













SCAN Technical Report

Friday, April 17, 2020

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Erratum: This version was created on April 23, 2020, and corrects two errors ("might be" \rightarrow "might not be" on page 3; "1,600" \rightarrow "225" on page 12) and several inadvertent omissions from the Acknowledgements (page 14).

1. What is SCAN?

The greater Seattle Coronavirus Assessment Network, or SCAN, is a public health surveillance (disease monitoring) program for SARS-CoV-2 (the virus that causes COVID-19) infection in greater Seattle and King County. SCAN is designed to help us better understand the COVID-19 outbreak and, with other sources of data, inform public health decisions. The SCAN platform launched on March 23, 2020 with an initial focus on COVID-19 testing of individuals comprising a broad representation of the greater Seattle and King County region using the at-home sample collection with a self-swabbing kit developed by the Seattle Flu Study (SFS).

The initial key objectives of SCAN are:

- Rapid, widespread collection and testing of community specimens to obtain a snapshot of the current extent of COVID-19 spread in King County
 - Is there an iceberg of cases below the currently recognized tip?
- Ongoing tracking for SARS-CoV-2 circulation in King County for the duration of the COVID-19 outbreak with weekly snapshot updates

<u>Is viral spread increasing or decreasing? Do public health measures need to be stepped up or can they be relaxed?</u>

SCAN is a partnership between the team behind the <u>Seattle Flu Study</u> (SFS) and <u>Public Health</u> — <u>Seattle & King County</u> (PHSKC). It is being executed by the <u>Brotman Baty Institute for Precision Medicine</u> (BBI), which is a collaboration between <u>UW Medicine</u>, the <u>Fred Hutchinson Cancer Research Center</u>, and <u>Seattle Children's</u>. SCAN relies on data modeling support from the <u>Institute for Disease Modeling</u> (IDM). It is funded by Gates Ventures (the private office of Bill Gates) and receives technical guidance from the <u>Centers for Disease Control and Prevention</u> and the <u>Bill & Melinda Gates Foundation</u>.

2. What SCAN is not

- SCAN is a public health disease surveillance program and <u>not</u> a clinical service. Its purpose is to take samples from the community to build our understanding of how COVID-19 is moving through our region by testing people who otherwise might not be tested. Our primary goal is to more completely understand where the virus exists in our region to inform public health decision-making at both the local and national levels.
- SCAN is designed to include a higher proportion of people experiencing COVID-19-like symptoms than in the general community. However, even within this group, SCAN differs from nearly all other SARS-CoV-2 testing being conducted in the United States in that the individuals we are testing are generally <u>not</u> presenting to medical care.
- At this time, SCAN is <u>not</u> yet achieving a representative sample of the population in the
 greater Seattle and King County region. Relative to our population, SCAN participants
 differ in terms of age, geography, income, race/ethnicity and other factors. These
 differences are documented below, and we are working to reduce them. However, all
 results and conclusions of this report are limited by this lack of representativeness.

Please see https://scanpublichealth.org/faq for additional information.

3. SCAN enrollment & testing

SCAN uses the infrastructure and methods developed by the collaborative team behind the <u>Seattle Flu Study</u> (SFS), including an at-home collection and self-swabbing kit. This model enables simpler sample collection and a wider range of participants, both with and without symptoms, than would present for health care.

Residents of most of King County can request a "Swab-and-Send" kit by logging on to the SCAN website, www.scanpublichealth.org. Briefly, the SCAN web platform consists of a web-based screening and enrollment site tied to a central patient database as well as a sample- and data- tracking database. Back-end applications also link to kit-delivery and -return partners as well as to a HIPAA-compliant portal for returning results. Website visitors are screened by ZIP code and whether or not they report COVID-19-like illness (CLI), defined as new or worsening cough, fever, or shortness of breath in the past week. Enrollments are capped each day due to lab capacity and to increase geographic representativeness. Enrollees complete a short survey with questions about demographics, symptoms, and risk factors and receive a nasal self-swab kit at their home within a day, shipped and returned using a private courier. Clear instructions for self-swabbing are provided in the kit "QuickStart" guide, along with a video demonstration on the SCAN website. The participant schedules pick-up/return of the completed swab kit. Upon receipt by the lab, it is registered, unboxed, and prepared for testing following all appropriate biosafety procedures. Kits fulfill all shipping and regulatory safety requirements.

