Do not neglect SARS-CoV-2 hospitalization and fatality risks in the middle-aged adult population

Nathanael Lapidus, Juliette Paireau, Daniel Levy-Bruhl, Xavier de Lamballerie, Gianluca Severi, Mathilde Touvier, Marie Zins, Simon Cauchemez, Fabrice Carrat, Sapris-Sero Study Group

Do not neglect SARS-CoV-2 hospitalization and fatality risks in the middle-aged adult population.

Nathanael Lapidus [α 1]*, Juliette Paireau [α 2,3], Daniel Levy-Bruhl [3], Xavier de Lamballerie [4], Gianluca Severi [5,6], Mathilde Touvier [7] Marie Zins [8,9], Simon Cauchemez [ω 2], Fabrice Carrat [ω 1] for the SAPRIS-SERO study group[+]

[1] Sorbonne Université, Inserm, Institut Pierre-Louis d'Epidémiologie et de Santé Publique, Département de Santé Publique, Hôpital Saint-Antoine, APHP.Sorbonne Université, Paris, France

[2] Mathematical Modelling of Infectious Diseases Unit, Institut Pasteur, UMR2000, CNRS, Paris, France

[3] Santé Publique France, French National Public Health Agency, Saint-Maurice, France

[4] Unité des Virus Emergents, UVE: Aix Marseille Univ, IRD 190, INSERM 1207, IHU Méditerranée Infection, 13005, Marseille, France

[5] Department of Statistics, Computer Science and Applications, University of Florence, Italy

[6] CESP UMR1018, Université Paris-Saclay, UVSQ, Inserm, Gustave Roussy, Villejuif, France

[7] Sorbonne Paris Nord University, Inserm U1153, Inrae U1125, Cnam, Nutritional Epidemiology Research Team (EREN), Epidemiology and Statistics Research Center – University of Paris (CRESS), Bobigny, France

[8] Paris University, Paris, France

[9] Paris Saclay University, Inserm UMS 11 Villejuif, France

[α] These first authors contributed equally to this article.

[ω] These senior authors contributed equally to this article.

[+] Members of the SAPRIS-SERO study group are listed in Appendix 1.

* Correspondence: Institut Pierre Louis d'Épidémiologie et de Santé Publique, 27 rue Chaligny, 75571 Paris cedex 12, France; nathanael.lapidus@inserm.fr

Funding: The SAPRIS-SERO study was supported by Agence Nationale de la Recherche (ANR), #ANR-10-COHO-06, Fondation pour la Recherche Médicale (#20RR052-00), Inserm (Institut National de la Santé et de la Recherche Médicale, #C20-26.

Abstract:

Objectives

This study aimed at estimating the SARS-CoV-2 infection hospitalization (IHR) and infection fatality ratios (IFR) in France.

Patients and methods

A serosurvey was conducted in 9,782 subjects from two French regions with the highest incidence of COVID-19 during the first wave of the pandemic and coupled with surveillance data.

Results

IHR and IFR were 2.7% and 0.49% overall. Both were higher in men and increased exponentially with age. The relative risks of hospitalization and death were 2.1 (95% CI: 1.9-2.3) and 3.8 (2.4-4.2) per 10-year increase, meaning that IHR and IFR approximately doubled every 10 and 5 years, respectively. They were dramatically high in the very elderly (80-90 years: IHR: 26%, IFR: 9.2%), but also substantial in younger adults (40-50 years: IHR: 0.98%, IFR: 0.042%).

Conclusions

These findings support the need for comprehensive preventive measures to help reduce the spread of the virus, even in young or middle-aged adults.

Keywords: Adult; Age Specific Death Rate; COVID-19; France; SARS-CoV-2

1. Introduction

The SARS-CoV-2 infection hospitalization ratio (IHR, probability of hospitalization in infected individuals) and the infection fatality ratio (IFR, probability of death in infected individuals) are critical parameters in public health decision-making regarding prioritization of control measures. However, age- and sex-related estimates are scarce, as they need reliable cumulative estimates of past infections, hospitalizations and deaths. By May 11, 2020, the cumulative number of COVID-19-related hospitalizations and hospital deaths in France reached 96,000 and 17,000, respectively. At that time, knowledge was still limited regarding therapeutics likely to improve survival such as anticoagulants, corticosteroids or high-flow nasal oxygen. This study estimated the age- and sex-specific IFR and IHR in France for this period based on contemporary SARS-CoV-2 seroprevalence data.

