SARS-CoV-2 (COVID-19) infection in pregnant women: characterization of symptoms and syndromes predictive of disease and severity through real-time, remote participatory epidemiology.

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Abstract

Background: From the beginning of COVID-19 pandemic, pregnant women have been considered at greater risk of severe morbidity and mortality. However, data on hospitalized pregnant women show that the symptom profile and risk factors for severe disease are similar to those among women who are not pregnant, although preterm birth, Cesarean delivery, and stillbirth may be more frequent and vertical transmission is possible. Limited data are available for the cohort of pregnant women that gave rise to these hospitalized cases, hindering our ability to quantify risk of COVID-19 sequelae for pregnant women in the community.

Objective: To test the hypothesis that pregnant women in community differ in their COVID-19 symptoms profile and disease severity compared to non-pregnant women. This was assessed in two community-based cohorts of women aged 18-44 years in the United Kingdom, Sweden and the United States of America.

Study design: This observational study used prospectively collected longitudinal (smartphone application interface) and cross-sectional (web-based survey) data. Participants in the discovery cohort were drawn from 400,750 UK, Sweden and US women (79 pregnant who tested positive) who self-reported symptoms and events longitudinally via their smartphone, and a replication cohort drawn from 1,344,966 USA women (162 pregnant who tested positive) cross-sectional self-reports samples from the social media active user base. The study compared frequencies of symptoms and events, including self-reported SARS-CoV-2 testing and differences between pregnant and non-pregnant women who were hospitalized and those who recovered in the community. Multivariable regression was used to investigate disease severity and comorbidity effects.

Results: Pregnant and non-pregnant women positive for SARS-CoV-2 infection drawn from these community cohorts were not different with respect to COVID-19-related severity. Pregnant women

were more likely to have received SARS-CoV-2 testing than non-pregnant, despite reporting fewer clinical symptoms. Pre-existing lung disease was most closely associated with the severity of symptoms in pregnant hospitalized women. Heart and kidney diseases and diabetes were additional factors of increased risk. The most frequent symptoms among all non-hospitalized women were anosmia [63% in pregnant, 92% in non-pregnant] and headache [72%, 62%]. Cardiopulmonary symptoms, including persistent cough [80%] and chest pain [73%], were more frequent among pregnant women who were hospitalized. Gastrointestinal symptoms, including nausea and vomiting, were different among pregnant and non-pregnant women who developed severe outcomes.

Conclusions: Although pregnancy is widely considered a risk factor for SARS-CoV-2 infection and outcomes, and was associated with higher propensity for testing, the profile of symptom characteristics and severity in our community-based cohorts were comparable to those observed among non-pregnant women, except for the gastrointestinal symptoms. Consistent with observations in non-pregnant populations, comorbidities such as lung disease and diabetes were associated with an increased risk of more severe SARS-CoV-2 infection during pregnancy. Pregnant women with pre-existing conditions require careful monitoring for the evolution of their symptoms during SARS-CoV-2 infection.

Keywords: pregnancy; community SARS-CoV-2 symptoms; SARS-CoV-2 risk factors; SARS-CoV-2 severity; digital health; citizen science; syndromic surveillance; anosmia.

Main text

1. Introduction

The COVID-19 pandemic is caused by the SARS-CoV-2, a newly identified enveloped RNA β-coronavirus [1,2]. Early on, pregnant women were regarded as a vulnerable group considered at greater risk of severe morbidity and mortality, based on previous studies of smaller coronavirus outbreaks, and the theoretical risks associated with relative immunosuppression of pregnancy [3–5]. However, a substantial literature has now documented that among hospitalized pregnant women, antecedent symptoms and risk factors for severe disease are similar to those outside pregnancy [6], and few hospitalized pregnant women require admission to intensive care or intubation, although preterm birth, Caesarean delivery, and stillbirth may be increased compared with women without COVID-19, and vertical transmission possible (86 studies to 8 Jun 2020) [7–10]. SARS-CoV-2 positive patients develop dry cough, fever, dyspnea, fatigue and bilateral lung infiltrates on imaging in the severe cases [11]. Hospitalized pregnant women positive for SARS-CoV-2 manifest similar symptoms [7,12,13]. However, little is known about pregnant women affected by SARS-CoV-2 infection who recover in the community without hospitalization [14].