The SCAN lab facilities are CLIA-certified through the Washington State Department of Health (WA DOH). Our CLIA-certified SARS-CoV-2 assay is a real-time RT-PCR test. We also sequence the SARS-CoV-2 genomes of positive samples and test all samples for a broad panel of respiratory viral pathogens on a research basis. Positive test results are provided to the individual participant by phone consultation (including advice to follow up with referral to their health providers if they have any concerns), and all participants have online access to results and a downloadable, printable report. A line-list testing report of all negative and positive results is reported to the local health authorities (PHSKC and WA DOH). Aggregate data including demographic and geographic information is regularly reported to PHSKC and partners, and a public-facing dashboard is in development.

In addition to the primary recruitment mechanism described above, a small number of clinical residual samples that are not otherwise being tested for SARS-CoV-2 are sent from area hospitals. These are tested in a deidentified manner and aggregate results including age and ZIP code of residence are reported to public health.

4. Participant characteristics from March 23 to April 9

Respondents self-select to participate in SCAN and are not wholly representative of all King County residents at this time. **Table 1** describes some of the demographic and health attributes of the SCAN participants from launch on March 23 through April 9. Participants are most likely to report female sex at birth (55.2%), race and ethnicity as non-Hispanic White (66.7%) or Asian (17.1%), and household income greater than \$150,000 per year (31.2%). The vast majority of participants report that they did not recently seek healthcare (84.5%) and do not have chronic conditions associated with COVID-19 severity (87.9% report no underlying conditions).

Table 1. Characteristics of SCAN participants through April 9. Note that the ratio of those who reported and did not report COVID-like illness (CLI) is determined through sampling, and not representative of the population of respondents.

	Total (% of Total)	No reported CLI*	Reported CLI
All Participants	4092	1392	2700
Sex at Birth Female Male Other Missing	2260 (55.2%) 1812 (44.3%) 2 18	767 621 0 4	1493 1191 2 14
Race and Ethnicity White, not Hispanic Hispanic or Latino, any race Asian, not Hispanic Black, not Hispanic Native Hawaiian or Pacific Islander American Indian or Alaskan Native Other or multi-racial, not Hispanic Unknown	2731 (66.7%) 239 (5.8%) 699 (17.1%) 79 (1.9%) 29 (0.7%) 19 (0.5%) 213 (5.2%) 83 (2.0%)	1038 68 169 21 6 7 59	1693 171 530 58 23 12 154 59
Income (last year before taxes) <pre> < \$25,000 > \$25,000 - \$50,000 > \$50,000 - \$75,000 > \$75,000 - \$100,000 > \$100,000 - \$125,000 > \$125,000 - \$150,000 > \$150,000 Prefer not to say Don't know Missing</pre>	229 (5.6%) 368 (9.0%) 442 (10.8%) 452 (11.0%) 397 (9.7%) 364 (8.9%) 1275 (31.2%) 523 (12.8%) 41 (1.0%)	58 105 133 142 173 140 453 176 12 0	171 263 309 310 224 224 822 347 29 1

Sought Care** No Yes, at Doctor's or Urgent Care Yes, at Pharmacy Yes, at Hospital or Emergency Department Yes, Other Missing	3458 (84.5%)	1328	2130
	344 (8.4%)	40	304
	13 (0.3%)	1	12
	11 (0.3%)	2	9
	285 (7.0%)	24	261
	4 (0.1%)	0	4
Underlying Conditions (individuals may have more than one)			
Chronic heart disease Chronic lung disease Diabetes Immunosuppressed None Missing	63	20	43
	126	33	93
	147	55	92
	205	58	147
	3598 (87.9%)	1238	2360
	4	0	4

^{*} CLI = self=reported new COVID-like illness (cough, fever, or shortness of breath) in the past 7 days

Figure 1 shows the age distribution of SCAN participants in comparison with the <u>estimated 2019 age distribution of all residents in King County</u>. The most common participant age range is 30-39 years (30%). The current proportion of SCAN participants who are children or elderly is lower than that of the King County population.

