COVID-19 secondary attack rate and risk factors in household contacts in Castellon (Spain): Preliminary report

Alberto Arnedo-Pena[1,5,7], Susana Sabater-Vidal[2], Noemí Meseguer-Ferrer[1], Mª Rosario Pac-Sa[1], Pilar Mañes-Flor[3], Juan Carlos Gascó-Laborda[1], Rosa Mª Larrea[4], Mª Dolores Tirado-Balaguer[2], Mª Ángeles Romeu-García[1], María Gil-Fortuño[2], Lourdes Safont-Adsuara[1], Aurora Blasco[2], Bárbara Gomila-Sar[2], Mª Rosario Moreno-Muñoz[2], Juan B Bellido-Blasco[1,5,6]

[1]Sección de Epidemiología. Centro de Salud Pública de Castellón. Generalitat Valenciana. [2]Laboratorio de Microbiología. Hospital General Universitario de Castellón. Generalitat Valenciana. [3]Servicio de Medicina Preventiva. Hospital Universitario de La Plana. Villarreal. Castellón. [4]Servicio de Medicina Preventiva. Hospital General Universitario de Castelló. [5]CIBER-ESP grupo 41. [6]Facultad de Ciencias de la Salud. Universitat Jaume I (UJI). Castelló. [7]Departamento de Ciencias de la Salud. Universidad Pública de Navarra.

Summary

Introduction: In a high proportion, around 60%-70% of COVID-19 patients are not admitted to hospitals and remains at home. Know the secondary attack rate (SAR) of viral transmission in their household contacts is a priority in the disease control.

Methods: Notified COVID-19 cases in the Epidemiology Division of Public Health Center from February 26 to April 8, 2020, with confirmation of the Microbiology Laboratory of Hospital General of Castelló were follow-up. Secondary attack rate was estimated from cases in household contacts of index cases and their risk factors by the inverse probability weighting.

Results: 347 index cases were studied on 542 notified cases (64.0%), excluding cases associated with outbreaks and nursing homes. Eighty-three secondary cases from 745 household contacts, secondary attack rate 11.1% (95% CI 9.0-13.6), and 205 household contacts with acute infection symptoms without microbiologic confirmed, SAR and 27.5% (95% CI 24.3-30.9), were found. All together (83 plus 205) they achieve a secondary attack rate of 38.7% (95% CI 95% 35.1-42.3). Risk factors were age of secondary case, households with two members, and index case with higher age.

Conclusions: The secondary attack rate found is high. It is necessary to adopt rigorous measures to cut the transmission chain in this area of close contact.

Key words:
COVID-19. Secondary attack rate. Risk factors. Household contacts.

Tasa de ataque secundaria y factores de riesgo en convivientes de pacientes por COVID-19 en Castellón (España). Resultados preliminares

Resumen

Introducción: Los pacientes de COVID-19 no ingresados en los hospitales y atendidos en sus domicilios alcanzan un 60%-70%. Conocer la tasa de ataque secundaria (TAS) de transmisión viral a los convivientes domiciliarios es prioritario para el control de la enfermedad.

Métodos: Se siguieron los casos de COVID-19 notificados a la Unidad de Epidemiología del Centro de Salud Pública de Castellón desde el 26 de febrero al 8 de abril de 2020 y confirmados por el Laboratorio de Microbiología del Hospital General de Castelló. TAS se estimó partiendo de los casos ocurridos entre los convivientes domiciliarios de los casos índices y sus factores de riesgo mediante la probabilidad inversa ponderada.

Resultados: Se estudiaron 347 casos índices de los 542 casos notificados (64,0%), excluyendo los asociados a brotes y residencias de ancianos. Se obtuvieron 745 convivientes con 83 casos secundarios, TAS fue del 11,1% (95% CI 9,0-13,6). Hubo 205 convivientes con síntomas de infección aguda sin confirmación microbiológica, TAS 27,5% (95% CI 24,3-30,9). Todos juntos (83 más 205) alcanzan una TAS de 38.7% (95% CI 95% 35.1-42.3). El riesgo fue mayor con la edad y en domicilios con dos convivientes, incrementándose con la edad de los casos índices.

Conclusiones: La TAS encontrada es elevada. Es necesario adoptar medidas rigurosas para cortar la cadena de transmisión en este ámbito de convivencia estrecha.

