Infection Fatality Ratios for COVID-19 Among Noninstitutionalized Persons 12 and Older: Results of a Random-Sample Prevalence Study

Background: Because many cases of coronavirus disease 2019 (COVID-19) are asymptomatic, generalizable data on the true number of persons infected are lacking. Mortality rates therefore are calculated from confirmed cases, which overestimates the infection fatality ratio (IFR). To calculate a true IFR, population prevalence data are needed from large geographic areas where reliable death data also exist. Most previous IFR estimates came from non-U.S. populations, including a cruise ship, or were calculated by using simulation techniques (1–3). Previous estimates also are not age specific, are relatively ungeneralizable, and are unsuitable for making clinical or policy decisions.

Objective: To estimate IFRs among noninstitutionalized (that is, community-dwelling) populations by age, race, ethnicity, and sex by using the first U.S. statewide random-sample study of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) prevalence.

Methods and Findings: We combined prevalence estimates from a statewide random sample with Indiana vital statistics data of confirmed COVID-19 deaths (4). In brief, our stratified random sample consisted of state residents aged 12 years and older. Known decedents and incarcerated persons were excluded. Because nursing homes were limiting residents’ ability to leave and re-enter the facilities, their participation was unlikely. Participants were tested from 25 April to 29 April 2020 for active viral infection and SARS-CoV-2 antibodies, which would indicate prior infection. Demographic information was collected.

We accounted for nonresponse by weighting prevalence estimates for age, race (dichotomized as White or non-White), and Hispanic ethnicity to reflect state demographics. Estimated prevalence included all current and past infections with bootstrapped 95% CIs. The prevalence of each demographic stratum was multiplied by the stratum-specific state population estimate to determine the number of cumulative infections by group.

We calculated the IFR by age, race, sex, and ethnicity on the basis of the cumulative number of confirmed COVID-19 deaths as of 29 April 2020, divided by the number of infections. Although nursing home residents were not tested, they represented 54.9% of Indiana’s deaths. Thus, we excluded nursing home residents from all calculations (that is, deaths and infections). To account for all infections, we added the number of patients hospitalized with COVID-19 during the testing period and noninstitutionalized COVID-19 deaths into the denominator.

As of 29 April 2020, Indiana had recorded 1099 COVID-19 deaths, 495 of which occurred in noninstitutionalized persons. Our random-sample study estimated 187,802 cumulative infections, to which 180 hospitalizations were added. The average age among all COVID-19 decedents was 76.9 years (SD, 13.1). The overall noninstitutionalized IFR was 0.26%. In order of magnitude, the demographic-stratified IFR varied most by age, race, ethnicity, and sex (Table). Persons younger than 40 years had an IFR of 0.01%; those aged 60 or older had an IFR of 1.71%. Whites had an IFR of 0.18%; non-Whites had an IFR of 0.59%.

Discussion: By using SARS-CoV-2 population prevalence data, we found that the risk for death among infected persons increased with age. Indiana’s IFR for noninstitutionalized persons older than 60 years is just below 2% (1 in 50). In comparison, the ratio is approximately 2.5 times greater than the es-

| Category       | Total Deaths, n | Mean Age at Death, y* | Noninstitutionalized Deaths, n† | Estimated Noninstitutionalized Infections (95% CI), n | Noninstitutionalized IFR (95% CI), % |
|----------------|-----------------|------------------------|----------------------------------|------------------------------------------------------|--------------------------------------|
| **Age, y**     |                 |                        |                                  |                                                      |                                      |
| <40            | 14              | 32.8                   | 13                               | 108 339 (73 041-142 095)                               | 0.01 (0.01-0.02)                     |
| 40-59          | 81              | 52.4                   | 63                               | 52 917 (33 963-71 546)                                | 0.12 (0.09-0.19)                     |
| ≥60            | 1004            | 79.5                   | 419                              | 24 493 (16 691-33 232)                                | 1.71 (1.28-2.58)                     |
| **Race**       |                 |                        |                                  |                                                      |                                      |
| White          | 715             | 78.9                   | 250                              | 141 026 (108 858-171 519)                             | 0.18 (0.15-0.23)                     |
| Non-White      | 384             | 73.3                   | 245                              | 41 583 (17 630-71 822)                                | 0.59 (0.34-1.41)                     |
| **Ethnicity**  |                 |                        |                                  |                                                      |                                      |
| Hispanic       | 17              | 72.9                   | 15                               | 39 783 (10 851-73 317)                                | 0.04 (0.02-0.14)                     |
| Non-Hispanic   | 1082            | 77.0                   | 480                              | 142 844 (118 830-172 653)                             | 0.34 (0.28-0.41)                     |
| **Sex**        |                 |                        |                                  |                                                      |                                      |
| Male           | 580             | 74.9                   | 300                              | 107 891 (64 803-169 979)                               | 0.28 (0.18-0.47)                     |
| Female         | 493             | 79.5                   | 169                              | 82 096 (53 116-109 200)                               | 0.21 (0.16-0.32)                     |
| **Total**      | 1099            | 76.9                   | 495                              | 187 378 (143 881-232 883)                              | 0.26 (0.21-0.35)                     |