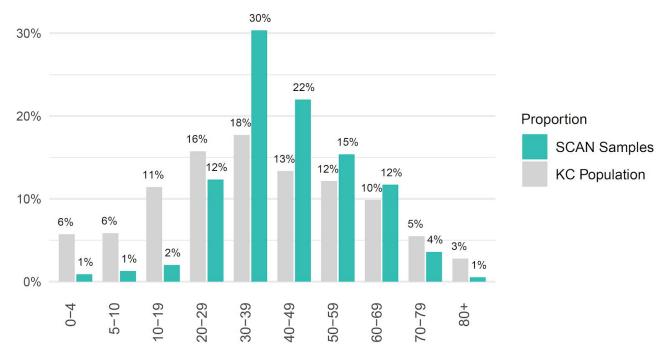


FIGURE 1: The distribution of SCAN community samples across age groups compared to the general King County population.

^{**}includes people who may have sought care for symptoms other than CLI

Figure 2 describes the residential location of SCAN participants in King County relative to estimated total population. Locations are grouped into census Public Use Microdata Areas (PUMAs). The representativeness ratio is a normalized measure of the ratio of the participant population relative to the total population residing in each PUMA. Ratios above (below) 1 indicate a residential location is overrepresented (underrepresented) relative to uniform sampling. Through April 9, participants more often live within Seattle city limits, Bellevue, and nearby eastside towns. South and rural eastern King County residents are underrepresented thus far.

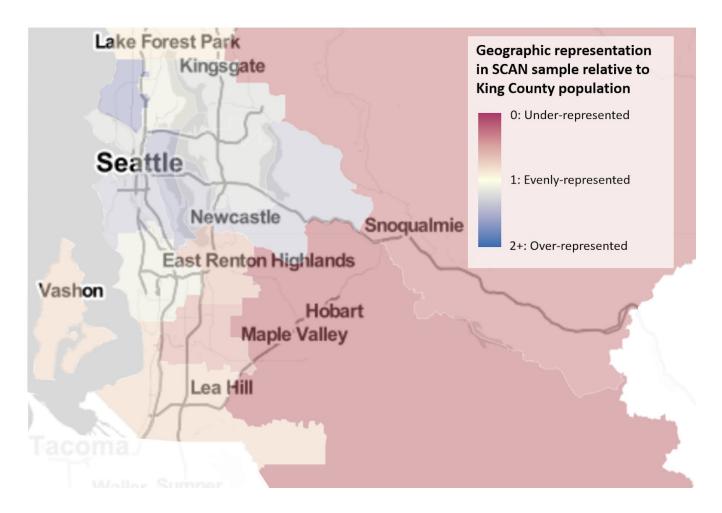


FIGURE 2: The distribution of residential locations for SCAN participants by census PUMA in King County. The representativeness ratio measures the frequency of participants relative to census population. PUMAs with ratios above (below) 1 are overrepresented (underrepresented) relative to uniform geographic sampling.

To reiterate, SCAN sampling is not wholly representative of all King County residents, and all results below should be interpreted with that caveat. Moving forward, we are adjusting our recruitment strategies to improve representativeness, so as to better identify how COVID-19 is affecting our entire community.

5. Does SCAN's symptom screener achieve risk stratification for SARS-CoV-2 infection?

Individuals who visit the SCAN website are screened with a three-question survey. Participants provide their ZIP code, age, and indicate whether they experienced COVID-like illness (CLI) in the past week in response to the question, "In the past week, have you been sick with a new fever, a new or worsening cough, or a new or worsening shortness of breath?" Respondents both with and without CLI are able to enroll.