Smartphone and web-based applications for population-based syndromic surveillance are citizen science tools that can facilitate rapid acquisition of extensive epidemiological data as a pandemic evolves [15]. These data can inform public-health policies, enhance the speed of the healthcare response, shape the community services, and alert the general population to urgent health threats [16]. Smartphone applications (apps) were used prior to the COVID-19 pandemic to remotely advise on prenatal health, and maternal health behaviors, including gestational weight gain and smoking cessation [17]. Many eHealth initiatives were launched at the onset of the pandemic, with most using single, one-off reporting methods to inform SARS-CoV-2 epidemiology [18]. We present findings from a unique, longitudinal symptom-tracking system that identified both test positive and

103 suspected (but untested) SARS-CoV-2 infected pregnant women in the community, who were
104 followed prospectively to assess the need for hospitalization. Furthermore, we evaluated whether
105 our findings could be replicated, using an independent, cross-sectional symptom survey tool.

106 We present data from pregnant women in the community who report testing positive for SARS-
107 CoV-2, yet who presented a wide spectrum of disease manifestations and who rarely required
108 hospitalization.
109 We sought to characterize the differences in the SARS-CoV-2 symptom profiles and severity
110 between pregnant and non-pregnant women who did and did not receive hospitalization. In
111 addition, we identified demographic characteristics and comorbidities that modified symptom
112 severity of SARS-CoV-2 in pregnancy.
113

114 ## 2. Materials and methods

115 ### 2.1 Study Populations

116 **Discovery Cohort.** The COVID Symptom Study smartphone-based application (app), developed by
117 Zoe Global Limited, and having more than four million users from the general population in UK,
118 and around 50,000 from Sweden. Users self-report daily information about their overall health
119 status, as well as a set of pre-specified symptoms [19, 14]. We included all pre-menopausal (if
120 menopausal status was reported) women aged 18 to 44 years, who specified their pregnancy status
121 at baseline (pregnant or not pregnant) included symptom profiles, outcomes on testing positive for
122 SARS-CoV-2, and hospitalization.
123 **Replication Cohort.** The Facebook COVID-19 Symptom survey, launched in the USA and hosted
124 by the Carnegie Mellon Delphi Research Center. The cross-sectional survey had 1,876,130 female
125 respondents who indicated their pregnancy status and age 18-44 years [20]. Users specified if they had
126 experienced specific symptoms over the last 24 hours, in addition to answering demographic and

infection-related questions. Survey weights were calculated to improve representation of the source population [21] (Supplementary Material 1).

2.2 Pregnancy groups, symptoms, syndromes and outcomes

Pregnancy status: Women were divided into pregnant and non-pregnant subgroups, based on self-reported pregnancy status, ascertained once near the start of follow-up in the discovery cohort, and at each survey for the replication cohort. Gestational age, at the time pregnancy was ascertained, was available only for the discovery cohort.

COVID-19 Test and Suspected Positive: Self-reported COVID-19 testing was used to identify women with SARS-CoV-2 infection (termed *test positive*). Test positives were considered *symptomatic positive* if they reported at least one of the tracked symptoms. The type of test (e.g. PCR, serology) was not ascertained, and those reporting a pending test were excluded.

Suspected positive cases were imputed, based on a previously published method for the computation of a test-positive prediction score [14], retrained for pregnancy age distribution, and using a strict mapping scheme to equate symptoms ascertained in the discovery and replication cohorts. We defined the outcome of suspected COVID-19 (termed *suspected positive*) for anyone with a score-based imputation probability above a computed threshold (Supplementary Material 2).

Hospitalization and Disease Severity: Individuals were considered to have been hospitalized when they indicated being either admitted to or discharged from hospital in their daily reporting, within one week before/after reporting at least one of the tracked symptoms. Symptom severity was defined as the weighted sum of symptoms based on peak presentation when comparing individuals reporting hospital visit with individuals who did not, in the training set (Supplementary Material 3). The weighting was then normalized so that the severity index ranges from 0 (no symptom) to 1 (all symptoms). Symptoms were equated in the two cohorts.

2.4 Statistical analysis

A power analysis was conducted to assess the suitability of the samples size. To account for the difference in age distributions between pregnant and non-pregnant groups, age-standardization was performed, by calculating weights for the non-pregnant women, to standardize to the age-distribution of the pregnant population (Supplementary materials 4 and 5).

Symptoms. To explore differences in the symptom profile between pregnant and non-pregnant women who tested or were suspected positive for SARS-CoV-2 and who also required hospitalization or sought care, we applied univariate unconditional age-weighted logistic regression for each of 18 symptoms ascertained in either the discovery cohort, the replication or in both. We then conducted multivariate analysis on symptoms grouped into clusters by body system, as shown in Table 2, and normalized to range from 0 to 1**.**

Severity of disease. To assess symptom severity between pregnant and non-pregnant women who tested or where suspected positive for SARS-CoV-2 infection and were hospitalized, univariate unconditional age-weighted regression was applied to the pregnant and non-pregnant groups of the discovery cohort, with the severity index as a response variable. As hospitalization data were not available for the replication cohort, the analysis was repeated for this cohort among those who were 'seen at a hospital for their symptoms', conditional on those who predicted or tested positive for SARS-CoV-2.

