The clinical spectrum of COVID-19: A population-based cohort study in Iceland

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The clinical spectrum of COVID-19: A population-based cohort study in Iceland

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Once the manuscript is published, dissemination of the findings will be carried out by issuing a press release that we anticipate will lead to domestic media coverage. The results will be shared on social media, both from individual authors and from our institutions, Landspitali–The National University Hospital and the University of Iceland. The results will be presented at medical conferences. Neither patients nor the public will be involved in dissemination of the findings, but will have access to the results.

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Key points

Question: What is the frequency and progression of symptoms experienced by SARS-CoV-2-positive persons?

Findings: In this population-based cohort study that included all persons who tested positive for SARS-CoV-2 by RT-PCR in Iceland, most (67.5%) had mild symptoms throughout their disease course. At the time of diagnosis, 5.3% were asymptomatic, of whom roughly half developed symptoms during follow-up. Common presenting symptoms included myalgia (55%), headache (51%), and non-productive cough (49%). At diagnosis, 13.8% and 22.3% did not meet the Centers for Disease Control and Prevention and World Health Organization case definitions for suspected COVID-19, respectively.

Meaning: In the setting of broad access to diagnostic testing, the majority of SARS-CoV-2-positive persons were found to have mild symptoms and almost one-fifth did not meet published clinical criteria for RT-PCR testing.
Abstract

Background: Previous studies on the epidemiology and clinical characteristics of COVID-19 have generally been limited to hospitalized patients. The aim of this study was to describe the clinical spectrum of COVID-19, based on a nationwide cohort with extensive diagnostic testing and a rigorous contact tracing approach.

Methods: A population-based cohort study examining symptom progression using prospectively recorded data on all individuals with a positive test (RT-PCR for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Cases were identified by three testing strategies: targeted testing guided by clinical suspicion, open-invitation population screening based on self-referral, and random population screening. All identified cases were enrolled in a telehealth monitoring service and symptoms were systematically monitored from diagnosis to recovery.

Results: Among 1564 SARS-CoV-2-positive persons who were enrolled into telehealth monitoring between March 17 and April 30, 2020, the most common presenting symptoms were myalgia (55%), headache (51%), and non-productive cough (49%). At the time of diagnosis, 83 (5.3%) individuals reported no symptoms, of whom 49 (59.0%) remained asymptomatic during follow-up. At the time of diagnosis, 216 (13.8%) and 349 (22.3%) persons respectively did not meet the case definition of the Centers for Disease Control and Prevention and the World Health Organization. The majority (67.5%) of SARS-CoV-2-positive patients had mild symptoms throughout the course of their disease.
Conclusion: In the setting of broad access to RT-PCR testing, the majority of SARS-CoV-2-positive persons were found to have mild symptoms. Fever and dyspnea were less common than previously reported. A substantial proportion of SARS-CoV-2-positive persons did not meet recommended case definitions at the time of diagnosis.
1 **Introduction**

2 On December 31 2019, the first cases of an atypical pneumonia of unidentified etiology were reported in Wuhan, China.\(^1\) One week later, a novel betacoronavirus, later named severe acute respiratory syndrome coronavirus (SARS-CoV-2), was identified as the causative pathogen\(^2,3\), and the disease subsequently termed coronavirus disease 2019 (COVID-19). The World Health Organization (WHO) declared the COVID-19 outbreak a pandemic on March 11, 2020.\(^4\)

3 COVID-19 has a wide range of clinical manifestations, ranging from an asymptomatic state or mild respiratory symptoms to severe viral pneumonia and acute respiratory distress syndrome.\(^5-7\) Previous publications have suggested that among identified symptomatic cases, approximately 81% have mild symptoms, 14% have severe symptoms, and 5% become critically ill.\(^8\) Besides respiratory symptoms, dysosmia, dysgeusia, abdominal pain, diarrhea, and rash have been described.\(^5,9\) Most published studies on the clinical characteristics of COVID-19 have been retrospective\(^5,8,10,11\) and limited to inpatients\(^12,13\) and therefore do not capture the full clinical spectrum of the disease.

4 The first case of COVID-19 in Iceland was diagnosed on February 27, 2020.\(^14\) Icelandic health authorities responded immediately by isolating infected persons and instituting systematic contact tracing and quarantine of exposed individuals.\(^15\) Broad access to real-time reverse-transcriptase polymerase chain reaction (RT-PCR) testing became available in Iceland early in the course of the pandemic, resulting in the highest rate of SARS-CoV-2 testing in the world.\(^16\) Approximately one month after the first case was
identified in Iceland, the incidence of undetected SARS-CoV-2 infections was found to
be only 0.6% by random population screening using RT-PCR. A subsequent study
found that only 56% of individuals positive for SARS-CoV-2 antibodies had been
diagnosed by RT-PCR. All SARS-CoV-2-positive individuals were actively monitored
at a newly established COVID-19 outpatient clinic at Landspitali–The National University
Hospital (LUH). The contact tracing and containment strategies implemented by the
Icelandic authorities rapidly curbed the epidemic, with only 12 new cases diagnosed
between May 1 and June 15.

In this paper, we describe the analysis of prospectively collected data on all persons
who tested positive for SARS-CoV-2 by RT-PCR in Iceland, and characterize the
epidemiology and full clinical spectrum of COVID-19 in this nationwide cohort.
Methods

Study population and design

This population-based cohort study included all persons who tested positive for SARS-CoV-2 by RT-PCR between February 27 and April 30, 2020, and were actively monitored at LUH. All individuals in Iceland who tested positive for SARS-CoV-2 were immediately contacted, instructed to isolate, and enrolled in a telehealth monitoring service. Monitoring involved frequent telephone interviews by a nurse or physician, through which the patient’s clinical status was evaluated. From February 27 to March 16, 2020, the content and documentation of these interviews was at the discretion of the nurse or physician making the call. On March 17, a standardized data entry form was built directly into the national electronic medical record system, facilitating a structured approach to the clinical evaluation of COVID-19 patients. The study was approved by the National Bioethics Committee (VSN-20-078). Neither patients nor the public were involved in the design, conduct, reporting, or dissemination planning of the research.

Virological testing

RT-PCR was used for detection of SARS-CoV-2 RNA in nasopharyngeal and oropharyngeal swabs, based on the WHO recommended protocol from Charité, Berlin or using a commercial kit (TaqMan 2019-nCoV Assay from Thermo Fisher Scientific) as previously described. Three testing protocols were implemented: targeted testing, open-invitation population screening and random population screening. Targeted testing was performed at the Department of Clinical Microbiology at LUH, whereas population screening was carried out by deCODE genetics, a biopharmaceutical company based in Iceland.
Targeted testing began on January 31, 2020, and included clinically suspected cases and individuals at high risk of exposure, though exposure was not a requirement for testing. Open-invitation population screening began on March 13, 2020, and was available to all Icelandic residents who were not in quarantine and did not have symptoms that prompted targeted testing. Finally, a randomly chosen sample of 6782 Icelanders was offered testing via telephone text message on March 31 and April 1, 2020.

Data collection

To confirm the completeness of telehealth enrollment, results of all SARS-CoV-2 testing were obtained from databases of LUH and deCODE genetics. Negative samples were used for denominator calculations. Baseline characteristics of SARS-CoV-2-positive patients and longitudinal data on symptom progression were obtained from the standardized data entry forms used by the COVID-19 Clinic. Data on clinical outcomes were extracted from LUH database. Data were linked using government issued national identification numbers. Population demographics were obtained from Statistics Iceland (www.statice.is).

The telehealth monitoring service

The initial patient interviews were conducted by a physician who informed the patients of the diagnosis, evaluated their health, and instructed them to self-isolate at home. A checklist of 19 specific symptoms was used during the initial and all subsequent interviews. The list of symptoms was developed based on findings reported in the literature at the time when the telehealth monitoring was being launched and with
1 respect to symptoms reported by the first 200 Icelanders who contracted COVID-19.
2 The list was subsequently refined, taking into account symptoms described by patients
3 during the early interviews and was formally introduced on March 17. From this point
4 onwards the checklist remained unchanged. Furthermore, the patients were asked
5 during every interview if additional symptoms were present. Finally, the patients’
6 baseline characteristics were documented, including past medical history, medication
7 use, and social history.
8 Based on the symptoms documented during the interviews, patients were classified into
9 one of three categories of clinical severity: low severity, defined as mild and improving
10 symptoms; moderate severity, defined as mild dyspnea, cough or fever for less than five
11 days; and high severity, defined as worsening dyspnea, worsening cough, high or
12 persistent fever for five days or longer, or severe fatigue. The frequency of follow-up
13 interviews ranged from daily to every fourth day, depending on clinical severity, age,
14 and underlying conditions. Patients with concerning symptoms were referred for
15 evaluation at the COVID-19 Clinic.
16 Patients were released from isolation and discharged from telehealth monitoring when
17 they met both of the following criteria: 14 days had passed since the diagnosis of
18 COVID-19, and they had been asymptomatic for the past seven consecutive days.
19 Case definitions
20 Patients were considered symptomatic due to COVID-19 using three different
21 definitions: 1) Reporting at least one of the 19 symptoms; 2) WHO case definition of
22 suspected COVID-19, which included fever and at least one other symptom of acute
respiratory infection, e.g. cough or shortness of breath; 3) Centers for Disease Control and Prevention (CDC) interim case definition of COVID-19, which included either two of the following symptoms: fever, rigor, myalgia, headache, sore throat, dysosmia or dysgeusia, or one of the following symptoms: cough, shortness of breath or difficulty breathing. Individuals who did not fulfill these definitions at the time of diagnosis or during follow-up, were determined to be asymptomatic. Otherwise, they were considered presymptomatic at the time of diagnosis.

