MAJOR ARTICLE







Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection Fatality Rate Among Elderly Danes: A Cross-sectional Study on Retired Blood Donors

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Background. Although the vast majority of individuals succumbing to infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are elderly, infection fatality rate (IFR) estimates for the age group \geq 70 years are still scarce. To this end, we assessed SARS-CoV-2 seroprevalence among retired blood donors and combined it with national coronavirus disease 2019 (COVID-19) survey data to provide reliable population-based IFR estimates for this age group.

Methods. We identified 60 926 retired blood donors aged ≥70 years in the rosters of 3 regionwide Danish blood banks and invited them to fill in a questionnaire on COVID-19-related symptoms and behaviors. Among 24 861 (40.8%) responders, we invited a random sample of 3200 individuals for blood testing. Overall, 1201 (37.5%) individuals were tested for SARS-CoV-2 antibodies (Wantai) and compared with 1110 active blood donors aged 17–69 years. Seroprevalence 95% confidence intervals (CIs) were adjusted for assay sensitivity and specificity.

Results. Among retired (aged \geq 70 years) and active (aged 17–69 years) blood donors, adjusted seroprevalences were 1.4% (95% CI, .3–2.5%) and 2.5% (95% CI, 1.3–3.8%), respectively. Using available population data on COVID-19–related fatalities, IFRs for patients aged \geq 70 years and for 17–69 years were estimated at 5.4% (95% CI, 2.7–6.4%) and .083% (95% CI, .054–.18%), respectively. Only 52.4% of SARS-CoV-2–seropositive retired blood donors reported having been sick since the start of the pandemic.

COVID-19 IFR in the age group >69 years is estimated to be 65 times the IFR for people aged 18–69 years. **Keywords.** COVID-19; infection fatality rate; epidemiology; SARS-Cov-2 antibody test; SARS-CoV-2 seroprevalence.

Since early in the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic it has been clear that comorbidities such as diabetes mellitus, chronic cardiovascular, obstructive pulmonary, and kidney diseases are common among patients who are hospitalized for coronavirus disease 2019 (COVID-19) and among patients who succumb to the infection [1–3].

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The comorbidities accumulating among deceased patients with COVID-19 are mostly prevalent in the elderly population [1]. Because of comorbidity and age-dependent frailty, the COVID-19 infection fatality rate (IFR) presumably is higher among older than among younger adults, but solid data to support this assumption are lacking.

Infection fatality rate may be approximated by relating agespecific number of COVID-19 deaths with corresponding measures of SARS-CoV-2 prevalence [4–6]. So far, only few studies have assessed how SARS-CoV-2 has spread among the elderly in the general population and with mixed results [7–10]. While a Spanish survey [8] found no strong association between age and SARS-CoV-2 seroprevalence, both a Swiss and a US investigation generally reported lower seroprevalence in the age group above 65 years than among younger adults [7, 10].

The aim of this study was to determine SARS-CoV-2 seroprevalence in an elderly retired blood-donor population in Denmark and to estimate the associated IFR for this age group. This knowledge will help tailor public health policies mitigating the impact of the pandemic.

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METHODS

Study Design and Participants

We contacted 60 926 elderly retired blood donors in 3 out of the 5 Danish administrative regions (the Danish Capital Region, the Zealand Region, and the Central Denmark Region). We have previously found that these regions had the lowest (0.7%) and highest (3.0%) seroprevalence of SARS-CoV-2 antibodies among active blood donors aged 17–69 years [4].

The 60 926 retired blood donors aged 70 years or older were invited to complete a digitalized questionnaire on COVID-19 symptoms and risk factors between 16 May and 25 May 2020. Within 2 weeks of the invitation, 24 861 (40.8%) donors had filled in the questionnaire.

In order to compare the symptoms and behavior of the older retired blood donors with younger active donors, we also mailed the questionnaire electronically to 75 934 participants in the Danish Blood Donor Study from all Danish regions aged 18–69 years on 28 May 2020 [11]. A total of 24 227 (31.9%) invitees responded to this questionnaire.