2. Materials and methods

Data from a seroprevalence study performed in May-June 2020 in 20-to 90-year old subjects were used. This study included subjects from three pre-existing general adult population cohorts from Île-de-France (N=6,348) and Grand Est (N=3,434), two regions of France with the highest incidence of COVID-19 during the first wave of the pandemic (1). All participants from these cohorts with regular access to online questionnaires were invited to participate in the study and dried-blood spots were collected in a random sample among them.

In all participants, an EuroImmun IgG test against the S1 domain of the spike protein (Elisa-S1) was performed. When the Elisa-S1 optical density ratio was ≥ 0.7, two further tests (EuroImmun IgG test against Nucleocapsid protein and an in-house micro-neutralization assay to detect neutralizing anti-SARS-CoV2 antibodies) were performed. We assumed that participants with at least one positive test and no negative test were truly infected. Among the participants assumed truly infected, 82% (278/338) had three positive tests, 15% (52/338) had two positive tests and 2% (8/338) had one positive test. Since the specificity was higher than 95% for each test independently (it was 100% for the neutralization assay (2)), the likelihood of two or three false positive tests in uninfected individuals could be considered negligible and the likelihood of one false positive test in uninfected individuals was very low and concerned very few participants. We therefore assumed the specificity to be 100%. However, in this imputation model, an Elisa-S1 < 0.7 was sufficient to be classified as non-infected which may have been biased by the imperfect sensitivity of this serological method. We estimated the sensitivity of Elisa-S1 at this threshold (0.7) in participants with positive RT-PCR result in the cohort. We found that 91 participants had a positive SARS-CoV-2 RT-PCR less than 3 months before the serological test, among whom 76 had an Elisa-S1 ≥ 0.7, suggesting a sensitivity of the Elisa-S1 test at this threshold of 84% (75%, 90%). This value was in line with the sensitivity reported at a threshold of 0.8 in an evaluation performed in SARS-CoV-2 PCR+ confirmed plasma donors (90.4% [84.4%, 94.7%]) (3). To account for the imperfect sensitivity of the serological tests, we assumed an 85% sensitivity in our analyses. Sensitivity analyses were conducted regarding this parameter, with sensitivities ranging from 80% to 100%. Multiple imputation using (log-transformed) numerical values from the three serological tests, region, age and sex was used to infer the probability of infection among participants who could not be classified as either infected or uninfected (Elisa-S1 ≥ 0.7 and at least one negative test).

Seroprevalence estimates were calibrated by generalized raking in relation to census data from the general adult population, excluding nursing home residents who were not part of the cohort target population. The cumulative numbers of hospital admissions and deaths for COVID-19 were obtained from the SI-VIC database, the national exhaustive inpatient surveillance system used during the pandemic. Patients from nursing homes were removed from these counts. Since the median date of sample collection in the serosurvey was May 14, hospital admissions and deaths were considered up to May 6 and May 13 to account for estimated 11- and 19- day delays from infection to hospitalization and seroconversion, respectively (4,5), and an estimated 7-day delay from hospitalization to death (SI-VIC data (6)). We report IHR and IFR by sex and 10-year age class. Multivariable random-effect meta-regression models were fitted to estimate the relative risks (RR) of hospitalization and death according to age and sex, using age class as a continuous covariate.

3. Results

Assuming an 85% sensitivity for the serological tests, the overall estimated IHR and IFR in the French adult population (excluding nursing homes) were 2.7% (95% CI: 2.4, 3.0) and 0.49% (95% CI: 0.44, 0.56), respectively. We found a strong log-linear relationship between age and the risk of hospitalization or death, corresponding to an exponential increase in risk with age (Figure 1). The estimated IHR in 20-30, 40-50, 60-70 and 80-90-year-old subjects were 0.39% (95% CI: 0.26, 0.61), 0.98% (95% CI: 0.82, 1.2), 5.9% (95% CI: 4.5, 7.6) and 26% (95% CI: 8.5, 84), respectively (RR: 2.1 (95% CI: 1.9, 2.3) per 10-year increase). The estimated IFR in these same age groups were 0.0065% (95% CI: 0.0043, 0.010), 0.042% (95% CI: 0.035, 0.051), 0.89 (95% CI: 0.68, 1.2) and 9.2% (95% CI: 3.0, 30), respectively (RR: 3.8 (95% CI: 2.4, 4.2) per 10-year increase). Both IHR and IFR were higher in men than in women for all age classes: RR 1.5 (95% CI: 1.1, 2.1) and 2.5 (95% CI: 1.8, 3.5), respectively. IHR and IFR estimates for sensitivities ranging from 80% to 100% are reported in supplementary tables S1 and S2, respectively. These estimates are directly proportional to the assumed sensitivities, which does not impact their order of magnitude.

