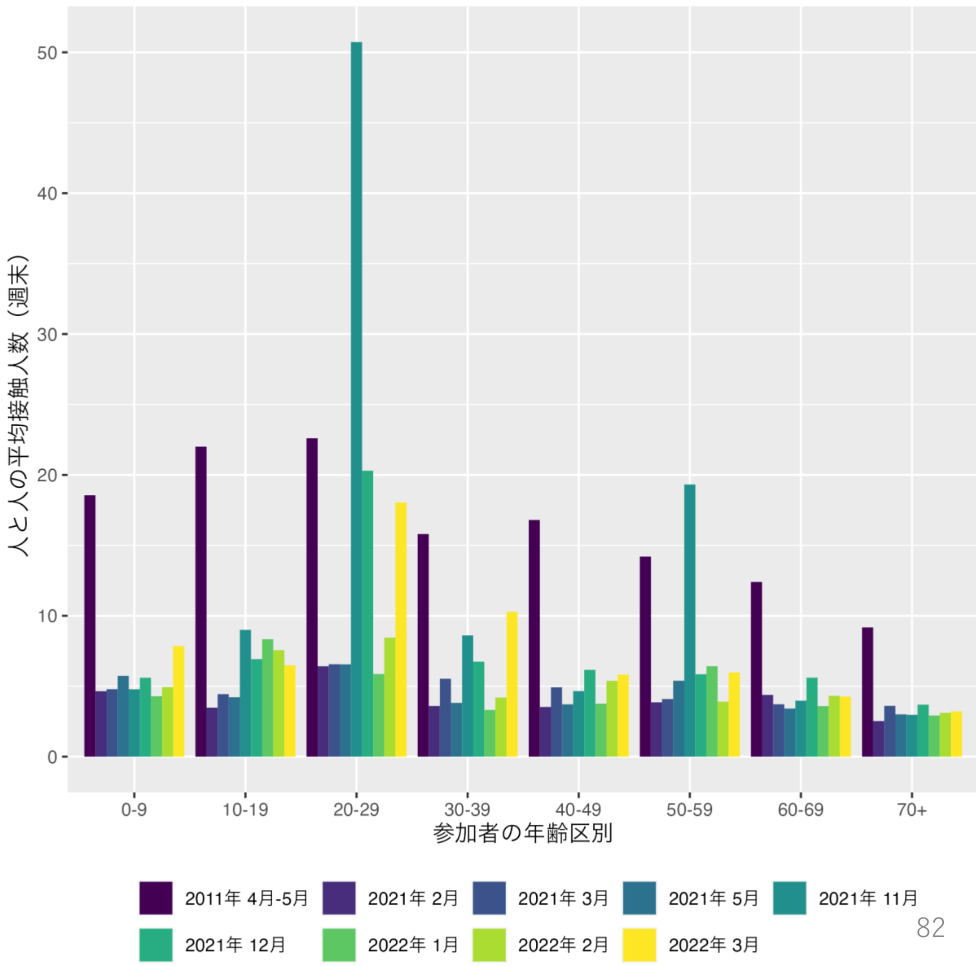


図２　週末における平均接触人数



Appendix 4. SEIR difference equations used for the mathematical model shown in Chapter 4.

Appendix 4:
SEIR Difference Equations

Difference equations used for the mathematical model are shown below.

N is defined as the total population of the prefecture and $n_i(t)$ is the number of people who have received i^{th} dose of vaccine on day t.

Prefecture-specific births and deaths are incorporated into the model. The birth rate (per day) is indicated as b and is incorporated in $S_1(t+1)$. The number of individuals who die at a death rate m is deducted from each compartment at rate $m \cdot$ *population of compartment*. For ease of reading, m is not indicated in the equations below.

$I(t)$ is the total number of people in all of the infected compartments as defined as follows:

$I(t) = I_1(t) + I_2(t) + I_3(t) + I_4(t) + I_5(t)$

V_{b} is the susceptible population recently boosted with a vaccine dose.

V_{w} is the vaccinated population with waning immunity.

Individuals who are partially vaccinated with 0-1 dose:

$$
\begin{aligned}
S_1(t+1) &= S_1(t) - n_{2S}(t+1) - \beta(t)\frac{S_1(t)\,I(t)}{N} + \rho R_1(t) + bN \\
E_1(t+1) &= E_1(t) - n_{2E}(t+1) + \beta(t)\frac{S_1(t)\,I(t)}{N} - \epsilon E_1(t) \\
I_1(t+1) &= I_1(t) - n_{2I}(t+1) + \epsilon E_1(t) - \gamma I_1(t) \\
R_1(t+1) &= R_1(t) - n_{2R}(t+1) + \gamma I_1(t) - \rho R_1(t)
\end{aligned}
$$

Individuals with 2 doses:

$$
\begin{aligned}
S_2(t+1) &= S_2(t) - n_{3S}(t+1) - \beta(t)\frac{S_2(t)\,I(t)}{N} + \rho R_2(t) + \kappa_2 V_{\mathrm{w},2}(t)\\
E_2(t+1) &= E_2(t) + n_{2E}(t+1) - n_{3E}(t+1) + \beta(t)\frac{S_2(t)\,I(t)}{N} + \beta(t)\frac{(1-\nu)\,V_{\mathrm{b},2}(t)\,I(t)}{N}\\
&\quad + \beta(t)\frac{(1-\nu)\,V_{\mathrm{w},2}(t)\,I(t)}{N} - \epsilon E_2(t)\\
I_2(t+1) &= I_2(t) + n_{2I}(t+1) - n_{3I}(t+1) + \epsilon E_2(t) - \gamma I_2(t)\\
R_2(t+1) &= R_2(t) + n_{2R}(t+1) - n_{3R}(t+1) + \gamma I_2(t) - \rho R_2(t)\\
V_{\mathrm{b},2}(t+1) &= V_{\mathrm{b},2}(t) + n_{2S}(t+1) - n_{3\mathrm{b}}(t+1) - \beta(t)\frac{(1-\nu)\,V_{\mathrm{b},2}(t)\,I(t)}{N} - \kappa_1\, V_{\mathrm{b},2}(t)\\
V_{\mathrm{w},2}(t+1) &= V_{\mathrm{w},2}(t) + \kappa_1\, V_{\mathrm{b},2}(t) - n_{3\mathrm{w}}(t+1) - \kappa_2 V_{\mathrm{w},2}(t) - \beta(t)\frac{(1-\nu)\,V_{\mathrm{w},2}(t)\,I(t)}{N}
\end{aligned}
$$

Individuals with 3 doses:

$$
\begin{aligned}
S_3(t+1) &= S_3(t) - n_{4S}(t+1) - \beta(t)\frac{S_3(t)I(t)}{N} + \rho R_3(t) + \kappa_2 V_{\mathrm{w},3}(t)\\
E_3(t+1) &= E_3(t) + n_{3E}(t+1) - n_{4E}(t+1) + \beta(t)\frac{S_3(t)\,I(t)}{N} + \beta(t)\frac{(1-\nu)\,V_{\mathrm{b},3}(t)\,I(t)}{N}\\
&\quad + \beta(t)\frac{(1-\nu)V_{\mathrm{w},3}(t)\,I(t)}{N} - \epsilon E_3(t)\\
I_3(t+1) &= I_3(t) + n_{3I}(t+1) - n_{4I}(t+1) + \epsilon E_3(t) - \gamma I_3(t)\\
R_3(t+1) &= R_3(t) + n_{3R}(t+1) - n_{4R}(t+1) + \gamma I_3(t) - \rho R_3(t)\\
V_{\mathrm{b},3}(t+1) &= V_{\mathrm{b},3}(t) + n_{3S}(t+1) + n_{3\mathrm{b}}(t+1) + n_{3\mathrm{w}}(t+1) - n_{4\mathrm{b}}(t+1)\\
&\quad - \beta(t)\frac{(1-\nu)\,V_{\mathrm{b},3}(t)\,I(t)}{N} - \kappa_1 V_{\mathrm{b},3}(t)\\
V_{\mathrm{w},3}(t+1) &= V_{\mathrm{w},3}(t) + \kappa_1 V_{\mathrm{b},3}(t) - n_{4\mathrm{w}}(t+1) - \kappa_2 V_{\mathrm{w},3}(t) - \beta(t)\frac{(1-\nu)\,V_{\mathrm{w},3}(t)\,I(t)}{N}
\end{aligned}
$$

Individuals with 4 doses:

$$
\begin{aligned}
S_4(t+1) &= S_4(t) - n_{5S}(t+1) - \beta(t)\frac{S_4(t)I(t)}{N} + \rho R_4(t) + \kappa_2 V_{\mathrm{w},4}(t)\\
E_4(t+1) &= E_4(t) + n_{4E}(t+1) - n_{5E}(t+1) + \beta(t)\frac{S_4(t)\,I(t)}{N} + \beta(t)\frac{(1-\nu)\,V_{\mathrm{b},4}(t)\,I(t)}{N}\\
&\quad + \beta(t)\frac{(1-\nu)\,V_{\mathrm{w},4}(t)\,I(t)}{N} - \epsilon E_4(t)\\
I_4(t+1) &= I_4(t) + n_{4I}(t+1) - n_{5I}(t+1) + \epsilon E_4(t) - \gamma I_4(t)\\
R_4(t+1) &= R_4(t) + n_{4R}(t+1) - n_{5R}(t+1) + \gamma I_4(t) - \rho R_4(t)\\
V_{\mathrm{b},4}(t+1) &= V_{\mathrm{b},4}(t) + n_{4S}(t+1) + n_{4\mathrm{b}}(t+1) + n_{4\mathrm{w}}(t+1) - n_{5\mathrm{b}}(t+1)\\
&\quad - \beta(t)\frac{(1-\nu)V_{\mathrm{b},4}(t)I(t)}{N} - \kappa_1 V_{\mathrm{b},4}(t)\\
V_{\mathrm{w},4}(t+1) &= V_{\mathrm{w},4}(t) + \kappa_1 V_{\mathrm{b},4}(t) - n_{5\mathrm{w}}(t+1) - \kappa_2 V_{\mathrm{w},4}(t) - \beta(t)\frac{(1-\nu)V_{\mathrm{w},4}(t)I(t)}{N}
\end{aligned}
$$

Individuals with 5 doses:

$$
\begin{aligned}
S_5(t+1) &= S_5(t) - \beta(t)\frac{S_5(t)I(t)}{N} + \rho R_5(t) + \kappa_2 V_{\mathrm{w},5}(t)\\
E_5(t+1) &= E_5(t) + n_{5E}(t+1) + \beta(t)\frac{S_5(t)\,I(t)}{N} + \beta(t)\frac{(1-\nu)\,V_{\mathrm{b},5}(t)\,I(t)}{N}\\
&\quad + \beta(t)\frac{(1-\nu)\,V_{\mathrm{w},5}(t)\,I(t)}{N} - \epsilon E_5(t)\\
I_5(t+1) &= I_5(t) + n_{5I}(t+1) + \epsilon E_5(t) - \gamma I_5(t)\\
R_5(t+1) &= R_5(t) + n_{5R}(t+1) + \gamma I_5(t) - \rho R_5(t)\\
V_{\mathrm{b},5}(t+1) &= V_{\mathrm{b},5}(t) + n_{5S}(t+1) + n_{5\mathrm{b}}(t+1) + n_{5\mathrm{w}}(t+1) - \beta(t)\frac{(1-\nu)\,V_{\mathrm{b},5}(t)\,I(t)}{N} - \kappa_1 V_{\mathrm{b},5}(t)\\
V_{\mathrm{w},5}(t+1) &= V_{\mathrm{w},5}(t) + \kappa_1 V_{\mathrm{b},5}(t) - \kappa_2 V_{\mathrm{w},5}(t) - \beta(t)\frac{(1-\nu)\,V_{\mathrm{w},5}(t)\,I(t)}{N}
\end{aligned}
$$

For the individuals that are flowing from 0-1 dose to 2 doses, n are defined as follows:

l is a snapshot in time, and the sum of all l so far is equal to t.

$$
\begin{aligned}
n_{2S}(t) &= n_2(t+1)\frac{S_1(t)}{N - \sum_{l=0}^{t} n_2(l)}\\
n_{2E}(t) &= n_2(t+1)\frac{E_1(t)}{N - \sum_{l=0}^{t} n_2(l)}\\
n_{2I}(t) &= n_2(t+1)\frac{I_1(t)}{N - \sum_{l=0}^{t} n_2(l)}\\
n_{2R}(t) &= n_2(t+1)\frac{R_1(t)}{N - \sum_{l=0}^{t} n_2(l)}
\end{aligned}
$$

For the individuals that are flowing into 3 doses, 4 doses or 5 doses, n are defined with the following conditions:

Individuals who are flowing from the $V_{\mathrm{b},i}$ compartments when $\sum_{l=0}^{t} n_{i-1}(l) - \sum_{l=0}^{t} n_i(l) \neq 0$ are defined as $n_{i\mathrm{b}}(t+1) = n_i(t+1)\frac{V_{\mathrm{b},i}(t)}{\sum_{l=0}^{t} n_{i-1}(l) - \sum_{l=0}^{t} n_i(l)}$; but when $\sum_{l=0}^{t} n_{i-1}(l) - \sum_{l=0}^{t} n_i(l) = 0$, then the individuals are defined as $n_{i\mathrm{b}}(t+1) = 0$.