Hospitalization. To reveal differences in the symptom profiles between hospitalized and non-hospitalized pregnant women positive for SARS-CoV-2, the frequency and percentage of women reporting each symptom were calculated for the discovery cohort. Symptoms were ranked from the most to the least frequently reported.

Disease modifiers. To identify demographic characteristics, comorbidities and pre-conditions associated with COVID-19 symptom severity in pregnancy, a multivariate unconditional regression was applied to each dataset, with the severity index as a response variable and age, diabetes, heart,

lung (and asthma) and kidney diseases as factors. As the regression investigated within-group factors, age-weighting was not applied. Bonferroni correction for multiple tests was applied.

Statistical analyses were performed using STATA version 16 (discovery cohort) and R 3.6.3 (replication cohort).

3. Results

Cohort Characteristics and COVID-19 Outcomes. The discovery cohort (N=400,750 participants) includes records from 14,049 pregnant and 386,701 non-pregnant women who had an average duration of follow-up of 11 days and contributed to an average of 6.6 reports per woman. Among the 45% of pregnant women who self-reported their gestation week at baseline, 14% were in the first trimester, 43% were in the second trimester, and 43% were in the third trimester. The replication cohort (N= 1,344,966 reports) included about 149 thousand surveys administered to women each week over 9 weeks. There were 41,796 surveys from women who indicated they were pregnant (3.2% of the source population). Demography was consistent with US age-specific pregnancy rates and stable over the survey period (https://www.cdc.gov/nchs/data/databriefs/db136.pdf).

Demographic details are shown in Table 1, together with testing rates. In the discovery cohort, we identified 629 and 25,061 pregnant and non-pregnant women, respectively, who were suspected positive for SARS-CoV-2 infection based on the symptom-score-based imputation method. Of these suspected positive, 21 and 591 were hospitalized, respectively. In the replication cohort, the proportion of 1,076 (2.9%) suspected positive pregnant was slightly lower compared to 44,772 (4.0%) suspected positive non-pregnant.

In the replication cohort, age-standardized testing proportions increased over time overall from the study launch (1.5%) through the most recent week (3.8%) as access to testing increased. Coincident

with the decline in COVID-19 infection in many areas of the USA over the study period, the number of suspected positive individuals imputed using the symptom score declined from 4.4% to 2.9%.

Insert Table 1 about here

Validation of the imputation method in a subset of the discovery cohort, and in the replication cohort is depicted in Figure 1, with additional sensitivity analyses in Supplementary Material 2.

Insert Figure 1 about here

Symptomatic, Syndromic and Severity Predictors: Frequency of symptoms and body system clusters is reported in Table 2, and graphically in Figure 2. In the discovery cohort, the most frequent symptoms in the hospitalized pregnant women positive for SARS-CoV-2 were persistent cough, headache and anosmia (all 80.0%), chest pain (73.3%), sore throat and fatigue (66.7%). In the replication cohort, among pregnant test positive women who were seen at the hospital for their illness, the most frequent symptoms were fatigue (87.5%), cough (84.6%), nausea or vomiting (78.2%), muscle pain (76.2) and anosmia (75.2%).

Insert Table 2 about here

In the discovery cohort, univariate analysis on each symptom found significant effect of pregnancy for decreased cases of *skipped meals* (t=-9.8) and of *delirium* (t=-16.2) but not for the other symptoms. Multivariate logistic regression found lower frequency of neurologic symptoms (t=-7.6) for the hospitalized pregnant vs. non pregnant women. In the replication cohort, pregnancy status was most strongly associated with increased *nausea or vomiting* (t=+10.9) and the *gastrointestinal* cluster (t=+6.0), even among those seen at a hospital for their illness (t=+4.1 and t=+3.7, respectively), indicating how questions are asked can impact symptom profiles in this population. Other symptoms common in pregnancy including *shortness of breath* (t=+5.1) and *nasal congestion*

(t=+3.6) were also predictive of pregnancy status (all age-standardized and p<5e-05 Bonferroni corrected).