From among the retired blood donors aged 70 years or older, who completed the questionnaire, we invited a random sample of 3203 individuals living within geographical proximity of 12 bleeding sites (2 in the Central Denmark Region, 6 in the Zealand Region, and 4 in the Capital Region) for serological SARS-CoV-2 antibody measurements. The number of retired blood donors invited was determined by capacity for blood sampling in the different regions.

A total of 1201 (38%) of the invited retired blood donors showed up for testing between 2 and 19 June 2020 (Figure 1). Characteristics of the cohort in the different steps are summarized in Table 1.

For comparison, we also tested a random sample of 360, 250, and 500 active blood donors (aged 17–69 years) who had given blood between 1 and 12 June 2020 in the Central Denmark Region and between 22 and 26 June 2020 in the Zealand and Capital Regions, respectively. This testing was done after anonymization of samples.

All 1201 elderly participants gave informed consent to participate in the Danish Blood Donor Study before samples were taken

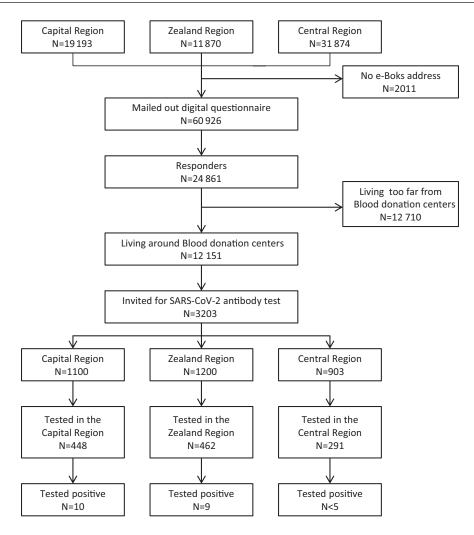


Figure 1. Patient testing flowchart. Abbreviation: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Table 1. Cohort Age and Sex Distribution at Different Selection Steps

	Received Question- naire (n = 60 926)	Responded to Question- naire (n = 24 861)	Р	Eligible for Testing ^a (n = 12 151)	Tested for SARS-CoV-2 Antibodies (n = 1201)	Р
Age, median (25th, 75th percentile), y	75 (72,79)	73 (71,76)	<.0001 ^b	73 (71,77)	73 (71,76)	.002 ^b
Women, n (%)	26 451 (43.4)	10 519 (42.3)	.44 ^c	5288 (43.5)	517 (43.1)	.78 ^c

Abbreviation: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

for SARS-CoV-2 antibody measurements. The study was approved by the Zealand Regional Committee on Health Research Ethics (approval number: SJ-740) and the data protection agency of the Capital Region (P-2019-99). According to Danish legislation, analysis of anonymous material does not require consent.

Questionnaire Data

The questionnaire included the following items: symptoms of disease during the previous 3 months, including fever, nasal symptoms (sneezing, affected sense of smell and/or taste), airways (sore throat, coughing, shortness of breath), and abdominal discomfort (diarrhea, vomiting); changes in behavior including hand-washing, using a handkerchief, sneezing in the elbow, avoiding handshakes, wearing a facemask, avoiding hugging people, reduced use of public transport, avoiding crowded places, and staying at home; and history of previous polymerase chain reaction (PCR) test for COVID-19 and the test result. The questions on disease symptoms were graded on a 4-point scale ranging from no symptoms (1); yes, a few (2); yes, a lot (3); and yes, many (4). The respondents were also allowed to answer "I do not know." For analysis, we dichotomized the scale into none (1) versus any (2-4); if the response was "I do not know" this answer was omitted from the analysis.

Laboratory Measurements

SARS-CoV-2 antibodies were measured **EDTA** (ethylenediaminetetraacetic acid) plasma samples using a double-sandwich enzyme-linked immunosorbent assay (ELISA) to estimate antibodies regardless of immunoglobulin type (IgTotal) (catalog no. WS-1096; Beijing Wantai Biological Pharmacy Enterprise, Beijing, China). We have previously estimated the sensitivity and specificity of this assay to be 96.7% (95% confidence interval [CI], 92.4–98.6%) and 99.5% (95% CI, 98.7-99.8%), respectively. This estimate was obtained through a nationwide validation effort across laboratories in Denmark on 150 SARS-CoV-2 PCR-positive samples covering the disease spectrum from mild (24.6%) and moderate (50%) to severe (20.6%) symptoms and 650 control samples (L Harritshøj 2020, unpublished data). One of the 1201 ELISA measurements in the present investigation was inconclusive and omitted from analysis.