Statistical analysis

The incidence of COVID-19 was calculated by age and sex, using both the Icelandic population and all SARS-CoV-2 tested individuals as denominators. Patients were followed until discharge from the telehealth monitoring service, hospital admission, death or end of the study period (May 22, 2020). Patients enrolled prior to the implementation of the standardized data entry form (March 17, 2020) were excluded from the analysis of symptoms and symptom progression.

The progression of COVID-19 symptoms was analyzed using parametric cure-mixture models and logistic regression. The time frame used in the analyses was days from symptom onset to discharge from telehealth monitoring. The data were interval censored due to the intermittent schedule of the interviews. To account for this, the cumulative incidence of symptom occurrence was estimated with the non-parametric Turnbull estimator and a parametric cure-mixture model using the log-logistic distribution. The proportion of patients experiencing a specific symptom per day was estimated employing logistic regression that allowed for non-linear effects using a three-
knot restricted cubic spline. Missing information between interviews was addressed by multiple imputation using chained equations, performed by additive regression, bootstrapping and predictive mean matching procedure.\textsuperscript{22} The number of imputations equaled the highest proportion of missing data for any variable, multiplied by 100. The added uncertainty due to imputation was fully accounted for in the logistic regression models. The result was compared with a complete-case analysis and naive up-down filling procedure.

All statistical analyses were performed in R version 3.6.3.
Results

Demographics and clinical characteristics

A total of 45,105 individuals (12% of the Icelandic population) underwent 47,800 RT-PCR tests for SARS-CoV-2 from January 31 to April 30, 2020. Of those, 16,750 (37.1%) underwent targeted testing, 26,762 (59.3%) participated in open-invitation population screening and 3924 (8.7%) in random population screening (Figure 1). The participation rate in the random screening was 56%. The population incidence of SARS-CoV-2-positive cases was 4.9 per 1000 individuals, and 39 per 1000 individuals tested were positive. This rate differed between the three testing strategies; the rate was 96 per 1000 individuals tested in case of targeted testing, 5.9 per 1000 tested for open-invitation population screening and 5.1 per 1000 tested for random population screening.

All persons who tested positive were enrolled in telehealth monitoring or admitted to hospital, with no exceptions. The median time from symptom onset until RT-PCR diagnosis and the enrollment interview was four days (interquartile range [IQR], 2-7) and a median of six (IQR, 4-8) interviews were conducted per individual during telehealth monitoring. The median time between interviews was two days (IQR, 1-3).

The clinical progression from symptom onset for the 1797 positive individuals is shown in Figure 2. Thirty-two of those patients were diagnosed after being admitted to hospital of whom one was diagnosed post-mortem (Figure 1). Characteristics of the SARS-CoV-2-positive cohort categorized by testing strategy is presented in Table 1. Individuals diagnosed by targeted testing, open-invitation population screening and random
population screening were similar at baseline. In total, 101 (5.6%) patients were hospitalized, 27 (1.5%) were admitted to an intensive care unit and 16 (0.9%) required mechanical ventilation. The median length of hospital stay was 8 days (IQR, 3.5-19) and 10 (0.6%) patients died. The total number of documented symptoms at diagnosis was lower among persons diagnosed before the implementation of standardized symptom monitoring compared to those diagnosed following the implementation (Supplemental Figure 1). The latter group was therefore used to study the symptom development and progression (Figure 1).

Of the 1564 (87%) persons who were followed using the standardized data entry form, 791 (51%) were female and the median age was 40 years (IQR, 26-53; range, 0-103). Among these, 1055 (67.5%) were classified as having low disease severity throughout the follow-up period, 55 (3.5%) were admitted to hospital and 13 (0.8%) required intensive care, six (0.4%) of whom received mechanical ventilation. Two (0.1%) patients died. The median follow-up was 15 days (IQR, 14-18), resulting in 69.2 person-years of follow-up time. A total of 1509 persons completed the telehealth follow-up from diagnosis until discharge. The observation time of the remaining 55 patients who were hospitalized was censored at the time of admission, after a median follow-up of 4 days (IQR, 2.5-8).

**Symptoms at diagnosis**

Of the 1564 persons with standardized symptom documentation, 42.7% had experienced fever at diagnosis. Cough (60.1%), dyspnea (31.7%), and gastrointestinal symptoms (35.7%) were also commonly reported. Eighty-three (5.3%) persons reported
no symptoms at diagnosis, which was more commonly noted among those diagnosed through open-invitation population screening (n=32, 23.7%) and random population screening (n=6, 30.0%), as compared with individuals diagnosed by targeted testing (n=45, 3.2%). Of the persons who were asymptomatic at diagnosis, 49 (59.0%) did not develop any symptoms throughout the telehealth monitoring, while the remaining 34 (41.0%) individuals developed symptoms after a median of 3 days (IQR, 3-4.75). All persons diagnosed by random population screening who were asymptomatic at diagnosis remained so during follow-up, compared with 19 (59.4%) individuals identified by open-invitation population screening and 24 (53%) diagnosed by targeted testing.

Using the CDC case definition, the symptoms reported by 216 (13.8%) SARS-CoV-2-positive persons were not consistent with COVID-19 at the time of diagnosis. This was more common among individuals diagnosed through open-invitation population screening (n=54, 40.0%) and random population screening (n=9, 45.0%), than by targeted testing (n=153, 10.9%). Seventy-two (4.6%) of those persons developed symptoms compatible with the CDC case definition at a median of 5 days (IQR, 3-6) from diagnosis, whereas the other 144 (9.2%) never met the CDC criteria. Similarly, 349 (22.3%) individuals did not fulfill the WHO case definition at the time of diagnosis, a finding that was more commonly observed among those diagnosed through open-invitation population screening (n=59, 43.7%) and random population screening (n=12, 60.0%), than by targeted testing (n=278, 19.7%). The WHO criteria were later met by 115 (7.4%) individuals at a median of 4 days (IQR, 3-6) from diagnosis, while the remaining 234 (15.0%) persons never fulfilled the criteria.
The cumulative incidence and proportion of infected individuals meeting CDC and WHO criteria by number of days from symptom onset is shown in Supplemental Figure 2. Among the 216 individuals who did not meet CDC criteria at diagnosis, four (1.9%) were hospitalized later in the course of their disease, and one required mechanical ventilation. Similarly, four (1.1%) of the 349 individuals who did not fulfill the WHO criteria at diagnosis were admitted to hospital for illness related to COVID-19, two of whom required intensive care. Among persons who did not have symptoms consistent with the WHO or CDC criteria at diagnosis, the most common symptoms were headache 140 (37.6%), rhinorrhea 128 (34.4%), dysosmia 123 (33.0%) and dysgeusia 122 (32.8%), with 241 (64.6%) individuals experiencing at least one of these symptoms.

**Symptoms at disease onset**

As shown in Table 2, the most common symptoms at the onset of COVID-19 were myalgia (54.6%, 95%CI, 50.6-58.6), headache (51.2%, 95%CI, 46.8-55.7), and non-productive cough (49.3%, 95%CI, 45.2-53.3). Overall, 83.0% (95%CI, 80.6-85.1) of individuals experienced at least one generalized symptom and 62.9% (95%CI, 59.1-66.6) at least one upper respiratory symptom. Multiple imputation logistic regression produced acceptable results as compared with complete case analysis and a naive up-down filling procedure (Supplemental Figures 3-6). Symptoms occurring on days when interviews were not conducted were imputed. The proportion of persons with missing information on symptoms was highest during the first days following symptom onset (Supplemental Table 1).
Compared with persons diagnosed by targeted testing, those diagnosed through either open-invitation or random population screening were less likely to have experienced cardinal symptoms of COVID-19 at disease onset, including fever (30.2% vs. 42.5%), cough (47.9% vs. 59.5%), dyspnea (18.8% vs. 25.9%) and gastrointestinal symptoms (23.1% vs. 30.8%). Other symptoms categorized according to testing strategy are shown in Supplemental Figures 7-10.

The proportion of patients experiencing specific symptoms by sex and age group is displayed in Supplemental Figures 11-14. The initial presentation of COVID-19 varied only slightly between the sexes. The proportion experiencing fever or gastrointestinal symptoms at onset was similar between age groups, but cough and dyspnea were more common among older individuals (Supplemental Figure 13).

Differences in symptoms at onset between hospitalized and non-hospitalized patients are shown in Supplemental Figures 15-18. Symptoms at disease onset were more common among patients who were later admitted to hospital, including generalized symptoms (93.5% vs 82.6%), lower respiratory symptoms (70.2% vs 62.8%) and gastrointestinal symptoms (48.1% vs 29.2%). However, the proportion of patients who experienced upper respiratory symptoms was lower, 47.8% compared with 63.5% of those who were never hospitalized.

