

## **SUPPLEMENTARY MATERIAL**

Supplement to: Pérez-Gómez B, Pastor-Barriuso R, Pérez-Olmeda M, et al. ENE-COVID nationwide serosurvey served to characterize asymptomatic infections and to develop a symptom-based risk score to predict COVID-19. *J Clin Epidemiol* 2021.

<b>Contents</b>	<b>Page</b>
ENE-COVID Study Group	2
Supplementary Table 1	7
Supplementary Table 2	9
Supplementary Table 3	10
Supplementary Table 4	11
Supplementary Figure 1	13
Supplementary Figure 2	14
Supplementary Figure 3	15
Supplementary Figure 4	16

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**Supplementary Table 1.** Difference in prevalence of asymptomatic SARS-CoV-2 infection by participant characteristics, case contact, and residential features, ENE-COVID study, April 27–June 22, 2020, Spain.\*

Characteristic	No. of asymptomatic <sup>†</sup> / positive cases	Asymptomatic prevalence <sup>‡</sup> (%; 95% CI)	Crude prevalence difference (%; 95% CI)	Standardized prevalence difference <sup>§</sup> (%; 95% CI)
Overall	781/2,669	28.7 (26.1–31.4)		
Sex				
Men	406/1,246	31.8 (28.4–35.5)	0.0 (reference)	0.0 (reference)
Women	375/1,423	25.8 (22.5–29.5)	–6.0 (–10.6 to –1.4)	–5.0 (–9.6 to –0.5)
Age (years)				
0–19	118/280	44.9 (36.4–53.7)	23.1 (13.7 to 32.5)	18.9 (7.4 to 30.3)
20–39	143/585	25.0 (20.6–30.0)	3.2 (–2.2 to 8.6)	4.1 (–1.6 to 9.8)
40–59	259/1,071	21.8 (18.8–25.1)	0.0 (reference)	0.0 (reference)
60–79	215/621	31.1 (26.3–36.4)	9.3 (3.5 to 15.2)	5.5 (–1.8 to 12.8)
≥80	46/112	36.1 (25.4–48.5)	14.3 (2.1 to 26.5)	10.3 (–2.5 to 23.1)
Nationality				
Spain	754/2,555	29.3 (26.7–32.2)	0.0 (reference)	0.0 (reference)
Other	27/114	17.7 (10.6–28.2)	–11.6 (–20.6 to –2.6)	–8.9 (–18.5 to 0.6)
Occupation				
Online work	126/651	19.6 (15.9–23.9)	0.0 (reference)	0.0 (reference)
Non-healthcare on-site	163/555	27.7 (22.9–33.0)	8.1 (1.9 to 14.3)	5.3 (–1.2 to 11.8)
Healthcare	43/211	16.9 (11.9–23.6)	–2.6 (–9.3 to 4.1)	–0.4 (–8.3 to 7.5)
Unemployed	44/143	31.8 (22.3–43.1)	12.2 (0.8 to 23.7)	7.6 (–3.0 to 18.2)
Not economically active	405/1,107	36.1 (31.6–40.9)	16.5 (10.6 to 22.5)	6.2 (–1.4 to 13.7)
Smoking				
No	634/2,229	27.8 (25.0–30.8)	0.0 (reference)	0.0 (reference)
Yes	143/433	33.0 (27.2–39.4)	5.2 (–1.4 to 11.8)	7.3 (0.5 to 14.2)
Body mass index <sup>¶</sup> (kg/m <sup>2</sup> )				
<25	260/1,019	25.6 (22.0–29.6)	0.0 (reference)	0.0 (reference)
25–30	275/912	26.9 (23.0–31.2)	1.3 (–4.2 to 6.8)	–1.9 (–7.2 to 3.3)
≥30	128/458	23.9 (18.9–29.8)	–1.6 (–7.9 to 4.7)	–3.9 (–9.9 to 2.1)
No. of chronic conditions <sup>  </sup>				
0	269/999	23.5 (20.3–27.1)	0.0 (reference)	0.0 (reference)
1	134/412	27.8 (22.6–33.6)	4.2 (–1.9 to 10.4)	0.3 (–5.9 to 6.4)
2	79/255	32.3 (25.8–39.7)	8.8 (1.1 to 16.5)	1.4 (–5.7 to 8.5)
≥3	38/138	27.4 (18.5–38.6)	3.9 (–6.9 to 14.6)	–1.8 (–11.9 to 8.3)
Contact with COVID-19 case				
No known contact	497/1,189	41.4 (37.3–45.8)	0.0 (reference)	0.0 (reference)
Non-cohab. suspected case	35/225	15.5 (10.0–23.4)	–25.9 (–33.9 to –18.0)	–22.1 (–30.4 to –13.7)
Non-cohab. confirmed case	93/492	18.8 (14.3–24.3)	–22.7 (–28.9 to –16.5)	–16.6 (–23.7 to –9.4)
Cohab. suspected case	72/397	18.8 (13.8–25.3)	–22.6 (–29.7 to –15.5)	–20.2 (–26.9 to –13.4)
Cohab. confirmed case	81/360	22.9 (17.1–30.0)	–18.5 (–26.0 to –11.0)	–16.4 (–23.8 to –9.0)
Household size (residents)				
1	65/225	27.0 (20.7–34.3)	–3.9 (–12.0 to 4.2)	–1.7 (–10.1 to 6.6)
2	204/667	28.7 (24.2–33.7)	–2.1 (–8.6 to 4.4)	–2.1 (–8.5 to 4.4)
3	191/644	28.4 (23.7–33.7)	–2.4 (–8.5 to 3.7)	–1.5 (–7.8 to 4.8)
4	231/806	30.8 (26.4–35.6)	0.0 (reference)	0.0 (reference)
≥5	90/327	24.3 (17.6–32.5)	–6.6 (–15.5 to 2.4)	–4.6 (–12.5 to 3.3)
Census tract average income				
<25th percentile	232/737	29.0 (24.2–34.4)	0.0 (reference)	0.0 (reference)
25–50th percentile	183/561	30.7 (25.1–36.9)	1.7 (–6.1 to 9.5)	3.0 (–3.9 to 10.0)
50–75th percentile	168/559	27.4 (22.4–33.0)	–1.6 (–9.0 to 5.8)	0.7 (–5.7 to 7.0)
≥75th percentile	198/812	27.5 (22.6–33.0)	–1.5 (–8.8 to 5.8)	0.5 (–6.5 to 7.6)