Insert Figure 2 about here

Univariate weighted regression also showed that pregnancy had no statistically significant effect on the severity of manifestation of SARS-CoV-2 infection, when expressed as 'severity index' in both cohorts (p>0.001, uncorrected to test the null hypothesis). In the discovery cohort, overall duration of disease was similar for pregnant and non-pregnant women. However, time to peak of symptom manifestation was longer in pregnant women (mean time = 2.8 days) than in non-pregnant (2.2 days, p=5.5e-7). In the replication cohort, pregnant women who tested positive and reported being seen at the hospital similarly reported a longer duration of illness.

As mentioned above, in the discovery cohort hospitalized positive pregnant women manifested persistent cough, headache and anosmia (all 80%), chest pain (73.3%), sore throat and fatigue (66.7%) as the most frequent symptoms. Non-hospitalised pregnant women positive for SARS-CoV-2 reported headache (71.9%), anosmia (62.5%), persistent cough (57.8%) and skipped meals (48.4%) most commonly (Figure 3). See Supplementary Material 6 for full list of symptoms and their associated prevalence.

Insert Figure 3 about here

Comorbidities: Lung disease was the comorbidity that most impacted on the severity of symptoms in pregnant positive women (t=4.1 for discovery cohort; t=14.1 for replication cohort, all p-val<0.0001 Bonferroni corrected).

Insert Table 3 about here

In the replication cohort heart disease (t=7.1) also impacted on the severity of symptoms, followed by kidney disease (t=4.6) and diabetes (t=3.6, all significant after Bonferroni correction at p-val<0.0001).

4. Discussion

Principal Findings. We studied two large cohorts of women with self-reported pregnancy status, symptoms and COVID-19 outcomes through participative surveillance. Pregnant women reported more frequent testing for SARS-CoV-2, but generally did not experience more severe disease. Disease trajectories were similar, and the time from onset to peak of symptoms was only slightly longer in pregnant than non-pregnant women (2.8 vs. 2.2 days).

Gastrointestinal symptoms were different in pregnant and non-pregnant women with poor outcomes, with decreased *skipped meals* in the discovery cohort and increased *nausea or vomiting* in the replication cohort. Neurologic symptoms (only surveyed in the discovery cohort) were decreased in pregnant women while *nasal congestion* (only surveyed in the replication cohort) was increased.

The current epidemiologic literature is largely based on pregnant women admitted to the hospital, which provides a narrow view of the spectrum of SARS-CoV-2 infection in all pregnant women. Our data show the preponderance of test positive and even suspected positive pregnant women were not seen at or admitted to the hospital for their illness; most pregnant women reported they recover in the community, as was observed by Lokken et al. [22]. Cardiopulmonary symptoms were more frequently reported by pregnant women who were hospitalised. Notably, pre-existing lung disease was confirmed as the major risk factor to develop more severe COVID-19 in pregnancy, as it is outside of pregnancy. Heart disease, kidney disease and diabetes were also risk factors.

Contextually, we developed a symptom-based prediction method to identify suspected COVID-19 cases among women 18-44 years of age, and validated this in an independent cohort with different symptom sets and reporting methodology.

Results in the context of what is known. Pregnant women are considered a high-risk group in UK and were considered high risk in the USA early in the pandemic. This likely contributed to the higher testing proportion but lower positives results among pregnant women vs. non-pregnant. Hospitalized pregnant women presented lower frequency of neurologic symptoms, especially *delirium*, which were only measured in the discovery cohort. The replication cohort showed higher frequency of *gastrointestinal* symptoms among pregnant women with more severe outcomes, especially *nausea or vomiting* in pregnancy, which may be a feature of pregnancy itself (e.g. hyperemesis gravidum). Diarrhoea in positive pregnant women has been previously reported (rates between 8.8% and 14%) [23,24].

Disease severity did not differ between pregnant and non-pregnant women in both datasets. This posits an equivalent manifestation of SARS-CoV-2 infection in pregnant and non-pregnant, as already reported by Chen and others [9,12].

Pre-existing lung disease is the comorbidity with strongest impact on the SARS-CoV-2 infection severity in pregnant women in both cohorts. Lokken et al. [22] similarly reported asthma as a primary risk factor for severe COVID-19 in pregnancy. Heart disease, kidney diseases and diabetes were also associated with severity in the replication cohort which had high enough prevalence of these conditions (related to survey-sampling to the general population) to detect an effect. These comorbidities are consistent with risk factors in the general, non-pregnant population; Li et al. observed chronic obstructive pulmonary disease, diabetes, hypertension, coronary heart disease and cerebrovascular diseases had the highest odd ratio for SARS-CoV-2 and admission to the intensive

care unit (ICU) [25], while Kumar et al. found diabetes increased SARS-CoV-2 severity and mortality two-fold [26].

