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The impact of the COVID-19 preventive measures on influenza transmission: molecular and epidemiological evidence

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A R T I C L E   I N F O

A B S T R A C T

Objective: We quantify the impact of COVID-19-related control measures on the spread of human influenza virus H1N1 and H3N2.
Methods: We analyzed case numbers to estimate the end of the 2019−2020 influenza season and compared it with the median of the previous 9 seasons. In addition, we used influenza molecular data to compare within-region and between-region genetic diversity and effective population size from 2019 to 2020. Finally, we analyzed personal behavior and policy stringency data for each region.
Results: The 2019−2020 influenza season ended earlier than the median of the previous 9 seasons in all regions. For H1N1 and H3N2, there was an increase in between-region genetic diversity in most pairs of regions between 2019 and 2020. There was a decrease in within-region genetic diversity for 12 of 14 regions for H1N1 and 9 of 12 regions for H3N2. There was a decrease in effective population size for 10 of 13 regions for H1N1 and 3 of 7 regions for H3N2.
Conclusions: We found consistent evidence of a decrease in influenza incidence after the introduction of preventive measures due to COVID-19 emergence.

Introduction

The emergence and spread of COVID-19 in 2020 led to a number of large-scale public health measures to limit international travel, reduce gatherings and increase mask-wearing. While these preventive measures were implemented to curtail the spread of COVID-19, they seem to have also impacted the spread of other respiratory illnesses. There have been several reports on the decrease in case numbers during the 2019−2020 influenza season in the northern hemisphere (Kuo et al., 2020) and the lack of a 2020 influenza season in the southern hemisphere (The Economist Newspaper, 2020). We quantify the impact of COVID-19 preventive measures on the spread of influenza in terms of incidence and viral molecular diversity (Bedford et al., 2015).

Methods

Case count data

We analyzed weekly case count data of influenza available in FluNet (World Health Organization, 2021) from various regions during the 2010−2020 influenza seasons. We defined T_S and T_E as the weeks during which the estimated number of cases reached 10% and 90% of the total case numbers in each influenza season, respectively. Since the influenza outbreaks for most regions started before the COVID-19 pandemic, we compared T_E and durations of influenza seasons pre-onset and post-onset of the COVID-19 pandemic. We defined the duration of an influenza season as the

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Table 1
Comparison of influenza outbreaks before and after the emergence of COVID-19

Continent	Country	$T_{E,\ 19\text{-}20}$	Median of T_E in previous 9 seasons (range)	[£]Difference in T_E	Standardized duration in 2019-2020 season
Northeast and Southeast Asia	Singapore	[ᵗ]4	27 (21, 29)	-23	-2.12
	Korea	[*]4	15 (4, 17)	-11	-1.20
	China	4	20 (7, 29)	-16	-1.42
	Taiwan[#]	15	24 (21, 27)	-9	-2.47
	Thailand	9	26 (11, 29)	-17	-1.34
	Japan	[*]6	13 (10, 16)	-7	-0.77
Western Asia	Afghanistan	7	15 (0, 25)	-8	-0.33
	Turkey	4	10 (6, 15)	-6	-1.84
	Israel	6	10 (6, 12)	-4	0.52
	Lebanon[ε]	12	14 (8, 17)	-2	-0.08
North America	Canada	11	14 (10, 17)	-3	-0.07
	USA	11	11 (8, 15)	0	0.78
	Mexico	11	11 (1, 24)	0	0.10
Central and South America	Brazil	12	27 (19, 28)	-15	-0.26
	Guatemala	13	23 (18, 27)	-10	0.12
Europe	Sweden	11	13 (9, 16)	-2	0.07
	Norway	11	14 (5, 17)	-3	0.15
	Denmark[ε]	11	11 (3, 15)	0	0.65
	Finland	8	11 (8, 12)	-3	1.10
	Germany	10	12 (9, 13)	-2	-0.49
	France	10	11 (6, 14)	-1	-0.04
	UK	10	13 (4, 15)	-3	0.98
	Spain	8	10 (5, 13)	-2	-0.20
	Italy	9	10 (6, 12)	-1	0.32
Africa	South Africa	7	27 (26, 29)	-20	-2.67

[£] Difference in T_E is equal to $T_{E,\ 19\text{-}20}$ minus the median of T_E in previous 9 seasons.

[ᵗ] Here n means the nth week in the second year of that season. For example, for the 2019−2020 season, we expressed T_E by the nth week in 2020.

[#] Since there is no data for Taiwan on Flunet, we used the data of outpatient visits for influenza-like illness from the Taiwan National Infectious Disease Statistics System (https://nidss.cdc.gov.tw/en/Home/Index).

[*] In the 2019−2020 season, there was no processed specimen listed on Flunet since week 4 and week 6 in Korea and Japan, respectively.

[ε] In Denmark, the 2011−2012 season was excluded because there was no apparent influenza outbreak that year.

difference between T_S and T_E and standardized the duration in the 2019−2020 season by the average and standard deviation of the duration from the previous 9 seasons.

