Title
SARS-CoV-2: An Empirical Investigation of Rose's Population-based Logic

Journal
Epidemiology, 32(6)

ISSN
1044-3983

Authors
Bruckner, Tim
Das, Abhery
Singh, Parvati
et al.

Publication Date
2021-11-01

DOI
10.1097/ede.0000000000001405

Peer reviewed

SARS-CoV-2: An Empirical Investigation of Rose's Population-based Logic

Tim Bruckner,[a,b] *Abhery Das,*[a] *Parvati Singh,*[c] *and Bernadette Boden-Albala*[a]

Background: Geoffrey Rose's paper "Sick Individuals, Sick Populations" highlights the counterintuitive finding that the largest share of morbidity arises from populations engaging in low- to moderate-risk behavior. Scholars refer to this finding as the prevention paradox. We examine whether this logic applies to SARS-CoV-2 infected persons considered low to moderate risk.

Methods: We conducted a population-representative survey and sero-surveillance study for SARS-CoV-2 among adults in Orange County, California. Participants answered questions about health behaviors and provided a finger-pin-prick sample from 10 July to 16 August 2020.

Results: Of the 2979 adults, those reporting low- and moderate-risk behavior accounted for between 78% and 92% of SARS-CoV-2 infections. Asymptomatic individuals, as well as persons with low and moderate scores for self-reported likelihood of having had SARS-CoV-2, accounted for the majority of infections.

Conclusions: Our findings support Rose's logic, which encourages public health measures among persons who self-identify as unlikely to have SARS-CoV-2. See video abstract at, http://links.lww.com/EDE/B860.

Keywords: SARS-CoV-2; COVID-19; pandemic; asymptomatic; risk behaviors; low risk

(*Epidemiology* 2021;32: 807–810)

California reported the first case of local spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causing COVID-19 disease in the United States and, over the following 8 months, recorded >904,100 cases and >17,400 deaths from this disease.[1] Public health measures to reduce SARS-CoV-2 involve adherence to physical distancing, use of face masks, ventilation, and hand hygiene. These measures appear widely endorsed in high-risk situations. Public support for these measures, however, diminishes without public mandates in lower-risk situations.[2,3]

In his seminal paper, "Sick Individuals, Sick Populations," Geoffrey Rose highlighted the phenomenon of the prevention paradox in which, for many diseases, the largest share of morbidity arises from populations engaging in low- to moderate-risk behavior.[4] This circumstance holds for two reasons. First, epidemiologists and clinicians have developed only a limited capacity to screen people into high risk in any meaningful way. Second, despite the fact that the greatest likelihood of infection and death concentrates among high-risk groups, an overwhelming share of the population resides in the low- to moderate-risk behavior categories.[4] Rose and other epidemiologists have extended this logic to the design of interventions.[5,6] Policy scholars, moreover, have recently applied Rose's argument to SARS-CoV-2 to further recommend continued vigilance to "population-based" public health strategies that focus on lowering the mean level of risk behaviors.[7]

Despite the intuitive appeal of Rose's logic to SARS-CoV-2, we know of no empirical evidence using a representative population that quantifies whether persons who do not engage in high-risk behavior—and those who self-identify as low-risk—account for the majority of SARS-CoV-2 infections. This gap in the evidence base arises because few regions have enacted routine population-based surveillance of SARS-CoV-2 and coupled this information with surveys on health behaviors. Instead, most regions test for individual clinical diagnostic purposes; other institutions focus on a small targeted subgroup to assist with planning (e.g., surveillance of healthcare workers by hospitals).[8,9] SARS-CoV-2 infection, however, may cause minimal or no symptoms.[10,11] Since persons without (or with minor) symptoms may not seek care, clinic-based estimates may considerably undercount the true incidence of SARS-CoV-2 infections—and especially among persons considered low to moderate risk.[12]