About 20.6% of participants who fill out the screener questionnaire report experiencing CLI. Through April 9, of those who self-reported CLI in response to the screener question and enrolled in SCAN (N=2700), 44 participants (1.6%) tested positive for SARS-CoV-2. Of those who reported no CLI in response to the screener question and enrolled in SCAN (N=1392), 1 participant (0.1%) tested positive for SARS-CoV-2. Of note and as discussed further below, this participant appears to have inaccurately answered the screener question, as their responses to the full-length illness questionnaire indicated that they had experienced CLI in the preceding seven days and had visited a health care provider for their illness.

The fact that nearly all positive test results were among participants who self-identified as having CLI indicates that the screener question was quite specific for COVID-19. As public health officials develop plans for relaxing social- and physical-distancing policies, it is unlikely that repeated testing of entire populations will be an effective use of resources. Therefore, the ability to easily distinguish between high- and low-risk populations will be critical to direct limited testing resources. These results suggest that a simple self-reported symptom-checker will be a useful source of information for such stratification for adults. As we enroll more children, we will understand how effectively this question predicts risk in younger age groups.

As we discuss in the following section, although one participant not reporting CLI had a positive test result, because of the relatively small number of persons without CLI tested, this is still consistent with the possibility that there are thousands of infections among people in the non-CLI sub-population. It is also likely that the population that has so far self-selected to visit the SCAN website and enroll in the non-CLI arm is biased compared to the general population of King County; this group may be at lower risk of coronavirus infection than the general population in King County.

For the time being, SCAN will continue to sample from individuals reporting no CLI; this could change in future if low yield of positives suggests the costs are greater than the benefits.

6. What does SCAN tell us about infections in the community?

In this section, we describe results from the first 18 days of testing SCAN community samples (March 23 to April 9, 2020). The small number of clinical residual samples that SCAN has processed are not included in this report. These results must be interpreted with caution for the following reasons:

- As described above, SCAN data are drawn from a self-selected sample of individuals who are drawn from an unknown sampling frame within a defined set of zip codes. As such, there may be biases due to sampling that we cannot adjust for. Our working assumption is that our sample so far is biased toward lower-risk individuals who may be more likely to heed public health messaging around reducing transmission risk, have regular access to the internet and a stable home address, and are aware of SCAN through mass media and word of mouth. Furthermore, individuals who know one another are more likely to enroll in SCAN: one-third of SCAN participants live with another SCAN participant. This means that individual risk of infection within the sample is correlated among individuals.
- Most SCAN participants report no or only mild symptoms and have not sought care at the time of enrollment. In other words, they are mostly drawn from a separate population than cases observed through clinical sampling. While SCAN gives us insight into this often hidden part of the "iceberg" of cases, it does not describe the population that seeks health care -- the classic "tip of the iceberg." In future reports, we plan to integrate clinically reported cases with SCAN data to present a fuller picture of the disease iceberg or pyramid.
- We rely on respondents to self-report CLI. While all enrollees responded to the same screener question, how they interpreted the questions might vary across subjects. Furthermore, we set a target of 3 participants reporting CLI for every one participant not reporting CLI, so it is possible that some respondents without CLI falsely reported symptoms as a way to get around the cap on enrollment for those without CLI. As such, results for those reporting CLI and those not reporting CLI must be interpreted in light of this possible misclassification.

Table 2 describes data on testing for SARS-CoV-2 among those reporting CLI symptoms. For samples collected between March 23 and April 9, a total of 4092 conclusive tests have been returned; 1392 of these were from respondents who reported no CLI. A test from one respondent who reported no CLI in the screener returned a positive result. However, this individual appears to have misclassified their illness status, as their responses to the full-length illness questionnaire indicated that they had experienced cough, muscle or body aches, and sore throat in the preceding seven days, and had visited a health care provider for their illness.

The remaining 2700 samples belonged to respondents reporting new or worsening CLI in the past week. These results are summarized in Table 2. Overall, 44 tests (1.6%) returned positive results. There was no significant difference in the percent returning positive across age groups (under 20, adults 20-59, and adults 60 years and over), nor were there significant differences by sex at birth. Geographically, there have been positive test results from nearly all PUMAs in the county. There are too few samples to identify potential 'hot spots', but infections do appear to be present geographically throughout King County.