(Table continues)

**Supplementary Table 1** (continued).

<b>Characteristic</b>	<b>No. of asymptomatic<sup>†</sup>/ positive cases</b>	<b>Asymptomatic prevalence<sup>‡</sup> (%; 95% CI)</b>	<b>Crude prevalence difference (%; 95% CI)</b>	<b>Standardized prevalence difference<sup>§</sup> (%; 95% CI)</b>
Municipality size (inhabitants)				
<5,000	203/511	36.6 (30.8–42.9)	0.0 (reference)	0.0 (reference)
5,000–20,000	170/507	36.2 (31.2–41.5)	–0.4 (–8.4 to 7.6)	–2.0 (–9.4 to 5.4)
20,000–100,000	183/720	27.5 (22.3–33.3)	–9.2 (–17.4 to –1.0)	–7.9 (–15.2 to –0.5)
≥100,000	225/931	26.0 (22.1–30.2)	–10.7 (–18.0 to –3.4)	–6.8 (–14.0 to 0.3)
Province seroprevalence (%)				
<3	205/505	40.3 (35.0–45.9)	0.0 (reference)	0.0 (reference)
3–5	177/586	30.0 (25.2–35.4)	–10.3 (–17.8 to –2.8)	–8.8 (–15.7 to –1.9)
5–10	126/432	26.9 (21.9–32.7)	–13.4 (–21.1 to –5.7)	–8.3 (–15.6 to –1.0)
≥10	273/1,146	24.7 (20.6–29.4)	–15.6 (–22.6 to –8.6)	–9.9 (–16.6 to –3.3)
Entry round				
First (April 27–May 11)	674/2,291	28.5 (25.7–31.4)	0.0 (reference)	0.0 (reference)
Second (May 18–June 1)	83/305	28.0 (21.5–35.7)	–0.5 (–8.2 to 7.3)	0.7 (–6.9 to 8.3)
Third (June 8–June 22)	24/73	37.3 (22.1–55.5)	8.8 (–8.5 to 26.2)	1.5 (–12.3 to 15.4)

\* Analyses restricted to 2,669 seropositive participants with detectable IgG antibodies against SARS-CoV-2 by the chemiluminescent microparticle immunoassay.

<sup>†</sup> Number of seropositive participants without previous self-reported symptoms, including fever, chills, severe tiredness, sore throat, cough, shortness of breath, headache, nausea/vomiting/diarrhea, and anosmia/ageusia.

<sup>‡</sup> Population prevalence of asymptomatic SARS-CoV-2 infection and 95% confidence interval (CI) accounting for sampling weights, non-response rates by sex, age, and census tract average income, stratification by province and municipality size, and clustering by household and census tract.

<sup>§</sup> Prevalence difference of asymptomatic SARS-CoV-2 infection and 95% confidence interval (CI) standardized to the overall distribution of all other characteristics presented in the table in the entire seropositive population in Spain.

<sup>¶</sup> Among seropositive participants aged 20 years or older.

<sup>||</sup> Among seropositive participants aged 40 years or older.