4. Discussion

We estimated an overall IHR of 2.7% and an IFR of 0.49% in the adult population, excluding those in nursing homes. Though these ratios may be underestimated in the elderly as nursing home residents are likely to experience poorer outcomes, our estimates are in line with earlier models (5) and various age-specific IFR estimates, worldwide (7). The IFR exponentially increases with age (doubling every 5.2 years) and is higher in men. Both IHR and IFR were dramatically elevated in the very elderly but this should not obscure substantial estimates in the young or middle-aged adult population. For example, in 20- to 30-year-old adults, the risk of death is 5 to 10 times that of a skydiving jump (1 per 100,000 jumps (8)) and in 40 to 50-year-olds, this risk of death is close to that of a BASE jump (1 to 2 per 1000 jumps (8)). As a comparison with another pandemic respiratory disease, these IFR estimates for SARS-CoV-2 are approximately 100 times as high as those for influenza A(H1N1pdm09) (1 to 10 deaths per 100,000 infections) (9). From a public health perspective, and even though substantial therapeutic improvements have certainly improved survival since data for this study were collected, these findings support the need for comprehensive preventive measures to help reduce the spread of the virus, even in young or middle-aged adults.

References

1. Carrat F, de Lamballerie X, Rahib D, Blanche H, Lapidus N, Artaud F, et al. Seroprevalence of SARS-CoV-2 among adults in three regions of France following the lockdown and associated risk factors: a multicohort study. medRxiv. 2020 Sep 18;2020.09.16.20195693.

2. Gallian P, Pastorino B, Morel P, Chiaroni J, Ninove L, de Lamballerie X. Lower prevalence of antibodies neutralizing SARS-CoV-2 in group O French blood donors. Antiviral Research. 2020 Sep 1;181:104880.

3. Patel EU, Bloch EM, Clarke W, Hsieh Y-H, Boon D, Eby Y, et al. Comparative performance of five commercially available serologic assays to detect antibodies to SARS-CoV-2 and identify individuals with high neutralizing titers. J Clin Microbiol. 2020 Nov 2.

4. Zhao J, Yuan Q, Wang H, Liu W, Liao X, Su Y, et al. Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019. Clin Infect Dis. 2020 Mar 28.

5. Salje H, Kiem CT, Lefrancq N, Courtejoie N, Bosetti P, Paireau J, et al. Estimating the burden of SARS-CoV-2 in France. Science. 2020 Jul 10;369(6500):208–11.

6. Courtejoie N, Dubost C-L. Parcours hospitalier des patients atteints de la Covid-19 lors de la première vague de l'épidémie - Ministère des Solidarités et de la Santé. Direction de la Recherche, des Études, de l'Évaluation et des Statistiques; 2020 Oct. (Les Dossiers de la Drees). Report No.: 67.

7. O'Driscoll M, Dos Santos GR, Wang L, Cummings DAT, Azman AS, Paireau J, et al. Age-specific mortality and immunity patterns of SARS-CoV-2. Nature. 2020 Nov 2;1–9.

8. Wingsuiting death and risk statistics - infographic danger percentage [Accessed 16 Oct 2020]. http://www.wingsuitfly.com/risk/4572000812

9. Wong JY, Kelly H, Ip DKM, Wu JT, Leung GM, Cowling BJ. Case fatality risk of influenza A (H1N1pdm09): a systematic review. Epidemiology. 2013 Nov;24(6):830–41.