Viral molecular sequences

We analyzed the influenza A surface glycoprotein hemagglutinin protein segment of human influenza A H1N1 and H3N2 sequences available in the GISAID EpiFlu database. The collection dates of the sequences ranged from January 2016 to December 2020. We used BEAST (Bayesian evolutionary analysis by sampling trees) (Drummond and Rambaut, 2007) to estimate the effective population size (N_e) from 2016 to 2020 for each location. The numbers of sequences analyzed are indicated in Table S1. For each location and each influenza type, we calculated the within-location genetic diversity, Watterson's θ (Watterson, 1975), for the first halves of 2019 and 2020.

Results and discussion

To examine the indirect impact of COVID-19 on influenza dynamics, we compared the 2019−2020 influenza season with the previous 9 seasons in 25 locations across 4 continents (Table 1). We found that for locations in Asia, the 2019−2020 influenza season ended earlier, and all regions except Israel experienced a shorter flu season than in previous years. In the Americas, Europe and Africa, in 12 of 15 locations, the 2019−2020 flu season ended earlier than the flu seasons of previous years; the rest remained similar. For locations where influenza seasons usually end later in the year, such as Brazil, Guatemala and South Africa, the difference in duration between the 2019−2020 season and previous seasons was larger than for other locations. The flu season in the southern hemisphere, which usually starts much later in the year, disappeared in several countries in 2020 (; The Economist Newspaper, 2020).

In addition to case count data, we analyzed molecular data to evidence our findings. We found that genetic diversity (θ) decreased from 2019 to 2020 for 12 of 14 locations analyzed for H1N1 and 9 of 12 locations for H3N2 (Table S2). On the other hand, we calculated between-region genetic diversity for each pair of regions once in 2019 and 2020; in 11 of 14 locations for H1N1 and 9 of 13 locations for H3N2 between-region genetic diversity increased from 2019 to 2020 in at least 50% of pairs for which the location was involved, reflecting reduced travel between regions in 2020 (Table S3).

While θ measures overall viral diversity, the effective population size (N_e) quantifies genetic diversity over time (Frost and Volz, 2010). We estimated N_e for H1N1 in 13 countries and found a decrease in N_e in 10 countries, including Italy and Taiwan (Figure 1; Figure S1). For H3N2, we analyzed 7 countries and found a decrease in N_e in South Africa, the United Arab Emirates and Taiwan in 2020 (Figure 1; Figure S2). This genetic diversity analysis confirms that the observed reduction in influenza case numbers was not only due to under-reporting during the COVID-19 pandemic; this observed reduction is in line with other studies carried out without genetic analysis (Feng et al., 2021; Akhtar et al., 2021; Stojanovic et al., 2021, Olsen et al., 2020).

We noticed that Asian countries tended to act earlier than countries in other continents on personal measures and government policies against the spread of COVID-19, especially in wearing masks (Table S4). We observed an earlier end of the flu season in Asia than in Europe and America, which could be explained by the earlier implementation of non-pharmaceutical interventions.

While using publicly available influenza genetic data restricted our analysis to countries with sufficient data and may suffer from sampling bias, we were able to identify a general trend
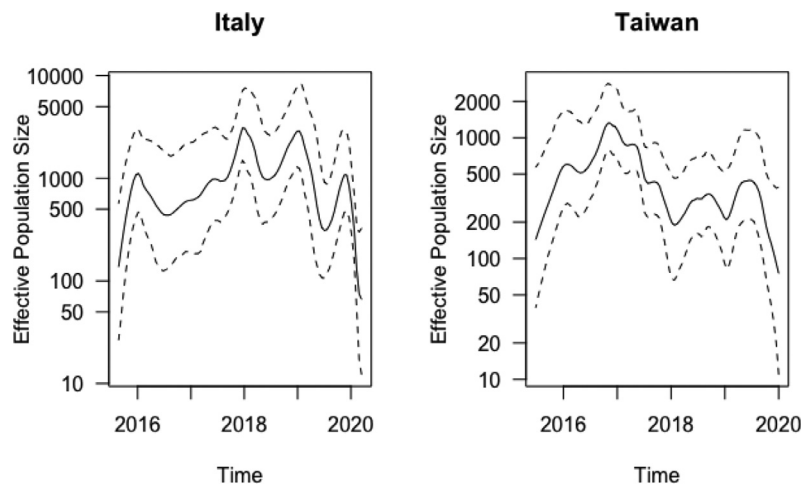
Italy / Taiwan

Figure 1. Effective population size trajectory of H1N1 in Italy and H3N2 in Taiwan

(with exceptions) with samples across multiple continents. Our combined analyses of case counts, genetic data and behavioral data support the conclusion that COVID-19 preventive measures led to the reduction of influenza transmission in several countries in 2020.

Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Ethical Approval

Approval was not required.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijid.2021.12.323.

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