**Supplementary Table 2.** Difference in SARS-CoV-2 seroprevalence among participants with self-reported symptoms compatible with COVID-19, ENE-COVID study, April 27–June 22, 2020, Spain.\*

Symptom	No. of positive cases†/ symptomatic participants	SARS-CoV-2 seroprevalence‡ (%; 95% CI)	Crude seroprevalence difference (%; 95% CI)	Standardized seroprevalence difference§ (%; 95% CI)
Overall	1,733/16,437	10.8 (10.0–11.7)		
Fever				
No	797/11,890	6.8 (6.1–7.5)	0.0 (reference)	0.0 (reference)
Yes	936/4,547	20.1 (18.2–22.2)	13.4 (11.4 to 15.3)	5.7 (4.2 to 7.3)
Chills				
No	1,006/12,232	8.5 (7.8–9.4)	0.0 (reference)	0.0 (reference)
Yes	727/4,205	17.5 (15.6–19.5)	8.9 (7.0 to 10.8)	0.2 (–1.2 to 1.6)
Severe tiredness				
No	774/11,127	6.9 (6.2–7.7)	0.0 (reference)	0.0 (reference)
Yes	959/5,310	19.1 (17.3–20.9)	12.1 (10.3 to 13.9)	3.2 (1.8 to 4.7)
Sore throat				
No	1,079/9,726	11.2 (10.2–12.3)	0.0 (reference)	0.0 (reference)
Yes	654/6,711	10.3 (9.2–11.6)	–0.9 (–2.3 to 0.5)	–3.0 (–4.2 to –1.9)
Cough				
No	799/8,320	9.6 (8.6–10.6)	0.0 (reference)	0.0 (reference)
Yes	934/8,117	12.1 (11.0–13.4)	2.6 (1.2 to 4.0)	0.2 (–1.0 to 1.3)
Shortness of breath				
No	1,266/13,213	9.7 (8.9–10.6)	0.0 (reference)	0.0 (reference)
Yes	467/3,224	15.5 (13.7–17.6)	5.8 (3.9 to 7.8)	–0.1 (–1.5 to 1.2)
Headache				
No	768/8,008	9.6 (8.7–10.6)	0.0 (reference)	0.0 (reference)
Yes	965/8,429	12.0 (10.8–13.2)	2.4 (1.0 to 3.7)	–0.9 (–2.1 to 0.2)
Nausea/vomiting/diarrhea				
No	1,136/12,533	9.4 (8.6–10.3)	0.0 (reference)	0.0 (reference)
Yes	597/3,904	15.3 (13.6–17.1)	5.9 (4.2 to 7.6)	0.6 (–0.5 to 1.8)
Anosmia/ageusia				
No	884/14,589	6.3 (5.7–7.0)	0.0 (reference)	0.0 (reference)
Yes	849/1,848	46.2 (42.8–49.7)	39.9 (36.5 to 43.3)	22.6 (19.7 to 25.6)
No. of symptoms				
1–2	547/9,157	5.8 (5.2–6.5)	0.0 (reference)	0.0 (reference)
3–4	446/4,115	11.7 (10.2–13.3)	5.8 (4.3 to 7.4)	4.8 (3.3 to 6.2)
5–6	432/2,124	19.4 (17.0–21.9)	13.5 (11.0 to 16.0)	10.2 (8.1 to 12.3)
7–9	308/1,041	31.0 (26.9–35.4)	25.1 (20.9 to 29.4)	17.2 (14.0 to 20.4)
Symptomatic risk score¶				
0–1	352/9,574	3.9 (3.4–4.5)	0.0 (reference)	0.0 (reference)
2–3	380/4,211	9.2 (8.0–10.7)	5.4 (4.0 to 6.8)	4.8 (3.4 to 6.2)
4–5	195/964	19.4 (16.2–23.2)	15.5 (12.0 to 19.1)	12.7 (9.8 to 15.7)
6–7	344/845	40.8 (36.2–45.5)	36.9 (32.3 to 41.6)	25.9 (21.7 to 30.0)
8–9	462/843	54.4 (49.5–59.2)	50.5 (45.7 to 55.3)	35.6 (31.3 to 39.8)

\* Analyses restricted to 16,437 symptomatic participants with symptom onset at least 21 days before blood draw.

† Number of symptomatic participants with detectable IgG antibodies against SARS-CoV-2 by the chemiluminescent microparticle immunoassay.

‡ Population seroprevalence of SARS-CoV-2 and 95% confidence interval (CI) accounting for sampling weights, non-response rates by sex, age, and census tract average income, stratification by province and municipality size, and clustering by household and census tract.

§ Difference of SARS-CoV-2 seroprevalence and 95% confidence interval (CI) standardized to the overall distribution of sex, age group, nationality, occupation, smoking, body mass index, number of chronic conditions, contact with COVID-19 case, household size, census tract average income, municipality size, province seroprevalence, and entry round in the entire symptomatic population in Spain. Seroprevalence differences for individual symptoms were further standardized to the overall distribution of all other symptoms.

¶ Symptomatic risk score assigning a weight of 1 to severe tiredness, 2 to fever, and 5 to anosmia/ageusia, together with a weight of 1 to absence of sore throat, which were proportional to their individual log-transformed standardized ratios and rounded to the nearest integer.