Palabras clave:
COVID-19. Tasa ataque secundaria. Factores riesgo. Convivientes.

Correspondencia: Juan B. Bellido-Blasco
E-mail: bellido_jua@gva.es

Introduction

COVID-19 pandemic is significant an enormous challenger to the world population and their extension results unstopped[1-2]. In China, cases in familial households represented 64% of cases in 1183 clusters[3]. Clinical forms of this disease comprise from mild to very severe symptoms, and an important number of patients remain at household if severity may be controlled. Hospitalization rates were estimated at 20.7%-31.4% in United States, and 23% in Iran[4-5]. In our area this figure is 42% of reported cases (unpublished data). Then 60%-70% COVID-19 patients remain at home. In these circumstances, disease transmission among household contacts may be a serious risk. And therefore the quantification of COVID-19 infection risk as the secondary attack rate is a priority to better understand epidemiologic aspects of this new disease and the accuracy of measures to prevent viral transmission[6].

Objective: the aim of this study is the estimation of the secondary attack rate of household contacts of COVID-19 index cases and their transmission risk factors in two health departments in the province of Castelló (Spain), with a population of 480,000 inhabitants.

Material and methods

As a part of epidemiological surveillance and control of COVID-19 pandemic in the health departments of Castelló and Vila-real-la Plana in the Valencia Community (Spain), the Epidemiology Division of the Public Health Center of Castelló has implemented the study of closed contacts of COVID-19 cases from the first day of the onset of the outbreak. Then a retrospective cohort study design was carried out with these closed contacts as the cohort of interest.

All COVID-19 cases must be notified to Epidemiology Division from physicians that diagnose cases and microbiologic confirmations are made in the Microbiology Laboratory of the *Hospital General Universitario de Castellón* in the public sector. In addition, other microbiology laboratories in the private sector could detect COVID-19 cases, but all positive cases must be communicated to Epidemiologic Division.

When a COVID-19 case was notified an epidemiological survey was implemented by the Epidemiologic Division to know circumstances of disease transmission and their closed contacts. After, a follow-up of the cases was carried out by telephone interview to know their evolution and the conditions of closed contacts. Information on demographic, health situation with disease`s symptoms and risk factors was obtained.

From February 26 to April 8, 2020, the first two months of COVID-19 pandemic in Castelló, 781 cases were notified and confirmed by the Epidemiologic Division. Of these, 239 were associated with outbreaks and nursing homes and were excluded from this study. With the remaining 542 the secondary attack rate has been calculated. Only household contacts were included in this preliminary report. The inclusion criteria were: closed contacts living in the same household of the index case and no other sources of transmission apart from the index case could be found. As exclusion criteria, COVID-19 cases of community outbreaks and from institutions as nursing homes. Closed contacts from work, social events, relatives live in other household were excluded and index cases live alone. Telephone interviews took place from February 27 to May 10.

Laboratory technique

Detection of SARS-CoV-2 RNA from upper or lower respiratory samples collected in viral transport medium[7], was performed by reverse transcription polymerase chain reaction (RT-PCR). The various Real Time PCR assays used in our/the laboratory amplify and detect different regions of the SARS-CoV-2 genome: nucleocapsid (N), envelope (E), RNA-dependent RNA polymerase (RdRp), and regions in the first open reading frame (ORF1ab)[8]. Depending on the availability of the different detection kits, we used: Roche Lightmix Modular SARS-CoV-2 (Roche-TIB MOLBIOL), VIASURE SARS-CoV-2 Real Time PCR Detection Kit (CerTest BIOTEC) and Abbott RealTime SARS-CoV-2 (Abbott).

Statistical methods

Secondary attack rate was defined as the proportion of secondary cases from the total of contacts that live in the household of index case. Acute infection symptoms included fever, cough, headache, sore throat, weakness, loss of smell and taste, vomits and diarrhea, symptoms associated with COVID-19 disease. Poisson regression was used in the univariate analysis. Confidence interval (CI) of 95% was calculated. Secondary case was dependent variable and potential risk factors were independent variables, including age, gender, number of household members, and residence (urban, semi-urban, and rural). For the index case: age, gender, hospitalization, suffer pneumonia, cough and health profession (physicians, nurses, auxiliary nurses and assistants) were studied. Directed Acyclic Graphs (DAG) program[9] was used to study relationships among secondary cases and independent variables with a number of household contacts as exposure and secondary case as outcome after a review of secondary cases of influenza and SARS epidemics[10-12]. Inverse probability weighting to adjust for confounding factors[13] with Stata® version 14 was used in the multivariate statistical analysis.