Individuals who are flowing from the $V_{\mathrm{w},i}$ compartments when $\sum_{l=0}^{t} n_{i-1}(l) - \sum_{l=0}^{t} n_i(l) \neq 0$ are defined as $n_{i\mathrm{w}}(t+1) = n_i(t+1)\frac{V_{\mathrm{w},i}(t)}{\sum_{l=0}^{t} n_{i-1}(l) - \sum_{l=0}^{t} n_i(l)}$; but when

$\sum\limits_{l=0}^{t} n_{i-1}(l) - \sum\limits_{l=0}^{t} n_i(l) = 0$, then the individuals are defined as $n_{i\mathrm{w}}(t+1) = 0$.

Individuals who are flowing from the S_i compartments when $\sum\limits_{l=0}^{t} n_{i-1}(l) - \sum\limits_{l=0}^{t} n_i(l) \neq 0$ are defined as $n_{iS}(t+1) = n_i(t+1)\frac{S_i(t)}{\sum\limits_{l=0}^{t} n_{i-1}(l) - \sum\limits_{l=0}^{t} n_i(l)}$; but when $\sum\limits_{l=0}^{t} n_{i-1}(l) - \sum\limits_{l=0}^{t} n_i(l) = 0$, then the individuals are defined as $n_{iS}(t+1) = 0$.

Individuals who are flowing from the E_i compartments when $\sum\limits_{l=0}^{t} n_{i-1}(l) - \sum\limits_{l=0}^{t} n_i(l) \neq 0$ are defined as $n_{iE}(t+1) = n_i(t+1)\frac{E_i(t)}{\sum\limits_{l=0}^{t} n_{i-1}(l) - \sum\limits_{l=0}^{t} n_i(l)}$; but when $\sum\limits_{l=0}^{t} n_{i-1}(l) - \sum\limits_{l=0}^{t} n_i(l) = 0$, then the individuals are defined as $n_{iE}(t+1) = 0$.

Individuals who are flowing from the I_i compartments when $\sum\limits_{l=0}^{t} n_{i-1}(l) - \sum\limits_{l=0}^{t} n_i(l) \neq 0$ are defined as $n_I(t+1) = n_i(t+1)\frac{I_i(t)}{\sum\limits_{l=0}^{t} n_{i-1}(l) - \sum\limits_{l=0}^{t} n_i(l)}$; but when $\sum\limits_{l=0}^{t} n_{i-1}(l) - \sum\limits_{l=0}^{t} n_i(l) = 0$, then the individuals are defined as $n_{iI}(t+1) = 0$.

Individuals who are flowing from the R_i compartments when $\sum\limits_{l=0}^{t} n_{i-1}(l) - \sum\limits_{l=0}^{t} n_i(l) \neq 0$ are defined as $n_R(t+1) = n_i(t+1)\frac{R_i(t)}{\sum\limits_{l=0}^{t} n_{i-1}(l) - \sum\limits_{l=0}^{t} n_i(l)}$; but when $\sum\limits_{l=0}^{t} n_{i-1}(l) - \sum\limits_{l=0}^{t} n_i(l) = 0$, then the individuals are defined as $n_{iR}(t+1) = 0$.

Appendix 5. SEIR differential equations and calculation of the effective reproduction number (R_e) used for the mathematical model shown in Chapter 5.

Appendix 5: SEIR Differential Equations and Calculation of R_e

Ordinary Differential Equations used for the model with an age structure.

N is defined as the total simulated population.

$I(t)$ is defined as the total number of people in all of the Infected compartments as defined as follows: $I(t) = I_1(t) + I_2(t) + I_3(t)$

Note that in the R script, $\beta \frac{I(t)}{N}$ was defined as λ, or in other words force of infection, that is defined as follows: $\lambda(t) = \beta I(t)$

The Ordinary Differential Equations (ODEs) that were used for the model are as follows:

Individuals with 0 or 1 dose:

$$\begin{aligned}
\frac{dS_1}{dt} &= -\beta \frac{S_1(t)I(t)}{N} + \rho R_1(t) \\
\frac{dE_1}{dt} &= \beta \frac{S_1(t)I(t)}{N} - \epsilon E_1(t) \\
\frac{dI_1}{dt} &= \epsilon E_1(t) - \gamma I_1(t) \\
\frac{dR_1}{dt} &= \gamma I_1(t) - \rho R_1(t)
\end{aligned}$$

Individuals with 2 doses:

$$\begin{aligned}
\frac{dS_2}{dt} &= -\beta \frac{S_2(t)I(t)}{N} + \rho R_2(t) + \kappa_2 V_{\mathrm{w},2}(t) \\
\frac{dE_2}{dt} &= \beta \frac{S_2(t)I(t)}{N} + \beta \frac{(1-\nu)V_{\mathrm{b},2}(t)I(t)}{N} + \beta \frac{(1-\nu)V_{\mathrm{w},2}(t)I(t)}{N} - \epsilon E_2(t) \\
\frac{dI_2}{dt} &= \epsilon E_2(t) - \gamma I_2(t) \\
\frac{dR_2}{dt} &= \gamma I_2(t) - \rho R_2(t) \\
\frac{dV_{\mathrm{b},2}}{dt} &= -\beta \frac{(1-\nu)V_{\mathrm{b},2}(t)I(t)}{N} - \kappa_1 V_{\mathrm{b},2}(t) \\
\frac{dV_{\mathrm{w},2}}{dt} &= \kappa_1 V_{\mathrm{b},2}(t) - \kappa_2 V_{\mathrm{w},2}(t) - \beta \frac{(1-\nu)V_{\mathrm{w},2}(t)I(t)}{N}
\end{aligned}$$

Individuals with 3 doses:

$$
\begin{aligned}
\frac{dS_3}{dt} &= -\beta\frac{S_3(t)I(t)}{N} + \rho R_3(t) + -\kappa_2 V_{\mathrm{w},3}(t) \\
\frac{dE_3}{dt} &= \beta\frac{S_3(t)I(t)}{N} + \beta\frac{(1-\nu)V_{\mathrm{b},3}(t)I(t)}{N} + \beta\frac{(1-\nu)V_{\mathrm{w},3}(t)I(t)}{N} - \epsilon E_3(t) \\
\frac{dI_3}{dt} &= \epsilon E_3(t) - \gamma I_3(t) \\
\frac{dR_3}{dt} &= \gamma I_3(t) - \rho R_3(t) \\
\frac{dV_{\mathrm{b},3}}{dt} &= -\beta\frac{(1-\nu)V_{\mathrm{b},3}(t)I(t)}{N} - \kappa_1 V_{\mathrm{b},3}(t) \\
\frac{dV_{\mathrm{w},3}}{dt} &= \kappa_1 V_{\mathrm{b},3}(t) - \kappa_2 V_{\mathrm{w},3}(t) - \beta\frac{(1-\nu)V_{\mathrm{w},3}(t)I(t)}{N}
\end{aligned}
$$

Calculation of the effective reproduction number (R_e)

In a simple SEIR model without any vaccination compartments, R_0 would be defined as $\frac{\beta}{\gamma}$. However, since this model captures a specific time during an epidemic that incorporates a population that consists of individuals who gained immunity from natural infection and vaccination, the reproduction number must reflect this. This is referred as the effective reproduction number or R_e.

Referring to the Diekmann et al. method in calculating R_0, the same logic was applied to calculate R_e. ODEs that were used to set up the Next Generation Matrix (NGM) are the E and I compartments since we are only referring to the generation of new infected individuals and changes in the states of already existing infected individuals. For this model, it is a closed population so there are no births or deaths.

The ODEs used for the calculation of R_e are as follows:

$$
\begin{aligned}
\frac{dE_1}{dt} &= \beta\frac{S_1(t)I(t)}{N} - \epsilon E_1(t) \\
\frac{dI_1}{dt} &= \epsilon E_1(t) - \gamma I_1(t) \\
\frac{dE_2}{dt} &= \beta\frac{S_2(t)I(t)}{N} + \beta\frac{(1-\nu)V_{\mathrm{b},2}(t)I(t)}{N} + \beta\frac{(1-\nu)V_{\mathrm{w},2}(t)I(t)}{N} - \epsilon E_2(t) \\
\frac{dI_2}{dt} &= \epsilon E_2(t) - \gamma I_2(t) \\
\frac{dE_3}{dt} &= \beta\frac{S_3(t)I(t)}{N} + \beta\frac{(1-\nu)V_{\mathrm{b},3}(t)I(t)}{N} + \beta\frac{(1-\nu)V_{\mathrm{w},3}(t)I(t)}{N} - \epsilon E_3(t) \\
\frac{dI_3}{dt} &= \epsilon E_3(t) - \gamma I_3(t)
\end{aligned}
$$

We define matrix **T** as transmissions and matrix **E** as transitions.

Based on the Diekmann et al. method, in the infection-free (or in other words, equilibrium) state, $\beta SI/N$ becomes βI since $S = N$. However in our model, $N = S_1 + E_1 + I_1 + R_1 + V_{\mathrm{b},2} + V_{\mathrm{w},2} +$

$S_2+E_2+I_2+R_2+V_{\mathrm{b},3}+V_{\mathrm{w},3}+S_3+E_3+I_3+R_3$ so in an infection-free state, all the individuals in the E, I, and $R=0$.

Thus, $N=S_1+V_{\mathrm{b},2}+V_{\mathrm{w},2}+S_2+V_{\mathrm{b},3}+V_{\mathrm{w},3}+S_3$.