We address these limitations and recruit a large representative sample from Orange County (OC), California, to assess health behaviors, symptoms, and history of SARS-CoV-2 infection (via antibodies from a blood test). OC includes a large, ethnically diverse (34.0% Hispanic, 21.7%

Submitted January 19, 2021; accepted July 19, 2021
From the [a]Program in Public Health, University of California, Irvine, CA; [b]Center for Population, Inequality, and Policy, University of California, Irvine, CA; and [c]Division of Epidemiology, College of Public Health, The Ohio State University, Columbus, OH.
This work was supported by Orange County Healthcare Agency.
The authors declare no conflicts of interest.
The corresponding author can provide de-identified and aggregated data, as well as program code, upon request.
SDC Supplemental digital content is available through direct URL citations in the HTML and PDF versions of this article (www.epidem.com).
Correspondence: Tim Bruckner, Program in Public Health, University of California, 653 E. Peltason Drive, Irvine, CA 92697. E-mail: tim.bruckner@uci.edu.

ISSN: 1044-3983/21/326-807
DOI: 10.1097/EDE.0000000000001405

Asian) metropolitan region and is the sixth most populous county in the United States.[13] We intend for our study to quantify the share of SARS-CoV-2 infected persons that arise from populations considered low to moderate risk.

METHODS

Recruitment

This study represents a joint effort between the University of California, Irvine, and the Orange County Health Care Agency. We received human subjects approval from the University of California, Irvine, Institutional Review Board (HS no. 2020-5952) and obtained informed consent from all study participants. Full details regarding the recruitment and testing procedures appear elsewhere.[14]

We focused on adults 18 years or older residing in OC on 1 July 2020. We used a proprietary database reflecting the age, income, and racial-ethnic diversity of OC and maintained by SoapBoxSample, an LRW Group Company, to recruit participants. Using this database, we invited (via email or telephone) one resident per household to participate in a study about their opinions of COVID-19 without initial mention of SARS-CoV-2 antibody testing. Participants received a $10 gift card as compensation for completing a survey regarding socio-demographics, daily activities, health behaviors, any known previous infection with SARS-CoV-2, and history of SARS-CoV-2 symptoms in the last few months. To minimize selection bias and skewing of the sample to people with suspected SARS-CoV-2 infection, subjects completed the survey before being offered an antibody test. We aimed to reach specific quotas for enrollment for age, race/ethnicity, income, and gender subgroups, using the US Census ACS 2018 estimates as benchmarks.

Variables and Analysis

To gauge behavior related to SARS-CoV-2 prevention, we asked respondents to rank whether each of the following statements described their behavior for the past week: "I avoided leaving the home," "I kept a distance of at least 6 feet from others when outside my home," and "I washed my hands more frequently than the month before." Persons could rank whether their behavior over the past week cohered with each of these statements by scoring on a scale of 1 to 10, in which 1 indicates "none of the time" and 10 indicates "all of the time." We grouped individuals answering 1–3 high risk, 4–7 moderate risk, and 8–10 low risk. We did not ask questions about indoor dining at bars and restaurants as well as indoor gym activity because California law prohibited these activities at the time of the survey.

We then asked participants about symptoms and likelihood of having COVID-19. With regard to each symptom (i.e., fever [temperature over 100.4°], chills, cough, wheezing or shortness of breath, chest pain, runny nose, sore throat, loss of sense of or taste, other respiratory symptoms), we asked, "Have you experienced any of these symptoms in the past 2 weeks? Which have you experienced in the past 2 months?" We categorized those reporting no symptoms as "asymptomatic" and those reporting any symptoms as "symptomatic." Finally, we asked: "On a scale of 1 to 10, where 1 means very unlikely and 10 means very likely, how likely do you think it is you have had COVID-19 ("Coronavirus")? Similarly, we grouped individuals answering 1–3 low risk, 4–7 moderate risk, and 8–10 high risk.