Results

In total, 347 index cases were included that represents 64.0 % of 542 cases notified. Eighty-three secondary cases with laboratory confirmation were found in 745 household contacts that represent a secondary attack rate of 11.1% (95% CI 9.0-13.6). Apart from confirmed secondary cases, acute infection symptoms were found in 205 of household contacts, 27.5% (95% CI 24.3-30.9); they could be secondary 'only symptoms based' cases. All together (83 plus 205) they achieve a secondary attack rate of 38.7% (95% CI 95% 35.1-42.3).

In 268 households no cases occurred (77.2%), in 75 households one case (21.6%), and in 4 households two cases (1.2 %).

An estimation of the incubation period may be calculated from the difference of onset day between index cases and secondary cases. The median of this serial period was 4 days (range 1-23) with mean 5.9±4.8 days.

Characteristics of index cases and household contacts are shown in Table 1. Household contacts were younger that index case with similar presence of females. Residence distribution was similar in both groups. Hospitalization, pneumonia, and lethality were higher in secondary cases than index cases.

In the univariate analysis (Table 2) several risk factors of secondary cases were found: patient`s age and two household members were important risks and from the index case, hospitalization, pneumonia, and cough. The health profession of index case was a protective factor. Incidence of acute infection symptoms by age groups (Table 3) a percent of affectation between 27.0% (0-24 age group) and 35.3% (45-64 age group) without significant difference.

Table 1. Characteristics of COVID-19 index cases and their household contacts, in Castellón (Spain), Feb 26th-April 8th, 2020.

Variables	Household contacts N=745 (%)	Index cases N=347 (%)
Age (mean±SD)	38.7±24.2[I]	54.8±16.5
Gender		
Female	409 (54.9)	182 (52.5)
Male	336 (45.1)	165 (47.0)
Nº of household members		
2	132 (17.7)	66 (19.0)
3	189 (25.4)	63 (18.2)
4 or more	424(56.9)	218 (62.8)
Residence		
≥50,000 inhabitants	293 (39.3)	134 (38.6)
49,000-5,000 inhabitants	416 (55.8)	194 (55.9)
<5,000 inhabitants	36 (4.8)	19 (5.5)
Health professions	-	106 (31.1)[II]
Secondary cases		
Laboratory confirmed	83 (11.1)	-
Only symptoms based	205 (27.5)[III]	-
All together	228 (38.7)	
Cases		
Hospitalization	48 (57.8%)[IV]	167 (48.1%)
Pneumonia	40 (48.2)[IV]	147 (42.4%)
Fatalities	8 (9.6%)[IV]	15 (4.3%)

[I]Missing age of 8 household contacts. [II]Missing health professions 6 index case. [III]Missing symptoms of 7 household contacts. [IV]Percent of 83 secondary confirmed cases.

By the DAGs approach potential risk factors were studied (Figure 1) adjusted by different covariates with inverse probability weighting (Table 4). High age of secondary cases, two household members, and higher age of index case had more elevated risk.

Figure 1. Directed Acyclic Graphs (DAG) of household contacts index case (exposure) effect on secondary COVID-19 cases (outcome). Ancestors of exposure and outcome (red color). Based on DAGitty version 3.0.