Cough, chest pain and dyspnea showed much higher incidence in the hospitalized pregnant women, indicating that cardiopulmonary symptoms are the major discriminant for hospitalization. Similarly, Ellington et al [27], found increased ICU admissions and need of mechanical ventilation in pregnant women, although the cohort studied had higher frequency of underlying medical conditions, and might be less representative of the general pregnant population.

Clinical implications. Pregnant women with pre-existing lung disease or prominent cardiopulmonary symptoms may need special attention during the COVID-19 pandemic; lung disease had strongest impact on disease severity while cardiopulmonary symptoms were the major discriminant for hospitalization in pregnancy. Indeed, in pregnancy, cardiopulmonary reserve is limited which increases morbidity and complicates management when there are added physiologic stressors (e.g. asthma exacerbation) [28–30] [31]. Diabetes was more common in the pregnant women in our cohorts, likely related to gestational diabetes. We confirmed diabetes is associated to increased severity of SARS-CoV-2 presentation [32].

Research implications. This study leveraged two cohorts followed through remote, participatory epidemiology, enabling rapid assessment of COVID-19 in pregnancy. The longitudinal nature of the discovery dataset enabled the comparison of disease duration, time from onset to peak of symptoms, and hospitalization between pregnant and non-pregnant women, prospectively. Broadly, pregnancy does not substantially contribute to morbidity. Clinicians should be more vigilant with pregnant who have pre-existing health conditions, prominent respiratory symptoms or a higher severity index -- as is the case in the general population. Further studies specifically targeting high-risk pregnancies and outcomes across the three trimesters may be warranted, to better define outcomes in this population. Also, we point out the need to interpret hospitalization rates and severity results in light of the policy changes, which can be dependent on the context or country.

Strengths and limitations. Participatory surveillance tools are crucial to epidemiological research and citizen science, as they increase population's awareness of urgent public health risks, promote public participation into science and enable inclusion in studies of large samples from the community within short time periods. Real-time public health data has been crucial in decision-making during the COVID-19 pandemic. However, user of smartphone applications and web-based surveys may not be representative of the general population, potentially limiting generalizability. Self-reported events may suffer from misclassification bias, which may be differential. The replication cohort was designed to be representative of the social media site user-base (the vast majority of US population), and it showed similar results to the detailed longitudinal discovery cohort of technology-aware smartphone users. Additionally, we applied age-standardization to account for demographic structure inherent to pregnancy. Despite the differences in the UK, Sweden and USA testing guidelines and healthcare systems, morbidity with COVID-19 in pregnancy were comparable. While the timing and symptoms profiled varied across platforms, we were able to develop and validate a prediction score for suspected positive, as well as a severity score for use in women of childbearing age. This may be useful for obstetricians in the context of limited access to SARS-CoV-2 testing during this pandemic.

Conclusions. Our findings from two large real-time syndromic surveillance technologies provide no evidence that pregnant women positive for SARS-CoV-2 are at higher risk of developing either increased morbidity or complex symptomatology compared with non-pregnant women. However, pre-existing lung disease or prominent cardiopulmonary symptoms may exacerbate cardiopulmonary stress of pregnancy. Pregnant women with comorbidities appear to be at increased risk for severe disease, consistent with evidence from COVID-19 infection in the general population.

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Declaration of interest

EM and CMA, JB, MFG, MM have no conflict of interest. ATC previously served as an investigator on a clinical trial of diet and lifestyle using a separate mobile application that was supported by Zoe Global Ltd.

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Table 1. Characteristics of the two cohorts, presented as percentages and means (standard deviations) in the cohorts. Except for group age, percentages and means are age standardized to the pregnant population age distribution in each cohort. Adjustment for survey weights was applied to the replication cohort. Self-report of being seen at a hospital was used as a proxy for hospitalization in the replication cohort.