Population Data and COVID-19 Surveillance Data

The samples for this study were collected between 2 and 19 June 2020. Public surveillance data on the number of individuals tested for SARS-CoV-2, hospitalized for COVID-19, and dying of COVID-19 are updated daily from Statens Serum Institute [12]. We retrieved population statistics from Statistics Denmark based on the Danish population in the first quarter of 2020 [13].

Statistical Analysis

Self-reported risk factors and symptoms were reported as percentages with 99.8% CIs because of multiple testing (exact CIs), and for differences between groups we reported the risk ratios (RRs). To compare age and sex compositions between groups we used Mann-Whitney U test and chi-square tests. We used the Rogan Gladen estimate to calculate the true prevalence. Confidence intervals were derived by 10⁸-sample percentile bootstrapping independently of sampling sensitivity, specificity, and apparent prevalence using posterior binomial distributions based on the observations. Prevalences were reported as percentages with 95% CIs. The analysis was performed in RStudio 1.2 and R 4.0.2 (R Foundation for Statistical Computing, Vienna, Austria) using the EpiR package to adjust measured seroprevalence for sensitivity and specificity of the diagnostic assay as well as weighing the estimate based on population size of the bleeding sites' recruitment areas. The weights of the geographical areas were based on the number of inhabitants in the municipalities (exact weights can be found in Supplementary Table 1).

RESULTS

The age and sex distributions of the different selection steps in the present investigation are summarized in Table 1.

A total of 24 861 (40.9%) retired blood donors aged 70 years or older and a total of 24 227 (31.9%) active blood donors aged 17–69 years answered the questionnaire on health behaviors and COVID-19 symptoms (Table 2). Adherence to official recommendations varied between 40% (staying at home) and 95% (frequent hand-washing) among the retired blood donors. For the same items, adherence among the younger active donors varied between 31% (staying at home) and 91% (frequent hand-washing), with estimates generally being lower

^aPersons living within a 10-20-km radius of a testing station.

^bMann-Whitney *U* test of difference in median age. ^cChi-square test of difference in percentage women.

Table 2. Questionnaire Data on Active Blood Donors Aged 18–69 Years and Retired Blood Donors Aged 70 Years or Older

	Responders Aged ≥70 Years	Responders Aged 18–69 Years	RR ^a (99.8% CI), P
Total N	24 861	24 722	
Women, n (%)	10 519 (42.3)	13 709 (55.5)	
Symptoms and tests			
Sick within the last 3 m	12.7 (12.1-13.4), 24 302	21.9 (21.0-22.7), 24 475	.70 (.6673), <.0001
Previous test for SARS-CoV-2	17.1 (15.1–19.3), 3080	35.8 (33.8–37.9), 5319	.51 (.45–.58), <.0001
Previous positive SARS-CoV-2 test	4.3 (1.9–8.0), 467	7.2 (5.5–9.3), 1839	.63 (.32-1.21), .02
Health behavior			
Washing hands often	94.6 (94.1–95.0), 24 861	90.9 (90.4–91.5), 24 722	1.36 (1.27–1.45), <.0001
Using handkerchief	42.7 (41.7–43.7), 24 861	14.7 (14.0–15.4), 24 722	1.85 (1.80–1.90), <.0001
Sneezing in the elbow	77.0 (76.2–77.8), 24 861	81.2 (80.5–82.0), 24 722	.88 (.8691), <.0001
Avoiding handshake	93.5 (93.0–94.0), 24 861	91.7 (91.1–92.2), 24 722	1.15 (1.09-1.22), <.0001
Using facemask	1.8 (1.6–2.1), 24 861	1.8 (1.6–2.1), 24 722	.99 (.90-1.10), .85
Avoiding hugging people	83.8 (83.0–84.5), 24 861	83.7 (83.0–84.5), 24 722	1.00 (.96-1.04), .93
Reduced use of public transport	46.3 (45.4–47.3), 24 861	33.9 (32.9–34.8), 24 722	1.29 (1.25-1.33), <.0001
Avoiding crowded places	75.5 (74.7–76.4), 24 861	67.4 (66.4–68.3), 24 722	1.23 (1.19–1.27), <.0001
Staying home	41.3 (40.3-42.3), 24 861	31.5 (30.6–32.4), 24 722	1.23 (1.20-1.26), <.0001