**Supplementary Table 3.** Discrimination of symptomatic risk score for predicting SARS-CoV-2 seropositivity among participants with self-reported symptoms compatible with COVID-19, ENE-COVID study, April 27–June 22, 2020, Spain.\*

Characteristic	Seropositive cases		Seronegative individuals		Discrimination index§ (95% CI)
	No.†	Symptomatic risk score‡	No.†	Symptomatic risk score‡	
Overall	1,733	4.70 (2.88)	14,704	1.75 (1.79)	0.789 (0.771–0.806)
Sex					
Men	790	4.66 (2.75)	6,161	1.73 (1.69)	0.805 (0.782–0.828)
Women	943	4.73 (2.99)	8,543	1.77 (1.86)	0.775 (0.750–0.802)
Age (years)					
0–19	133	3.37 (2.06)	1,875	1.90 (1.39)	0.685 (0.614–0.755)
20–39	404	4.77 (2.58)	4,125	1.78 (1.80)	0.792 (0.758–0.829)
40–59	761	5.11 (3.19)	5,868	1.68 (1.93)	0.813 (0.789–0.835)
60–79	377	4.63 (2.85)	2,470	1.70 (1.92)	0.806 (0.773–0.837)
≥80	58	4.05 (2.94)	366	1.56 (1.44)	0.727 (0.623–0.829)
Smoking					
No	1,469	4.66 (2.87)	10,373	1.69 (1.72)	0.794 (0.775–0.812)
Yes	263	4.91 (2.93)	4,328	1.91 (1.95)	0.777 (0.733–0.821)
Body mass index¶ (kg/m <sup>2</sup> )					
<25	711	4.67 (2.90)	5,902	1.74 (1.89)	0.785 (0.758–0.808)
25–30	590	4.90 (2.94)	4,542	1.67 (1.79)	0.810 (0.782–0.838)
≥30	299	5.23 (2.97)	2,385	1.77 (1.97)	0.825 (0.788–0.861)
No. of chronic conditions					
0	682	5.00 (3.16)	4,781	1.67 (1.96)	0.806 (0.778–0.832)
1	260	4.99 (2.90)	2,032	1.60 (1.82)	0.836 (0.800–0.871)
2	164	4.29 (2.98)	1,135	1.71 (1.87)	0.779 (0.725–0.831)
≥3	90	4.80 (3.13)	756	1.93 (1.87)	0.764 (0.687–0.840)
Contact with COVID-19 case					
No known contact	613	4.19 (2.84)	10,095	1.67 (1.71)	0.763 (0.733–0.792)
Non-cohab. suspected case	178	4.84 (2.61)	1,444	1.88 (1.82)	0.776 (0.721–0.827)
Non-cohab. confirmed case	378	4.99 (2.89)	1,508	1.85 (1.90)	0.810 (0.776–0.842)
Cohab. suspected case	304	4.95 (2.98)	1,408	1.94 (1.98)	0.787 (0.744–0.831)
Cohab. confirmed case	259	5.04 (2.86)	246	2.43 (2.18)	0.741 (0.676–0.804)
Province seroprevalence (%)					
<3	266	4.08 (3.08)	6,917	1.64 (1.72)	0.735 (0.691–0.775)
3–5	370	4.59 (3.53)	3,811	1.73 (2.00)	0.787 (0.756–0.819)
5–10	281	5.18 (2.59)	1,645	1.77 (1.52)	0.810 (0.768–0.853)
≥10	816	4.70 (2.69)	2,331	2.02 (1.80)	0.770 (0.743–0.796)

\* Analyses restricted to 16,437 symptomatic participants with symptom onset at least 21 days before blood draw.

† Number of symptomatic participants with detectable and undetectable IgG antibodies against SARS-CoV-2 by the chemiluminescent microparticle immunoassay.

‡ Weighted mean (standard deviation) of symptomatic risk score among seropositive and seronegative individuals, assigning a weight of 1 to severe tiredness and absence of sore throat, 2 to fever, and 5 to anosmia/ageusia.

§ The population discrimination index was calculated as the weighted proportion of seropositive-negative pairs in which the seropositive case had a higher symptomatic risk score on 1,000 design-based bootstrap samples, obtaining an overfitting-corrected discrimination index and 95% confidence interval (CI) as the mean and the 2.5th to 97.5th percentiles of the bootstrap replications.

¶ Among symptomatic participants aged 20 years or older.

|| Among symptomatic participants aged 40 years or older.

**Supplementary Table 4.** Diagnostic performance and predictive value of symptomatic risk score equal to or greater than 3 for SARS-CoV-2 seropositivity among participants with self-reported symptoms compatible with COVID-19, ENE-COVID study, April 27–June 22, 2020, Spain.\*