For participants who agreed to the antibody test, we invited them to 1 of 11 drive-thru test sites that span the geography of OC. We assessed past SARS-CoV-2 infection using a coronavirus antigen microarray.[15]

RESULTS

We recruited 2979 adults who completed the survey and provided a viable blood sample for coronavirus antigen microarray analysis from 10 July to 16 August 2020.[14] The overall unadjusted seroprevalence of SARS-CoV-2 was 11.8% (351/2979; 95% confidence intervals: 11.6% to 12.0%). Formal bias analysis (reported elsewhere)[14] indicates that nonresponse was unlikely to account for this relatively high prevalence (i.e., compared with other estimates in the US save for that in New York City).[16,17]

The Figure plots, by low-, moderate-, and high-risk behavior category, the percentage of persons that tested positive for SARS-CoV-2. Persons reporting low- and moderate-risk behavior accounted for 78% to 92% of SARS-CoV-2 infections (depending on the particular behavior).

Given the potential systematic bias of under-reporting high-risk behaviors (e.g., not keeping a 6 ft distance) due to social desirability,[18] we then assessed SARS-CoV-2 among low- to moderate-risk categories in other ways. Specifically, we used a composite score of self-reported symptoms in which we classified SARS-CoV-2 positive tests by whether the respondent reported any symptom (i.e., ≥1) or none in the past 2 weeks or in the past 2 months. We reasoned that persons reporting any SARS-CoV-2 symptoms would be more likely to have been infected,[9] thereby raising the possibility of being placed in a higher transmission risk category (although the extent of viral shedding among symptomatic vs. asymptomatic persons continues to be debated).[19] We arrayed SARS-CoV-2 by the response to the question on self-reported likelihood of having COVID. Consistent with the previous inference, low and moderate scores on the self-reported COVID question (i.e., 1–7) account for 70% of SARS-CoV-2 tests (eFigure 1; http://links.lww.com/EDE/B840). eFigure 2; http://links.lww.com/EDE/B840, moreover, indicates that the majority of persons with positive SARS-CoV-2 tests *and* with symptoms considered themselves of low to moderate risk of having contracted COVID. Confidence intervals for these and all other percentages appear in the eFigures 4 to 6; http://links.lww.com/EDE/B840.

DISCUSSION

Drawing from a diverse population-based sample of adults in a large Southern California county, we examined