Unless otherwise stated, the data are presented as percentage that responded yes (99.8% CI), n. If n is different from the total number it is because not all responded to this item. Abbreviations: CI, confidence interval; RR, risk ratio; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

than among the elderly retired donors (Table 2). By June 2020, use of facemasks was neither recommended nor mandatory except under certain circumstances and therefore infrequently reported by either group of blood donors (1.8%).

Overall, 1201 (38%) elderly retired donors were tested for antibodies to SARS-CoV-2. Compared with non-invitees and nonattendees who had answered the questionnaire, those who were tested for SARS-CoV-2 antibodies were marginally more compliant with the official precautionary recommendations (Table 3). Of the 1200 elderly retired blood donors with a valid test result, 22 (1.8%) were positive for SARS-CoV-2 antibodies. The 22 SARS-CoV-2 antibody-positive individuals were more likely to report a history of symptoms compatible with COVID-19 compared with those who tested negative for SARS-CoV-2 antibodies (52.4% [99.8% CI, 20.1–83.3%] vs 15.1% [99.8% CI, 12.0–18.6%]), although individually, the distribution of specific symptoms was not statistically significantly different between the 2 groups (Table 3).

For 4 out of 5 officially recommended precautions against spread of disease, self-reported compliance was lower among the elderly blood donors who tested positive for SARS-CoV-2 antibodies than among those who did not have antibodies, although this difference was statistically significant only for 1 recommendation (avoiding hugging or kissing on the cheeks) (54.5% [99.8% CI, 22.3–84.2%] vs 87.4% [99.8% CI, 84.2–90.2%]) (Table 3). With regard to staying at home as much as possible, compliance was higher among SARS-CoV-2–positive participants than among SARS-CoV-2–negative participants (Table 3).

The adjusted SARS-CoV-2 seropositivity prevalences for men and women combined among those 70 years or older were 2.2% (95% CI, .6–4.1%), 1.9% (95% CI, .4–3.7%), and .7% (95% CI, -.4–3.0%) in the Capital, Zealand, and Central Regions, respectively (Table 4). In these 3 regions we also tested for SARS-CoV-2 antibodies in an anonymized sample of active blood donors aged 17–69 years, yielding corresponding adjusted prevalences of 5.3% (95% CI, 2.3–9.2%), 2.5% (95% CI, .6–5.3%), and 1.1% (95% CI, -.3–2.8%), respectively.

These 3 regions represent the entire spectrum of regional-level COVID-19 seroprevalences detected in Denmark so far [4, 12]. Thus, according to official statistics, the 2 administrative regions not included in this investigation (the North and South Denmark Regions) have a slightly lower prevalence of patients treated for COVID-19 than the Central Region [12].

Assuming that the SARS-CoV-2 seroprevalence observed for the Central Region in the present investigation also applies to the North and South Regions, and that blood donors are representative of the general population, we estimate an adjusted nationwide SARS-CoV-2 seroprevalence of 2.2% (95% CI, 1.0–3.4%) in the age group of 17–69 years and of 1.2% (95% CI, .1–2.4%) among individuals aged 70 years or older in the Danish population. For the entire age group aged 17 years or older the adjusted seroprevalence was 1.6% (95% CI, .58–2.5%).

On 22 June 2020, the official nationwide number of individuals aged 70 years or older registered with SARS-CoV-2 since the beginning of the pandemic was 2180. The seroprevalence estimated in the present investigation suggests that this number corresponds to only 21.6% (95% CI, 10.8–28.9%) of all COVID-19 cases in the age group at the time.