Table 2. How many people with COVID-like illness had a positive test result?

	Number with positive results for SARS-CoV-2 / Number reporting COVID-Like Illness	% positive for SARS-CoV-2 among those reporting CLI (Range of Likely Values)*
Total	44/2700	1.6% (1.2% - 2.2%)
Age Group 0-19 years 20-59 years 60+ Missing	2/130 31/1867 11/336 0/7	1.5% (0.2% - 5.4%) 1.7% (1.1% - 2.3%) 3.3% (1.6% - 5.8%)
Sex at Birth Female Male Other Missing	20/1493 23/1191 0/2 1/14	1.3% (0.8% - 2.1%) 1.9% (1.2% - 2.9%)

^{*} These 95% confidence intervals for binomial distributions assume random independent sampling, which is not the case for SCAN. These percentages reflect only the proportion positive among people tested through SCAN and do not reflect percentages in the overall population. As SCAN continues to collect samples from more people, the variability in the percentages will decrease and the proportion positive among people tested through SCAN can be used to estimate the prevalence of SARS-CoV-2 infection in the King County population.

In addition to these results, 11 tests were returned with inconclusive results, meaning that only two of four SARS-CoV-2 targets for the RT-PCR test were positive.

Figure 3 shows the daily total of tests, results, and proportion positive by day over the first 18 days of results, stratified by reported CLI. A sample ratio of about 75:25 CLI:non-CLI is maintained most days as it is controlled by the screener questionnaire. There is a declining trend of proportion testing positive over time, but this needs to be interpreted with caution as these include both CLI and non-CLI, and the split of CLI to non-CLI can vary by day. In the following section we discuss an adjusted time trend which accounts for these issues.

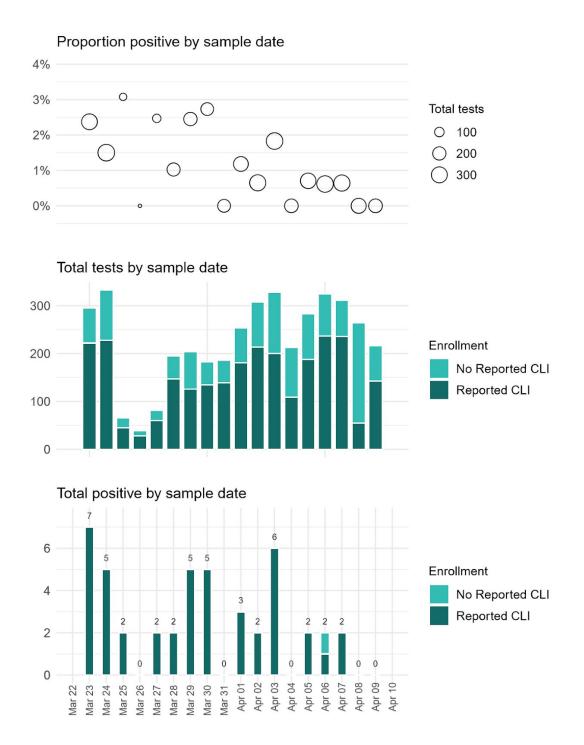


FIGURE 3: SCAN tests results by enrollment date, between 23 March and 9 April. Top: proportion of tests returning a positive result. Circle sizes represent the number of samples taken that day. Middle: Total tests for samples taken each day, stratified by self-reported CLI symptoms. Bottom: Total positive test results for samples taken each day, stratified by self-reported CLI symptoms. CLI = COVID-like illness (new or worsening cough, fever, or shortness of breath in the past week).

We developed a statistical model to adjust for several of the known data issues outlined above. The details of the statistical model are described in the technical appendix (Section 8 of this report). Briefly, we pooled data from the self-reported CLI and non-CLI samples and fit a logistic regression controlling for CLI/non-CLI sample and age group. We also included a random effect for residence to account for added variance due to household membership. Each observation was also assigned two weights based on sample membership and age group. Respondents in the CLI sample were weighted 0.2, and those in non-CLI sample 0.8, as approximately 20% of SCAN respondents report CLI symptoms on the screener (based on 30,499 responses including from people who visited the site but were not able to enroll and be tested due to caps). Age groups were weighted relative to the King County population distribution, such that observations belonging to under-represented ages were given a higher weight. Using this model, we make estimates of population period prevalence with 95% credible intervals.