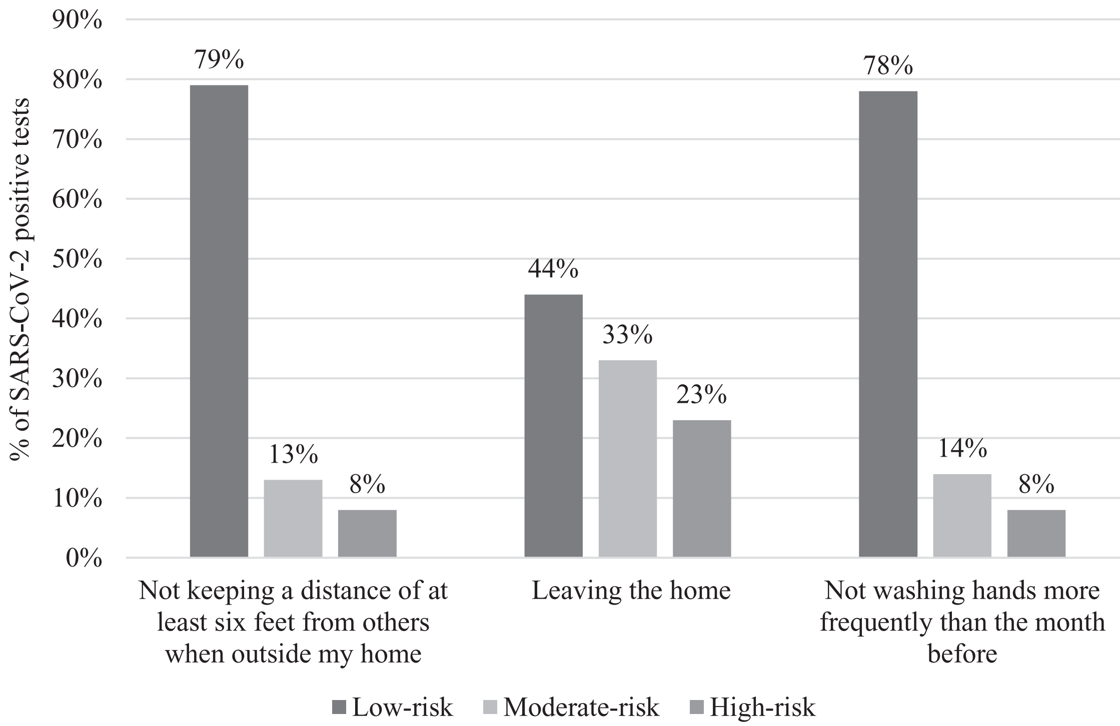

FIGURE. Percent of SARS-CoV-2 seroprevalence by self-reported risk category for three specific health behaviors among 351 SARS-CoV-2 positive adults in Orange County, CA, July 10 to August 16, 2020. Low-risk (participating in the behavior rarely); moderate-risk (participating in the behavior some of the time); high-risk (participating in the behavior most of the time). These values sum to 100% for each behavior.

whether persons considered low and moderate risk of SARS-CoV-2 account for actual infections. We found that consistent with Geoffrey Rose's logic, persons self-reporting low- to moderate-risk behaviors pertaining to SARS-CoV-2 accounted for the overwhelming majority of SARS-CoV-2 infections. This finding arises due to the fact that—despite popular media reports which highlight high-risk events—most of the population practices low-to-moderate-risk health behaviors.[20]

Asymptomatic persons, as well as those who ranked themselves as "highly unlikely to have COVID," constituted the majority of SARS-CoV-2 infections. This circumstance is consistent with the theory of widespread transmission by asymptomatic individuals as well as by those who remain unaware of their own infection.[21] We cannot determine from our data what fraction of SARS-CoV-2 infections arose from which behavior or from which risk group. It remains possible, for instance, that attendance of "super-spreader" events, considered high-risk, may account for substantial SARS-CoV-2 transmission. However, if others replicate our results, another explanation for continued spread involves low- and moderate-risk behaviors driving SARS-CoV-2 transmission.

Further research should scrutinize reported symptoms since persons who test positive with SARS-CoV-2 (especially younger adults) may have mild symptoms but report "no symptoms" on surveys. We also note the key limitation that, given the low ability to predict individual SARS-CoV-2 cases, nondifferential measurement error in risk behaviors may affect results. Furthermore, we omitted a question on wearing cloth masks given that, at the time of the survey, its preventive value remained unclear. Nevertheless, our results add to the empirical evidence that supports population-based strategies that encourage public health measures—even among persons who self-identify as unlikely to have, or unlikely to transmit, SARS-CoV-2.[21,22]

ACKNOWLEDGMENTS

The Orange County Health Care Agency funded this study. We are grateful to the entire actOC team that conducted the drive-thru SARS-CoV-2 antibody study: Daniel M. Parker, Scott Bartell, Veronica Vieira, Saahir Khan, Andrew Noymer, Emily Drum, Bruce Albala, Matthew Zahn, and Bernadette Boden-Albala. We also thank actOC site leaders, volunteers, and the Orange County community for their support. Lastly, we thank Neeraj Sood from the University of Southern California who provided the initial survey from which our Orange County survey was based.

REFERENCES

1. State of California. Tracking COVID-19 in California. 2020. Available at: https://covid19.ca.gov/state-dashboard/. Accessed October 27, 2020.
2. Haischer MH, Beilfuss R, Hart MR, et al. Who is wearing a mask? Gender-, age-, and location-related differences during the COVID-19 pandemic. *PLoS One*. 2020;15:e0240785.