IFR = infection fatality ratio.
* Mean age in years at the time of death, among total deaths.
† Excludes deaths among nursing home residents.

This article was published at Annals.org on 2 September 2020.
Estimated IFR for seasonal influenza, 0.8% (1 in 125), among those aged 65 years and older (5). Of note, the IFR for non-Whites is more than 3 times that for Whites, despite COVID-19 decedents in that group being 5.6 years younger on average.

We are unaware of any similar IFR estimates by demographic group but recognize several limitations of our analysis. First, despite random selection and weighting for nonresponse, the potential for response bias remains. Second, imperfections in tests have the potential for false-positives, which may bias estimated infections upward. Separately, use of confirmed COVID-19 deaths may undercount the true number of deaths; both issues might result in lower IFRs. Third, because children and non-state tax filers were excluded, our estimates may lack generalizability to persons who were not studied. Fourth, we could not account for disease severity among random-sample participants with positive test results. Although participants represented persons with less severe illness, some with positive test results may have later died of COVID-19, resulting in a potential underestimation of the IFR. However, accounting for right-censoring bias also might overestimate the IFR, because we cannot distinguish deaths among persons we randomly tested from those among patients who were hospitalized during the testing period. Race and ethnicity data for confirmed COVID-19 deaths may have been inaccurate, thus biasing these IFR estimates. Lastly, IFR is a population-based measure and should be interpreted cautiously as a measure of individual risk.

Justin Blackburn, PhD
Constantin T. Yiannoutsos, PhD
Indiana University Richard M. Fairbanks School of Public Health, Indianapolis, Indiana

Aaron E. Carroll, MD, MS
Indiana University School of Medicine, Indianapolis, Indiana

Financial Support: This study was funded by the State of Indiana.

Disclosures: Disclosures can be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M20-5352.

Reproducible Research Statement: Study protocol: Available from Dr. Blackburn (e-mail, jblackb@iu.edu). Statistical code: Not available. Data set: Available from the Indiana State Department of Health (www.coronavirus.in.gov/2397.htm).

Corresponding Author: Justin Blackburn, PhD, 1050 Wishard Boulevard, Indianapolis, IN 46202; e-mail, jblackb@iu.edu.

Correction: This article was corrected on 3 September 2020 to fix inaccurate values within the male and female categories in the table.

doi:10.7326/M20-5352

References
1. Park M, Cook AR, Lim JT, et al. A systematic review of COVID-19 epidemiology based on current evidence. J Clin Med. 2020;9. [PMID: 32244365] doi:10.3390/jcm9040967
2. Russell TW, Hellewell J, Jarvis CI, et al. Estimating the infection and case fatality ratio for coronavirus disease (COVID-19) using age-adjusted data from the outbreak on the Diamond Princess cruise ship, February 2020. Euro Surveill. 2020;25. [PMID: 32234121] doi:10.2807/1560-7917.ES.2020.25.12.2000256
3. Basu A. Estimating the infection fatality rate among symptomatic COVID-19 cases in the United States. Health Aff (Millwood). 2020;39:1229-1236. [PMID: 32379502] doi:10.1377/hlthaff.2020.00455
4. Menachemi N, Yiannoutsos CT, Dixon BE, et al. Population point prevalence of SARS-CoV-2 infection based on a statewide random sample - Indiana, April 25-29, 2020. MMWR Morb Mortal Wkly Rep. 2020;69:960-964. [PMID: 32701938] doi:10.15585/mmwr.mm6929e1
5. Centers for Disease Control and Prevention. Estimated influenza illnesses, medical visits, hospitalizations, and deaths in the United States—2018–2019 influenza season. Accessed at www.cdc.gov/flu/about/burden/2018-2019.html on 4 June 2020.