The equations used for matrix $\mathbf{T}$ are as follows:

$$\begin{aligned}
\dot{E}_1 &= \beta I\\
\dot{I}_1 &= 0\\
\dot{E}_2 &= \beta I+\beta I\frac{(1-\nu)V_{\mathrm{b},2}}{N}+\beta I\frac{(1-\nu)V_{\mathrm{w},2}}{N}\\
\dot{I}_2 &= 0\\
\dot{E}_3 &= \beta I+\beta I\frac{(1-\nu)V_{\mathrm{b},3}}{N}+\beta I\frac{(1-\nu)V_{\mathrm{w},3}}{N}\\
\dot{I}_3 &= 0
\end{aligned}$$

The equations used for matrix $\mathbf{E}$ are as follows:

$$\begin{aligned}
\dot{E}_1 &= -\epsilon E_1\\
\dot{I}_1 &= \epsilon E_1-\gamma I_1\\
\dot{E}_2 &= -\epsilon E_2\\
\dot{I}_2 &= \epsilon E_2-\gamma I_2\\
\dot{E}_3 &= -\epsilon E_3\\
\dot{I}_3 &= \epsilon E_3-\gamma I_3
\end{aligned}$$

With the above equations, the NGMs are written as follows:

$$\mathbf{T}=\begin{bmatrix}
0 & \beta & 0 & \beta & 0 & \beta\\
0 & 0 & 0 & 0 & 0 & 0\\
0 & \beta+\beta(1-\nu)(V_{\mathrm{b},2}+V_{\mathrm{w},2}) & 0 & \beta+\beta(1-\nu)(V_{\mathrm{b},2}+V_{\mathrm{w},2}) & 0 & \beta+\beta(1-\nu)(V_{\mathrm{b},2}+V_{\mathrm{w},2})\\
0 & 0 & 0 & 0 & 0 & 0\\
0 & \beta+\beta(1-\nu)(V_{\mathrm{b},3}+V_{\mathrm{w},3}) & 0 & \beta+\beta(1-\nu)(V_{\mathrm{b},3}+V_{\mathrm{w},3}) & 0 & \beta+\beta(1-\nu)(V_{\mathrm{b},3}+V_{\mathrm{w},3})\\
0 & 0 & 0 & 0 & 0 & 0
\end{bmatrix}$$

$$\mathbf{E}=\begin{bmatrix}
-\epsilon & 0 & 0 & 0 & 0 & 0\\
\epsilon & -\gamma & 0 & 0 & 0 & 0\\
0 & 0 & -\epsilon & 0 & 0 & 0\\
0 & 0 & \epsilon & -\gamma & 0 & 0\\
0 & 0 & 0 & 0 & -\epsilon & 0\\
0 & 0 & 0 & 0 & \epsilon & -\gamma
\end{bmatrix}$$

The dominant eigenvalue, indicated as $\mathbf{K_L}$, is calculated as follows:

$$\begin{aligned}
\mathbf{K_L} &= -\mathbf{TE^{-1}}\\
\mathbf{K_L} &= \frac{\beta(-\nu V_{\mathrm{b},2}-\nu V_{\mathrm{b},3}-\nu V_{\mathrm{w},2}-\nu V_{\mathrm{w},3}+V_{\mathrm{b},2}+V_{\mathrm{b},3}+V_{\mathrm{w},2}+V_{\mathrm{w},3}+3)}{\gamma}
\end{aligned}$$

Since at the start of the simulated epidemic, there is one infected individual per age category, so all compartments except for the Infected compartments are equal to 0. Thus, the above equation is simplied as follows:

$\mathbf{K_L} = R_e = \frac{3\beta}{\gamma}$

Calculation of the probability of an effective contact

Another key component in infectious disease transmission, in addition to age-stratified contacts, is the probability of each contact that results in transmission. This is defined as q. Since β is defined as the rate at which two specific individuals contact one another per unit time that results in transmission, β can also be written as $\beta = qc$ where c is the average contact rate per individual.

Since c can be derived directly from the contact surveys, $c = 8.07$ which was the average weekday contact rate per individual (weighted by age and sex) reported from the contact surveys in Fukuoka and Osaka prefectures in December 2022.

Based on the Wuhan study by Kucharski et al. (2020), R_0 of SARS-CoV-2 was estimated as 2.2 (IQR: $1.6 - 3.0$). In December 2022, the main SARS-COV-2 variant that was circulating was BA.5 of Omicron which was reported to have higher transmissibility than the original virus. Thus, the higher end of the IQR, an estimate of $R_0 = 3.0$, was taken in the calculation of q. γ was 0.9 based on the model parameters that were used for these simulations. q was calculated as follows:

$$\begin{aligned} R_e &= \frac{3\beta}{\gamma} \\ 3 &= \frac{3qc}{\gamma} \\ 1 &= \frac{8.07q}{0.9} \\ q &= 0.112 \end{aligned}$$