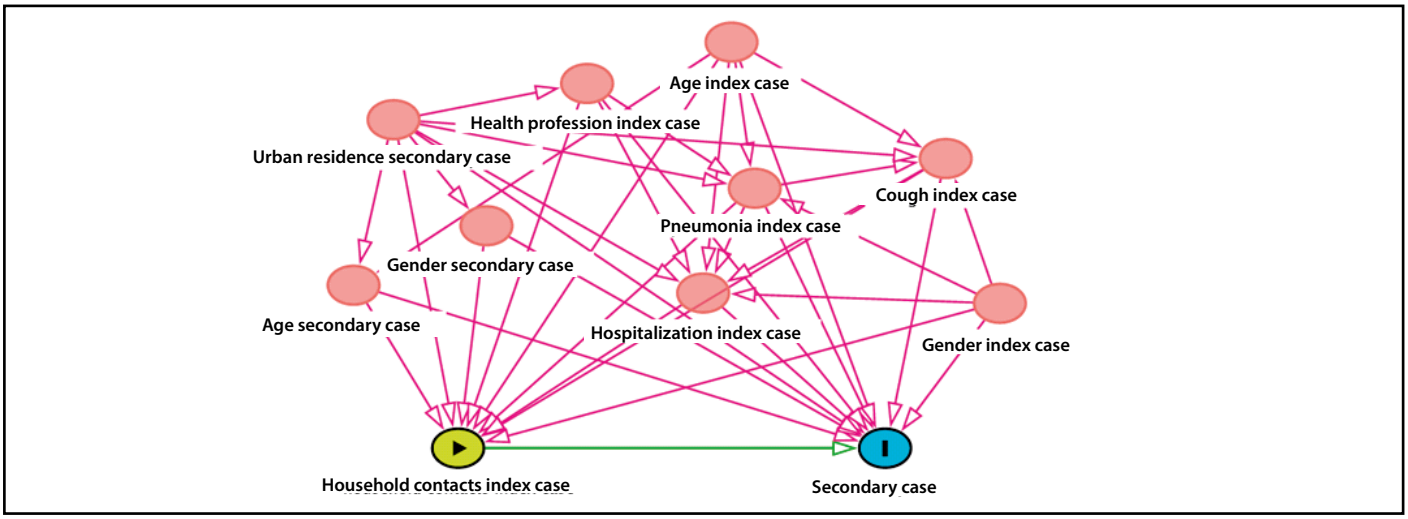

Table 2. Risk factors of confirmed secondary COVID-19 cases, in Castellón (Spain), Feb 26th-April 8th, 2020. Univariate Poisson regression.

Variable	Cases n=83	No cases n=662	Total	RR	95% CI	P value
Age ±SD[I]	60.7±17.5	35.9±23.5		1.04	1.03-1.05	<0.001
Ages groups (years)[I]						
0-24	1	272	273	1.00		
25-44	14	112	126	30.3	4.00-230.6	0.001
45-64	28	187	215	35.5	4.8-261.3	<0.001
64-74	19	46	65	79.8	10.7-596.4	<0.001
75 and more	21	37	58	98.8	13.3-734.8	<0.001
Gender						
Male	38	298	336	1.03	0.67-1.58	0.901
Female	45	364	409	1.00		
Nº of household members						<0.001
2	40	92	132	4.76	2.93-7.25	<0.001
3	16	173	189	1.32	0.72-2.47	0.367
4 or more	27	397	424	1.00		
Residence						
≥50,000 inhabitants	32	261	293	0.99	0.63-1.56	0.957
49,000-5,000 inhabitants	45	371	416	1.53	0.64-3.65	0.342
<5,000 inhabitants	6	30	36	1.00	0.49-3.25	0.984
Index case						
Age ±SD	-	-		1.03	1.02-1.05	<0.001
Gender						
Male	36	308	344	0.89	0.56-1.38	0.439
Female	47	354	401	1.00		
Cough						
Yes	71	480	551[II]	1.85	1.00-3.41	0.049
No	12	160	172			
Pneumonia						
Yes	45	252	297	1.79	1.16-2.7	0.008
No	38	416	448	1.00		
Hospitalization						
Yes	56	285	341	2.46	1.55-3.85	<0.001
No	27	377	404	1.00		
Health profession						
Yes	16	218	234[III]	0.45	0.27-0.81	0.007
No	67	424	491	1.00		

[I]Missing age 8 household contacts. [II]Missing cough 7 index cases. [III]Missing health professions 6 index cases.

Hospitalization, pneumonia, and the cough of index cases lost their relationship with the disease. Health profession remains associated with low risk of transmission at home.

Discussion

The results of this study suggest that household contacts of COVID-19 index cases have a high risk to suffer the disease, considering that only laboratory confirmed cases are included. When acute infection symptoms were contemplated, a higher increase of attack rate was observed, increasing the risk fourfold.