**Progression of symptoms**

By day 21 from disease onset, the most commonly experienced symptoms were lethargy (74.7%, 95%CI 72.5-76.9), headache (73.0%, 95%CI, 70.6-75.2), and productive or non-productive cough (72.8%, 95%CI, 70.2-75.1). Overall, 93.1% (95%CI,
91.6-94.3) had experienced at least one generalized symptom, 87.2% (95%CI, 85.2-88.8) at least one upper respiratory symptom, and 80.3% (95%CI, 78.2-82.3) at least one lower respiratory symptom. The cumulative incidence of fever, dyspnea, and gastrointestinal symptoms by day 21 were 47.8%, 52.0%, and 50.1%, respectively (Figure 3). Of those who eventually developed fever, 85.2% had done so by the third day of their illness. Similarly, 80.2% had experienced cough 52.2% dyspnea and 62.0% gastrointestinal symptoms by day three. The proportion of persons who had developed each symptom was comparable regardless of sex or age group (Supplemental Figures 19-30).

Of the 19 symptoms, only dysosmia and dysgeusia were more common later in the disease course than at symptom onset. Both symptoms peaked on day eight from diagnosis. The trend was most pronounced among individuals aged 25 to 55 years and was more marked among females (Supplemental Figure 12). Other symptoms attributed to COVID-19 were most prevalent during the onset of the disease. No symptom exhibited a bimodal pattern (Supplemental Figures 11-14). The cumulative incidence of each specific symptom was lower among persons diagnosed through population screening compared with targeted testing, except for rhinorrhea and vomiting (Supplemental Figures 31-34). By day 21, a large proportion of patients who were ever admitted to hospital for COVID-19 had experienced fever, cough, dyspnea and gastrointestinal symptoms, or 91.0% (95%CI, 68.6-95.7), 96.0% (95%CI, 76.3-98.4), 82.7% (95%CI, 65.7-91.1), and 84.8% (95%CI, 64.7-91.5), respectively (Supplemental Figures 35-38).


Discussion

In this study, we examined the clinical characteristics of COVID-19 among persons diagnosed by RT-PCR in a national population-based cohort. Our prospectively collected data on symptoms and disease progression revealed that 48% experienced fever, 73% cough, and 52% dyspnea. At the time of diagnosis, 5% were completely asymptomatic, 13% did not meet the CDC case definition, and 22% did not fulfill the WHO criteria. Due to aggressive contact tracing and widespread virological testing it is likely that the cohort includes the majority of symptomatic cases in the population. This assumption is supported by the low prevalence of SARS-CoV-2 infection detected by random population screening using RT-PCR during the peak of the epidemic (0.6%) and by a subsequent population-based study estimating that 56% of seropositive persons had previously been diagnosed by RT-PCR.

The comprehensive, nationwide characterization of COVID-19 symptoms was facilitated by broad access to diagnostic testing in Iceland. The SARS-CoV-2 RT-PCR test was free of charge for both targeted testing and population screening, resulting in over 12% of the population being tested, which was higher than in any other country during the study period. As a result, we were able to describe the true spectrum of symptomatic SARS-CoV-2 infection, while previous studies were largely based on hospitalized cohorts or cases identified in the setting of more restrictive testing. Furthermore, subgroup analysis allowed us to quantify the degree by which cohorts that included only hospitalized patients might overestimate the presence of specific symptoms, for instance fever which was considerably more common at symptom onset in patients who
were later admitted to hospital (74%) than in patients who never were hospitalized (40%).

The proportion of persons with COVID-19 who remain completely asymptomatic has been a focus of interest during the pandemic with implications for the risk of disease dissemination. In the current study, 83 individuals reported no symptoms at the time of diagnosis, approximately half of whom developed symptoms in the ensuing days. Thus only 3.1% of cases diagnosed by RT-PCR remained completely symptom-free during follow-up. However, as some degree of suspicion of COVID-19 was needed to prompt an individual to be tested or to seek testing, symptomatic patients are likely to be overrepresented in our sample. The true proportion of SARS-CoV-2-positive persons who never develop symptoms can be estimated by longitudinal follow-up of individuals diagnosed by random population screening. In the current study, 6 of the 20 (30%) individuals diagnosed by random population screening never developed symptoms. This finding is supported by a recent seroprevalence study in Iceland that found that 44% of individuals with antibodies against SARS-CoV-2 had either not undergone RT-PCR testing or had tested negative, suggesting only mild or no symptoms among this group. A potential limitation of the random screening approach are uncertainties regarding the sensitivity and specificity of RT-PCR for detection of SARS-CoV-2.

Most of the included persons experienced only minor symptoms. Only 22% of patients developed moderate symptoms, 8% severe symptoms, and 3.5% required hospitalization. The standardized prospective recording of clinical symptoms made it possible to evaluate the sensitivity of the widely used CDC and WHO case definitions for the diagnosis of COVID-19 throughout the course of the disease. By
applying these definitions, we demonstrate that a substantial number of cases would have been missed; approximately 9% by the CDC criteria and 15% by the WHO criteria. The identification of additional 4% and 7% of cases would have been delayed by a median of 5 and 4 days, respectively. These are concerning observations with immediate implications for current efforts to curtail the pandemic. Our data show that most patients have mild symptoms that may not have prompted the consideration of COVID-19 by either patients or healthcare providers in more resource-limited settings, and indicates a need for revising and widening the CDC and WHO case definitions to increase their sensitivity.

Symptoms observed among patients with mild forms of COVID-19 have previously been examined in a multicenter European study of 1420 RT-PCR-positive persons who answered a questionnaire. Severely ill patients were excluded and the remaining cohort was predominantly female (68%), young (94% <60 years of age), and biased towards healthcare workers (31% of the group). While these results are not easily generalizable to the entire population, the investigators found that only 7% of patients required hospitalization compared to 3.5% in the present study. Headache, loss of smell, and nasal obstruction were the most common symptoms identified. Although these symptoms were also frequently identified in our cohort, we found cough and myalgias to be more common. The predominance of loss of smell identified in the aforementioned study agrees with our observation that olfactory symptoms are most common in the younger age groups.

We found that slightly less than 50% of patients developed fever during the course of the disease, already present in 85% of those by day 3. This is consistent with the study
by Lechien et al. who noted fever ≥38.0°C in 45.4% of cases\(^1\), while it is higher than was reported by Guan et al. (21.7%)\(^5\) and Goyal et al. (25%)\(^12\). A meta-analysis by Sun et al. found that 89% of COVID-19 patients had a fever ≥37.3°C\(^6\), but this definition of fever is rarely used in clinical practice. Over the follow-up period, 70% of patients experienced cough which is consistent with the findings of Lechien et al. who observed cough in 63% of cases\(^10\). In total, 52% of patients reported any dyspnea and only 14% described dyspnea at rest during the disease. The reported incidence of dyspnea ranges from 22-49%\(^7,10,24\) but most previous studies do not differentiate between dyspnea at rest and dyspnea on exertion. Gastrointestinal symptoms were common, reported by almost half of patients at some point during the first 14 days. Abdominal pain (22%) and diarrhea (28%) were frequent as in previous studies\(^12,25\). Interestingly, although one-fourth of patients experienced nausea, vomiting was rare.

Our findings indicate a lower rate of hospital admissions and mortality in Iceland compared with many other countries. The reasons for these disparate outcomes are likely multifactorial. Iceland has a relatively young population, with 85.8% younger than 65 years, compared to 77.1% in Italy, 80.6% in Spain, 81.6% in the United Kingdom, and 83.5% in the USA\(^26,27\). The relatively young age of the population, in addition to a strong emphasis on limiting the exposure of elderly and multimorbid individuals, resulted in a low median age of confirmed COVID-19 cases of 40 years (IQR, 26-53) in Iceland compared to 51 years (IQR, 36-65) among all cases reported to the WHO\(^26\) and 48 years (IQR, 33-63) in the USA\(^29\). The strategy to protect susceptible individuals seems to have been effective. In the recent seroprevalence study in Iceland, the infection fatality rate was estimated to be 0.3%\(^17\). Different rates of specific risk factors for inferior
outcomes in COVID-19 are unlikely to explain this difference as they appear to have a
similar distribution in Iceland as in other countries. For instance 28.8% of Icelandic
adults have hypertension\cite{30} and 27% are obese.\cite{31} Nevertheless, these differences and
the homogenous population in Iceland may limit the generalizability of our findings to
other nations and geographical areas.

This study does have limitations. We do not have information on SARS-CoV-2-negative
individuals and therefore the baseline rate of symptoms that resemble those of COVID-
19 in the population is unknown. The rate of such symptoms in the community is not
zero and thus some of the symptoms attributed to SARS-CoV-2 in this study may be
due to other causes. However, this is unlikely to affect the overall interpretation of our
findings as there was a strong temporal relationship between the diagnosis and the
onset and resolution of symptoms. It is also noteworthy that in order to accurately
describe symptom progression, cases diagnosed before the implementation of the
standardized clinical data entry form were excluded from the analysis of symptom
development, representing 11% of all SARS-CoV-2-positive cases in Iceland. The date
of implementation of the standardized data entry form was not influenced by the clinical
characteristics of the patients being diagnosed, and therefore should not introduce bias.
Furthermore, the demographics and clinical characteristics of excluded cases were
largely comparable to those that were included in the study. Another limitation is that
daily standardized documentation of symptoms was not available during hospital
admission. This could conceivably lead to an underestimation of severe symptoms such
as dyspnea. However, only 3.5% of the included patients were hospitalized and
symptoms prior to hospitalization were included in the analysis. It is important to note
that the data were based on self-reported symptoms via telephone calls. This shortcoming is mitigated by the fact that experienced nurses and physicians conducted the interviews. Finally, our study was concerned with the symptomatology of the acute phase of COVID-19. It has become apparent that patients may experience prolonged symptoms following their initial infection. Telehealth monitoring was discontinued after the resolution of the acute illness, and we therefore cannot characterize the nature of long-term symptoms of COVID-19. A principal strength of the study is its population-based approach, which included all confirmed cases in the country during the study period, regardless of their need for medical care.