Appendix 6. R script used for the mathematical model simulations covered in Chapter 5

```
library(deSolve)
library(ggplot2)
library(scico)
library(readxl)
library(dplyr)
library(tidyr)
library(reshape2)

# First, test by developing an SEIR model without any vax/un-vax groups
rm(list = ls(all = TRUE))


# -----------------------------------------------------------------------------------------
# 1. Select which prefecture's contact rates you want to use in your model
# Note: The wd() of the script where the weekday and weekend contacts were developed belong here:
# "~/Dropbox/LSHTM PhD/JP Model/Contact survey"
# the R scripts start off with "ctcagematrix" and for each pref for Dec 2022 survey

# -----------------------------------------------------------------------------------------

# Import the age-stratified matrix first (includes the >10 contacts)
setwd("~/Dropbox/LSHTM PhD/Tomoka PhD Project Shared/Modeling/JP Model/Contact matrix") #may need to
change wd() here when sharing

# select which prefecture you want for contact rates and weekday vs. weekend
whichpref <- "okinawa_wkday"

# Weekday contacts
if (whichpref %in% "fukuoka_wkday"){
  contactmatr <- read.csv("totalmatrix_dec2022_fukuoka_wkday_withplus10.csv", row.names = 1, header =
TRUE)}
if (whichpref %in% "osaka_wkday"){
  contactmatr <- read.csv("totalmatrix_dec2022_osaka_wkday_withplus10.csv", row.names = 1, header =
TRUE)}
if (whichpref %in% "okinawa_wkday"){
  contactmatr <- read.csv("totalmatrix_dec2022_okinawa_wkday_withplus10.csv", row.names = 1, header =
TRUE)}

# Weekend contacts
if (whichpref %in% "fukuoka_wkend"){
  contactmatr <- read.csv("totalmatrix_dec2022_fukuoka_weekend_withplus10.csv", row.names = 1, header =
TRUE)}
if (whichpref %in% "osaka_wkend"){
  contactmatr <- read.csv("totalmatrix_dec2022_osaka_weekend_withplus10.csv", row.names = 1, header =
TRUE)}
if (whichpref %in% "okinawa_wkend"){
  contactmatr <- read.csv("totalmatrix_dec2022_okinawa_weekend_withplus10.csv", row.names = 1, header =
TRUE)}


#re-label the column names into the approp age categories
colnames <- c("0-9", "10-19", "20-29", "30-39", "40-49", "50-59", "60-69", "70+")
colnames(contactmatr) <- colnames


# -----------------------------------------------------------------------------------------
# 2. Create the plot of the age stratified matrix
# -----------------------------------------------------------------------------------------

contactmatr <- as.matrix(contactmatr) # convert back into matrix format to prep for plot
age.cat <- colnames(contactmatr)

tmp <- expand.grid(contacts=age.cat,part=age.cat)

agedat <- data.frame(x=as.vector(contactmatr))
agedat$contacts <- tmp$contacts
agedat$participants <- tmp$part

#using another color scheme using scico package
ggplot(agedat,aes(x=participants, y=contacts, fill=x, label=x)) +
  geom_tile(aes(fill = x)) +
```

```
  geom_text(aes(label = round(x, 2)),
            color = ifelse(agedat$x > 1, "white", "black")) +
  #you need to identify as "agedat$x" for the variable
  #because I am not putting the color inside aes()
  #need to put it outside of aes() to identify the colors
  scale_fill_scico("Log Number \n of Contacts",
                   palette = "tokyo", direction = -1,
                   #invert the colors, put -1 in direction
                   breaks = c(0.01, 0.1, 1, 10),
                   limits = c(0.01, 20),
                   trans = "log") +
  xlab("Age Categories of Participants") +
  ylab("Age Categories of Contacts") +
  theme(axis.text = element_text(size = 10, face = "bold", color = "black"),
        legend.text = element_text(size = 12, color = "black"),
        legend.title = element_text(size = 12, face = "bold", color = "black"),
        axis.title = element_text(size = 12, face = "bold", color = "black"))

# ------------------------------------------------------------------------------------------
# 3. Then, we need to make the contact matrix symmetrical in prep for the simulations
# ------------------------------------------------------------------------------------------
xsym <- (contactmatr+t(contactmatr))/2

# check this whether this is a matrix
is.matrix(xsym)

# make this as a matrix
xsym <- as.matrix(xsym)


# ------------------------------------------------------------------------------------------
# 4. Create a stacked bar chart of the demographics of all the prefectures
# ------------------------------------------------------------------------------------------
setwd("~/Dropbox/LSHTM PhD/Tomoka PhD Project Shared/Modeling/JP Model/Demography")

# Source of this excel: 2022 JP census data from the website below:
# https://www.e-stat.go.jp/stat-search/files?stat_infid=000032224635
# each row indicates the total # of population per prefecture and each column shows the age category

demography <- read_excel("Fukuoka_Osaka_Okinawa_Pop_2022_Census_byagegroups.xlsx")

# Create stacked bar chart of the demography % by age category for each prefecture

dem_percent <- demography[,-1] / demography$Total * 100

dem_percent <- cbind(demography[,1], dem_percent)
dem_percent <- dem_percent[,1:9]
dem_percentlong <- melt(dem_percent, id.vars = "Prefecture")
colnames(dem_percentlong) <- c("prefecture", "agecat", "percent")

# list the prefecture in this specific order
pref_order <- c("Osaka", "Fukuoka", "Okinawa")

dem_percentlong$agecat <- factor(dem_percentlong$agecat, levels = rev(levels(dem_percentlong$agecat)))
#dem_percentlong$prefecture <- factor(dem_percentlong$prefecture, levels = c("Osaka", "Fukuoka",
"Okinawa"))
dem_percentlong$prefecture <- factor(dem_percentlong$prefecture, levels = pref_order)

# Calculate total population for each prefecture
total_pop <- aggregate(Total ~ Prefecture, data = demography, FUN = sum)
total_pop <- total_pop[match(pref_order, total_pop$Prefecture),]

# Combine prefecture names with total population as part of the x-axis label
prefecture_labels <- paste(total_pop$Prefecture, "\n(Total N: ", total_pop$Total, ")", sep = "")


# plot the stacked bar chart
ggplot(dem_percentlong, aes(x = prefecture, y = percent, fill = agecat)) +
  geom_bar(stat = "identity") +
  geom_text(aes(label = paste(round(percent), "%")),
            position = position_stack(vjust = 0.5)) +
  scale_fill_brewer(palette = "Set3") + # you can change the palette if needed
  theme_minimal() +
  theme(axis.text = element_text(size = 10, color = "black"),
        legend.text = element_text(size = 10, color = "black"),
        legend.title = element_text(size = 10, face = "bold", color = "black"),
```

```
        axis.title = element_text(size = 12, face = "bold", color = "black"),
        legend.position = "right") +
  scale_x_discrete(labels = prefecture_labels) +
  labs(x = "Prefecture", y = "Population per Prefecture (%)", fill = "Age Category")



# ------------------------------------------------------------------------------------------
# 5. Create a vector for the initial conditions of the simulation
# Note: Remember that we are dealing with 7 age categories so we need to have 8 different
# compartments of S (S1 to S7), 7 compartments of I (I1 to I7), etc.
# ------------------------------------------------------------------------------------------

# Calculate the proportion of the pop in each age category and multiply by the total N that you are
# using for your simulation (e.g. 100,000 as total N)

sim_totalN <- 100000

demography_prop <- demography %>%
  group_by(Prefecture) %>%
  summarize(
    age_0_9 = `0-9`/Total * sim_totalN,
    age_10_19 = `10-19`/Total * sim_totalN,
    age_20_29 = `20-29`/Total * sim_totalN,
    age_30_39 = `30-39`/Total * sim_totalN,
    age_40_49 = `40-49`/Total * sim_totalN,
    age_50_59 = `50-59`/Total * sim_totalN,
    age_60_69 = `60-69`/Total * sim_totalN,
    age_70plus = `70+`/Total * sim_totalN

  )

# check the total per row to make sure it adds up to sim_totalN
rowSums(demography_prop[,2:9]) #yes it matches with sim_totalN

# ------------------------------------------------------------------------------------------
# 6. Select the prefecture of the demography you want to incorporate in your model
# ------------------------------------------------------------------------------------------

# select which prefecture for the demography data
whichpref <- "okinawa"

if (whichpref %in% "fukuoka"){
  pop <- demography_prop %>%
  filter(Prefecture=="Fukuoka") %>% select(2:ncol(demography_prop))}
if (whichpref %in% "osaka"){
  pop <- demography_prop %>%
    filter(Prefecture=="Osaka") %>% select(2:ncol(demography_prop))}
if (whichpref %in% "okinawa"){
  pop <- demography_prop %>%
    filter(Prefecture=="Okinawa") %>% select(2:ncol(demography_prop))}


# check the total that should come out to sim_totalN
rowSums(pop)


# ------------------------------------------------------------------------------------------
# 7. Import the vax coverage data from 10 Jan 2023 to create bar graph to show
# different levels of coverage across the different age categories and for each prefecture
# ------------------------------------------------------------------------------------------
setwd("~/Dropbox/LSHTM PhD/Tomoka PhD Project Shared/Modeling/JP Model/Vaccine Coverage")

vaxcov <- read_excel("Fukuoka_Osaka_Okinawa_Vax_Coverage_bydose_pref_12Apr2024.xlsx")
# this spreadsheet shows the N of vax individuals per dose and by prefecture
# Each N is calculated by DOSE (different from the spreadsheet imported in step #8)
# The total N of all doses for each prefecture adds up to the total pop of each prefecture.

vaxcov$dose <- rep(c("Dose 0-1", "Dose 2", "Dose 3"), times = 3)
vaxcov$prefecture <- rep(c("Osaka", "Fukuoka", "Okinawa"), each = 3)
vaxcov <- vaxcov[,2:ncol(vaxcov)]
vaxcov$total <- rowSums(vaxcov[,1:8])

#reorder the vaxcov df and then put it into % per dose and per prefecture
vaxcov <- vaxcov %>%
  select(prefecture, dose, "0-9", "10-19", "20-29", "30-39", "40-49",
```

```
         "50-59", "60-69", "70+", ends_with("total")) %>%
  mutate_at(vars(-c(prefecture, dose)), ~./total * 100)

vaxcov <- vaxcov[,2:ncol(vaxcov)-1] #eliminate the total (which is shown as 100%)


#put it into long format in prep for plot
vaxcov_long <- vaxcov %>%
  pivot_longer(cols      = -c(prefecture, dose),
               names_to  = "age",
               values_to = "N")

#set the order of the prefecture in prep for the plot
vaxcov_long$prefecture <- factor(vaxcov_long$prefecture, levels = c("Osaka", "Fukuoka", "Okinawa"))

# plot
ggplot(vaxcov_long, aes(x = age, y = N, fill = prefecture)) +
  geom_bar(stat = "identity", position = "dodge") +
  facet_wrap(~dose) +
  labs(title, title, x = "Age", y = "Vaccination Coverage (%)", fill = "Prefecture",
       caption = "Source: COVID-19 vaccination coverage data reported on 10 Jan 2023
       by the Prime Minister's Office of Japan") +
  theme_bw() +
  scale_y_continuous(breaks = seq(0,100,by=5)) +
  scale_fill_brewer(palette = "Set2") +
  theme(axis.text.x = element_text(angle = 45, hjust =1, color = "black"),
        legend.text = element_text(size = 10,  color = "black"),
        legend.title = element_text(size = 10, face = "bold", color = "black"),
        axis.title = element_text(size = 10, face = "bold",color = "black"),
        plot.caption = element_text(hjust=0))


# ---------------------------------------------------------------------------------------------
#  8. Import the vax coverage data from 10 Jan 2023 to incorporate in the model
# ---------------------------------------------------------------------------------------------
setwd("~/Dropbox/LSHTM PhD/Tomoka PhD Project Shared/Modeling/JP Model/Vaccine Coverage")

vaxcoverage_byage <- read_excel("Fukuoka_Osaka_Okinawa_Vax_Coverage_Prop_byage_24Mar2024.xlsx")
# this spreadsheet shows the proportion of vaccinated individuals per age category and by prefecture.
# The proportion is calculated BY AGE CATEGORY
# (ie it adds up to 1 by adding ALL incl 0-1 dose, exact 2 dose, exact 3 dose for each age cat)


# ---------------------------------------------------------------------------------------------
# 9. Select the prefecture of the vax coverage you want to incorporate in your model
# ---------------------------------------------------------------------------------------------

# select which prefecture for the vax coverage data
whichpref <- "okinawa"

# Filter first to Fukuoka vax coverage data
if (whichpref %in% "okinawa") {
  vax_prop_by_age <- vaxcoverage_byage %>%
  filter(Prefecture=="Okinawa_0-1dose" | Prefecture=="Okinawa_exact_2dose" |
Prefecture=="Okinawa_exact_3dose")}
if (whichpref %in% "fukuoka") {
  vax_prop_by_age <- vaxcoverage_byage %>%
    filter(Prefecture=="Fukuoka_0-1dose" | Prefecture=="Fukuoka_exact_2dose" |
Prefecture=="Fukuoka_exact_3dose")}
if (whichpref %in% "osaka") {
  vax_prop_by_age <- vaxcoverage_byage %>%
    filter(Prefecture=="Osaka_0-1dose" | Prefecture=="Osaka_exact_2dose" |
Prefecture=="Osaka_exact_3dose")}


# Double check with the proportion that should add to 1 by age cat
colSums(vax_prop_by_age[,2:length(vax_prop_by_age)]) #yes adds up to 1 for each age cat

# transform into long format and get the proportion of vax'd per age category
# by dividing with the total population of each age category (from 2022 census)

vax_long <- vax_prop_by_age %>%
  pivot_longer(cols = 2:ncol(vax_prop_by_age),
               names_to = "age_cat",
               values_to = "prop_vax") %>%
  mutate(sim_population_byage = case_when(
```

```r
    age_cat=="0-9"   ~ pop$age_0_9,
    age_cat=="10-19" ~ pop$age_10_19,
    age_cat=="20-29" ~ pop$age_20_29,
    age_cat=="30-39" ~ pop$age_30_39,
    age_cat=="40-49" ~ pop$age_40_49,
    age_cat=="50-59" ~ pop$age_50_59,
    age_cat=="60-69" ~ pop$age_60_69,
    age_cat=="70+"   ~ pop$age_70plus),
    sim_vax_n = prop_vax * sim_population_byage
  )

# double check that the grand total of N adds up to the total N needed for simulation
sum(vax_long$sim_vax_n)
# double check that each N of age category adds up to the sum of N for each age cat needed for
simulation
test <- vax_long %>% group_by(age_cat) %>%
  summarize(sum = sum(sim_vax_n))
print(test)
print(pop) #yes the "test" matches with this total sum needed for simulation



# ---------------------------------------------------------------------------------------------
# 10. Select again the prefecture of the vax coverage you want to incorporate in your model
# and separate out the 0-1 dose, exactly 2 dose, and exactly 3 dose buckets
# ---------------------------------------------------------------------------------------------
whichpref <- "okinawa"

if (whichpref %in% "okinawa") {
bucket_0_1dose <- vax_long  %>% filter(Prefecture=="Okinawa_0-1dose") %>%
  select("age_cat", "sim_vax_n") %>%
  pivot_wider(names_from = age_cat, values_from = sim_vax_n)

bucket_2dose <- vax_long  %>% filter(Prefecture=="Okinawa_exact_2dose") %>%
  select("age_cat", "sim_vax_n") %>%
  pivot_wider(names_from = age_cat, values_from = sim_vax_n)

bucket_3dose <- vax_long  %>% filter(Prefecture=="Okinawa_exact_3dose") %>%
  select("age_cat", "sim_vax_n") %>%
  pivot_wider(names_from = age_cat, values_from = sim_vax_n)

# subtract 1 from each N so we can start off with 1 infected person per age category in our
# initial condition. Do the same for all other buckets (including those who received exactly 2 doses
# and those who received exactly 3 doses)
bucket_0_1dose_sim <- bucket_0_1dose %>%
  mutate(across(everything(), ~. -1))
# transform into a list to prep for putting this as the initial condition
bucket_0_1dose_sim <- as.numeric(unlist(bucket_0_1dose_sim))

bucket_2dose_sim <- bucket_2dose %>%
  mutate(across(everything(), ~. -1))
# transform into a list to prep for putting this as the initial condition
bucket_2dose_sim <- as.numeric(unlist(bucket_2dose_sim))

bucket_3dose_sim <- bucket_3dose %>%
  mutate(across(everything(), ~. -1))
# transform into a list to prep for putting this as the initial condition
bucket_3dose_sim <- as.numeric(unlist(bucket_3dose_sim))
}

if (whichpref %in% "osaka") {
  bucket_0_1dose <- vax_long  %>% filter(Prefecture=="Osaka_0-1dose") %>%
    select("age_cat", "sim_vax_n") %>%
    pivot_wider(names_from = age_cat, values_from = sim_vax_n)

  bucket_2dose <- vax_long  %>% filter(Prefecture=="Osaka_exact_2dose") %>%
    select("age_cat", "sim_vax_n") %>%
    pivot_wider(names_from = age_cat, values_from = sim_vax_n)

  bucket_3dose <- vax_long  %>% filter(Prefecture=="Osaka_exact_3dose") %>%
    select("age_cat", "sim_vax_n") %>%
    pivot_wider(names_from = age_cat, values_from = sim_vax_n)

  bucket_0_1dose_sim <- bucket_0_1dose %>%
    mutate(across(everything(), ~. -1))
  # transform into a list to prep for putting this as the initial condition
```

```r
  bucket_0_1dose_sim <- as.numeric(unlist(bucket_0_1dose_sim))

  bucket_2dose_sim <- bucket_2dose %>%
    mutate(across(everything(), ~. -1))
  # transform into a list to prep for putting this as the initial condition
  bucket_2dose_sim <- as.numeric(unlist(bucket_2dose_sim))

  bucket_3dose_sim <- bucket_3dose %>%
    mutate(across(everything(), ~. -1))
  # transform into a list to prep for putting this as the initial condition
  bucket_3dose_sim <- as.numeric(unlist(bucket_3dose_sim))

  }

if (whichpref %in% "fukuoka") {
  bucket_0_1dose <- vax_long  %>% filter(Prefecture=="Fukuoka_0-1dose") %>%
    select("age_cat", "sim_vax_n") %>%
    pivot_wider(names_from = age_cat, values_from = sim_vax_n)

  bucket_2dose <- vax_long  %>% filter(Prefecture=="Fukuoka_exact_2dose") %>%
    select("age_cat", "sim_vax_n") %>%
    pivot_wider(names_from = age_cat, values_from = sim_vax_n)

  bucket_3dose <- vax_long  %>% filter(Prefecture=="Fukuoka_exact_3dose") %>%
    select("age_cat", "sim_vax_n") %>%
    pivot_wider(names_from = age_cat, values_from = sim_vax_n)

  bucket_0_1dose_sim <- bucket_0_1dose %>%
    mutate(across(everything(), ~. -1))
  # transform into a list to prep for putting this as the initial condition
  bucket_0_1dose_sim <- as.numeric(unlist(bucket_0_1dose_sim))

  bucket_2dose_sim <- bucket_2dose %>%
    mutate(across(everything(), ~. -1))
  # transform into a list to prep for putting this as the initial condition
  bucket_2dose_sim <- as.numeric(unlist(bucket_2dose_sim))

  bucket_3dose_sim <- bucket_3dose %>%
    mutate(across(everything(), ~. -1))
  # transform into a list to prep for putting this as the initial condition
  bucket_3dose_sim <- as.numeric(unlist(bucket_3dose_sim))

  }


# ------------------------------------------------------------------------------------------
# 11. Set your initial conditions of your model simulation
# ------------------------------------------------------------------------------------------


yinit <- c(
  S_v0 = bucket_0_1dose_sim,
  E_v0 = c(rep(0,8)),
  I_v0 = c(rep(1,8)),
  R_v0 = c(rep(0,8)),

  S_v1 = c(rep(0,8)),
  E_v1 = c(rep(0,8)),
  I_v1 = c(rep(1,8)),
  R_v1 = c(rep(0,8)),
  Vb_v1 = bucket_2dose_sim,
  Vw_v1 = c(rep(0,8)),

  S_v2 = c(rep(0,8)),
  E_v2 = c(rep(0,8)),
  I_v2 = c(rep(1,8)),
  R_v2 = c(rep(0,8)),
  Vb_v2 = bucket_3dose_sim,
  Vw_v2 = c(rep(0,8))

)

print(yinit)

# check the total that should come out to sim_totalN
sum(yinit)
```

```
# ------------------------------------------------------------------------------------------
# 12. Create index for each compartment so the codes that follow can be easier to follow
# to see which compartment belongs to which
# ------------------------------------------------------------------------------------------
sindex <- 1:8
eindex <- 9:16
iindex <- 17:24
rindex <- 25:32

sindex2 <- 33:40
eindex2 <- 41:48
iindex2 <- 49:56
rindex2 <- 57:64
vbindex2 <- 65:72
vwindex2 <- 73:80

sindex3 <- 81:88
eindex3 <- 89:96
iindex3 <- 97:104
rindex3 <- 105:112
vbindex3 <- 113:120
vwindex3 <- 121:128


# ------------------------------------------------------------------------------------------
# 13. Set your parameters and run your simulation!
# ------------------------------------------------------------------------------------------

# a. call out the source where you have the script with the functions saved
setwd("~/Dropbox/LSHTM PhD/Tomoka PhD Project Shared/Modeling/JP Model")

source("seir_testrun_functioncode_ko_ver6.R")

# b. Set the parameters for SEIR model

#times <- seq(0, 65*200, 0.5)
#times <- seq(0, 10, 0.1)
times <- seq(0,60,1)
#times <- seq(0,365*40,1)


# the below parameters are constant so define them as your parameters
rho     <- 1/(365*9/12) #rate from R back to S
epsilon <- 0.9  #rate from E to I
gamma   <- 0.9 #rate from I to R
kappa1  <- 1/30 #rate from Vb1 to Vw1
kappa2  <- 1/142 #rate from Vw1 to S1
nu      <- 0.7 #vax efficacy

# multiplying the beta with the probability of contact that results in transmission
# this is based on the R0 equation that I calculated from getting the dominant eigenvalue of
# the ODEs of my model. R0 = 3*beta/gamma = (3*q*c)/gamma

q <-  0.112  #this is when R0 = 3.0 (higher end of IQR)

beta <- q*xsym  # new matrix created with the beta indicated in each cell across all age cats

is.matrix(beta) # check again to see if it's in matrix format


# c. Define the parameters for my simulation

# define what parms are equal to here so when you put "parms" in lsoda(),
# the ODEs will be solved accordingly based on how these parameters
# were defined in the earlier code above.

# make sure to add beta here b/c we've defined beta as q * xsym in the above code
# with the age-stratified contact matrix. If beta changes, it will be reflected
# in your simulation b/c you added beta as part of your list of "parms."

parms <- list(rho = rho, epsilon = epsilon,
           gamma = gamma, kappa1 = kappa1, kappa2 = kappa2,
           nu = nu, beta = beta)
```

```
# need to make sure 'parms' here is a LIST!

# d. Solve the ODE and run the simulation w/ above parameters using lsoda()

seir_sim <- lsoda(
  y = yinit,
  times = times,
  func  = seir_mod,
  parms = parms)


# Check if each row (excluding time) adds up to the N_total
# to make sure you are adding/subtracting ppl from the compartments properly
seir_sim <- as.data.frame(seir_sim)
# create new variable to add up the sums of each row
seir_sim$total_n = rowSums(seir_sim[,2:ncol(seir_sim)])

# check the model doesn't change the total size (indicates equations are not balanced)
summary(seir_sim$total_n)


# -----------------------------------------------------------------------------------------
# 14. Prepare to create graphs of each compartment of my simulation
# -----------------------------------------------------------------------------------------

# a. create vectors for each compartment in prep to create graphs
times <- seir_sim[,1]
suscept_novax <- seir_sim[,1+sindex]
exposed_novax <- seir_sim[,1+eindex]
infectd_novax <- seir_sim[,1+iindex]
recovds_novax <- seir_sim[,1+rindex]

suscept_dose2  <- seir_sim[,1+sindex2]
exposed_dose2 <- seir_sim[,1+eindex2]
infectd_dose2 <- seir_sim[,1+iindex2]
recovds_dose2 <- seir_sim[,1+rindex2]
vb1_dose2     <- seir_sim[,1+vbindex2]
vw1_dose2     <- seir_sim[,1+vwindex2]

suscept_dose3  <- seir_sim[,1+sindex3]
exposed_dose3 <- seir_sim[,1+eindex3]
infectd_dose3 <- seir_sim[,1+iindex3]
recovds_dose3 <- seir_sim[,1+rindex3]
vb2_dose3     <- seir_sim[,1+vbindex3]
vw2_dose3     <- seir_sim[,1+vwindex3]



# b. Plot the sum of individuals in each compartment

par(mfrow=c(2,2))
plot(times,apply(suscept_novax,1,sum),type='l',col='turquoise',main="Susceptible \n dose 0-
1",ylab="N",xlab="days")
plot(times,apply(exposed_novax,1,sum),type='l',col='violet',main="Exposed \n dose 0-
1",ylab="N",xlab="days")
plot(times,apply(infectd_novax,1,sum),type='l',col='salmon2',main="Infected \n dose 0-
1",ylab="N",xlab="days")
plot(times,apply(recovds_novax,1,sum),type='l',col='springgreen2',main="Recovered \n dose 0-
1",ylab="N",xlab="days")


par(mfrow=c(3,4))
plot(times,apply(suscept_dose2,1,sum),type='l',col='blue2',main="Susceptible \n dose
2",ylab="N",xlab="days")
plot(times,apply(exposed_dose2,1,sum),type='l',col='violetred1',main="Exposed \n dose
2",ylab="N",xlab="days")
plot(times,apply(infectd_dose2,1,sum),type='l',col='red',main="Infected \n dose2",ylab="N",xlab="days")
plot(times,apply(recovds_dose2,1,sum),type='l',col='limegreen',main="Recovered \n dose
2",ylab="N",xlab="days")
plot(times,apply(vb1_dose2,1,sum),type='l',col='orangered3',main="Vaccinated \n dose
2",ylab="N",xlab="days")
plot(times,apply(vw1_dose2,1,sum),type='l',col='orange',main="Vaccinated \n waning
dose2",ylab="N",xlab="days")
```

```
plot(times,apply(suscept_dose3,1,sum),type='l',col='navy',main="Susceptible \n
dose3",ylab="N",xlab="days")
plot(times,apply(exposed_dose3,1,sum),type='l',col='orchid3',main="Exposed \n
dose3",ylab="N",xlab="days")
plot(times,apply(infectd_dose3,1,sum),type='l',col='red3',main="Infected \n
dose3",ylab="N",xlab="days")
plot(times,apply(recovds_dose3,1,sum),type='l',col='forestgreen',main="Recovered \n
dose3",ylab="N",xlab="days")
plot(times,apply(vb2_dose3,1,sum),type='l',col='orangered4',main="Vaccinated \n
dose3",ylab="N",xlab="days")
plot(times,apply(vw2_dose3,1,sum),type='l',col='orange2',main="Vaccinated \n waning dose
3",ylab="N",xlab="days")


#reorder the plots differently
par(mfrow=c(3,4))
plot(times,apply(suscept_novax,1,sum),type='l',col='blue2',main="Susceptible \n dose 0-
1",ylab="N",xlab="days")
plot(times,apply(exposed_novax,1,sum),type='l',col='violetred1',main="Exposed \n dose 0-
1",ylab="N",xlab="days")
plot(times,apply(infectd_novax,1,sum),type='l',col='red',main="Infected \n dose 0-
1",ylab="N",xlab="days")
plot(times,apply(recovds_novax,1,sum),type='l',col='springgreen2',main="Recovered \n dose 0-
1",ylab="N",xlab="days")
plot(times,apply(suscept_dose2,1,sum),type='l',col='blue2',main="Susceptible \n dose
2",ylab="N",xlab="days")
plot(times,apply(exposed_dose2,1,sum),type='l',col='violetred1',main="Exposed \n dose
2",ylab="N",xlab="days")
plot(times,apply(infectd_dose2,1,sum),type='l',col='red',main="Infected \n dose2",ylab="N",xlab="days")
plot(times,apply(recovds_dose2,1,sum),type='l',col='springgreen2',main="Recovered \n dose
2",ylab="N",xlab="days")
plot(times,apply(suscept_dose3,1,sum),type='l',col='blue2',main="Susceptible \n
dose3",ylab="N",xlab="days")
plot(times,apply(exposed_dose3,1,sum),type='l',col='violetred1',main="Exposed \n
dose3",ylab="N",xlab="days")
plot(times,apply(infectd_dose3,1,sum),type='l',col='red',main="Infected \n dose3",ylab="N",xlab="days")
plot(times,apply(recovds_dose3,1,sum),type='l',col='springgreen2',main="Recovered \n
dose3",ylab="N",xlab="days")

par(mfrow=c(2,2))
plot(times,apply(vb1_dose2,1,sum),type='l',col='orangered3',main="Vaccinated \n dose
2",ylab="N",xlab="days")
plot(times,apply(vw1_dose2,1,sum),type='l',col='orange',main="Vaccinated \n waning
dose2",ylab="N",xlab="days")
plot(times,apply(vb2_dose3,1,sum),type='l',col='orangered3',main="Vaccinated \n
dose3",ylab="N",xlab="days")
plot(times,apply(vw2_dose3,1,sum),type='l',col='orange2',main="Vaccinated \n waning dose
3",ylab="N",xlab="days")


#c. Summary stats for summing the total number of infected from each simulation

#create a list of the df's you want to summarize the N from
df_list <- list(
  infected_novax = infectd_novax,
  infectd_dose2  = infectd_dose2,
  infectd_dose3  = infectd_dose3,
  recovds_novax  = recovds_novax,
  recovds_dose2  = recovds_dose2,
  recovds_dose3  = recovds_dose3)

#results <- list()
#create an empty vector to store the max_sum values in prep for the loop
max_sums <- c()

#loop to get the max N of the sum of the individuals in each compartment after the simulation
for (i in seq_along(df_list)) {
  sums <- rowSums(df_list[[i]]) #calculate sum of each row in current df
  max_sum <- max(sums) #finds the max sum among all rows in current df
  max_sums <- c(max_sums, max_sum) #stores the max sum of current df to the max_sums vector
  #results[[i]] <- list(sums = sums, max_sum = max_sum)
  #cat("Maximum N of individuals for", names(df_list)[i], ":", max_sum, "\n")
}

# Create a data frame with the max_sum values
results_df <- data.frame(df_name = names(df_list), max_sum = max_sums)
```

```
# Print the data frame
print(results_df)


#create another list of the df's to summarize the susceptible population
df_list2 <- list(suscept_novax, suscept_dose2, suscept_dose3)

sums <- numeric(length(df_list2)) #get ready for the loop
grand_total <- 0 #get ready for the loop to put the grand total sum

for (i in seq_along(df_list2)) {
  # get the last row of each df and sum all columns (ie all age categories summed up)
  sums[i] <- sum(tail(df_list2[[i]], n = 1))

  # add the sum to the total sum
  grand_total <- grand_total + sums[i]

  prop_S      <- grand_total/sim_totalN #proportion of S out of total N

  r0_endemic  <- 1/prop_S #calculate the R0 at endemic state equilibrium
}

# print the values
print(prop_S)
print(r0_endemic)
```