The secondary attack rate founded in this study is in line with recent studies of household contacts of COVID-19 patients, between 7.5% and 30%[14-19]. In some of these studies COVID-19 tests (RT-PCR) for all household contacts were performed, studies size ranged from 15 to 686 participants in several countries. When tests were performed secondary attack rate was more elevated in China, 30%[14] and France 73%[15], but not in two studies in the United States[16] and another in China[17], with attack rates of 10.5% and 16.3%, respectively. In China, Bi and co-authors[18] estimated a secondary attack rate of 11.2% and in South Korea 7.6%[19] without the tests performed for all household contacts. In household clusters the transmission rate was 20.5%[20], in close contacts of COVID-19 cases 11.7%[21], and transmission from a family member 31% of cases[22]. In our study, household transmission rate is on line with some these papers, and it may suppose an important source of new cases.

Index case appeared more contagious in the first 5 days from the started symptoms[23]. A comparison in the 2009 pandemic influenza, the secondary attack rates in household contacts rise from 4% to 37%, suggesting differences in study designs[24].

Table 3. Incidence of acute infection symptoms by age groups distribution of household contacts excluding secondary cases, in Castellón (Spain), Feb 26th-April 8th, 2020. Relative risk (RR) and confidence intervals (CI) by univariate Poisson regression.

Ages groups (years)[I]	Households contacts with symptoms[II]	Total	%	RR	96% CI	P value
0-24	73	370	27.0	1.00		
25-44	36	111	32.4	1.20	0.80-1.79	0.372
45-64	65	184	35.3	1.31	0.94-1.83	0.117
64-74	16	46	34.8	1.29	0.78-2.21	0.361
75 and more	10	36	27.8	1.02	0.53-1.99	0.936
TOTAL	200	647				

[I]Missing age of 8 household contacts. [II]Missing symptoms 7 household contacts.

Table 4. Adjusted secondary attack rates and relative risk (RR) of COVID-19 secondary case in household contacts using inverse probability weighting.

Variable	Adjusted[I-VII] secondary attack rate (%)	Adjusted RR	95% Confidence interval	P value
Age groups (years)[I]				
0-24	0.3	1.00		
25-44	10.6	36.25	4.81-273.23	0.000
45-64	12.7	43.45	5.97-316.30	0.000
65-74	25.6	87.47	11.81-647.69	0.000
75 and more	16.7	56.82	7.52-429.37	0.000
Gender[II]				
Male	11.3	1.03	0.69-1.55	0.884
Female	11.0	1.00		
Nº of household members[III]				
2	19.6	2.05	1.21-3.49	0.008
3	7.0	0.79	0.43-1.46	0.450
4	9.5	1.00		
Index case: Cough[IV]				
Yes	13.0	1.80	0.94-3.45	0.074
No	7.2			
Pneumonia[V]				
Yes	11.5	1.03	0.66-1.61	0.901
No	11.1			
Hospitalization[VI]				
Yes	13.6	1.10	0.65-1.88	0.714
No	12.2			
Health profession[VII]				
Yes	6.5	0.48	0.28-0.82	0.008
No	13.5			

[I]Adjusted for index case age and residence. [II]Adjusted for residence. [III] Adjusted for household contacts (age groups and gender), residence and index case (age, gender, hospitalization, pneumonia, cough, and health profession). [IV]Adjusted for residence and index case (age, gender, pneumonia). [V]Adjusted for index case (age and gender, health profession) and residence. [VI]Adjusted for index case (age, gender, cough), health profession and residence; pneumonia was removed from the model due collinearity. [VII]Adjusted for residence.

Transmission risk factors were age, presence of only two household members, and index case age. Bi and co-authors[18] have indicated that age affectation in household contacts has little difference, suggesting that children may have an important role in the transmission. At this moment, and here, transmissions are associated with adults, but disease symptoms in children were found and in general few COVID-19 tests performed. This point merits attention and surveillance in the next development of the

pandemic. In our study acute infection symptoms by age groups were similar with affectation of the age group 0-24 years. A high risk of secondary cases has been indicated in spouses of index cases[17]. Pneumonia, hospitalization, and the cough of index cases are markers of disease severity associated with secondary cases in the univariate analysis, but with adjusted for different variables, the associations were not maintained. Health professions as a protective factor may be related to the low severity of the disease in more young health professional than the general population, the use of screening COVID-19 tests in health professions, and more compliance of preventive measures.

Convenience sampling was used for this study with a high percentage of the first 781 COVID-19 cases notified in Castelló and Vila-real health departments. Secondary cases were obtained from laboratory confirmation, hospitalization, medical records, and interviews with patients and household contacts. The estimation of risk factors was adjusted for different variables that permit more precision.