**Conclusion**

This report describes the symptomatology and clinical severity of the of COVID-19 in Iceland. The incidence of COVID-19 was high due to extensive testing of both symptomatic and asymptomatic individuals, while disease severity was lower than previously reported. Symptoms such as fever and dyspnea were less frequent than has been observed in earlier studies. Our findings suggest that both the CDC and WHO case definitions of COVID-19 lack sensitivity and miss a substantial proportion of patients, including those who later develop severe disease.
References


1. 72314 cases from the Chinese Center for Disease Control and Prevention.
2. JAMA. 2020. Advance online publication.


31. OECD/European Observatory on Health Systems and Policies (2019), Iceland:
1 Country Health Profile 2019, State of Health in the EU. 


### Tables

**Table 1. Characteristics of SARS-CoV-2-positive persons according to testing strategy.**

<table>
<thead>
<tr>
<th></th>
<th>Targeted testing</th>
<th>Open population screening</th>
<th>Random population screening</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n</strong></td>
<td>1619</td>
<td>158</td>
<td>20</td>
</tr>
<tr>
<td>Age (median [IQR])</td>
<td>42.0 [26.0-55.0]</td>
<td>39.0 [29.0-49.0]</td>
<td>45.0 [33.75-54.75]</td>
</tr>
<tr>
<td>Females (%)</td>
<td>822 (50.8)</td>
<td>72 (45.6)</td>
<td>9 (45.0)</td>
</tr>
<tr>
<td>BMI (median [IQR])</td>
<td>24.5 (22.6-29.6)</td>
<td>27.5 (23.6-30.9)</td>
<td>27.6 (24.5-31.2)</td>
</tr>
<tr>
<td>Lung disease (%)</td>
<td>237 (14.6)</td>
<td>22 (13.9)</td>
<td>1 (5.0)</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>71 (4.4)</td>
<td>3 (1.9)</td>
<td>1 (5.0)</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>254 (15.7)</td>
<td>19 (12.0)</td>
<td>4 (20.0)</td>
</tr>
<tr>
<td>Cardiovascular disease (%)</td>
<td>141 (8.7)</td>
<td>6 (3.8)</td>
<td>1 (5.0)</td>
</tr>
<tr>
<td>Chronic kidney disease (%)</td>
<td>36 (2.2)</td>
<td>1 (0.6)</td>
<td>1 (5.0)</td>
</tr>
<tr>
<td>Cancer (%)</td>
<td>81 (5.0)</td>
<td>4 (2.5)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Current smoking (%)</td>
<td>77 (4.8)</td>
<td>7 (4.4)</td>
<td>2 (10.0)</td>
</tr>
<tr>
<td>Clinical severity at enrollment (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severity Level</td>
<td>Low Severity</td>
<td>Moderate Severity</td>
<td>High Severity</td>
</tr>
<tr>
<td>---------------</td>
<td>--------------</td>
<td>-------------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Cases</td>
<td>1276 (78.8)</td>
<td>147 (93.0)</td>
<td>19 (95)</td>
</tr>
<tr>
<td>Percentage</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Severity Level</th>
<th>Low Severity</th>
<th>Moderate Severity</th>
<th>High Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital admission (%)</td>
<td>100 (6.2)</td>
<td>1 (0.6)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Percentage</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Severity Level</th>
<th>Low Severity</th>
<th>Moderate Severity</th>
<th>High Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Admission to intensive care unit (%)</td>
<td>27 (1.7)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Percentage</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1 BMI, body mass index; IQR, interquartile range.

2 Table 2. Proportion of SARS-CoV-2-positive persons who experienced specific symptoms and symptom constellations on days 1, 3, 7, and 14 from symptom onset.

3 The cumulative incidence of the specific symptoms by day 14 is shown in the last column. All values are reported as percentages with 95% confidence intervals (CI).

<table>
<thead>
<tr>
<th>Constellation of symptoms</th>
<th>Specific symptoms</th>
<th>Proportion of persons experiencing a symptom per day (%), 95%CI</th>
<th>Cumulative incidence by day 14 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Symptom onset Day 3 Day 7 Day 14</td>
<td></td>
</tr>
<tr>
<td>Generalized</td>
<td></td>
<td>83.0 (80.6-85.1) 78.0 (75.9-85.1) 65.3 (63.9-66.9) 40.2 (39.0-41.2)</td>
<td>92.7 (91.2-93.8)</td>
</tr>
<tr>
<td></td>
<td>Fever ≥38°C</td>
<td>Rigor, chills</td>
<td>Headache</td>
</tr>
<tr>
<td>------------------</td>
<td>-------------</td>
<td>---------------</td>
<td>----------</td>
</tr>
<tr>
<td>-</td>
<td>41.3 (36.9-45.8)</td>
<td>32.0 (29.2-34.9)</td>
<td>17.8 (16.6-19.2)</td>
</tr>
<tr>
<td>-</td>
<td>31.4 (27.3-35.9)</td>
<td>23.5 (21.0-26.3)</td>
<td>12.5 (11.5-13.6)</td>
</tr>
<tr>
<td>-</td>
<td>51.2 (46.8-55.7)</td>
<td>45.7 (42.4-48.9)</td>
<td>35.1 (33.5-36.6)</td>
</tr>
<tr>
<td>-</td>
<td>54.6 (50.6-58.6)</td>
<td>44.6 (41.7-47.5)</td>
<td>26.9 (25.6-28.3)</td>
</tr>
<tr>
<td>-</td>
<td>37.5 (33.3-41.9)</td>
<td>37.1 (34.1-40.3)</td>
<td>35.7 (34.3-37.2)</td>
</tr>
<tr>
<td></td>
<td>Loss of appetite</td>
<td>Upper respiratory</td>
<td>Rhinorrhea</td>
</tr>
<tr>
<td>------------------</td>
<td>------------------</td>
<td>-------------------</td>
<td>------------</td>
</tr>
<tr>
<td></td>
<td>23.1 (19.9-26.8)</td>
<td>62.9 (59.1-66.6)</td>
<td>33.3 (29.2-37.8)</td>
</tr>
<tr>
<td></td>
<td>22.1 (19.7-24.7)</td>
<td>60.2 (57.4-63.0)</td>
<td>28.8 (26.0-31.7)</td>
</tr>
<tr>
<td></td>
<td>19.6 (18.3-20.9)</td>
<td>54.0 (52.5-55.5)</td>
<td>21.0 (19.7-22.4)</td>
</tr>
<tr>
<td></td>
<td>11.8 (11.0-12.6)</td>
<td>36.9 (35.7-38.1)</td>
<td>12.0 (11.2-12.9)</td>
</tr>
<tr>
<td></td>
<td>44.4 (41.8-46.9)</td>
<td>85.9 (84.1-87.6)</td>
<td>52.9 (50.4-55.3)</td>
</tr>
<tr>
<td></td>
<td>28.4)</td>
<td>31.2)</td>
<td>25.0)</td>
</tr>
<tr>
<td>------------------</td>
<td>-------</td>
<td>-------</td>
<td>-------</td>
</tr>
<tr>
<td><strong>Lower</strong></td>
<td>63.1 (59.5-66.6)</td>
<td>61.0 (58.4-63.6)</td>
<td>56.3 (54.9-57.7)</td>
</tr>
<tr>
<td><strong>respiratory</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-productive</td>
<td>49.3 (45.2-53.3)</td>
<td>45.2 (42.3-48.0)</td>
<td>37.1 (35.7-38.5)</td>
</tr>
<tr>
<td>cough</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Productive</td>
<td>13.4 (11.1-16.4)</td>
<td>14.4 (12.5-16.6)</td>
<td>16.0 (14.8-17.2)</td>
</tr>
<tr>
<td>cough</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any dyspnea</td>
<td>25.2 (22.1-28.6)</td>
<td>26.0 (23.7-28.5)</td>
<td>27.0 (25.7-28.3)</td>
</tr>
<tr>
<td>Dyspnea at rest</td>
<td>4.5 (3.3-6.2)</td>
<td>4.6 (3.6-5.8)</td>
<td>4.5 (3.9-5.2)</td>
</tr>
</tbody>
</table>
### Gastrointestinal

<table>
<thead>
<tr>
<th>Symptom</th>
<th>30.0 (26.0-34.4)</th>
<th>26.9 (24.1-29.9)</th>
<th>21.0 (19.6-22.5)</th>
<th>11.1 (10.3-12.0)</th>
<th>48.2 (45.7-50.6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Nausea</td>
<td>13.0 (10.6-15.7)</td>
<td>11.8 (10.2-13.6)</td>
<td>9.6 (8.7-10.5)</td>
<td>5.1 (4.6-5.6)</td>
<td>25.0 (22.9-27.2)</td>
</tr>
<tr>
<td>- Vomiting</td>
<td>3.4 (2.2-5.3)</td>
<td>2.7 (1.9-3.8)</td>
<td>1.7 (1.3-2.2)</td>
<td>0.9 (0.6-1.3)</td>
<td>4.8 (3.9-5.9)</td>
</tr>
<tr>
<td>- Abdominal pain</td>
<td>11.1 (8.7-14.0)</td>
<td>9.2 (7.6-11.0)</td>
<td>6.3 (5.6-7.2)</td>
<td>3.8 (3.4-4.4)</td>
<td>22.3 (20.3-24.2)</td>
</tr>
<tr>
<td>- Diarrhea</td>
<td>13.7 (11.1-16.9)</td>
<td>12.5 (10.6-14.6)</td>
<td>10.1 (9.2-11.1)</td>
<td>6.0 (5.4-6.6)</td>
<td>28.0 (25.7-30.2)</td>
</tr>
</tbody>
</table>

1. The predicted proportion of SARS-CoV-2-positive individuals who experience a symptom at the designated day from symptom onset, as estimated by multiple imputation logistic regression.