As of 22 June, the total number of registered deaths in Denmark from COVID-19 was 71 and 542 for the age group below and above 70 years, respectively. Given the estimated

^aRR of difference in prevalence of symptoms or behavior between the 2 age groups, 99.8% CI, and *P* value

Table 3. Self-reported Symptoms in Tested and Not Tested Participants Aged 70 Years or Older

	Not Invited for Testing	But Did Not Accept Invitation	Tested Negative	Tested Positive	RR ^a (99.8% CI), P
Total N	21 658	2002	1178	22	
Women, % (99.8% CI), n	42.2 (41.1–43.2), 21 658	43.3 (39.9–46.8), 2002	42.9 (38.4–47.4), 1178	50 (19.0–81.0), 22	1.33 (.35–4.89), .50
Symptoms and tests					
Sick within the last 3 m ^b	12.6 (11.9–13.3), 21 170	12.1 (10.0–14.6), 1954	15.1 (12.0–18.6), 1156	52.4 (20.,1–83.3), 21	5.86 (1.55–22.1), <.00
Fever ^c	51.9 (48.2–55.6), 1751	51.2 (38.9–63.4), 162	55.4 (41.0–69.1), 121	57.1 (7.7–96.8), 7	1.07 (.11–10.6), .93
Running or blocked nose	72.6 (69.3–75.8), 1793	76.3 (64.6–85.7), 160	79.7 (66.6–89.4), 123	66.7 (16.3–97.6), 9	.54 (.07–4.32), .35
Loss of sense of smell ^c	27.8 (24.2–31.7), 1379	27.5 (16.0–41.5), 120	32.7 (19.1–48.6), 98	66.7 (9.4–99.2), 6	3.78 (.28–50.8), .09
Loss of sense of taste ^c	26.3 (22.7–30.1), 1375	25.2 (14.3–38.8), 123	33.0 (19.3–49.0), 97	66.7 (9.4–99.2), 6	3.72 (.28–50.1), .09
Sneezing ^c	75.8 (72.4–78.9), 1712	80.5 (68.9–894), 149	76.7 (62.8–87.5), 116	50 (6.4–93.5), 8	.33 (.04–2.69), .09
Sore throat ^c	58.5 (54.8–62.2), 1717	56.1 (43.4–68.3), 155	65.9 (51.6–78.3), 123	33.3 (2.4–83.7), 9	.29 (.03–2.36), .05
Coughing ^c	77.8 (74.7–80.6), 1920	75.6 (64.2–85.0), 168	82.4 (70.2–91.2), 131	90 (37.6–99.9), 10	1.85 (.08–44.5), .54
Dyspnea ^c	49.9 (46.1–53.7), 1643	44.4 (31.7–57.6), 142	36.1 (22.6–51.4), 108	37.5 (2.7-88.0), 8	1.05 (.12-9.32), .94
Vomiting ^c	8.7 (6.5-11.2), 1405	9.2 (3.2–19.6), 130	8.8 (2.5–20.8), 102	11.7 (0.0–71.1), 8	1.29 (.03–11.7), .82
Diarrhea ^c	28.9 (25.3–32.7), 1491	36.7 (24.6–50.1), 139	27.4 (15.3-42.3), 106	11.1 (0.0–66.5), 9	.35 (.01–8.79), .29
Previous test for SARS-CoV-2 ^b	17.3 (15.2–19.6), 2660	14.9 (8.6–23.3), 235	14.4 (7.3–24.2), 174	18.2 (0.4–67.9), 11	1.30 (.13–13.3), .72
Previous positive SARS-CoV-2 test ^b	3.8 (1.6–7.5), 412	3.3 (0.0–26.9), 30	4.3 (0.0–33.7), 23	100 (3.1–100), 2	
Health behavior					
Washing hands often ^b	94.5 (94.1–95.0), 21 658	94.4 (92.6–95.9), 2003	95.6 (93.4–97.2), 1178	86.3 (52.7–99.1), 22	.30 (.05–1.98), .04
Using handkerchief ^b	42.7 (41.7–43.7), 21 658	44.2 (40.8–47.7), 2003	43.2 (38.8–47.7), 1178	40.9 (12.9–74.1), 22	.91 (.24–3.44), .83
Sneezing in the elbow ^b	76.8 (76.0–77.7), 21 658	75.7 (72.6–78.6), 2003	81.1 (77.3–84.5), 1178	63.6 (29.7–89.8), 22	.42 (.11–1.61), .04
Avoiding handshake ^b	89.2 (88.6–89.8), 21 658	93.3 (91.4–94.9), 2003	94.4 (92.0–96.3), 1178	90.9 (58.5–99.8), 22	.60 (.06–5.75), .48
Using facemask ^b	1.8 (1.5–2.1), 21 658	2.0 (1.2–3.2), 2003	2.2 (1.1–3.9), 1178	0 (0–22.9), 22	
Avoiding hugging people ^b	83.6 (82.8–84.3), 21 658	84.7 (81.3–86.4), 2003	87.4 (84.2–90.2), 1178	54.5 (22.3–84.2), 22	.18 (.05–.67), <.000
Reduced use of public transport ^b	46.1 (45.1–47.1), 21 658	50.4 (47.0–53.9), 2003	52.0 (47.4–56.5), 1178	45.5 (15.8–77.7), 22	.77 (.21–2.87), .55
Avoiding crowded places ^b	75.5 (74.6–76.3), 21 658	76.3 (73.2–79.2), 2003	76.3 (72.3–80.0), 1178	68.2 (33.7–92.3), 22	.67 (.17–2.72), .38
Staying home ^b	41.5 (40.5–42.5), 21 658	41.9 (38.5–45.4), 2003	37.5 (33.2–42.0), 1178	45.5 (15.8–77.7), 22	1.38 (.37–5.11), .45
Other risk factors					
Current smoking ^b	8.7 (8.2–9.3), 21 557	8.2 (6.4–10.3), 1995	9.1 (6.7–11.9), 1178	9.1 (0.2-41.1), 22	1.01 (.10–9.69), 1.00
Current alcohol consumption, median standard drinks/week (25%, 75%)		5 (2,10)	5 (2,10)	2 (0,5)	