	Discovery Cohort			Replication Cohort		
	All (N=400,750)	Non-pregnant (N=386,701)	Pregnant (N=14,049)	All (N=1,344,966)	Non-pregnant (N=1,303,170)	Pregnant (N=41,796)
Age (years) (not age-standardized)	32.1 (7.2)	32.1 (7.3)	32.4 (4.9)	29.0 (0.02)	29.0 (0.01)	29.0 (0.05)
Tested	7.0%	6.1%	8.0%	2.5%	2.4%	2.7%
Positive	0.6%	0.7%	0.6%	0.4%	0.4%	0.4%
Negative	5.5%	4.9%	6.2%	2.2%	2.1%	2.2%
Suspected	5.6%	6.7%	4.5%	3.5%	4.0%	3.0%
Comorbidities						
Diabetes	1.8%	1.2%	2.3%	3.9%	3.5%	4.3%
Lung	12.9%	12.8%	11.3%	19.3%	19.8%	18.8%
Heart	0.6%	0.5%	0.6%	0.8%	0.9%	0.7%
Kidney	0.3%	0.4%	0.3%	0.6%	0.7%	0.5%
Cancer	0.1%	0.2%	0.1%	0.9%	1.1%	0.8%
Symptom Severity	0.07 (0.11)	0.07 (0.11)	0.04 (0.09)	0.08 (0.0005)	0.08 (0.0003)	0.07 (0.001)
Test positive and hospitalized*	0.09%	0.07%	0.1%	0.06 %	0.03%	0.09%
Suspected positive and Hospitalized*	0.16%	0.16%	0.15%	0.17 %	0.12%	0.23%

462 * Hospitalization not queried in replication cohort. Proportion of who tested positive or were
463 suspected positive and who reported seeking care at a hospital for symptoms in the prior 24 hours
464 provided as a proxy.

Table 2. Frequencies and percentage values of presentation of each symptom among hospitalized in the discovery cohort, and among all women who self-reported being seen at a hospital for their illness in the replication cohort (as hospitalization data were not available). Data are reported by pregnancy status and further subdivided by SARS-CoV-2 test positive or suspected COVID-19 status. Data are reported as N (%) in the discovery cohort, and N surveys (survey-weight adjusted %) in the replication cohort. *Fatigue* was mapped to *tiredness/exhaustion* and *unusual muscle pain* to *pain in muscle and joints* in the replication cohort. Symptoms not ascertained or mapped in either cohort are marked as not available (NA).

		Discovery Cohort				Replication Cohort			
Cluster (body system)	Symptom	Hospitalised non pregnant positive (N=229)	Hospitalised non pregnant suspected positive (N=591)	Hospitalised pregnant positive (N=15)	Hospitalised pregnant suspected positive (N=21)	Seen at hospital, non-pregnant positive (N=300-)	Seen at hospital, non-pregnant suspected positive (N=1395-)	Seen at hospital, pregnant positive (N=29)	Seen at hospital, pregnant suspected positive (N= 75-)
Inflammation	Fever	151 (65.9)	359 (60.7)	8 (53.3)	12 (57.1)	135 (48.1)	514 (39.0)	12 (50.6)	19 (29.9)
	Unusual muscle pain	121 (52.8)	338 (57.2)	9 (60.0)	9 (42.9)	199 (69.0)	1,048(77.0)	19 (76.2)	52 (71.8)
	Fatigue	125 (54.6)	345 (58.4)	10 (66.7)	8 (38.1)	207 (65.9)	1,142(79.8)	24 (87.5)	()61 (84.0)
Neurologic	Headache	185 (80.8)	516 (87.3)	12 (80.0)	17 (81.0)	NA	NA	NA	NA

	Delirium	88 (38.4)	253 (42.8)	4 (26.7)	1 (4.8)	NA	NA	NA	NA
Cardiopulmonary	Dyspnea	113 (49.3)	316 (53.5)	9 (60.0)	11 (52.4)	166 (54.8)	913(65.1	20 (73.6)	47 (66.9)
	Persistent cough	178 (77.7)	438 (74.1)	12 (80.0)	19 (90.5)	202 (68.2)	1,161 82.3	24(84.6)	61 (81.0)
	Chest pain	170 (74.2)	463 (78.3)	11 (73.3)	14 (66.7)	156 (53.2)	787(56.8)	17 (62.3)	34 (51.9)
	Difficulty breathing	NA	NA	NA	NA	144 (47.7)	710 (51.6)	16 (56.0)	36 (55.1)
Oropharyngeal	Hoarse voice	117 (51.1)	309 (52.3)	6 (40.0)	11 (52.4)	NA	NA	NA	NA
	Sore throat	148 (64.6)	371 (62.8)	10 (66.7)	14 (66.7)	118 (38.3)	552(39.1)	15 (59.0)	29 (46.7)
	Nasal congestion	NA	NA	NA	NA	146 (48.4)	719 (51.5)	19 (61.5)	45 (56.2)
	Runny nose	NA	NA	NA	NA	116 (35.9)	636 (48.5)	14 (57.0)	33 (51.4)
Anosmia/ageusia	Anosmia	177 (77.3)	481 (81.4)	12 (80.0)	19 (90.5)	182 (63.1)	786 (56.7)	20 (75.2)	47 (70.4_)
Gastrointestinal	Skipped meals	153 (66.8)	400 (67.7)	7 (46.7)	11 (52.4)	NA	NA	NA	NA
	Abdominal pain	115 (50.2)	274 (46.4)	9 (60.0)	10 (47.6)	NA	NA	NA	NA
	Diarrhoea	126 (55.0)	275 (46.5)	7 (46.7)	11 (52.4)	137 (49.2)	611(44.4)	17 (59.8)	39 (56.1)