Characteristic	Symptomatic risk score in seropositive cases†		Symptomatic risk score in seronegative individuals†		Sensitivity‡ (%; 95% CI)	Specificity§ (%; 95% CI)	Positive predictive value‡ (%; 95% CI)	Negative predictive value§ (%; 95% CI)
	0–2	3–9	0–2	3–9				
Overall	503	1,230	11,157	3,547	71.4 (68.1–74.4)	74.2 (73.1–75.2)	25.1 (23.1–27.3)	95.5 (94.9–96.1)
Sex								
Men	220	570	4,683	1,478	73.6 (69.3–77.4)	74.2 (72.7–75.7)	27.2 (24.5–30.2)	95.5 (94.7–96.2)
Women	283	660	6,474	2,069	69.5 (65.1–73.5)	74.1 (72.7–75.4)	23.5 (21.3–25.9)	95.5 (94.7–96.2)
Age (years)								
0–19	53	80	1,240	635	62.4 (50.6–72.9)	65.9 (62.8–68.8)	10.8 (8.1–14.3)	96.3 (94.7–97.5)
20–39	101	303	3,073	1,052	73.4 (67.2–78.8)	73.1 (71.2–74.8)	23.6 (20.6–26.9)	96.0 (94.9–96.9)
40–59	213	548	4,572	1,296	73.7 (69.2–77.7)	77.4 (75.9–78.8)	30.2 (27.0–33.6)	95.7 (94.8–96.4)
60–79	110	267	1,971	499	71.8 (65.5–77.3)	78.1 (75.8–80.3)	35.8 (31.0–40.9)	94.2 (92.6–95.5)
≥80	26	32	301	65	54.9 (37.5–71.2)	82.4 (76.6–87.0)	38.7 (25.0–54.5)	90.0 (84.2–93.8)
Smoking								
No	419	1,050	7,926	2,447	71.3 (67.8–74.5)	74.7 (73.3–75.9)	28.8 (26.4–31.4)	94.8 (94.0–95.4)
Yes	84	179	3,228	1,100	71.8 (64.1–78.4)	72.8 (71.0–74.5)	14.4 (11.9–17.3)	97.6 (96.8–98.2)
Body mass index¶ (kg/m <sup>2</sup> )								
<25	203	508	4,503	1,399	70.7 (66.5–74.6)	74.8 (73.3–76.3)	26.5 (23.5–29.6)	95.2 (94.2–96.1)
25–30	173	417	3,595	947	72.4 (67.1–77.1)	78.1 (76.5–79.6)	31.9 (28.5–35.4)	95.2 (94.2–96.1)
≥30	74	225	1,819	566	76.6 (69.8–82.3)	75.5 (73.2–77.7)	30.2 (25.3–35.5)	95.9 (94.5–97.0)
No. of chronic conditions								
0	198	484	3,752	1,029	72.0 (67.0–76.5)	77.8 (76.2–79.2)	32.5 (29.0–36.2)	94.9 (93.8–95.8)
1	75	185	1,635	397	74.2 (66.3–80.8)	79.8 (77.5–82.0)	35.2 (30.0–40.8)	95.5 (93.8–96.7)
2	46	118	887	248	70.1 (60.4–78.3)	76.4 (73.0–79.5)	30.1 (24.2–36.6)	94.6 (92.4–96.3)
≥3	30	60	570	186	67.7 (54.7–78.5)	74.8 (70.3–78.8)	26.2 (19.3–34.6)	94.6 (91.6–96.6)
Contact with COVID-19 case								
No known contact	211	402	7,850	2,245	67.8 (62.3–72.8)	75.8 (74.6–77.1)	14.6 (12.7–16.8)	97.5 (96.9–97.9)
Non-cohab. suspected case	48	130	1,053	391	70.4 (61.0–78.3)	70.1 (66.7–73.4)	27.0 (22.1–32.6)	93.8 (91.3–95.6)
Non-cohab. confirmed case	100	278	1,117	391	74.8 (68.7–80.0)	74.1 (70.7–77.2)	41.1 (35.5–47.0)	92.4 (90.3–94.1)
Cohab. suspected case	72	232	975	433	73.2 (65.5–79.8)	69.5 (65.8–73.0)	32.0 (26.9–37.5)	93.0 (90.1–95.1)
Cohab. confirmed case	72	187	159	87	73.5 (64.9–80.6)	59.9 (50.9–68.2)	67.5 (58.5–75.4)	66.5 (56.7–75.1)

(Table continues)

**Supplementary Table 4** (continued).

Characteristic	Symptomatic risk score in seropositive cases†		Symptomatic risk score in seronegative individuals†		Sensitivity‡ (%; 95% CI)	Specificity§ (%; 95% CI)	Positive predictive value‡ (%; 95% CI)	Negative predictive value§ (%; 95% CI)
	0–2	3–9	0–2	3–9				
Province seroprevalence (%)								
<3	113	153	5,392	1,525	59.5 (52.1–66.4)	77.0 (75.6–78.4)	8.8 (7.1–10.9)	98.1 (97.5–98.5)
3–5	103	267	2,870	941	72.4 (66.8–77.4)	74.1 (72.0–76.1)	19.8 (16.7–23.5)	96.8 (95.9–97.5)
5–10	75	206	1,231	414	75.0 (67.3–81.4)	74.6 (71.2–77.6)	31.5 (25.5–38.2)	95.0 (93.4–96.3)
≥10	212	604	1,664	667	72.8 (67.8–77.4)	67.2 (64.1–70.1)	41.7 (37.5–46.0)	88.5 (85.8–90.7)

\* Analyses restricted to 16,437 symptomatic participants with onset of symptoms at least 21 days before blood draw. The value of 3 for the symptomatic risk score corresponded to the optimal diagnostic threshold that minimized the overall misclassification rate.