Abbreviations: CI, confidence interval; RR, risk ratio; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

seroprevalences, these numbers correspond to IFRs of .083% (95% CI, .054–.18%) and 5.4% (95% CI, 2.7–64.0%) among people aged 17–69 years and aged 70 years or older, respectively. Thus, the IFR among people aged 70 years or older is 65 (95% CI, 40–356) times the IFR among people aged 17–69 years. The IFR for the adult Danish population aged 17 years or older was .81% (95% CI, .52–2.2%).

DISCUSSION

This Danish study on health behavior, COVID-19 symptoms, and SARS-CoV-2 antibody prevalence among retired and active blood donors suggests that older adults (here, those aged 70 years or older) in general are more likely to adhere to official

recommendations to reduce SARS-CoV-2 transmission than younger adults (here, those aged 17–69 years). Consistent with this age-dependent difference in guideline adherence, our study also indicated that the SARS-CoV-2 seroprevalence in Denmark is lower (1.2%) among older than among younger (2.2%) adults, even though this difference was not statistically significant. In support of the suspected underlying mechanism, questionnaire data showed that older retired blood donors who tested positive for SARS-CoV-2 antibodies were less likely to have adhered to official recommendations to prevent COVID-19 than older retired blood donors testing negative for antibodies. Overall, our data indicate that the IFR for COVID-19 among individuals aged 70 years or older is 5.4% (95% CI, 2.7–64%)—that is, 65 times that estimated for younger adults aged 17–69 years.

^aRR of difference in prevalence of symptoms and behavior between those who tested positive and those who tested negative for SARS-CoV-2, 99.8% CI, and P value.

^bPresented data are percentage "yes" (99.8% CI), n. When n does not equal the number in the group it is because not all responded to the item.

Data are percentage "more than a little" (99.8% Cl), n. When n does not equal the number in the group it is because not all responded to the item.