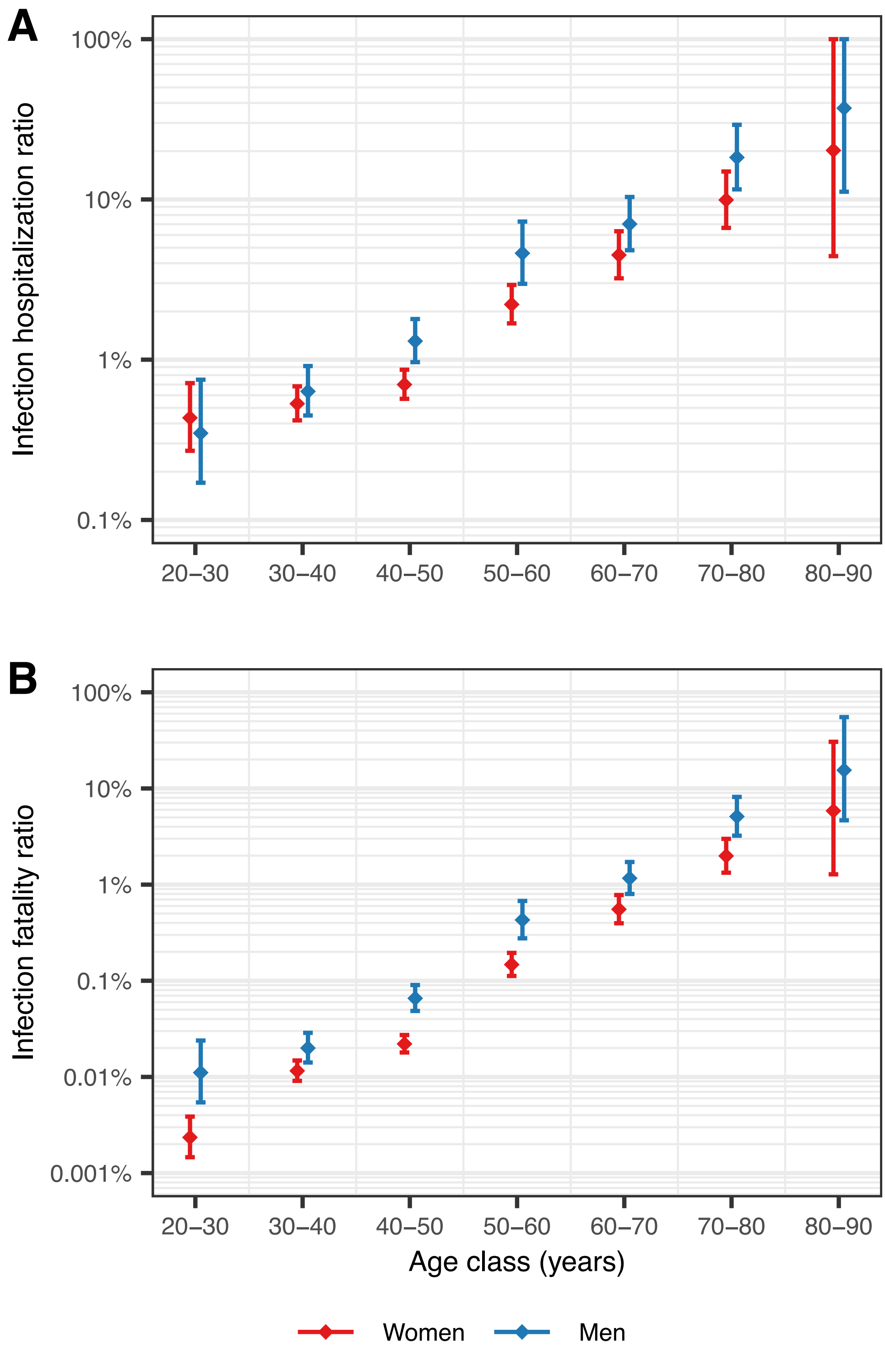

Figure 1. Infection hospitalization ratio and infection fatality ratio with 95% confidence intervals by sex and age class: **A.** Infection hospitalization ratio. **B.** Infection fatality ratio.