Limitations of this study include the following: First we did not carry out a screening of COVID-19 test of household members in order to find secondary cases, considering the existence of asymptomatic and mild clinical cases[25]. Second, more risk factors may play a role in viral transmission like environmental condition of homes. Third, higher severity of secondary cases may be due some selection bias, because it is more difficult following of hospitalized index cases. Fourth, unknown factors of transmission may be present in the household contacts of this new disease.

Although it was not a main objective of this study, we have applied the formula given by T. Olbadia *et al*[26] to estimate the transmission parameter Ro, a context with 99% of susceptibles. The result was R0 = 1.07, taking the confirmed rate (11.1%) and R0 = 1.27 taking the global rate, that is, confirmed and symptomatic cases (38.7%).

The findings of this study suggest a high secondary attack rate in household contacts and emphasize the importance of preventing the transmission in homes, considering the high contagiousness of COVID-19[27] and a potential fecal-oral transmission[28-29]. In this regard, COVID-19 screening tests for all household contacts appeared very convenient considering that it is a high risk population[30], who took care of COVID-19 patients and some have suffered acute infections without microbiology confirmation. And still more, the uncertainty can add mental distress to the contacts. To know their COVID-19 situation will be useful for their performer. In addition, a better understanding of the epidemiology of this disease may be achieved.

In conclusion, the secondary attack rate in household contacts is elevated with old age and householders with two members as risk factors. To avoid viral transmission strength measures are needed.

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References

1. Pan A, Liu L, Wang C, Guo H, Hao X, Wang Q, *et al*. Association of public health interventions with the epidemiology of the COVID-19 outbreak in Wuhan, China. *JAMA*. 2020:e206130.
2. Khachfe HH, Chahrour M, Sammouri J, Salhab H, Makki BE, Fares M. An epidemiological study on COVID-19: A rapidly spreading disease. *Cureus*. 2020;12:e7313.
3. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: Summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. *JAMA* 2020; doi: 10.1001/jama.2020.2648.
4. CDC COVID-19 Response Team. Severe outcomes among patients with coronavirus disease 2019 (COVID-19) - United States, February 12-March 16, 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69:343-346.
5. Nikpouraghdam M, Jalali Farahani A, Alishiri G, Heydari S, Ebrahimnia M, Samadinia H, *et al*. Epidemiological characteristics of coronavirus disease 2019 (COVID-19) patients in IRAN: A single center study. *J Clin Virol*. 2020;127:104378.
6. Liu Y, Eggo RM, Kucharski AJ. Secondary attack rate and superspreading events for SARS-CoV-2. *Lancet*. 2020;395(10227):e47.
7. https://www.cdc.gov/coronavirus/2019-nCoV/guidelines-clinical-specimens-html (Accessed on May 11, 2020)
8. https://www.who.int/publications-detail/laboratory-testing-for-2019-novel-coronavirus-in-suspected-human-cases-20200117 (Accessed on May 11, 2020)
9. Textor J, van der Zander B, Gilthorpe MS, Liskiewicz M, Ellison GT. Robust causal inference using directed acyclic graphs: the R package 'dagitty'. *Int J Epidemiol*. 2016;45:1887-1894.
10. Cauchemez S, Donnelly CA, Reed C, Ghani AC, Fraser C, Kent CK, *et al*. Household transmission of 2009 pandemic influenza A (H1N1) virus in the United States. *N Engl J Med*. 2009;361:2619-27.
11. Vargas-Leguas H, Caylà JA, Ballester I, Burgui R, Morteruel M, Horna O, *et al*. Factores asociados en la transmisión a los convivientes de gripe (H1N1) 2009. *Rev Esp Salud Publica*. 2011;85:57-62.
12. Casado I, Martínez-Baz I, Burgui R, Irisarri F, Arriazu M, Elía F, *et al*. Primary Health Care Sentinel Network of Navarra. Household transmission of influenza A(H1N1)pdm09 in the pandemic and post-pandemic seasons. *PLoS One*. 2014;9:e108485.
13. Robins JM, Hernán MA, Brumback B. Marginal structural models and causal inference in epidemiology. *Epidemiology*. 2000;11:550-60.
14. Wang Z, Ma W, Zheng X, Wu G, Zhang R. Household transmission of SARS- CoV-2. *J Infect*. 2020:S0163-4453(20)30169-9.