2. The cumulative incidence of a symptom by day 21 from symptom onset, as estimated by the parametric cure-mixture model.
SARS-CoV-2-positive patients (n = 1797)

Enrolled in telehealth monitoring (n = 1765)

#include paraphrasing(if needed)

Included in analysis of symptom progression (n = 1564)

Hospitalized at LUH at the time of diagnosis (n = 31)
Diagnosed post mortem (n = 1)

Enrolled in telehealth before implementation of standardized data entry form (n = 200)
RT-PCR positive several weeks after exposure and symptom resolution (n = 1)

Targeted testing (1619 positive, of 16750 tested)
Open invitation population screening (158 positive, of 26762 tested)
Random population screening (20 positive, of 3924 tested)
List of Figures

S1 The total number of documented symptoms by date of diagnosis. The y-axis ranges from 0 to 19 symptoms, and the x-axis from February 27 to May 1, 2020. The median number of documented symptoms by date is depicted with a red dot and the date at which the standardized data entry form was implemented (March 17) is illustrated with a dotted vertical line. The relationship between date of diagnosis and the total number of documented symptoms is further illustrated with a generalized additive model with integrated smoothness estimation, which is depicted as a blue line.

S2 The cumulative incidence and daily proportion of SARS-CoV-2-positive patients (by RT-PCR) who fulfilled the WHO and CDC case definition criteria for suspected COVID-19 by age group and days from symptom onset. The x-axis ranges from symptom onset to day 21, and the y-axis shows the proportion or cumulative incidence as a percentage. The range of the y-axis varies between panels. The logistic regression estimate of the daily proportion of patients meeting criteria (panels A and B) are illustrated as lines with 95% confidence intervals depicted as shaded areas. The cumulative incidence of patients meeting criteria (panels C and D) are illustrated both as dots (representing the Turnbull estimate) and as lines, estimated using parametric cure-mixture models using a log-logistic distribution.

S3 The proportion of SARS-CoV-2-positive patients (by RT-PCR) experiencing generalized symptoms by day from symptom onset, estimated using different methods. The x-axis ranges from symptom onset until day 21, and the y-axis shows the proportion as a percentage. The range of the y-axis varies between panels. Four methods are shown. The daily proportion based on persons with no missing data (complete cases) is depicted with a closed circle, and a similar daily proportion based on a naive upward filling procedure is illustrated as a closed triangle. Estimates based on logistic regression using only cases with no missing data (blue, dotted line) and logistic regression with multiple imputation (red, solid line) are shown with 95% confidence intervals illustrated as a shaded area.

S4 The proportion of SARS-CoV-2-positive patients (by RT-PCR) experiencing upper respiratory symptoms by day from symptom onset, estimated using different methods. The x-axis ranges from symptom onset until day 21, and the y-axis shows the proportion as a percentage. The range of the y-axis varies between panels. Four methods are shown. The daily proportion based on persons with no missing data (complete cases) is depicted with a closed circle, and a similar daily proportion based on a naive upward filling procedure is illustrated as a closed triangle. Estimates based on logistic regression using only cases with no missing data (blue, dotted line) and logistic regression with multiple imputation (red, solid line) are shown with 95% confidence intervals illustrated as a shaded area.

S5 The proportion of SARS-CoV-2-positive patients (by RT-PCR) experiencing lower respiratory symptoms by day from symptom onset, estimated using different methods. The x-axis ranges from symptom onset until day 21, and the y-axis shows the proportion as a percentage. The range of the y-axis varies between panels. Four methods are shown. The daily proportion based on persons with no missing data (complete cases) is depicted with a closed circle, and a similar daily proportion based on a naive upward filling procedure is illustrated as a closed triangle. Estimates based on logistic regression using only cases with no missing data (blue, dotted line) and logistic regression with multiple imputation (red, solid line) are shown with 95% confidence intervals illustrated as a shaded area.

S6 The proportion of SARS-CoV-2-positive patients (by RT-PCR) experiencing gastrointestinal symptoms by day from symptom onset, estimated using different methods. The x-axis ranges from symptom onset until day 21, and the y-axis shows the proportion as a percentage. The range of the y-axis varies between panels. Four methods are shown. The daily proportion based on persons with no missing data (complete cases) is depicted with a closed circle, and a similar daily proportion based on a naive upward filling procedure is illustrated as a closed triangle. Estimates based on logistic regression using only cases with no missing data (blue, dotted line) and logistic regression with multiple imputation (red, solid line) are shown with 95% confidence intervals illustrated as a shaded area.

S7 The proportion of SARS-CoV-2-positive patients (by RT-PCR) experiencing generalized symptoms by testing strategy. The x-axis ranges from symptom onset until day 21, and the y-axis shows the proportion as a percentage. The range of the y-axis varies between panels. The 95% confidence intervals are illustrated as a shaded area.
S8 The proportion of SARS-CoV-2-positive patients (by RT-PCR) experiencing upper respiratory symptoms by testing strategy. The x-axis ranges from symptom onset until day 21, and the y-axis shows the proportion as a percentage. The range of the y-axis varies between panels. The 95% confidence intervals are illustrated as a shaded area.

S9 The proportion of SARS-CoV-2-positive patients (by RT-PCR) experiencing lower respiratory symptoms by testing strategy. The x-axis ranges from symptom onset until day 21, and the y-axis shows the proportion as a percentage. The range of the y-axis varies between panels. The 95% confidence intervals are illustrated as a shaded area.

S10 The proportion of SARS-CoV-2-positive patients (by RT-PCR) experiencing gastrointestinal symptoms by testing strategy. The x-axis ranges from symptom onset until day 21, and the y-axis shows the proportion as a percentage. The range of the y-axis varies between panels. The 95% confidence intervals are illustrated as a shaded area.

S11 Proportion of SARS-CoV-2-positive patients (by RT-PCR) experiencing generalized symptoms by age group, sex and day from symptom onset. The x-axis ranges from symptom onset to day 21, and the y-axis shows the proportion as a percentage. The range of the y-axis varies between panels. The logistic regression estimate of the proportion is illustrated with a colored line and the 95% confidence interval shown as a shaded area.

S12 Proportion of SARS-CoV-2-positive patients (by RT-PCR) experiencing upper respiratory symptoms by age group, sex and day from symptom onset. The x-axis ranges from symptom onset to day 21, and the y-axis shows the proportion as a percentage. The range of the y-axis varies between panels. The logistic regression estimate of the proportion is illustrated with a colored line and the 95% confidence interval shown as a shaded area.

S13 Proportion of SARS-CoV-2-positive patients (by RT-PCR) experiencing lower respiratory symptoms by age group, sex and day from symptom onset. The x-axis ranges from symptom onset to day 21, and the y-axis shows the proportion as a percentage. The range of the y-axis varies between panels. The logistic regression estimate of the proportion is illustrated with a colored line and the 95% confidence interval shown as a shaded area.

S14 Proportion of SARS-CoV-2-positive patients (by RT-PCR) experiencing gastrointestinal symptoms by age group, sex and day from symptom onset. The x-axis ranges from symptom onset to day 21, and the y-axis shows the proportion as a percentage. The range of the y-axis varies between panels. The logistic regression estimate of the proportion is illustrated with a colored line and the 95% confidence interval shown as a shaded area.

S15 Proportion of SARS-CoV-2-positive patients (by RT-PCR) experiencing generalized symptoms by hospitalization status. The x-axis ranges from symptom onset to day 21, and the y-axis shows the proportion as a percentage. The range of the y-axis varies between panels. The logistic regression estimate of the proportion is illustrated with a red or blue line the 95% confidence interval shown as a shaded area.

S16 Proportion of SARS-CoV-2-positive patients (by RT-PCR) experiencing upper respiratory symptoms by hospitalization status. The x-axis ranges from symptom onset to day 21, and the y-axis shows the proportion as a percentage. The range of the y-axis varies between panels. The logistic regression estimate of the proportion is illustrated with a red or blue line the 95% confidence interval shown as a shaded area.