Table 4. SARS-CoV-2 Seropositivity in Retired Blood Donors Aged 70 Years or Older and Active Blood Donors Aged 17–69 Years

	Region			
	Capital	Zealand	Central Denmark	Total
Tested, ≥70 y, n				
Nonreactive, n	439	452	288	1179
Reactive, n	10	9	<5	22
Total, n	449	461	291	1201
≥70 years, seroprevalence				
Unadjusted, %	2.2 (1.1-4.1)	2.0 (0.9-3.7)	1.0 (0.2-3.0)	1.8 (1.2-2.8)
Adjusted, %	2.2 (0.6-4.1)	1.9 (0.4-3.7)	0.7 (-0.4-3.0)	1.4 (0.3-2.5)
Citizens, ≥70 y, n	231 731	139 827	184 324	555 882
Expected seropositives, n	5098 (1390-9501)	2656 (559-5174)	1290 (0-5529)	7782 (1668–13 897)
Confirmed cases, n	1194	394	243	1831
Ratio of confirmed cases to expected seropositives, %	23.4 (12.6-85.9)	14.8 (7.6–70.5)	18.8 (4.4-100)	23.5 (13.2-100)
Confirmed deaths, n	311	107	60	478
IFR, %	6.1 (3.3-22.4)	4.0 (2.1-19.1)	4.7 (1.1–100)	6.1 (3.4-28.6)
Tested, 17–69 y, n				
Nonreactive, n	479	243	355	1077
Reactive, n	21	7	5	33
Total, n	500	250	360	1110
17–69 y, seroprevalence				
Unadjusted, %	4.2 (2.6-6.3)	2.8 (1.1-5.7)	1.4 (0.5–3.2)	3.0 (2.1-4.1)
Adjusted, %	3.9 (2.1-6.0)	2.5 (0.6-5.3)	1.1 (-0.3-2.8)	2.5 (1.3-3.8)
Citizens, 17–69 y, n	1 268 536	544 560	887 939	2 701 035
Expected seropositives, n	49 472 (26 639–76 112)	13 614 (3267–28 861)	9767 (0-24 862)	67 525 (35 113–102 639)
Confirmed cases, n	5575	1543	1320	8438
Ratio of confirmed cases to expected seropositives, %	11.3 (7.3–20.9)	11.3 (5.3–47.2)	13.5 (5.3–100)	12.5 (8.2-24.0)
Confirmed deaths, n	45	17	9	71
IFR, %	0.09 (0.06 -0.17)	0.12 (0.06-0.52)	0.09 (0.04-100)	0.11 (0.07-0.2)

Abbreviations: IFR, infection fatality rate; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

In our study, only about half of the older retired blood donors who tested positive for SARS-CoV-2 antibodies recollected feeling sick with COVID-19 symptoms since the start of the pandemic. This proportion of apparently asymptomatic infections with SARS-CoV-2 is in the same range as in previous reports from both the United States and South America [14, 15]. Although based on a small number of SARS-CoV-2–seropositive participants and even disregarding potential underreporting of symptoms in our investigation, our findings show that, also among the elderly, the course of COVID-19 is highly variable and that silent sero-converters may not be a negligible source of infection.

Only a small minority of participants with self-reported COVID-19 symptoms reported having had a PCR test for SARS-CoV-2 and even fewer had had a positive PCR test. This could be the result of the early Danish recommendation of staying home and not consulting one's general practitioner if sick to avoid virus transmission to frail patients. Regardless, our findings suggest that individuals with COVID-19 may previously have escaped detection by the testing efforts implemented by Danish health authorities. This notion is further corroborated by the seemingly small fraction (21.6%) of SARS-CoV-2 infections among

the elderly recognized by the health authorities as estimated from the present study.

We surveyed health-related behavior among the participants in our study. The official Danish recommendations are as follows: (1) stay home if you are sick, (2) clean your hands regularly, (3) sneeze in your elbow, (4) avoid hugging or close contact, and (5) avoid crowded places. The Danish political interventions towards the COVID-19 pandemic are summarized in Supplementary Table 2. In our investigation, retired blood donors aged 70 years or older who tested positive for SARS-CoV-2 antibodies had been less inclined (54.5-90.9%) to follow official recommendations than those who tested negative (76.6–95.6%), with the exception of staying at home more. Whether this tendency to stay at home more has resulted in a more relaxed attitude towards other precautions cannot be ruled out. This finding may also be an example of reverse causality—that is, individuals who experience symptoms may be more likely to report that they stayed at home. Regardless, although based on small numbers, the association between taking SARS-CoV-2 precautions and testing negative for antibodies is reassuring in terms of their effectiveness.