Appendix 1: The SAPRIS-SERO study group

Sofiane Kab, Adeline Renuy, Stephane Le-Got, Celine Ribet, Emmanuel Wiernik, Marcel Goldberg, Marie Zins (Constances cohort),

Fanny Artaud, Pascale Gerbouin-Rérolle, Mélody Enguix, Camille Laplanche, Roselyn Gomes-Rima, Lyan Hoang, Emmanuelle Correia, Alpha Amadou Barry, Nadège Senina, Gianluca Severi (E3N-E4N cohort)

Fabien Szabo de Edelenyi, Nathalie Druesne-Pecollo, Younes Esseddik, Serge Hercberg, Mathilde Touvier (NutriNet-Santé cohort)

Marie-Aline Charles, Pierre-Yves Ancel, Valérie Benhammou, Anass Ritmi, Laetitia Marchand, Cecile Zaros, Elodie Lordmi, Adriana Candea, Sophie de Visme, Thierry Simeon, Xavier Thierry, Bertrand Geay, Marie-Noelle Dufourg, Karen Milcent (Epipage2 and Elfe child cohorts)

Clovis Lusivika-Nzinga, Gregory Pannetier, Nathanael Lapidus, Frédéric Chau, Isabelle Goderel, Céline Dorival, Jérôme Nicol, Fabrice Carrat (IPLESP – methodology and coordinating data center)

Cindy Lai, Hélène Esperou, Sandrine Couffin-Cadiergues (Inserm)

Jean-Marie Gagliolo (Institut de Santé Publique)

Hélène Blanché, Jean-Marc Sébaoun, Jean-Christophe Beaudoin, Laetitia Gressin, Valérie Morel, Ouissam Ouili, Jean-François Deleuze (Fondation Jean-Dausset, CEPH-Biobank)

Stéphane Priet, Paola Mariela Saba Villarroel, Toscane Fourié, Souand Mohamed Ali, Abdenour Amroun, Morgan Seston, Nazli Ayhan, Boris Pastorino, Xavier de Lamballerie (Unité des Virus Émergents)

Appendix 2: Supplementary tables

Supplementary table S1: Estimated infection hospitalization ratios by sex and age class (years), for different hypotheses of serological test sensitivity