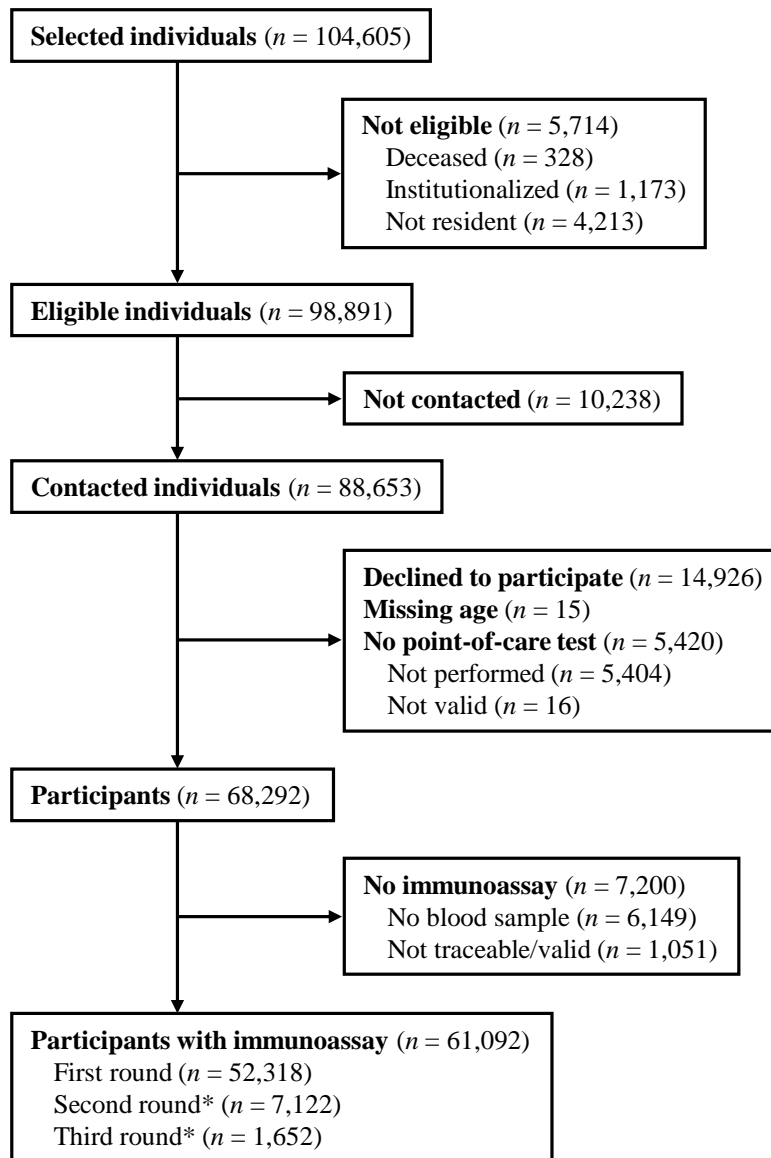
† Number of seropositive and seronegative participants with symptomatic risk score of 0–2 and 3–9, assigning a weight of 1 to severe tiredness and absence of sore throat, 2 to fever, and 5 to anosmia/ageusia.

‡ Population sensitivity and positive predictive value with 95% confidence intervals (CIs) for symptomatic risk score equal to or greater than 3, accounting for sampling weights, non-response rates by sex, age, and census tract average income, stratification by province and municipality size, and clustering by household and census tract.

§ Population specificity and negative predictive value with 95% confidence intervals (CIs) for symptomatic risk score less than or equal to 2, accounting for sampling weights, non-response rates by sex, age, and census tract average income, stratification by province and municipality size, and clustering by household and census tract.