Appendix 7. Continuation of the R script used for the mathematical model simulations covered in Chapter 5. This script shows the SEIR model in a function that is used in the main script shown in Appendix 6.

```
seir_mod <- function(t, y, parms) {
  beta     <- parms$beta # parms$beta from parms being a list
  rho      <- parms$rho
  epsilon  <- parms$epsilon
  gamma    <- parms$gamma
  kappa1   <- parms$kappa1  #this was initially just "kappa"
  kappa2   <- parms$kappa2  #this was initially "lambda"
  nu       <- parms$nu


  #Those in the 0-1 dose group
  #these indeces were defined in the main code (outside of the function)
  # and these indeces are to define the compartments stratified by age category (i.e. S1 to S8,
  # E1 to E8, etc.) We need these indeces defined in a vector format
  S_v0 <- y[sindex]
  E_v0 <- y[eindex]
  I_v0 <- y[iindex]
  R_v0 <- y[rindex]

  #Those in the group with 2nd dose vax
  S_v1 <- y[sindex2]
  E_v1 <- y[eindex2]
  I_v1 <- y[iindex2]
  R_v1 <- y[rindex2]
  Vb_v1 <- y[vbindex2]
  Vw_v1 <- y[vwindex2]

  #Those in the group with 3rd dose vax
  S_v2 <- y[sindex3]
  E_v2 <- y[eindex3]
  I_v2 <- y[iindex3]
  R_v2 <- y[rindex3]
  Vb_v2 <- y[vbindex3]
  Vw_v2 <- y[vwindex3]

  # the total N by adding up all compartments
  N <- S_v0+E_v0+I_v0+R_v0+S_v1+E_v1+I_v1+R_v1+Vb_v1+Vw_v1+
       S_v2+E_v2+I_v2+R_v2+Vb_v2+Vw_v2

  # check here to make sure that beta is in matrix format
  if(is.matrix(beta)==F ) {  #if this statement is true, then the error message
    # will be provided here and the message within the curly bracket will be shown.
    # check to make sure that this works
    stop("beta not matrix")} #it stops the function with this error message if
  # beta is not a matrix. If it's a matrix then the function will carry through
  # to the next line of code.

  #lambda <- beta%*%sum(I_v0 + I_v1 + I_v2)/sum(N)
  lambda <- beta%*%(I_v0 + I_v1 + I_v2)/N
  # force of infection calculated by multiplying beta with I/N
  # this is multiplying a matrix with a vector.
  # impt note: when multiplying a matrix with a vector, the vector MUST
  # have the same number of columns as the matrix.
  # we defined above in the sindex, iindex, etc. as a vector with the same # of items
  # as the different age categories (i.e. 8 age categories)
  #browser()

  # # take the sum of all compartments in each vax bucket in prep for the ODEs
  # N_v0 <- sum(S_v0+E_v0+I_v0+R_v0)
  # N_v1 <- sum(S_v1+E_v1+I_v1+R_v1+Vb_v1+Vw_v1)

  #ODEs for those who received 0-1 dose
  S_v0_new <- -lambda*S_v0 + rho*R_v0

  E_v0_new <-  lambda*S_v0 - epsilon*E_v0

  I_v0_new <-  epsilon*E_v0 - gamma*I_v0

  R_v0_new <-  gamma*I_v0 - rho*R_v0
```

```
  #ODEs for those who received 2nd dose vax

  S_v1_new     <-  -lambda*S_v1  + rho*R_v1 + kappa2*Vw_v1

  E_v1_new     <-  (lambda*S_v1) + (lambda*(1-nu)*Vb_v1) + (lambda*(1-nu)*Vw_v1) - (epsilon*E_v1)

  I_v1_new     <-  (epsilon*E_v1) - (gamma*I_v1)

  R_v1_new     <-  (gamma*I_v1) - (rho*R_v1)

  #ODE for waning immunity for those who received 2nd dose vax
  Vb_v1_new    <-   -(lambda*(1-nu)*Vb_v1) - (kappa1*Vb_v1)

  Vw_v1_new    <-   (kappa1*Vb_v1) - (kappa2*Vw_v1) - (lambda*(1-nu)*Vw_v1)

  #ODEs for those who received 3rd dose vax
  S_v2_new    <-  -lambda*S_v2 + rho*R_v2 + kappa2*Vw_v2

  E_v2_new    <-   (lambda*S_v2) + (lambda*(1-nu)*Vb_v2) + (lambda*(1-nu)*Vw_v2) - (epsilon*E_v2)

  I_v2_new    <-  (epsilon*E_v2) - (gamma*I_v2)

  R_v2_new    <-  (gamma*I_v2) - (rho*R_v2)

  #ODE for waning immunity for those who received 3rd dose vax
  Vb_v2_new   <-  -(kappa1*Vb_v2) -  (lambda*(1-nu)*Vb_v2)

  Vw_v2_new   <-  (kappa1*Vb_v2) - (kappa2*Vw_v2) - (lambda*(1-nu)*Vw_v2)


  # write the return list containing all the outputs from the differential equations
  return(list(c( S_v0=S_v0_new, E_v0=E_v0_new, I_v0=I_v0_new, R_v0=R_v0_new,
                 S_v1=S_v1_new, E_v1=E_v1_new, I_v1=I_v1_new, R_v1=R_v1_new,
                 Vb_v1=Vb_v1_new, Vw_v1=Vw_v1_new,
                 S_v2=S_v2_new, E_v2=E_v2_new, I_v2=I_v2_new, R_v2=R_v2_new,
                 Vb_v2=Vb_v2_new, Vw_v2=Vw_v2_new
                 )))

}
```