While this approach accounts for some sources of bias and added variability, it does not account for all of them: these estimates are likely to be affected by using a self-selected sample that may tend to be at lower risk of infection. Furthermore, the prevalence estimates are to be interpreted as a community sample, distinct from a clinical sample of patients with more severe illness. These factors could result in underestimation of population prevalence in King County. On the other hand, it is possible that individuals with CLI are more likely to participate in SCAN than the general population (*i.e.* that much less than 20% of King County has experienced CLI in the previous 7 days), which would result in overestimation of population prevalence in King County. These biases are likely to be fairly constant over the first 18 days of SCAN data collection, as we have yet to undertake active recruitment. As such, we believe prevalence estimates over time can be directly interpreted relative to one another.

We estimate that the average population prevalence between March 23 and April 9 was 0.24% [95% CI 0.05% - 0.75%]. In other words, at any given time during that period, we estimate the infected population in King County was between 1,100 and 16,900 individuals. Among those reporting CLI symptoms, prevalence over the period was estimated at 1.47% [95% CI 0.95% - 2.25%]. Among those not reporting CLI symptoms, we estimate the upper bound of the 95% CI of the period prevalence to be 0.49%.

We found evidence that community prevalence has been declining in King County. **Figure 4** shows the decline in population prevalence over the period from March 23 through April 9 across three discrete six-day periods. During the period from Monday March 23 to Saturday March 28, we estimate prevalence was 0.32% [0.08%-1.18%], from Sunday March 29 to Friday April 3, we estimate prevalence was 0.27% [0.07%-0.95%], and from Saturday April 4 to Thursday April 9, we estimate prevalence declined to 0.07% [0.01%-0.36%]. During this most recent period, we estimate that between 225 and 8,100 King County community residents were infected with SARS-CoV-2, subject to the aforementioned caveats. Note that not all

samples collected in the last period had been returned to or tested by the lab at the time that this report was prepared, and these results are thus subject to change as data are updated.

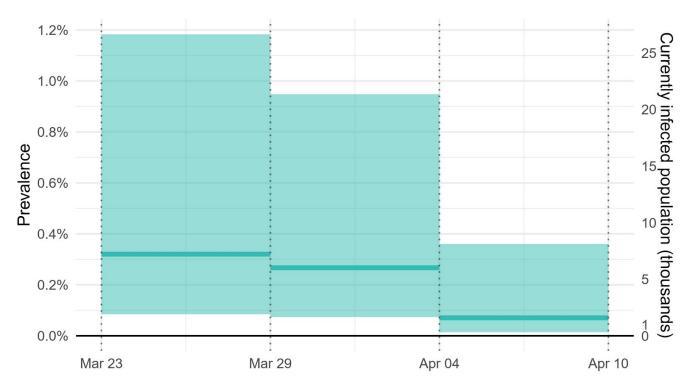


FIGURE 4: Model-based estimate of population period prevalence in the community from March 23 through April 9, with time split into three six-day periods. The estimate for the third period, Apr 4-9, is provisional at the time of writing.

7. How will SCAN continue to serve public health?

SCAN plans to continue assessment of the community prevalence of SARS-CoV-2 for the duration of King County's COVID-19 outbreak and for future COVID-19 seasons if these occur. Immediate next steps for SCAN include efforts to:

- Increase inclusion and representation of children 18 years and under. As noted above, children are currently underrepresented in SCAN. However, they may be an important source of unrecognized COVID-19 due to asymptomatic or milder presentations. The extent of positivity in kids, including within different age ranges, may inform our understanding of the relative impact of school closures vs. other social-distancing strategies, as well as the risk of rebound when schools reopen.
- Increase representation of other key groups in King County that are not yet participating in high enough numbers in SCAN. These include residents in South and East King County, essential workers, adults greater than 65 years of age, males, and non-English speakers.