	Nausea or vomiting	NA	NA	NA	NA	138 (49.4)	633 (49.8)	21 (78.2)	51 (79.4)

Table 3. Frequencies and percentages of comorbidities and pre-existing conditions in the discovery and replication cohorts. Columns refer to pregnant women tested and suspected positive for SARS-CoV-2 infection. Data are reported as N (%). Data from the replication cohort are reported as N surveys (survey-weight adjusted %). Conditions not ascertained or mapped in either cohort are marked as not available (NA).

	Discovery Cohort		Replication Cohort	
Comorbidity or pre-existing condition	Pregnant test positive (N=79)	Pregnant suspected positive (N=629)	Pregnant test positive (N=134)	Pregnant suspected positive (N=1076)
Diabetes	3 (3.8)	15 (2.4)	11 (8.9)	76 (7.4)
Lung disease	8 (10.1)	80 (12.7)	37 (31)	376 (34.2)
Heart disease	1 (1.3)	5 (0.8)	5 (6.3)	41 (4.8)
Kidney disease	0 (0.0)	2 (0.3)	8 (7.8)	30 (43.3
Hypertension	NA	NA	17 (13.9)	170 (15.4)
Autoimmune	0 (0.0)	8 (1.3)	14 (11.5)	106 (9.3)
Cancer	0 (0.0)	1 (0.2)	5 (4.7)	29 (3.2)
Smoking / Past smoker	6 (7.6) 13 (16.5)	36 (5.7) 121 (19.2)	NA	NA

Figure 1. Receiver Operating Characteristics curve showing validation of the imputation of SARS-CoV-2 test status using the mapped symptom score probability in the replication cohort. Area under the curve is 74%.

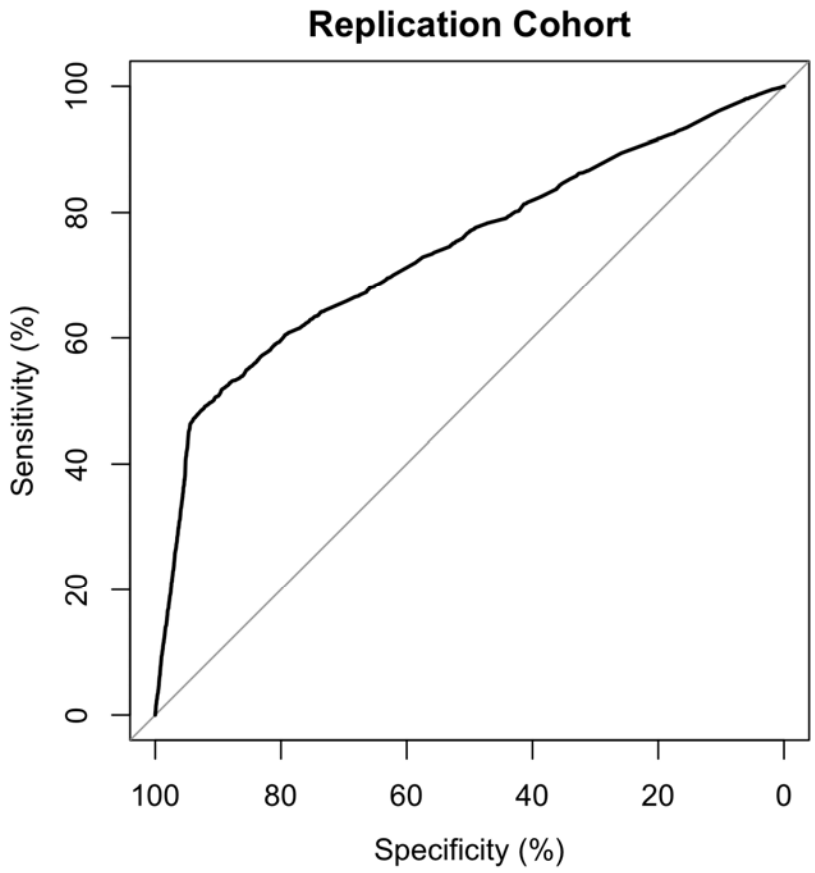

Figure 2. Comparison of symptoms presentation in the discovery (DC) and replication (RC) cohorts. Results refer to non-pregnant (orange) and pregnant (blue) women tested positive and suspected positive for SARS-CoV-2 and who required hospitalization (in DC, darker shade) or were seen at the hospital (RC, lighter shade). Results are reported as age-standardized percentage of women reporting each symptom in each subcohort.