Sex	Age	Sensitivity = 80%	Sensitivity = 85%	Sensitivity = 90%	Sensitivity = 95%	Sensitivity = 100%
All	All	0.025 (0.023, 0.029)	0.027 (0.024, 0.030)	0.029 (0.025, 0.032)	0.030 (0.027, 0.034)	0.032 (0.028, 0.036)
	20-30	0.0037 (0.0024, 0.0058)	0.0039 (0.0026, 0.0061)	0.0042 (0.0027, 0.0065)	0.0044 (0.0029, 0.0069)	0.0046 (0.0030, 0.0072)
	30-40	0.0054 (0.0044, 0.0068)	0.0058 (0.0047, 0.0072)	0.0061 (0.0050, 0.0076)	0.0065 (0.0053, 0.0080)	0.0068 (0.0055, 0.0084)
	40-50	0.0092 (0.0077, 0.011)	0.0098 (0.0082, 0.012)	0.010 (0.0087, 0.012)	0.011 (0.0092, 0.013)	0.012 (0.0096, 0.014)
	50-60	0.031 (0.024, 0.04)	0.033 (0.026, 0.043)	0.035 (0.027, 0.045)	0.037 (0.029, 0.048)	0.039 (0.03, 0.050)
	60-70	0.055 (0.043, 0.072)	0.059 (0.045, 0.076)	0.062 (0.048, 0.081)	0.066 (0.051, 0.085)	0.069 (0.053, 0.090)
	70-80	0.13 (0.096, 0.18)	0.14 (0.10, 0.19)	0.15 (0.11, 0.20)	0.16 (0.11, 0.21)	0.16 (0.12, 0.22)
	80-90	0.24 (0.080, 0.79)	0.26 (0.085, 0.84)	0.27 (0.09, 0.89)	0.29 (0.095, 0.94)	0.30 (0.10, 0.99)
Women	All	0.019 (0.017, 0.022)	0.020 (0.018, 0.023)	0.022 (0.019, 0.025)	0.023 (0.020, 0.026)	0.024 (0.021, 0.028)
	20-30	0.0041 (0.0025, 0.0067)	0.0043 (0.0027, 0.0071)	0.0046 (0.0029, 0.0076)	0.0048 (0.0030, 0.0080)	0.0051 (0.0032, 0.0084)
	30-40	0.0050 (0.0039, 0.0064)	0.0053 (0.0042, 0.0068)	0.0056 (0.0044, 0.0072)	0.0059 (0.0047, 0.0076)	0.0063 (0.0049, 0.0080)
	40-50	0.0066 (0.0054, 0.0081)	0.0070 (0.0057, 0.0087)	0.0074 (0.0060, 0.0092)	0.0078 (0.0064, 0.0097)	0.0082 (0.0067, 0.010)
	50-60	0.021 (0.016, 0.028)	0.022 (0.017, 0.029)	0.023 (0.018, 0.031)	0.025 (0.019, 0.033)	0.026 (0.02, 0.034)
	60-70	0.042 (0.030, 0.060)	0.045 (0.032, 0.063)	0.048 (0.034, 0.067)	0.05 (0.036, 0.071)	0.053 (0.038, 0.074)
	70-80	0.093 (0.063, 0.14)	0.099 (0.066, 0.15)	0.11 (0.070, 0.16)	0.11 (0.074, 0.17)	0.12 (0.078, 0.18)
	80-90	0.19 (0.042, 1.0)	0.20 (0.044, 1.0)	0.21 (0.047, 1.0)	0.23 (0.049, 1.0)	0.24 (0.052, 1.0)
Men	All	0.032 (0.027, 0.039)	0.034 (0.028, 0.042)	0.036 (0.030, 0.044)	0.038 (0.032, 0.047)	0.040 (0.033, 0.049)
	20-30	0.0033 (0.0016, 0.0071)	0.0035 (0.0017, 0.0075)	0.0037 (0.0018, 0.0079)	0.0039 (0.0019, 0.0084)	0.0041 (0.0020, 0.0088)
	30-40	0.0060 (0.0042, 0.0086)	0.0063 (0.0045, 0.0091)	0.0067 (0.0048, 0.0097)	0.0071 (0.005, 0.010)	0.0075 (0.0053, 0.011)
	40-50	0.012 (0.0091, 0.017)	0.013 (0.0097, 0.018)	0.014 (0.010, 0.019)	0.015 (0.011, 0.020)	0.015 (0.011, 0.021)
	50-60	0.043 (0.028, 0.068)	0.046 (0.03, 0.073)	0.049 (0.031, 0.077)	0.052 (0.033, 0.081)	0.054 (0.035, 0.086)
	60-70	0.066 (0.045, 0.098)	0.07 (0.048, 0.10)	0.074 (0.051, 0.11)	0.078 (0.054, 0.12)	0.083 (0.057, 0.12)
	70-80	0.17 (0.11, 0.28)	0.18 (0.12, 0.29)	0.19 (0.12, 0.31)	0.20 (0.13, 0.33)	0.22 (0.14, 0.34)
	80-90	0.35 (0.11, 1.0)	0.37 (0.11, 1.0)	0.39 (0.12, 1.0)	0.41 (0.12, 1.0)	0.44 (0.13, 1.0)

Supplementary table S2: Estimated infection fatality ratios by sex and age class (years), for different hypotheses of serological test sensitivity