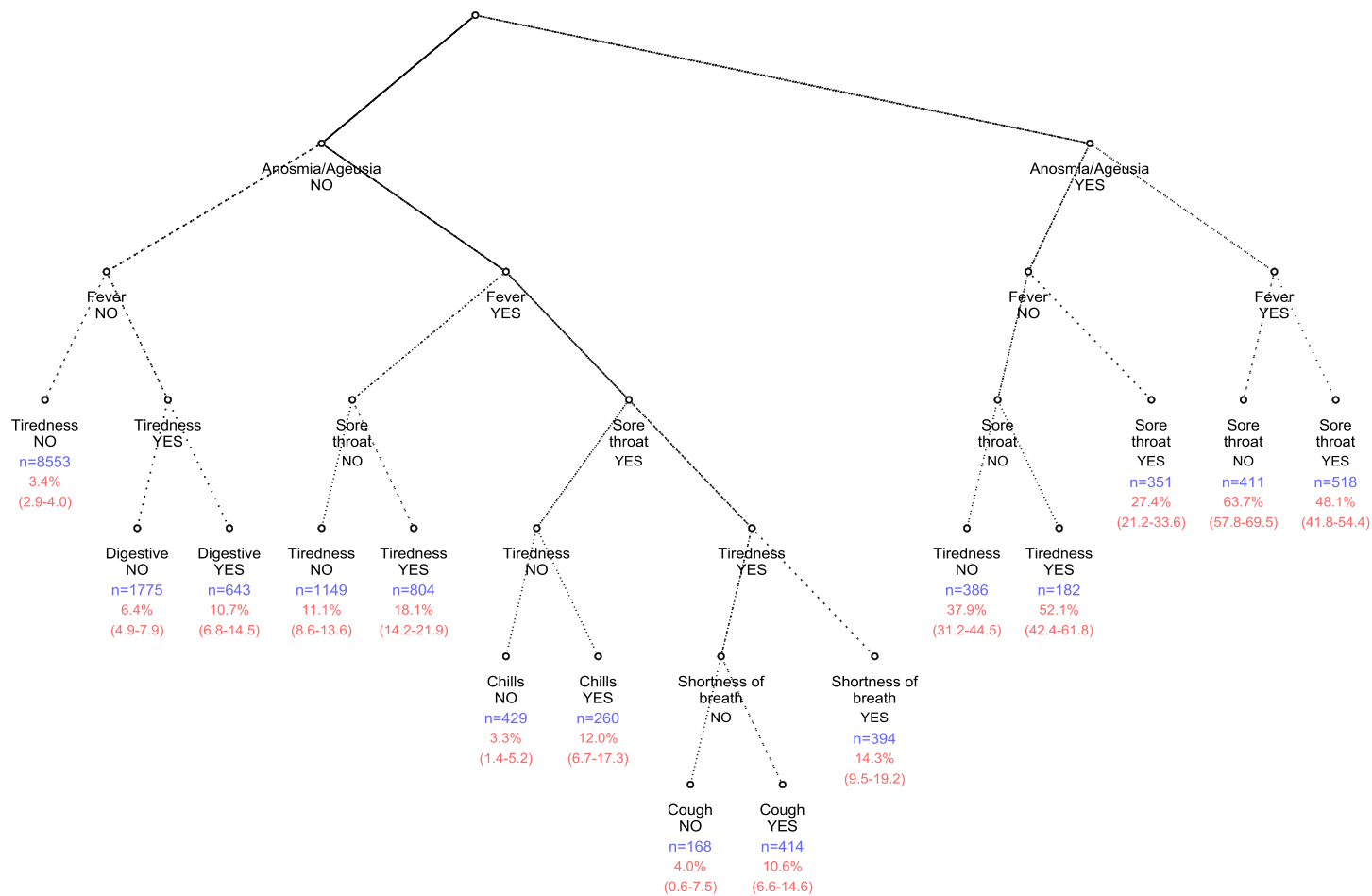
¶ Among symptomatic participants aged 20 years or older.

|| Among symptomatic participants aged 40 years or older.



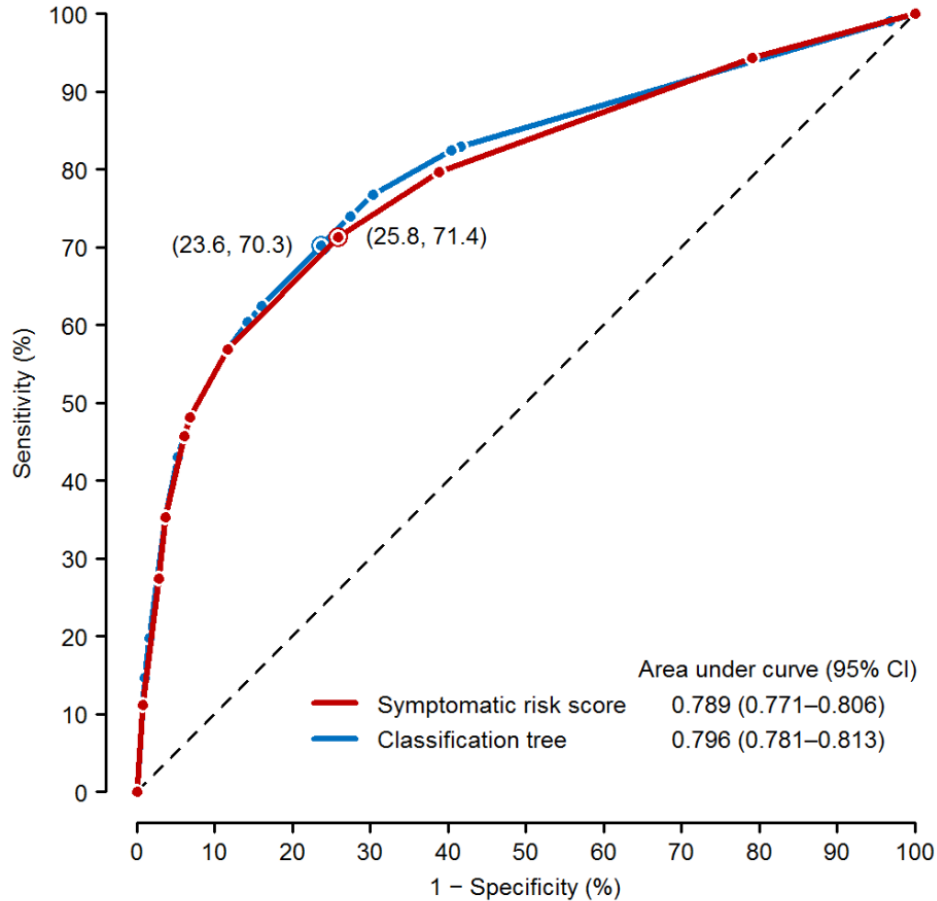
**Supplementary Figure 1.** Flow chart of participants, ENE-COVID study, April 27–June 22, 2020, Spain.