S17 Proportion of SARS-CoV-2-positive patients (by RT-PCR) experiencing lower respiratory symptoms by hospitalization status. The x-axis ranges from symptom onset to day 21, and the y-axis shows the proportion as a percentage. The range of the y-axis varies between panels. The logistic regression estimate of the proportion is illustrated with a red or blue line the 95% confidence interval shown as a shaded area.

S18 Proportion of SARS-CoV-2-positive patients (by RT-PCR) experiencing gastrointestinal symptoms by hospitalization status. The x-axis ranges from symptom onset to day 21, and the y-axis shows the proportion as a percentage. The range of the y-axis varies between panels. The logistic regression estimate of the proportion is illustrated with a red or blue line the 95% confidence interval shown as a shaded area.
S19 Cumulative incidence of generalized symptoms experienced by SARS-CoV-2-positive patients (by RT-PCR) by day from symptom onset. The x-axis ranges from symptom onset to day 21, and the y-axis shows the cumulative incidence as a percentage. The range of the y-axis varies between panels. The non-parametric Turnbull estimate of the cumulative incidence is depicted with dots and the parametric cure-mixture estimate illustrated as a shaded grey area.

S20 Cumulative incidence of generalized symptoms experienced by SARS-CoV-2-positive patients (by RT-PCR) by age group and day from symptom onset. The x-axis ranges from symptom onset to day 21, and the y-axis shows the cumulative incidence as a percentage. The range of the y-axis varies between panels. The non-parametric Turnbull estimate of the cumulative incidence is depicted with dots and the parametric cure-mixture estimate illustrated as a line with the 95% confidence interval shown as a shaded grey area.

S21 Cumulative incidence of generalized symptoms experienced by SARS-CoV-2-positive patients (by RT-PCR) by sex and day from symptom onset. The x-axis ranges from symptom onset to day 21, and the y-axis shows the cumulative incidence as a percentage. The range of the y-axis varies between panels. The non-parametric Turnbull estimate of the cumulative incidence is depicted with dots and the parametric cure-mixture estimate illustrated as a line with the 95% confidence interval shown as a shaded grey area.

S22 Cumulative incidence of upper respiratory symptoms experienced by SARS-CoV-2-positive patients (by RT-PCR) by day from symptom onset. The x-axis ranges from symptom onset to day 21, and the y-axis shows the cumulative incidence as a percentage. The range of the y-axis varies between panels. The non-parametric Turnbull estimate of the cumulative incidence is depicted with dots and the parametric cure-mixture estimate illustrated as a line with the 95% confidence interval shown as a shaded grey area.

S23 Cumulative incidence of upper respiratory symptoms experienced by SARS-CoV-2-positive patients (by RT-PCR) by age group and day from symptom onset. The x-axis ranges from symptom onset to day 21, and the y-axis shows the cumulative incidence as a percentage. The range of the y-axis varies between panels. The non-parametric Turnbull estimate of the cumulative incidence is depicted with dots and the parametric cure-mixture estimate illustrated as a line with the 95% confidence interval shown as a shaded grey area.

S24 Cumulative incidence of upper respiratory symptoms experienced by SARS-CoV-2-positive patients (by RT-PCR) by sex and day from symptom onset. The x-axis ranges from symptom onset to day 21, and the y-axis shows the cumulative incidence as a percentage. The range of the y-axis varies between panels. The non-parametric Turnbull estimate of the cumulative incidence is depicted with dots and the parametric cure-mixture estimate illustrated as a line with the 95% confidence interval shown as a shaded grey area.

S25 Cumulative incidence of lower respiratory symptoms experienced by SARS-CoV-2-positive patients (by RT-PCR) by day from symptom onset. The x-axis ranges from symptom onset to day 21, and the y-axis shows the cumulative incidence as a percentage. The range of the y-axis varies between panels. The non-parametric Turnbull estimate of the cumulative incidence is depicted with black dots and the parametric cure-mixture estimate illustrated with a black line with the 95% confidence interval shown as a shaded grey area.

S26 Cumulative incidence of lower respiratory symptoms experienced by SARS-CoV-2-positive patients (by RT-PCR) by age group and day from symptom onset. The x-axis ranges from symptom onset to day 21, and the y-axis shows the cumulative incidence as a percentage. The range of the y-axis varies between panels. The non-parametric Turnbull estimate of the cumulative incidence is depicted with black dots and the parametric cure-mixture estimate illustrated as a line with the 95% confidence interval shown as a shaded grey area.

S27 Cumulative incidence of lower respiratory symptoms experienced by SARS-CoV-2-positive patients (by RT-PCR) by sex and day from symptom onset. The x-axis ranges from symptom onset to day 21, and the y-axis shows the cumulative incidence as a percentage. The range of the y-axis varies between panels. The non-parametric Turnbull estimate of the cumulative incidence is depicted with black dots and the parametric cure-mixture estimate illustrated with a line with the 95% confidence interval shown as a shaded grey area.
S28 Cumulative incidence of gastrointestinal symptoms experienced by SARS-CoV-2-positive patients (by RT-PCR) by day from symptom onset. The x-axis ranges from symptom onset to day 21, and the y-axis shows the cumulative incidence as a percentage. The range of the y-axis varies between panels. The non-parametric Turnbull estimate of the cumulative incidence is depicted with black dots and the parametric cure-mixture estimate illustrated as a black line with the 95% confidence interval shown as a shaded grey area.

S29 Cumulative incidence of gastrointestinal symptoms experienced by SARS-CoV-2-positive patients (by RT-PCR) by age group and day from symptom onset. The x-axis ranges from symptom onset to day 21, and the y-axis shows the cumulative incidence as a percentage. The range of the y-axis varies between panels. The non-parametric Turnbull estimate of the cumulative incidence is depicted with dots and the parametric cure-mixture estimate illustrated as a line with the 95% confidence interval shown as a shaded area.

S30 Cumulative incidence of gastrointestinal symptoms experienced by SARS-CoV-2-positive patients (by RT-PCR) by sex and day from symptom onset. The x-axis ranges from symptom onset to day 21, and the y-axis shows the cumulative incidence as a percentage. The range of the y-axis varies between panels. The non-parametric Turnbull estimate of the cumulative incidence is depicted with dots and the parametric cure-mixture estimate illustrated as a line with the 95% confidence interval shown as a shaded area.

S31 Cumulative incidence of generalized symptoms experienced by SARS-CoV-2-positive patients (by RT-PCR) by testing strategy. The x-axis ranges from symptom onset to day 21, and the y-axis shows the cumulative incidence as a percentage. The range of the y-axis varies between panels. The non-parametric Turnbull estimate of the cumulative incidence is depicted with dots and the parametric cure-mixture estimate illustrated as a line with the 95% confidence interval shown as a shaded area.

S32 Cumulative incidence of upper respiratory symptoms experienced by SARS-CoV-2-positive patients (by RT-PCR) by testing strategy. The x-axis ranges from symptom onset to day 21, and the y-axis shows the cumulative incidence as a percentage. The range of the y-axis varies between panels. The non-parametric Turnbull estimate of the cumulative incidence is depicted with dots and the parametric cure-mixture estimate illustrated as a line with the 95% confidence interval shown as a shaded area.

S33 Cumulative incidence of lower respiratory symptoms experienced by SARS-CoV-2-positive patients (by RT-PCR) by testing strategy. The x-axis ranges from symptom onset to day 21, and the y-axis shows the cumulative incidence as a percentage. The range of the y-axis varies between panels. The non-parametric Turnbull estimate of the cumulative incidence is depicted with dots and the parametric cure-mixture estimate illustrated as a line with the 95% confidence interval shown as a shaded area.

S34 Cumulative incidence of gastrointestinal symptoms experienced by SARS-CoV-2-positive patients (by RT-PCR) by testing strategy. The x-axis ranges from symptom onset to day 21, and the y-axis shows the cumulative incidence as a percentage. The range of the y-axis varies between panels. The non-parametric Turnbull estimate of the cumulative incidence is depicted with dots and the parametric cure-mixture estimate illustrated as a line with the 95% confidence interval shown as a shaded area.

S35 Cumulative incidence of generalized symptoms experienced by SARS-CoV-2-positive patients (by RT-PCR) by hospitalization status. The x-axis ranges from symptom onset to day 21, and the y-axis shows the cumulative incidence as a percentage. The range of the y-axis varies between panels. The non-parametric Turnbull estimate of the cumulative incidence is depicted with dots and the parametric cure-mixture estimate illustrated as a line with the 95% confidence interval shown as a shaded area.

S36 Cumulative incidence of upper respiratory symptoms experienced by SARS-CoV-2-positive patients (by RT-PCR) by hospitalization status. The x-axis ranges from symptom onset to day 21, and the y-axis shows the cumulative incidence as a percentage. The range of the y-axis varies between panels. The non-parametric Turnbull estimate of the cumulative incidence is depicted with dots and the parametric cure-mixture estimate illustrated as a line with the 95% confidence interval shown as a shaded area.
Cumulative incidence of lower respiratory symptoms experienced by SARS-CoV-2-positive patients (by RT-PCR) by hospitalization status. The x-axis ranges from symptom onset to day 21, and the y-axis shows the cumulative incidence as a percentage. The range of the y-axis varies between panels. The non-parametric Turnbull estimate of the cumulative incidence is depicted with dots and the parametric cure-mixture estimate illustrated as a line with the 95% confidence interval shown as a shaded area.