Appendix 8. Publication titled “Public Perspectives on COVID-19 Public Health and Social Measures in Japan and the United Kingdom: A Qualitative Study” published in BMC Public Health.

Kawamitsu *et al. BMC Public Health* (2024) 24:1393
https://doi.org/10.1186/s12889-024-18866-3

BMC Public Health

RESEARCH

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Public perspectives on COVID-19 public health and social measures in Japan and the United Kingdom: a qualitative study

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Abstract

Background The COVID-19 pandemic, caused by SARS-CoV-2, was one of the greatest modern public health crises that the world has faced. Countries undertook sweeping public health and social measures (PHSM); including environmental actions such as disinfection and ventilation; surveillance and response, such as contact tracing and quarantine; physical, such as crowd control; and restrictions on travel. This study focuses on the public perceptions of PHSM in two countries, Japan and the United Kingdom (UK) as examples of high-income countries that adopted different measures over the course of the pandemic.

Methods This study was conducted between November 2021 and February 2022, a period in which the Omicron variant of SARS-CoV-2 was predominant. Fourteen online focus group discussions were conducted in each country. Overall, 106 total participants (50 from the UK and 56 from Japan) participated in 23 focus groups (11 in the UK and 12 in Japan) with an average of three to six participants per group. Both countries were compared using a thematic analysis method.

Results Both countries' participants agreed that vaccination was an effective measure. However, they did not favor mandatory vaccination policies. Working from home was well accepted by both sides, but they reported that schools should have continued to be opened as before COVID-19. Both sides of participants expressed that temperature testing alone in indoor facilities was ineffective as a COVID-19 control measure. There were contrasting views on face covering rules in public spaces, international and domestic movement restrictions. High acceptance of mask-wearing was reflective of Japanese customs, while it was accepted as a strong recommendation for participants in the UK. Japanese participants favored quarantine for international travel, while the UK participants supported banning non-essential travel.

Conclusion Similar and contrasting views on PHSM against COVID-19 between Japan and the UK demonstrated how policies in controlling an epidemic should be tailored by country with respect to its norms, cultures, economic and disease burden. Our findings may guide how policy makers can engage with the public through effective health communication and consider regulations that are aligned with the public's views and capacities in changing their behavior for future pandemic preparedness.

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Keywords COVID-19, SARS-CoV-2, Public health and social measures, Japan, United Kingdom, England, Pandemic preparedness, Focus groups

Introduction

The COVID-19 pandemic caused by SARS-CoV-2 was one of the greatest public health crises the world has faced, and in response countries undertook considerable public health and social measures (PHSM). PHSM is defined by the World Health Organization (WHO) as measures or actions by individuals, institutions, communities, local and national governments, and international bodies to slow or stop the spread of infectious disease, such as COVID-19 [1]. PHSMs include but are not limited to vaccination policies, face covering rules, working and teaching hours for businesses and schools, testing requirements to access indoor events, and international and domestic travel restrictions. The adoption of PHSMs was the subject of much debate during the COVID-19 pandemic [2]. Although all countries aimed to achieve the same outcome – to stop or dampen the spread of the diseases and death without burdening their health resources and economic vigor – there was a recognition that there exists no one-size fits all policy.

In 2021 the British Academy funded a small portfolio of projects focusing on vaccine engagement across the G7 countries [3]. The funded project; Adapting to the 'New Normal': Implications for post-COVID-19 Health Communication and Education [4], specifically focused on Japan and the United Kingdom (UK) as the only G7 island nations. Despite with similar constitutional governments, these nations were influenced by distinct socio-cultural and economic factors. This allowed for a comparative analysis of population responses to public health measures across diverse social-cultural settings but under similar government policy frameworks.

In align with this, the current study focused on Japan and the United Kingdom (UK), countries that adopted different PHSM over the course of the pandemic; albeit with slight variations within different prefectures of Japan and regions of the UK. Both Japan and the UK are islands, high-income countries, with similar demographic profiles including large proportions of elderly in their populations. The study aimed to identify why public voices should be considered when designing long-term plans for PHSMs to help prepare for future pandemics, and to identify culturally specific traits of populations as displaying homogenous behaviors. This could help with the curation of messages in terms of knowing when and how to approach the public about policy changes.

Methods

Study setting and study participants

The funded project; Adapting to the 'New Normal': Implications for post-COVID-19 Health Communication and Education used a mixed methods design; (i) survey with experimental design and (ii) focus groups. The discrete choice experiment aimed to assess the cost-benefit preferences the public would make while the focus groups provided a sample of qualitative insights creating a rationale for making these choices. While the large-scale survey provided patterns of choices, the focus groups were important to complement the survey as it helped us understand the rationale behind these choices.

In this study, we utilized the mixed-gender focus group discussions (FGDs) part only with the aim of providing insights into the public assessment and understanding of the advantages and disadvantages that individuals may envision when considering COVID-19 public health and social measures (PHSMs). Six PHSM categories were chosen (Table 1) for the FGDs. The discussions were held online, because the study was conducted when the Omicron variant of SARS-CoV-2 was predominant, and the prevailing COVID-19 preventive measures prohibited group gatherings.

The participants were recruited through snowball sampling and online platforms (Facebook, Twitter, and website introducing the project) by purposive convenience sampling between November 2021 and February 2022. The study obtained information on age, gender, ethnicity, residence, occupation, the number of COVID-19 vaccinations that they had received and specific dates and times if and when they could participate for focus group discussions. Individuals aged more than 18 years old were eligible for FGDs, if they lived in the Kansai region (Japan) or Greater London (the UK). The Kansai region is located on the west side of Japan and consists of six prefectures: Osaka, Hyogo, Kyoto, Nara, Wakayama, and Shiga. Approximately 20.4 million people lived in the region, which comprised 16.7% of the total population of Japan in 2021 [5]. Osaka is the second largest city after the capital of Tokyo. The population and businesses are mainly dispersed among the three major cities of Osaka (Osaka prefecture), Kobe (Hyogo prefecture), and Kyoto (Kyoto prefecture). Greater London is the administrative area of London, the capital of the United Kingdom and England. It is organized into 33 local administrative divisions, consisting of 32 London boroughs and the City of London. The population of Greater London was approximately 9 million in 2021 [6]. The researchers then grouped the participants according to the available dates and times so that they were as mixed in age and gender as possible, in anticipation of the group dynamics that would emerge from interactions among participants with diverse backgrounds.

Data collection

Online focus groups were conducted separately in Japan and the UK. The focus group topic guides included questions on the six main categories of PHSMs: (1) vaccination; (2) face covering rules; (3) working and teaching hours for businesses, schools, and universities; (4) testing required to access indoor events; (5) domestic movement restriction; and (6) border closure and international travel restrictions. The participants were asked to select the level of control measures for each category according to the type of COVID-19 scenarios that differed in epidemiological profiles with varying cases, death rates, and hospitalization trends (Table 1). As these scenarios changed, the participants were asked anew whether they would alter their preference level of measures to adapt to these changes. This process provided participant views of PHSMs responding to 'shocks', or sharp changes in the headline levels of infections, hospitalizations, and deaths. The epidemiological profile of COVID-19 scenarios was based on (i) the number of new cases per million people per week (ranging from 200 to 4000), (ii) the percentage of excess deaths per month (ranging from −10 to 25%), and (iii) the overall trend in the number of hospitalizations over the previous 2 weeks (either 'rising' or 'falling').

Table 1 Public health and social measures (PHSM) categories and level options

PHSM Category	Level	Description
Vaccination policy (National)	**1**	General information campaign, no penalties if unvaccinated.
	2	Vaccine strongly advised and limited service if unvaccinated.
	3	Vaccines compulsory for everyone.
Face covering rules in public spaces	**1**	Face covering rules in public spaces, and recommended only, not forced.
	2	Mandatory fines for non-compliance.
Working and teaching hours for businesses and schools	**1**	Regular (maintains economy).
	2	Minimal (relieves health services).
Testing required to access indoor events	**1**	Temperature checks (easy but unreliable).
	2	Lateral flow/antigen (uncomfortable but more reliable).
International travel restriction	**1**	Fewer/limited flights (but no quarantine).
	2	Frequent/regular flights (but long quarantine).
	3	Bans on all non-essential entry and exit.
Domestic movement restrictions	**1**	Overnight curfew (stay indoors between 9 pm and 6 am).
	2	Commuting limited to local town, city or prefecture.

The participants were asked to explore the reasons for the selections in each phase. Based on the principle of focus group design, the PI was able to customize a design for the focus group integrated within the larger mixed-method design of the study [7]. The focus groups used similar prompts and references of the scenarios in the survey to elicit participants' detailed thought processes and choices, enhancing the validity of the overall mixed-methods design. Each group discussion lasted between 100 and 120 min.