As of now there are only few studies on health behavior and compliance with recommendations and their impact on

COVID-19. A previous questionnaire-based study from 27 different countries including Denmark reported that elderly people aged 70 years or older were less compliant than people aged 60–70 years [16]. We cannot confirm this finding in our study; rather, older retired donors tended to adhere more strongly to official guidelines than younger donors.

Compared with retired blood donors aged 70 years or older, active blood donors aged 17-69 years twice as often reported having been sick with COVID-19 symptoms (21.9% vs 12.7%), having been tested for SARS-CoV-2 (35.8% vs 17.1% of those reporting sickness), and having had a positive SARS-CoV-2 test (7.2% vs 4.3% of those reporting test results). These differences in both COVID-19 prevalence and in test seeking may reflect age-dependent variations in mobility and in physical distancing, also apparent in the present study. Whereas precautions to limit the spread of SARS-CoV-2 with regard to handwashing, hugging, and handshaking were followed by large proportions of both active and retired donors, active donors aged 18-69 years did not stay home or avoid public transport or crowded places to the same extent as the retired blood donors aged 70 years or older. It is not surprising that individuals of working age and with children at home face problems isolating themselves from other people. This could expose them to more infectious agents and explain why the active donors report much higher disease rates than the retired donors.

Based on official Danish reports on COVID-19-related deaths, we estimated the IFR to be 5.4% in the age group of 70 years or older. This was 65 times the IFR among active blood donors aged 17–69 years. Our IFR estimate among older individuals was only slightly lower than the 6.9% recently reported from rural settings in Latin America [17]. These estimates for the elderly population are, as expected, much higher than previously reported estimates for all ages from Greece [18], China [19], and cruise ships [20] as well as the estimate we reported in the younger donor population [4].

The strength of the present study is that we have combined questionnaire data and serological SARS-CoV-2 measurements on a large population of retired Danish blood donors aged 70 years or older. In particular, blood donors are more inclined to participate in public health studies than other Danes (T. Brodersen, 2019, unpublished results) and are also familiar with the process of blood sampling, both factors adding to the participation rate. Geographically, we carried out the investigation in 3 of the 5 Danish administrative regions to ensure that regional variation in COVID-19 prevalence was represented. Indeed, we found the same geographical variation in SARS-CoV-2 seroprevalence in the older age group as that we have reported among Danish blood donors aged 17-69 years [4], which also mirrors the official incidence of COVID-19 across Denmark. Active blood donors resemble the average general population, with the exception of people with low income, people who are marginalized, and men who have had sex with men [21].

We also know that the mortality among blood donors relative quickly approaches that of the general population after cessation of the donation activity (T. Brodersen, 2019, unpublished results).

While we assume that the same participation bias applied to active and retired blood donors concerning the questionnaire part of the study, low participation rates warrant caution in the interpretation of our results. With regard to the serological survey, participants invited to blood sampling were required to be free of symptoms of infectious disease and to be able to meet for testing at a bleeding site. Diseased and immobile elderly individuals are therefore likely to be underrepresented in our study population of older retired blood donors. There have been outbreaks at Danish nursing homes that will not be reflected by this study. It is therefore unknown which way this selection has biased the estimate. However, given that the proportion of individuals above the age of 70 years who live at nursing homes is less than 5%, we assume that this bias will have limited influence on the overall result. Another possible bias is the inadequate antibody responses that are frequently seen among elderly individuals. This phenomenon has primarily been reported in studies on vaccine responses [22]. Whether the antibody response to SARS-CoV-2 infection is as inadequate as has been reported from vaccine studies is uncertain and, thus, it is not possible to quantify the impact of this bias. However, if applicable to SARS-CoV-2 infection and to the present study, we may have underestimated the SARS-CoV-2 seroprevalence among the elderly retired blood donors and consequently overestimated the corresponding IFR for this age segment.

In conclusion, this cross-sectional study on seroprevalence, self-reported disease, and compliance indicates that social distancing reduces the risk of SARS-CoV-2. In the present study, retired blood donors aged 70 years or older were able to self-isolate to a higher extent than the younger age groups, which was associated with a lower seroprevalence in the elderly population. However, the IFR among individuals aged 70 years or older is 65 times that of younger individuals, which underscores the need for continuous precautions to avoid the general spread of SARS-CoV-2.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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