Cumulative incidence of gastrointestinal symptoms experienced by SARS-CoV-2-positive patients (by RT-PCR) by hospitalization status. The x-axis ranges from symptom onset to day 21, and the y-axis shows the cumulative incidence as a percentage. The range of the y-axis varies between panels. The non-parametric Turnbull estimate of the cumulative incidence is depicted with dots and the parametric cure-mixture estimate illustrated as a line with the 95% confidence interval shown as a shaded area.
Table S1: The proportion of missing information per variable by day from symptom onset. No data were missing for any variable for any patient during days on which interviews occurred. Information regarding the symptoms on days during which interviews did not occur can be considered to be missing.

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Figure S1: The total number of documented symptoms by date of diagnosis. The y-axis ranges from 0 to 19 symptoms, and the x-axis from February 27 to May 1, 2020. The median number of documented symptoms by date is depicted with a red dot and the date at which the standardized data entry form was implemented (March 17) is illustrated with a dotted vertical line. The relationship between date of diagnosis and the total number of documented symptoms is further illustrated with a generalized additive model with integrated smoothness estimation, which is depicted as a blue line.
Figure S2: The cumulative incidence and daily proportion of SARS-CoV-2-positive patients (by RT-PCR) who fulfilled the WHO and CDC case definition criteria for suspected COVID-19 by age group and days from symptom onset. The x-axis ranges from symptom onset to day 21, and the y-axis shows the proportion or cumulative incidence as a percentage. The range of the y-axis varies between panels. The logistic regression estimate of the daily proportion of patients meeting criteria (panels A and B) are illustrated as lines with 95% confidence intervals depicted as shaded areas. The cumulative incidence of patients meeting criteria (panels C and D) are illustrated both as dots (representing the Turnbull estimate) and as lines, estimated using parametric cure-mixture models using a log-logistic distribution.
Figure S3: The proportion of SARS-CoV-2-positive patients (by RT-PCR) experiencing generalized symptoms by day from symptom onset, estimated using different methods. The x-axis ranges from symptom onset until day 21, and the y-axis shows the proportion as a percentage. The range of the y-axis varies between panels. Four methods are shown. The daily proportion based on persons with no missing data (complete cases) is depicted with a closed circle, and a similar daily proportion based on a naive up-down filling procedure is illustrated as a closed triangle. Estimates based on logistic regression using only cases with no missing data (blue, dotted line) and logistic regression with multiple imputation (red, solid line) are shown with 95% confidence intervals illustrated as a shaded area.
Figure S4: The proportion of SARS-CoV-2-positive patients (by RT-PCR) experiencing upper respiratory symptoms by day from symptom onset, estimated using different methods. The x-axis ranges from symptom onset until day 21, and the y-axis shows the proportion as a percentage. The range of the y-axis varies between panels. Four methods are shown. The daily proportion based on persons with no missing data (complete cases) is depicted with a closed circle, and a similar daily proportion based on a naive up-down filling procedure is illustrated as a closed triangle. Estimates based on logistic regression using only cases with no missing data (blue, dotted line) and logistic regression with multiple imputation (red, solid line) are shown with 95% confidence intervals illustrated as a shaded area.
Figure S5: The proportion of SARS-CoV-2-positive patients (by RT-PCR) experiencing lower respiratory symptoms by day from symptom onset, estimated using different methods. The x-axis ranges from symptom onset until day 21, and the y-axis shows the proportion as a percentage. The range of the y-axis varies between panels. Four methods are shown. The daily proportion based on persons with no missing data (complete cases) is depicted with a closed circle, and a similar daily proportion based on a naive up-down filling procedure is illustrated as a closed triangle. Estimates based on logistic regression using only cases with no missing data (blue, dotted line) and logistic regression with multiple imputation (red, solid line) are shown with 95% confidence intervals illustrated as a shaded area.
Figure S6: The proportion of SARS-CoV-2-positive patients (by RT-PCR) experiencing gastrointestinal symptoms by day from symptom onset, estimated using different methods. The x-axis ranges from symptom onset until day 21, and the y-axis shows the proportion as a percentage. The range of the y-axis varies between panels. Four methods are shown. The daily proportion based on persons with no missing data (complete cases) is depicted with a closed circle, and a similar daily proportion based on a naive up-down filling procedure is illustrated as a closed triangle. Estimates based on logistic regression using only cases with no missing data (blue, dotted line) and logistic regression with multiple imputation (red, solid line) are shown with 95% confidence intervals illustrated as a shaded area.
Figure S7: The proportion of SARS-CoV-2-positive patients (by RT-PCR) experiencing generalized symptoms by testing strategy. The x-axis ranges from symptom onset until day 21, and the y-axis shows the proportion as a percentage. The range of the y-axis varies between panels. The 95% confidence intervals are illustrated as a shaded area.
Figure S8: The proportion of SARS-CoV-2-positive patients (by RT-PCR) experiencing upper respiratory symptoms by testing strategy. The x-axis ranges from symptom onset until day 21, and the y-axis shows the proportion as a percentage. The range of the y-axis varies between panels. The 95% confidence intervals are illustrated as a shaded area.
Figure S9: The proportion of SARS-CoV-2-positive patients (by RT-PCR) experiencing lower respiratory symptoms by testing strategy. The x-axis ranges from symptom onset until day 21, and the y-axis shows the proportion as a percentage. The range of the y-axis varies between panels. The 95% confidence intervals are illustrated as a shaded area.
**Figure S10:** The proportion of SARS-CoV-2-positive patients (by RT-PCR) experiencing gastrointestinal symptoms by testing strategy. The x-axis ranges from symptom onset until day 21, and the y-axis shows the proportion as a percentage. The range of the y-axis varies between panels. The 95% confidence intervals are illustrated as a shaded area.
Figure S11: Proportion of SARS-CoV-2-positive patients (by RT-PCR) experiencing generalized symptoms by age group, sex and day from symptom onset. The x-axis ranges from symptom onset to day 21, and the y-axis shows the proportion as a percentage. The range of the y-axis varies between panels. The logistic regression estimate of the proportion is illustrated with a colored line and the 95% confidence interval shown as a shaded area.
Figure S12: Proportion of SARS-CoV-2-positive patients (by RT-PCR) experiencing upper respiratory symptoms by age group, sex and day from symptom onset. The x-axis ranges from symptom onset to day 21, and the y-axis shows the proportion as a percentage. The range of the y-axis varies between panels. The logistic regression estimate of the proportion is illustrated with a colored line and the 95% confidence interval shown as a shaded area.
Figure S13: Proportion of SARS-CoV-2-positive patients (by RT-PCR) experiencing lower respiratory symptoms by age group, sex and day from symptom onset. The x-axis ranges from symptom onset to day 21, and the y-axis shows the proportion as a percentage. The range of the y-axis varies between panels. The logistic regression estimate of the proportion is illustrated with a colored line and the 95% confidence interval shown as a shaded area.
Figure S14: Proportion of SARS-CoV-2-positive patients (by RT-PCR) experiencing gastrointestinal symptoms by age group, sex and day from symptom onset. The x-axis ranges from symptom onset to day 21, and the y-axis shows the proportion as a percentage. The range of the y-axis varies between panels. The logistic regression estimate of the proportion is illustrated with a colored line and the 95% confidence interval shown as a shaded area.
Figure S15: Proportion of SARS-CoV-2-positive patients (by RT-PCR) experiencing generalized symptoms by hospitalization status. The x-axis ranges from symptom onset to day 21, and the y-axis shows the proportion as a percentage. The range of the y-axis varies between panels. The logistic regression estimate of the proportion is illustrated with a red or blue line the 95% confidence interval shown as a shaded area.
Figure S16: Proportion of SARS-CoV-2-positive patients (by RT-PCR) experiencing upper respiratory symptoms by hospitalization status. The x-axis ranges from symptom onset to day 21, and the y-axis shows the proportion as a percentage. The range of the y-axis varies between panels. The logistic regression estimate of the proportion is illustrated with a red or blue line the 95% confidence interval shown as a shaded area.
Figure S17: Proportion of SARS-CoV-2-positive patients (by RT-PCR) experiencing lower respiratory symptoms by hospitalization status. The x-axis ranges from symptom onset to day 21, and the y-axis shows the proportion as a percentage. The range of the y-axis varies between panels. The logistic regression estimate of the proportion is illustrated with a red or blue line the 95% confidence interval shown as a shaded area.
Figure S18: Proportion of SARS-CoV-2-positive patients (by RT-PCR) experiencing gastrointestinal symptoms by hospitalization status. The x-axis ranges from symptom onset to day 21, and the y-axis shows the proportion as a percentage. The range of the y-axis varies between panels. The logistic regression estimate of the proportion is illustrated with a red or blue line the 95% confidence interval shown as a shaded area.