The discussion guide was initially created in English, and then it was translated into Japanese to fit the Japanese context. A pilot test was conducted to scrutinize the content of the discussion guide. Before starting the data collection, the principal investigator (PI) conducted training sessions for the research assistants (RAs) on how to conduct the focus group discussions (FDGs). Specifically, the moderators were trained to ask participants individually and by name for their thoughts (promoting inclusivity), and to defuse any political contexts. Participants were given the option to turn the camera on or off, but were encouraged to keep them on as much as possible to allow for the observation of facial expressions. The study addressed the possibility of bias in data collection by training moderators to ensure that participants responded using their own words and phrases, and elaborated on their thoughts independently before being prompted by researchers.

In each country, the PI and/or the RAs moderated the group discussions. Each focus group had two researchers; specifically, one was mainly a moderator who ensured the smooth progression of the sessions and note taking, while the other was mainly an observer who made sure that all of the topics and questions were covered. The observer was responsible for recording the time, providing technical support, observing remarks and facial expressions, note taking, and had decision-making authority in the event of a tie in the number of votes. Each focus group conducted was moderated by native Japanese speaker in Japan and by native English speaker in the UK .

Overall, 106 participants were recruited and participated in the FDGs. In Japan, 56 participants participated in 12 FGDs, with an average of three to six participants per group. They were conducted between 8th January 2022 and 12th February 2022.

In the UK, 50 participants participated in 11 focus groups, with an average of three to six participants per group. FGDs in the UK were conducted between 28th December 2021 and 21st January 2022.

Data analysis

All recorded video and audio were transcribed by NVivo transcription software and checked by RAs. Japanese FGD transcripts were translated into English by the RAs.

To ensure data consistency, this study had two researchers in each session to compare each note and recorded data for the accuracy and consistency in the data collected. Additionally, to ensure data reliability, this study introduced variations in the scenarios to assess the participants' consistency in their choices. The transcripts were read multiple times to develop a deeper understanding of the data. Then, thematic analysis was used to analyze the data and present the results according to the main themes that emerged together with illustrative quotes.During the analysis phase, discussions were held between native speakers of Japanese and English to capture the nuances of the speakers and the cultural background necessary to interpret and discuss the results of all focus groups conducted in Japan and the UK.

Results

Characteristics of the participants in the focus group discussions are shown in Table 2. Findings from the FGDs in Japan are reported first, followed by the UK.

Response to COVID-19 preventive measures in Japan

In general, Japanese participants mainly emphasized the number of cases and hospitalizations rather than the number of deaths. There was a preference to maintain restrictions regardless of the number of cases, because they expected that the numbers would increase again. Many participants recognized the economic damage and agreed that economic activities should be prioritized when the number of cases decreased.

Table 2 Characteristics of participants

Characteristics	United Kingdom ($n=50$)	Japan ($n=56$)
Age		
18–39	36	42
40–59	13	11
60 and above	1	3
Sex		
Female	26	27
Male	24	29
Occupation		
Financial	1	0
Health service	5	3
Consultant	0	0
Services	3	2
Others	41	51
Vaccination		
None	5	5
1 dose	6	0
2 doses	7	51
3 doses	19	-
4 doses	13	-

Vaccination is an effective measure but should not be mandatory

The majority of Japanese participants believed in the effectiveness of the vaccine; but even under high infectious scenarios, they opposed making vaccination mandatory, in consideration of respect for human rights and the differing situations of individuals. Although 60% of participants chose the option of strongly recommending against limiting services to the unvaccinated, they preferred to make advantages for those who were vaccinated instead of imposing penalties or restrictions on those who were unvaccinated.

> *"We need to guarantee individual freedom, so I chose Level 2 (Vaccine strongly advised and limited service if unvaccinated). Rather than restricting services to the unvaccinated, I thought that vaccination would go more smoothly if there were benefits to those who had been vaccinated." (Female, 18–39 s, FG2).*

However, in the scenario that cases decreased, some participants who had experienced adverse reactions to vaccination reported preferring a general information campaign versus mandatory vaccination.

> *"I choose level 1(General information campaign, No penalties if unvaccinated). I had a very strong side effect from the vaccine, and my fever was not so bad, about 38 degrees Celsius, but I felt muscle pain so much that I was bedridden for about three days. Since I know the situation, I think that if more and more people get vaccinated twice, they will probably ask for a third and fourth vaccination. If it became a requirement and I was restricted from doing many things, I would not be happy." (Female, 18–39 s, FG5).*

Quarantine as an effective measure to control imported cases

Around 60% of participants in Japan believed that COVID-19 was repeatedly brought in from outside the country; and because of the effectiveness of quarantine, more emphasis should be placed on the quarantine period for international travel under high infectious scenarios.

> *"People are coming from overseas anyway. Even if there are restrictions on non-essential overseas travel, people will enter the country even if they don't need to, so it is better to have a quarantine period." (Male, 40–59 s, FG11).*

In the scenario that COVID-19 became stable, such as under low infectious scenarios, many participants reported preferring to have frequent or regular flights which provided for a quarantine period, because a total ban on unnecessary international travels was impossible given the economic damage.

> *"I have a very similar opinion to the person who just said, and that is level 2 (Frequent/regular flights (but long quarantine)). I think it is a compromise between the two. I think that setting a quarantine period will lead to a decrease in unnecessary travel, such as travel for entertainment and sightseeing. We can't eliminate such things. If we focus on the effect of drastically restricting such activities, I think this is better." (Male, 18–39 s, FG5).*

Domestic travel restrictions play a role in reducing the spread of infection

Many people in Japan thought that under high infectious scenarios, commuting limited to local towns, cities, or prefectures would be appropriate because the number of cases was large; and activities should be restricted during the daytime, when there was a lot of human activity. However, some thought that due to the economic impact, and based on their experience, restricting activities during the daytime would be too severe.

> *"...domestic travel should be restricted during the day. The number of infected people is high, exceeding 10,000. It depends on the virulence of the virus, but it is important not to spread the infection. The infection has spread without restrictions during the day." (Male, 18–39 s, FG10).*

The participants reported that they might change their preference if the severity of the COVID-19 pandemic were to reduce. Around 50% of participants reported that they may choose an overnight curfew, while the remaining chose commuting limited to local town, city, or prefecture. It was mentioned that it would be difficult to limit movement of people in the Kansai area, where people frequently come and go from neighboring prefectures for commuting to work and school.

> *"Within Kansai area is close to neighboring prefectures, and many people commute to school and work across the region, so level 2 (Commuting limited to local town, city or prefecture) is difficult." (Female, 18–39 s, FG6).*

Work from home is an appropriate measure but may not be good for schools

Most participants in Japan agreed that under high infectious scenarios businesspeople and companies should use telework to minimize direct human contact. However, they believed that schooling should be continued, especially for elementary and junior high schools, as virtual learning could impact student social skills, education, and physical activity.

> *"Even if students take online classes, it's not good for their health if they stay at home all the time and don't do any physical activity. School is also important for social skills, so I would like to make it level 1(Regular (maintains economy)) to respect the right of children to learn." (Female, 18–39 s, FG2).*

Participants reported that if the number of cases decreased, regulations should be loosened by accepting the presence of COVID-19 as the new normal, and schools should be reopened, considering the importance of student education.

> *"I think it would be good to weaken the restrictions on working/schooling. As everyone mentioned earlier, if commuting is restricted, I think the situation will change to the new normal where people will be able to live with this. If the COVID-19 situation is reduced to this level, I think that schools should return to normal, and everyone should be able to study to some extent." (Female, 18–39 s, FG4).*

Temperature checks alone are not a sufficient measure for indoor events

Almost all participants had the opinion that in their experience a temperature check alone was not effective. Most participants supported lateral flow or antigen testing due to its reliability.

> *"I also don't trust the temperature check alone, so I think the antigen test is more reliable. I think the more checks you do, the more likely you can find people who are positive." (Female, 60s, FG12).*

In the scenario that cases decreased, most participants reported that they would accept the use of temperature screening, in consideration of the financial costs, human resources, and time taken to implement antigen testing.

> *"The number of cases has decreased significantly, and the number of hospitalizations has gone down from the previous increase, so I am imagining the last part of a wave that came once. As for the num-*

ber of deaths, I don't feel that there is a significant difference between 9% fewer and 3% more deaths, so I'm thinking that we should loosen up the measures. I think vaccination is fine, but I don't think we need to spend so much money and time on antigen testing for events. I think it's also the right time to ensure people's freedom of movement without setting quarantine periods for restrictions on overseas travel." (Male, 40–59 s, FG11).

Mask wearing is a custom in Japan and an effective measure

All participants thought that wearing masks in public spaces should be recommended rather than forced, because almost all people in Japan wear masks, and new measures would not likely increase the rate of the mask use. They believed that wearing masks was important and effective in preventing infection.

> *"Considering the cost of establishing such laws and regulations, I thought it would be fine to leave it as it is, because all Japanese people are currently wearing masks." (Male, 18–39 s, FG3,)*

> *"I think people will wear masks just because it is cultural. If you look at the U.S., Europe, and other countries, you will find that there are many people who do not wear masks. In Japan, it is not compulsory to wear masks, and even if there is no fine, people would probably wear masks in public places, and I think people can cooperate in wearing masks even if there are no strict rules." (Female, 18–39 s, FG9).*

Response to COVID-19 preventive measures in the UK

Most participants made decisions based on the hospitalization and death rate rather than the number of cases.

Vaccination is an effective measure but should not be mandatory

As in Japan, participants in the UK did not recommend compulsory vaccination, out of consideration for human rights. But many participants were in favor of limiting services for the unvaccinated.

> *"I would go with level 2 (Vaccine strongly advised and limited service if unvaccinated) as well. Also, for this reason I don't think it should be compulsory to have vaccines, however if it is strongly advised and it's your choice not to have it then the consequences of you not having it affect what you can do." (Female, 40–59 s, FG2).*

> *"To keep such a good condition, I think a vaccine is necessary, but not mandatory because there must be someone who is concerned not to have the vaccine and they can still keep their freedom." (Female, 40–59 s, FG3).*

Limiting international travel to only essential trips may reduce the spread the viruses

Around 50% of participants reported preferring frequent or regular flights with long quarantine times; whilst the other half preferred a government ban on all non-essential international travel, with the expectation that the policy would impede the entry of new variants into the country.

> *"I would also choose level 3 (bans on all non-essential entry and exit). Just like [name removed] had said, there are people carrying viruses from other countries. So, I think, in regard to the case study, I think if we ban all non-essential entries and exits, then hopefully that'll crack down on any additional new variants." Female, 18–39 s FG6)*

Domestic travel restrictions do not have any impact on control measures

Most of the participants did not see any difference between an overnight curfew and limited commuting. They thought that both options still allowed people to contact each other.

> *"I think what we'd want to do is reduce contact as much as possible, so with the third kind of question with commuting limited to local towns versus not seeing each other, the curfew after hours, those two again I don't feel strongly about because they don't really make a difference. You're still seeing people either way. I guess still staying with the commuting within a limited local town reduces it from spreading to another geographical area." (Female, 18–39 s, FG9).*

Limited working hours is effective, but it may not be a good choice for the long term

Roughly 60% of the participants believed that activities such as schools, universities, and business should be reduced; as they could increase the number of cases and hospitalizations due to close contact. However, some participants were concerned about mental health issues and domestic violence resulting from isolation at home.

"You understand, when you reduce the number of times in school and businesses, people will not be in contact, hence the reduction in the number of people who would be going to hospital." (Male, 18–39 s, FG11).

"At the same time, I've also noticed within my profession that domestic abuse has risen and mental health has risen, and people have taken their lives and people have been very hurt in domestic abuse situations. So, that's the only reason I would go with regular." (Female, 18–39 s, FG1).

Temperature checks alone are not a sufficient measure for indoor events

Around 70% of participants preferred lateral flow or antigen testing, as they believed that a temperature check alone was not reliable. However, it was reported that lateral flow or antigen tests may be uncomfortable for some people.

"For me, I'd say level 2 (Lateral flow/antigen (uncomfortable but more reliable)) because it is a little uncomfortable but to get reliable data is quite important." (Male, 18–39 s, FG4).

"I would definitely choose level 1 (Temperature checks (easy but unreliable)). Because it's easy and I don't see if lateral flow or antigen tests can be comfortable for everyone." (Male, 18–39 s, FG4).