3. Lyu W, Wehby GL. Community use of face masks and COVID-19: evidence from a natural experiment of state mandates in the US: study examines impact on COVID-19 growth rates associated with state government mandates requiring face mask use in public. *Health Aff (Millwood)*. 2020;39:1419–1425.
4. Rose G. Sick individuals and sick populations. *Int J Epidemiol*. 1985;14:32–38.
5. Ahern J, Jones MR, Bakshis E, Galea S. Revisiting rose: comparing the benefits and costs of population-wide and targeted interventions. *Milbank Q*. 2008;86:581–600.
6. Rose G. Strategy of prevention: lessons from cardiovascular disease. *Br Med J (Clin Res Ed)*. 1981;282:1847–1851.
7. Halperin W, Ibrahim MA, Connell N. Geoffrey Rose's strategy of prevention applied to COVID-19. *Health Secur*. 2020;18:502–504.
8. Moscola J, Sembajwe G, Jarrett M, et al; Northwell Health COVID-19 Research Consortium. Prevalence of SARS-CoV-2 antibodies in health care personnel in the New York City Area. *JAMA*. 2020;324:893–895.
9. Yang R, Gui X, Xiong Y. Comparison of clinical characteristics of patients with asymptomatic vs symptomatic coronavirus disease 2019 in Wuhan, China. *JAMA Netw Open*. 2020;3:e2010182.
10. Long QX, Tang XJ, Shi QL, et al. Clinical and immunological assessment of asymptomatic SARS-CoV-2 infections. *Nat Med*. 2020;26:1200–1204.
11. Pan X, Chen D, Xia Y, et al. Asymptomatic cases in a family cluster with SARS-CoV-2 infection. *Lancet Infect Dis*. 2020;20:410–411.
12. Fauci AS, Lane HC, Redfield RR. Covid-19 - navigating the uncharted. *N Engl J Med*. 2020;382:1268–1269.
13. American Community Survey 2018. 2018. Available at: https://www.census.gov/programs-surveys/acs. Accessed 20 August 2020.
14. Bruckner TA, Parker DM, Bartell SM, et al. Estimated seroprevalence of SARS-CoV-2 antibodies among adults in Orange County, California. *Sci Rep*. 2021;11:3081.
15. de Assis RR, Jain A, Nakajima R, et al. Analysis of SARS-CoV-2 antibodies in COVID-19 convalescent blood using a coronavirus antigen microarray. *Nat Commun*. 2021;12:6.
16. Rosenberg ES, Tesoriero JM, Rosenthal EM, et al. Cumulative incidence and diagnosis of SARS-CoV-2 infection in New York. *Ann Epidemiol*. 2020;48:23–29.e4.
17. Havers F, Reed C, Lim T, et al. Seroprevalence of antibodies to SARS-CoV-2 in 10 sites in the United States, March 23-May 12, 2020. *JAMA Intern Med*. 2020;180:1576–1586.
18. Timmons S, McGinnity F, Belton C. It depends on how you ask: measuring bias in population surveys of compliance with COVID-19 public health guidance. *J Epidemiol Community Health*. 2021;75:387–389.
19. Li W, Su YY, Zhi SS, et al. Virus shedding dynamics in asymptomatic and mildly symptomatic patients infected with SARS-CoV-2. *Clin Microbiol Infect*. 2020;26:1556.e1–1556.e6.
20. Frieden TR, Lee CT. Identifying and interrupting superspreading events-implications for control of severe acute respiratory syndrome coronavirus 2. *Emerg Infect Dis*. 2020;26:1059–1066.
21. Gandhi M, Yokoe DS, Havlir DV. Asymptomatic transmission, the Achilles' heel of current strategies to control Covid-19. *N Engl J Med*. 2020;382:2158–2160.
22. Pollán M, Pérez-Gómez B, Pastor-Barriuso R, et al; ENE-COVID Study Group. Prevalence of SARS-CoV-2 in Spain (ENE-COVID): a nationwide, population-based seroepidemiological study. *Lancet*. 2020;396:535–544.