15. Danis K, Epaulard O, Bénet T, Gaymard A, Campoy S, Bothelo-Nevers E, *et al.* Cluster of coronavirus disease 2019 (Covid-19) in the French Alps, 2020. *Clin Infect Dis.* 2020:ciaa424.

16. Burke RM, Midgley CM, Dratch A, Fenstersheib M, Haupt T, Holshue M, *et al.* Active monitoring of persons exposed to patients with confirmed COVID-19—United States, January–February 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69:245–6.

17. Li W, Zhang B, Lu J, Liu S, Chang Z, Cao P, *et al.* The characteristics of household transmission of COVID-19. *Clin Infect Dis.* 2020:ciaa450.

18. Bi Q, Wu Y, Mei S, Ye C, Zou X, Zhang Z, *et al*. Epidemiology and transmission of COVID-19 in 391 cases and 1286 of their close contacts in Shenzhen, China: a retrospective cohort study. *Lancet Infect Dis.* 2020:S1473-3099(20)30287-5.

19. Dong XC, Li JM, Bai JY, Liu ZQ, Zhou PH, Gao L, *et al*. Epidemiological characteristics of confirmed COVID-19 cases in Tianjin. *Zhonghua Liu Xing Bing Xue Za Zhi.* 2020;41:638-642.

20. COVID-19 National Emergency Response Center, Epidemiology and Case Management Team, Korea Centers for Disease Control and Prevention. Coronavirus Disease-19: Summary of 2,370 contact investigations of the first 30 cases in the Republic of Korea. *Osong Public Health Res Perspect.* 2020;11:81-84.

21. Kwok KO, Wong VWY, Wei WI, Wong SYS, Tang JW. Epidemiological characteristics of the first 53 laboratory-confirmed cases of COVID-19 epidemic in Hong Kong, 13 February 2020. *Euro Surveill.* 2020;25:2000155.

22. Hua J, Chen R, Zhao L, Wu X, Guo Q, He C, *et al*. Epidemiological features and medical care-seeking process of patients with COVID-19 in Wuhan, China. *ERJ Open Res.* 2020;6:00142-2020.

23. Cheng HY, Jian SW, Liu DP, Ng TC, Huang WT, Lin HH. Taiwan COVID-19 Outbreak Investigation Team. Contact tracing assessment of COVID-19 transmission dynamics in Taiwan and risk at different exposure periods before and after symptom onset. *JAMA Intern Med.* 2020. doi: 10.1001/jamainternmed.2020.2020.

24. Lau LL, Nishiura H, Kelly H, Ip DK, Leung GM, Cowling BJ. Household transmission of 2009 pandemic influenza A (H1N1): a systematic review and meta-analysis. *Epidemiology.* 2012;23:531-42.

25. Mizumoto K, Kagaya K, Zarebski A, Chowell G. Estimating the asymptomatic proportion of coronavirus disease 2019 (COVID-19) cases on board the Diamond Princess cruise ship, Yokohama, Japan, 2020. *Euro Surveill.* 2020;25:2000180.

26. Obadia T, Haneef R. & Boëlle P. The R0 package: a toolbox to estimate reproduction numbers for epidemic outbreaks. *BMC Med Inform Decis Mak*. 2012;12:147. https://doi.org/10.1186/1472-6947-12-147.

27. Cheng HY, Jian SW, Liu DP, Ng TC, Huang WT, Lin HH, *et al.* Contact tracing assessment of COVID-19 transmission dynamics in Taiwan and risk at different exposure periods before and after symptom onset. *JAMA Intern Med*. 2020:e202020.

28. Jin X, Lian JS, Hu JH, Gao J, Zheng L, Zhang YM, *et al.* Epidemiological, clinical and virological characteristics of 74 cases of coronavirus-infected disease 2019 (COVID-19) with gastrointestinal symptoms. *Gut*. 2020;69:1002-1009.

29. Ding S, Liang TJ. Is SARS-CoV-2 also an enteric pathogen with potential fecal-oral transmission: A COVID-19 virological and clinical review. *Gastroenterology.* 2020:S0016-5085(20)30571-0.

30. Hu Z, Song C, Xu C, Jin G, Chen Y, Xu X, *et al.* Clinical characteristics of 24 asymptomatic infections with COVID-19 screened among close contacts in Nanjing, China. *Sci China Life Sci.* 2020;63:706-711.