Sex	Age	Sensitivity = 80%	Sensitivity = 85%	Sensitivity = 90%	Sensitivity = 95%	Sensitivity = 100%
All	All	0.0046 (0.0041, 0.0052)	0.0049 (0.0044, 0.0056)	0.0052 (0.0047, 0.0059)	0.0055 (0.0049, 0.0062)	0.0058 (0.0052, 0.0065)
	20-30	0.000061 (0.000040, 0.000096)	0.000065 (0.000043, 0.00010)	0.000069 (0.000045, 0.00011)	0.000073 (0.000048, 0.00011)	0.000077 (0.000050, 0.00012)
	30-40	0.00015 (0.00012, 0.00018)	0.00015 (0.00013, 0.00019)	0.00016 (0.00013, 0.00020)	0.00017 (0.00014, 0.00021)	0.00018 (0.00015, 0.00023)
	40-50	0.00040 (0.00033, 0.00048)	0.00042 (0.00035, 0.00051)	0.00045 (0.00037, 0.00054)	0.00047 (0.00039, 0.00057)	0.00050 (0.00041, 0.00060)
	50-60	0.0026 (0.0020, 0.0034)	0.0028 (0.0021, 0.0036)	0.0029 (0.0023, 0.0038)	0.0031 (0.0024, 0.0040)	0.0032 (0.0025, 0.0042)
	60-70	0.0083 (0.0064, 0.011)	0.0089 (0.0068, 0.012)	0.0094 (0.0072, 0.012)	0.0099 (0.0077, 0.013)	0.010 (0.0081, 0.014)
	70-80	0.033 (0.024, 0.044)	0.035 (0.026, 0.047)	0.037 (0.027, 0.050)	0.039 (0.029, 0.053)	0.041 (0.030, 0.056)
	80-90	0.087 (0.028, 0.28)	0.092 (0.030, 0.30)	0.098 (0.032, 0.32)	0.10 (0.034, 0.34)	0.11 (0.036, 0.35)
Women	All	0.0029 (0.0025, 0.0033)	0.0031 (0.0027, 0.0035)	0.0032 (0.0028, 0.0037)	0.0034 (0.0030, 0.0039)	0.0036 (0.0031, 0.0042)
	20-30	0.000022 (0.000014, 0.000036)	0.000023 (0.000015, 0.000039)	0.000025 (0.000015, 0.000041)	0.000026 (0.000016, 0.000043)	0.000028 (0.000017, 0.000045)
	30-40	0.00011 (0.000086, 0.00014)	0.00012 (0.000091, 0.00015)	0.00012 (0.000096, 0.00016)	0.00013 (0.00010, 0.00017)	0.00014 (0.00011, 0.00017)
	40-50	0.00021 (0.00017, 0.00026)	0.00022 (0.00018, 0.00027)	0.00023 (0.00019, 0.00029)	0.00025 (0.00020, 0.00030)	0.00026 (0.00021, 0.00032)
	50-60	0.0014 (0.0011, 0.0018)	0.0015 (0.0011, 0.0019)	0.0016 (0.0012, 0.0021)	0.0016 (0.0013, 0.0022)	0.0017 (0.0013, 0.0023)
	60-70	0.0052 (0.0037, 0.0073)	0.0055 (0.0040, 0.0078)	0.0059 (0.0042, 0.0083)	0.0062 (0.0044, 0.0087)	0.0065 (0.0047, 0.0092)
	70-80	0.019 (0.013, 0.028)	0.020 (0.013, 0.030)	0.021 (0.014, 0.032)	0.022 (0.015, 0.033)	0.023 (0.016, 0.035)
	80-90	0.055 (0.012, 0.29)	0.059 (0.013, 0.31)	0.062 (0.014, 0.32)	0.065 (0.014, 0.34)	0.069 (0.015, 0.36)
Men	All	0.0066 (0.0055, 0.0081)	0.0070 (0.0058, 0.0086)	0.0075 (0.0062, 0.0091)	0.0079 (0.0065, 0.0096)	0.0083 (0.0068, 0.010)
	20-30	0.00010 (0.000051, 0.00022)	0.00011 (0.000054, 0.00024)	0.00012 (0.000058, 0.00025)	0.00012 (0.000061, 0.00027)	0.00013 (0.000064, 0.00028)
	30-40	0.00019 (0.00013, 0.00027)	0.00020 (0.00014, 0.00029)	0.00021 (0.00015, 0.00030)	0.00022 (0.00016, 0.00032)	0.00023 (0.00017, 0.00034)
	40-50	0.00062 (0.00046, 0.00085)	0.00066 (0.00049, 0.00090)	0.00070 (0.00051, 0.00095)	0.00073 (0.00054, 0.0010)	0.00077 (0.00057, 0.0011)
	50-60	0.0040 (0.0026, 0.0064)	0.0043 (0.0028, 0.0068)	0.0045 (0.0029, 0.0072)	0.0048 (0.0031, 0.0076)	0.0050 (0.0033, 0.0080)
	60-70	0.011 (0.0075, 0.016)	0.012 (0.0080, 0.017)	0.012 (0.0085, 0.018)	0.013 (0.0089, 0.019)	0.014 (0.0094, 0.020)
	70-80	0.048 (0.030, 0.077)	0.051 (0.032, 0.082)	0.054 (0.034, 0.086)	0.057 (0.036, 0.091)	0.06 (0.038, 0.096)
	80-90	0.15 (0.044, 0.52)	0.15 (0.047, 0.55)	0.16 (0.049, 0.58)	0.17 (0.052, 0.62)	0.18 (0.055, 0.65)