\* Participants with chemiluminescent microparticle immunoassay in second or third round but not in previous rounds.



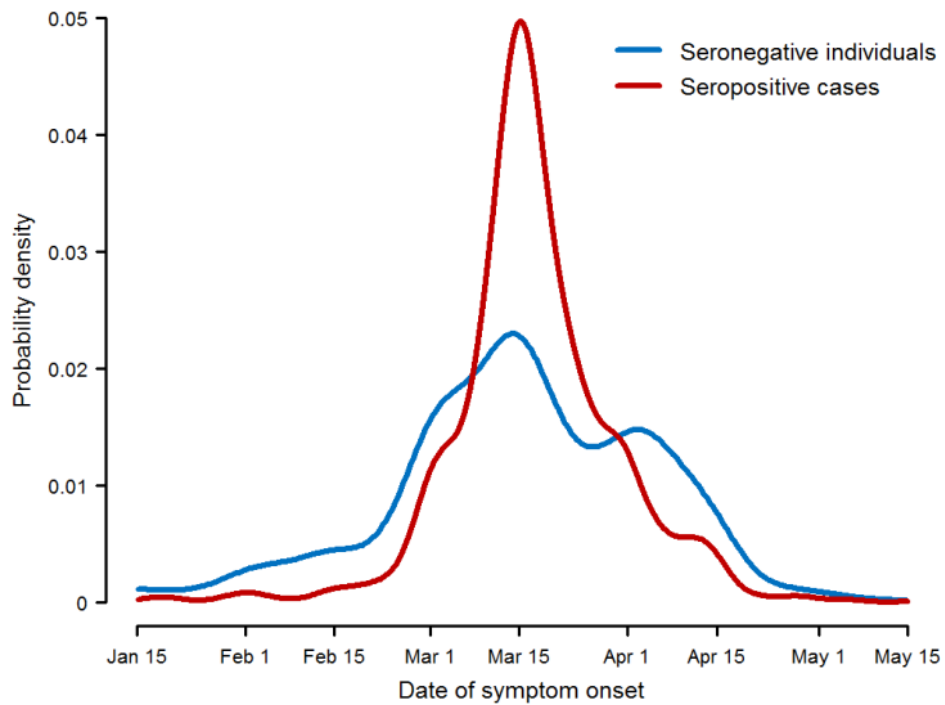
**Supplementary Figure 2.** Classification tree for SARS-CoV-2 seropositivity based on symptoms among participants with self-reported symptoms compatible with COVID-19, ENE-COVID study, April 27–June 22, 2020, Spain.

Analyses restricted to 16,437 symptomatic participants with onset of symptoms at least 21 days before blood draw. The classification tree used the chi-square automatic interaction detection algorithm to recursively split nodes based on symptoms with the lowest Bonferroni-corrected  $p$  values obtained from design-based logistic regression models. The numbers in blue under terminal nodes indicate participants and the percentages in red indicate SARS-CoV-2 seroprevalences and 95% confidence intervals.



**Supplementary Figure 3.** ROC curves of symptomatic risk score and classification tree for predicting SARS-CoV-2 seropositivity among participants with self-reported symptoms compatible with COVID-19, ENE-COVID study, April 27–June 22, 2020, Spain.

Analyses restricted to 16,437 symptomatic participants with onset of symptoms at least 21 days before blood draw. The symptomatic risk score assigned a weight of 1 to severe tiredness and absence of sore throat, 2 to fever, and 5 to anosmia/ageusia. The classification tree assigned predicted probabilities equal to SARS-CoV-2 seroprevalences at terminal nodes. Sensitivities and specificities were estimated accounting for sampling weights and non-response rates. The outlined point on the ROC curves corresponded to the optimal threshold that minimized the overall misclassification rate (symptomatic risk score  $\geq 3$  and tree-based predicted probability  $\geq 0.111$ ). The area under the ROC curves and its 95% confidence interval (CI) were calculated as the mean and the 2.5th to 97.5th percentiles of 1,000 design-based bootstrap replications.



**Supplementary Figure 4.** Distribution of date of symptom onset among seropositive and seronegative individuals for SARS-CoV-2, ENE-COVID study, April 27–June 22, 2020, Spain.

Analyses restricted to 16,437 symptomatic participants with onset of symptoms at least 21 days before blood draw. Probability density functions were estimated using Gaussian kernel smoothers with a bandwidth of one-fifth their standard deviations and accounted for sampling weights and non-response rates.