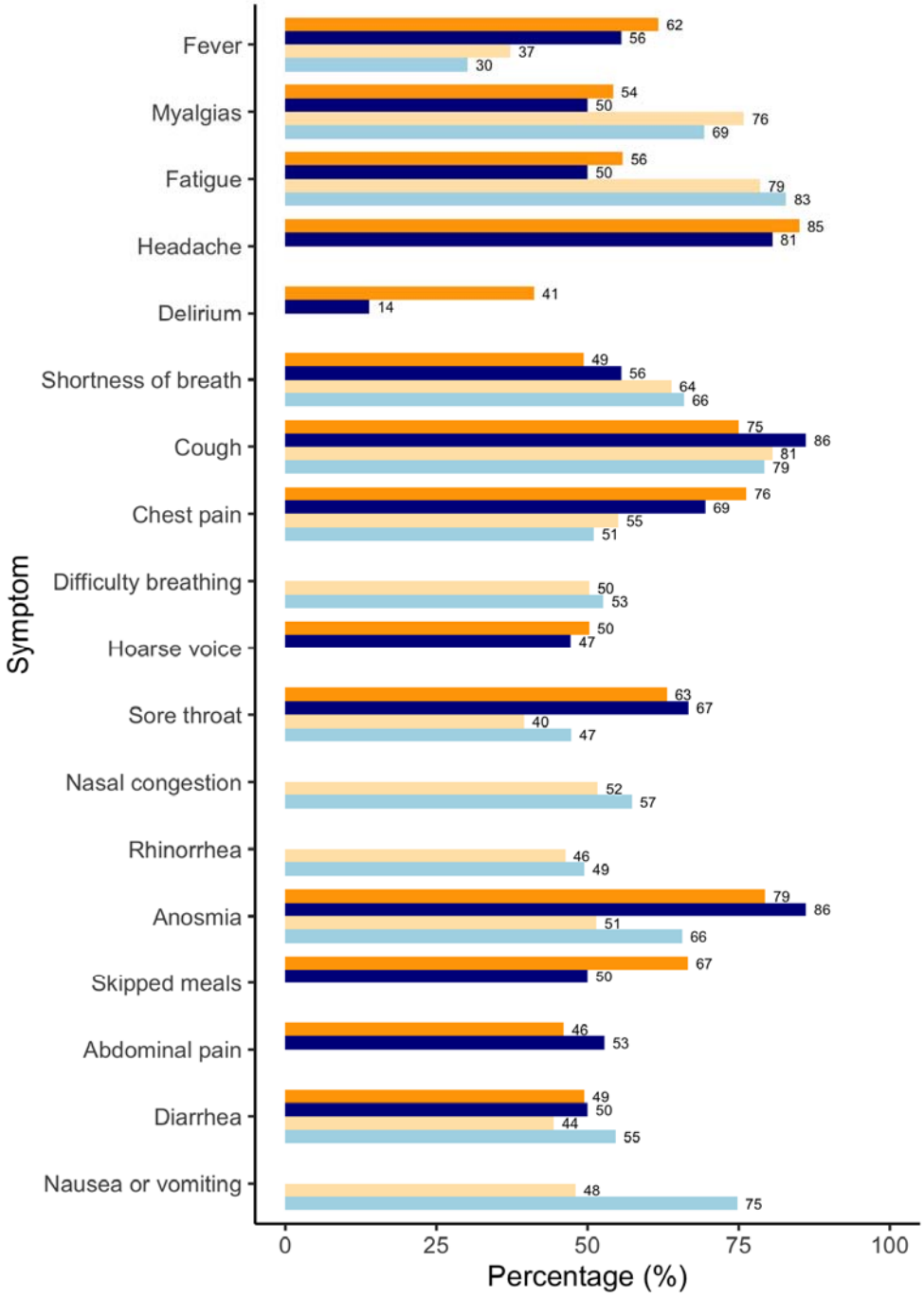

Figure 3. Symptom profile of hospitalized and non-hospitalized pregnant and non-pregnant women positive and suspected positive to SARS-CoV-2 in the discovery cohort. Results are reported in percentage of women reporting each symptom in each group.