Mask wearing prevents transmission but recommendation alone is not effective to public behavior changes

The majority of participants (88%) supported mandatory fines for non-compliance, since they were concerned that recommendations alone may be insufficient to change behaviors, and trusted that masks could reduce transmission due to a respiratory tract infection. However, there were disagreements about human rights if the government made mask-wearing a mandatory measure.

"I have somebody that I know that is from China background and they said that even before COVID, they've always had to wear masks in public transport, and they don't really get much colds and flu's anyway. Yes, I'll go with level 2 (Mandatory fines for non-compliance)." (Female,18–39 s, FG1).

"I think based on the data above that there's a lot of cases and hospital admissions are rising, I think I would opt for level 2 (Mandatory fines for non-compliance) because experience told me when it's recommended then most people don't follow. But if you have to then you may get slightly more people follow the rules." (Female, 40–59 s, FG2).

Table 3 describes the overall similarities and differences in the responses of participants to the selected PHSM of COVID-19.

Discussion

In this study we conducted focus group discussions with 106 people in Japan and the United Kingdom (UK), to investigate public perceptions of levels of COVID-19 prevention measures under different hypothetical degree scenarios of the pandemic. The study spanned from late 2021 to early 2022, a time at which the Omicron variant of SARS-CoV-2 was predominant. To the best of our knowledge, this is the first comparative study of its kind.

In the FGDs, participants in the UK judged the level of countermeasures based on the number of deaths and hospitalizations, while those in Japan focused on the number of cases and hospitalizations. There were similarities and differences between Japanese and the UK perspectives on different PHSMs.

Vaccines

Most participants in both countries accepted the strong recommendation for vaccination, and limiting services to the unvaccinated. However, a collective resistance to mandatory vaccination persisted across all conceivable COVID-19 scenarios. These findings were consistent with a discrete choice survey conducted in the USA, which explored preferences for strategies related to COVID-19 vaccine distribution [8]. The most common reasons against mandatory vaccination were human rights and the right to freedom of choice, and also considering those who were physically unable to be vaccinated. The perceptions of participants from both countries on rewarding the vaccinated were in line with a study in the Netherlands in which respondents particularly disliked the policies penalizing those who abstain from vaccination, while favoring approaches that reward vaccine acceptance [9]. The opposition to mandatory vaccination may be in consideration of human rights and the preservation of individual freedom of choice; as well as in recognition of those who had legitimate medical reasons for being ineligible for vaccination. Within the UK, the issue of mandated COVID-19 vaccination was a divisive one, leading to a polarization of public sentiment [10]. It is crucial to recognize that mandates and restrictions carry profound ethical implications [11]; and possess the potential to elicit a strong and often negative public reaction [12, 13].

The high acceptance of COVID-19 vaccination observed in our study is likely attributed to the

Table 3 Summary of participants responses to PHSM categories and level options

PHSMs	Similarities between the UK and Japan	Differences	
		United Kingdom	**Japan**
Vaccines	All participants did not agree to enforce the level 3 option: "Vaccines compulsory for everyone" (all case scenarios). Participants preferred either level 1: "General information campaign, No penalties if unvaccinated"; or level 2: "Vaccine strongly advised and limited service if unvaccinated" (all case scenarios).		
International travel		Participants chose level 3: "Bans on all non-essential entry and exit" on all case scenarios	Participants preferred the level 2 option: "Frequent/regular flights (but long quarantine)
Domestic travel restriction		Participants do not see domestic restrictions or curfews as effective. They believe people will have contact in some ways even with the restrictions.	Participants chose the level 1 option during the low number of cases of COVID-19. Participants chose the level 2 option when the case load is high.
Working/teaching hours for business/schools	Both countries had in common the encouragement of working from home or teleworking, depending on the type of work. Participants accepted level 2: "minimal hours" (or work from home or telework). (all scenarios)	The perspectives mainly focus on minimizing contact, encouraging people to reduce interaction in business settings.	The perspectives mainly concern the negative impact of school closures on children. Participants reported that schools should be reopened to ensure the continued education of students.
COVID-19 testing in indoor events	Participants reported that level 1 "temperature check alone" was not effective in high case scenarios	Participants chose the level 2 option "lateral flow/antigen testing", as they believe that testing temperature alone was not effective or reliable.	Participants chose level 1 (temperature check alone) during the low cases of COVID-19. But they chose level 2 "lateral flow/antigen testing" during the high case scenario.
Masks		The participants chose level 2: "Mandatory fines for non-compliance".	The participants reported that mask wearing is well accustomed in Japan and thus level 1 "recommendation for mask-wearing" is enough. They believed forced policy of mask wearing will not increase the already high rate of mask wearing.

widespread recognition that vaccination is the foremost efficacious measure for curtailing the incidence of COVID-19 cases and mitigating hospitalizations. It was reported that 64–70% in the UK [14], and 56–62% of individuals in Japan [15], had COVID-19 vaccine confidence; and the acceptance is related to the high effectiveness of the vaccine during the time of the study [16, 17]. Positive and pervasive media attention regarding the effectiveness of the vaccine may have influenced opinions; particularly in Japan where the government or media is perhaps the main source of information [8]. However, the participants suggested that there is a room for improvement in the transparency and clarity of government health communications to the public.

Travel restrictions

Both countries are geographically islands, and this might have influenced the shared concerns regarding the implementation of international and domestic travel restrictions. Participants in both countries recognized the importance of quarantine periods. Due to the economic impact of flight bans, most Japanese respondents focused on the quarantine system; while about half of respondents in the UK preferred to ban all non-essential travel, as they thought that every entry could bring the virus, or a new variant. It was estimated that in tourism revenue, Japan could lose 1.29 billion USD during the first quarter of 2020 [18]; and the UK could lose £7 billion during the Omicron pandemic [19]. Although both countries suffered from the economic impact, differences in participant responses could have been influenced by their governments' response to the pandemic and the current COVID-19 situation in their countries. It is worth noting that in Japan, a national lockdown is not possible by law, and therefore the willingness of the public to adhere to suggestions was considered important for the flattening of the COVID-19 curve [12]. In contrast, in the UK, a national lockdown required residents to stay home unless there was an essential need to go out. Public business activities may have a large impact on the behaviors of individuals.

Working hours

Individuals from both countries were adapting to new ways of teleworking under COVID-19 measures. They were in favor of continuing remote work situations beyond the conclusion of the pandemic. In the UK, telework was mainly discussed, with support for its introduction and minimizing the use of public transportation to reduce human contact as an essential infection control measure. On the other hand, in Japan, schooling was mainly discussed rather than telework. Participants expressed concerns about the negative impact of school closures on children's development and stressed the importance of schooling, even if it slightly increases the risk of infection, assuming that other policies such as vaccines are in place. Thisdifference could potentially be attributed to the relatively youthful composition of the Japanese participants, coupled with the potential challenges in effectively instituting online learning at the time of data collection comparing to the UK situation.

COVID-19 testing

Participants from both countries did not agree that temperature screening alone was an effective method for identifying suspected cases, especially when the COVID-19 cases were high, as was the case at the time of the study. Previous studies [20–22] supported this response, stating that temperature screening methods alone should not be the sole measure for case detection. A systematic review and meta-analysis found that 40–50% of confirmed COVID-19 cases were asymptomatic [23]; thus, perhaps undermining the reliability of temperature checks as a diagnostic tool. However, Japanese participants accepted the idea of taking temperature readings only, in the scenario with low number of COVID-19 cases; as they assumed that the lateral flow tests or polymerase chain reaction (PCR) tests required significant financial, human, and time resources.

Mask wearing

Participants from both countries acknowledged the effectiveness of wearing masks in preventing infection. In Japan, the participants indicated that there was no need for such regulations, citing the longstanding Japanese custom of wearing masks [24]. In contrast, the participants from the UK advocated for stricter regulation on mask-wearing, as the population is not as accustomed to this practice as in Japan. In 2020, approximately 80% of people in Japan wore masks to prevent COVID-19 transmission [25]. The cultural emphasis on self-restraint to curb the spread of infection may have contributed to the high compliance rate for mask-wearing as a control measure against COVID-19. Given the widespread acceptance of mask-wearing, the general population in Japan and in other Asian countries may have been strongly motivated to adhere to policies and guidelines that encourage the wearing of face masks in public spaces to combat the COVID-19 pandemic [26].

Strengths and limitations

This study captured the real-time opinions during the period of the Omicron pandemic, when infection levels and concerns about new variants were high. Although public opinions were dynamic, our findings retained significance as a historical record, and reflected individual viewpoints within the context of the COVID-19 pandemic. These insights could prove valuable to policymakers when contemplating hypothetical scenarios for future COVID-19 re-emergence or outbreaks of other pathogens.

Our study had some limitations. First, the study was conducted online, to avoid gathering people under COVID-19. This left us with online recruitment of participants, and convenience sampling restricted the group to only those with internet access and the capacity to engage in online interactions; and this was particularly noticeable among the younger participants in Japan. Second, the study was conducted during a specific period where the preferences of participants may have depended on their availabilities and the epidemiological situation when a new SARS-CoV-2 variant had just begun to circulate. Third, data collection occurred during a transitional phase in both countries and spanned a period of evolving infection scenarios and response strategies. Despite the guidance of the moderator to anchor responses to the hypothetical scenarios rather than current circumstances, the infection conditions at the time of the FGDs may still have influenced perceptions and replies. Fourth, inherent bias could arise from the likelihood of participation being skewed toward individuals interested in COVID-19 control measures; and leaving out the opinions of those entirely disinterested or those who may delineate from the views of the majority. Finally, there were slight variations to PHSMs within different prefectures of Japan and regions of the UK. Hence the public perspectives obtained from the Kansai and Greater London areas may not be representative those throughout both countries. Despite these limitations, our findings provide valuable information on the similar and contrasting views of COVID-19 measures in Japan and the UK.

Conclusions

Our study revealed similarities and differences in preferences for preventive measures among the respondents from both countries. While both groups agreed on certain PHSM categories (vaccination, working and teaching hours, and COVID-19 testing policy), the responses differed on face-covering rules in public spaces and international and domestic movement restrictions. This indicates that policy to control infection cannot be homogenous across the world. Our findings implicated how policy makers engage in health communication with the public; and for future pandemic preparedness could encourage policy makers to consider regulations which are in alignment with public capacities. Although the specific reasons of similarities and differences were not explored in this study, they warrant future studies to cover various aspects – such as norms, cultures, and the economic and disease burdens of each country – in understanding the public opinions on the PHSM responses.

Abbreviations

FGD	Focus Group Discussion
PCR	Polymerase Chain Reaction
PHSM	Public Health Social Measures
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
WHO	World Health Organization

Acknowledgements
The authors would like to thank Dr. James Gilleen, Mr. Kieron Scott Singh, Dr. Miho Sato, the research assistants Ms. Kimiko Uchiyama, Mr. Shun Okino, and all participants in Japan and the UK for partaking in this study.

Author contributions
SK: data collection, data analysis, data interpretation, and writing the original draft; TZW: data collection, data analysis, data interpretation, and writing the original draft; SMH: data interpretation and writing the original draft; TN: study design and conceptualization, data collection, data interpretation and translation, writing review, and editing; MJ: Principal Investigator (PI), study design and conceptualization, data collection, data interpretation, supervision, writing review, and editing; CS: study design and conceptualization, supervision, writing review, and editing. All authors reviewed the manuscript.

Funding
Financial support for this study was provided by the British Academy (Ref: COVG7210041, 'Adapting to the 'New Normal': Implications for post-COVID-19 Health Communication and Education). CS was supported by a Japan Ministry of Education, Culture, Sports, Science and Technology Young Researcher award on 'Improving the international travel experience in the time of COVID-19' (KAKENHI 22K18104). SMH and TN were supported by the WISE Program (Doctoral Program for World-leading Innovative & Smart Education) of Ministry of Education, Culture, Sports, Science and Technology. The funders of the study had no role in the study design, data collection, data analysis, data interpretation, or the writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Data availability
The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The study received ethical approval from the ethics committee of University of Roehampton London, UK (Ref: EDU 21/ 222) and the School of Tropical Medicine and Global Health (TMGH), Nagasaki University, Japan (Ref: NU_TMGH_2021_192_1). All participants provided informed consent.

Consent for publication
All participants provided informed consent for publication.

Competing interests
The authors declare no competing interests.

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Received: 1 November 2023 / Accepted: 16 May 2024
Published online: 23 May 2024

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