Figure S19: Cumulative incidence of generalized symptoms experienced by SARS-CoV-2-positive patients (by RT-PCR) by day from symptom onset. The x-axis ranges from symptom onset to day 21, and the y-axis shows the cumulative incidence as a percentage. The range of the y-axis varies between panels. The non-parametric Turnbull estimate of the cumulative incidence is depicted with black dots and the parametric cure-mixture estimate illustrated with a black line with the 95% confidence interval shown as a shaded grey area.
Figure S20: Cumulative incidence of generalized symptoms experienced by SARS-CoV-2-positive patients (by RT-PCR) by age group and day from symptom onset. The x-axis ranges from symptom onset to day 21, and the y-axis shows the cumulative incidence as a percentage. The range of the y-axis varies between panels. The non-parametric Turnbull estimate of the cumulative incidence is depicted with dots and the parametric cure-mixture estimate illustrated as a line with the 95% confidence interval shown as a shaded area.
Figure S21: Cumulative incidence of generalized symptoms experienced by SARS-CoV-2-positive patients (by RT-PCR) by sex and day from symptom onset. The x-axis ranges from symptom onset to day 21, and the y-axis shows the cumulative incidence as a percentage. The range of the y-axis varies between panels. The non-parametric Turnbull estimate of the cumulative incidence is depicted with dots and the parametric cure-mixture estimate illustrated as a line with the 95% confidence interval shown as a shaded area.
Figure S22: Cumulative incidence of upper respiratory symptoms experienced by SARS-CoV-2-positive patients (by RT-PCR) by day from symptom onset. The x-axis ranges from symptom onset to day 21, and the y-axis shows the cumulative incidence as a percentage. The range of the y-axis varies between panels. The non-parametric Turnbull estimate of the cumulative incidence is depicted with black dots and the parametric cure-mixture estimate illustrated with a black line with the 95% confidence interval shown as a shaded grey area.
Figure S23: Cumulative incidence of upper respiratory symptoms experienced by SARS-CoV-2-positive patients (by RT-PCR) by age group and day from symptom onset. The x-axis ranges from symptom onset to day 21, and the y-axis shows the cumulative incidence as a percentage. The range of the y-axis varies between panels. The non-parametric Turnbull estimate of the cumulative incidence is depicted with dots and the parametric cure-mixture estimate illustrated as a line with the 95% confidence interval shown as a shaded area.
Figure S24: Cumulative incidence of upper respiratory symptoms experienced by SARS-CoV-2-positive patients (by RT-PCR) by sex and day from symptom onset. The x-axis ranges from symptom onset to day 21, and the y-axis shows the cumulative incidence as a percentage. The range of the y-axis varies between panels. The non-parametric Turnbull estimate of the cumulative incidence is depicted with dots and the parametric cure-mixture estimate illustrated as a line with the 95% confidence interval shown as a shaded area.
Figure S25: Cumulative incidence of lower respiratory symptoms experienced by SARS-CoV-2-positive patients (by RT-PCR) by day from symptom onset. The x-axis ranges from symptom onset to day 21, and the y-axis shows the cumulative incidence as a percentage. The range of the y-axis varies between panels. The non-parametric Turnbull estimate of the cumulative incidence is depicted with black dots and the parametric cure-mixture estimate illustrated with a black line with the 95% confidence interval shown as a shaded grey area.
Figure S26: Cumulative incidence of lower respiratory symptoms experienced by SARS-CoV-2-positive patients (by RT-PCR) by age group and day from symptom onset. The x-axis ranges from symptom onset to day 21, and the y-axis shows the cumulative incidence as a percentage. The range of the y-axis varies between panels. The non-parametric Turnbull estimate of the cumulative incidence is depicted with dots and the parametric cure-mixture estimate illustrated as a line with the 95% confidence interval shown as a shaded area.
Figure S27: Cumulative incidence of lower respiratory symptoms experienced by SARS-CoV-2-positive patients (by RT-PCR) by sex and day from symptom onset. The x-axis ranges from symptom onset to day 21, and the y-axis shows the cumulative incidence as a percentage. The range of the y-axis varies between panels. The non-parametric Turnbull estimate of the cumulative incidence is depicted with dots and the parametric cure-mixture estimate illustrated with a line with the 95% confidence interval shown as a shaded area.
Figure S28: Cumulative incidence of gastrointestinal symptoms experienced by SARS-CoV-2-positive patients (by RT-PCR) by day from symptom onset. The x-axis ranges from symptom onset to day 21, and the y-axis shows the cumulative incidence as a percentage. The range of the y-axis varies between panels. The non-parametric Turnbull estimate of the cumulative incidence is depicted with black dots and the parametric cure-mixture estimate illustrated as a black line with the 95% confidence interval shown as a shaded grey area.
Figure S29: Cumulative incidence of gastrointestinal symptoms experienced by SARS-CoV-2-positive patients (by RT-PCR) by age group and day from symptom onset. The x-axis ranges from symptom onset to day 21, and the y-axis shows the cumulative incidence as a percentage. The range of the y-axis varies between panels. The non-parametric Turnbull estimate of the cumulative incidence is depicted with dots and the parametric cure-mixture estimate illustrated as a line with the 95% confidence interval shown as a shaded area.
Figure S30: Cumulative incidence of gastrointestinal symptoms experienced by SARS-CoV-2-positive patients (by RT-PCR) by sex and day from symptom onset. The x-axis ranges from symptom onset to day 21, and the y-axis shows the cumulative incidence as a percentage. The range of the y-axis varies between panels. The non-parametric Turnbull estimate of the cumulative incidence is depicted with dots and the parametric cure-mixture estimate illustrated as a line with the 95% confidence interval shown as a shaded area.
Figure S31: Cumulative incidence of generalized symptoms experienced by SARS-CoV-2-positive patients (by RT-PCR) by testing strategy. The x-axis ranges from symptom onset to day 21, and the y-axis shows the cumulative incidence as a percentage. The range of the y-axis varies between panels. The non-parametric Turnbull estimate of the cumulative incidence is depicted with dots and the parametric cure-mixture estimate illustrated as a line with the 95% confidence interval shown as a shaded area.
Figure S32: Cumulative incidence of upper respiratory symptoms experienced by SARS-CoV-2-positive patients (by RT-PCR) by testing strategy. The x-axis ranges from symptom onset to day 21, and the y-axis shows the cumulative incidence as a percentage. The range of the y-axis varies between panels. The non-parametric Turnbull estimate of the cumulative incidence is depicted with dots and the parametric cure-mixture estimate illustrated as a line with the 95% confidence interval shown as a shaded area.
Figure S33: Cumulative incidence of lower respiratory symptoms experienced by SARS-CoV-2-positive patients (by RT-PCR) by testing strategy. The x-axis ranges from symptom onset to day 21, and the y-axis shows the cumulative incidence as a percentage. The range of the y-axis varies between panels. The non-parametric Turnbull estimate of the cumulative incidence is depicted with dots and the parametric cure-mixture estimate illustrated as a line with the 95% confidence interval shown as a shaded area.
Figure S34: Cumulative incidence of gastrointestinal symptoms experienced by SARS-CoV-2-positive patients (by RT-PCR) by testing strategy. The x-axis ranges from symptom onset to day 21, and the y-axis shows the cumulative incidence as a percentage. The range of the y-axis varies between panels. The non-parametric Turnbull estimate of the cumulative incidence is depicted with dots and the parametric cure-mixture estimate illustrated as a line with the 95% confidence interval shown as a shaded area. The parametric cure-mixture model was unable to be fit to the cumulative incidence of vomiting among the different testing strategies as no individual diagnosed by random population screening experienced vomiting (panel C).
Figure S35: Cumulative incidence of generalized symptoms experienced by SARS-CoV-2-positive patients (by RT-PCR) by hospitalization status. The x-axis ranges from symptom onset to day 21, and the y-axis shows the cumulative incidence as a percentage. The range of the y-axis varies between panels. The non-parametric Turnbull estimate of the cumulative incidence is depicted with dots and the parametric cure-mixture estimate illustrated as a line with the 95% confidence interval shown as a shaded area.
Figure S36: Cumulative incidence of upper respiratory symptoms experienced by SARS-CoV-2-positive patients (by RT-PCR) by hospitalization status. The x-axis ranges from symptom onset to day 21, and the y-axis shows the cumulative incidence as a percentage. The range of the y-axis varies between panels. The non-parametric Turnbull estimate of the cumulative incidence is depicted with dots and the parametric cure-mixture estimate illustrated as a line with the 95% confidence interval shown as a shaded area.
A. One or more of any lower respiratory symptom

B. Non-productive cough

C. Productive cough

D. Any dyspnea

E. Dyspnea at rest

Figure S37: Cumulative incidence of lower respiratory symptoms experienced by SARS-CoV-2-positive patients (by RT-PCR) by hospitalization status. The x-axis ranges from symptom onset to day 21, and the y-axis shows the cumulative incidence as a percentage. The range of the y-axis varies between panels. The non-parametric Turnbull estimate of the cumulative incidence is depicted with dots and the parametric cure-mixture estimate illustrated as a line with the 95% confidence interval shown as a shaded area.
Figure S38: Cumulative incidence of gastrointestinal symptoms experienced by SARS-CoV-2-positive patients (by RT-PCR) by hospitalization status. The x-axis ranges from symptom onset to day 21, and the y-axis shows the cumulative incidence as a percentage. The range of the y-axis varies between panels. The non-parametric Turnbull estimate of the cumulative incidence is depicted with dots and the parametric cure-mixture estimate illustrated as a line with the 95% confidence interval shown as a shaded area.