We are currently developing and implementing strategies aimed at increasing participation of the above-mentioned groups. We will also roll out translations of the website in 12 different languages, beginning with Spanish, Vietnamese, and Chinese in the third week of April (week 4 since SCAN's launch). We implemented a 7-day follow-up questionnaire for participants starting April 15, and will report those results in a future brief. These data will help describe the course of illness of individuals who test positive despite reporting no or mild symptoms at the time of enrollment, which may contribute to a better understanding of asymptomatic and pre-symptomatic transmission.

In the longer term, we anticipate SCAN will play a key role, along with other data sources, in helping public health officials assess the prevalence of COVID-19 and track whether and the levels of infection change if we relax or strengthen community mitigation measures. Because SCAN offers testing to community members who are not sick enough to seek healthcare, including those without any symptoms, it will continue to provide a view onto the submerged portion of the disease iceberg or pyramid. Surveillance of these subsets of the community is key because people with mild or no illness are more likely to mix in the community once businesses and workplaces reopen and may transmit the virus.

As SCAN data further accrue, King County will accumulate more information to understand how many symptomatic and asymptomatic cases may be unrecognized in the community, as well as which groups (age, region) in the community might be at particular risk. Together with other sources of data, SCAN may also inform ongoing estimates of the reproductive rate of the SARS-CoV-2 virus in the community, a key parameter for understanding the extent of transmission and an indicator of whether the outbreak is under control.

8. Technical appendix

Model description

We used the following approach to adjust our estimates for CLI and non-CLI sampling split, under-representation of youngest and oldest age groups, and clustering of respondents by residence in order to make population prevalence estimates.

First, we fit the following hierarchical logistic regression:

$$\begin{split} C_{i,h} &\sim Bernoulli(p_{i,h}) \\ log(\frac{p_{i,h}}{1-p_{i,h}}) &= \beta_0 + \beta_c CLI_i + \beta_a AgeGroup_i + \beta_p Period_i + \epsilon_h \\ \epsilon_h &\sim Normal(0,\sigma^2) \end{split}$$

Where:

- $C_{i,h}$ is the test result (1=positive, 0=negative) for an individual i living in residence h. $C_{i,h}$ is assumed to follow a Bernoulli distribution, with risk of infection $p_{i,h}$.
- $p_{i,h}$ is modeled as the logit-transformed sum of the following components:
 - \circ β_0 is the intercept
 - \circ CLI_i is an indicator for self-report CLI (0=no CLI, 1=CLI) with regression coefficient β_c
 - o $AgeGroup_i$ is a vector of indicator variables for respondent age group (0-4, 5-19, 20-59, 60+) with vector of regression coefficients β_a .
 - \circ $Period_i$ is a vector of indicator variables for one of three periods under which the respondent enrolled (1 = March 23 to March 28, 2 = March 29 to April 3, 3 = April 4 to April 9) with vector of regression coefficients β_p . These fixed effects were used to make the time dependent prevalence estimates. In the case of prevalence estimates for the overall time period, the model was run without these terms.
 - \circ ε_h is a residence random effect term used to capture extra variance in prevalence arising from clustered data.

The model was fit in R version 3.5.1, using the <u>INLA package</u> (version 18.07.12). The INLA package allows for approximate Bayesian inference. Default priors were used for all unknown model parameters β and σ .

We drew 5000 predictive samples (posterior draws) for each individual, accounting for parameter uncertainty in the fitted model. Each individual was also assigned two weights:

- A CLI weight, $w_{1,i}$ which is 0.2 if the respondent reported CLI, otherwise 0.8. About 20% of respondents to the SCAN screener reported CLI.
- An age-based post-stratification weight, $w_{2,i}$. Using population age projections for King County in 2019, for each age group, the weight is defined as the ratio of the sum of population to the sum of samples in each age group.

Each of the 5000 predictive samples were collapsed across all individuals using a weighted mean with weight $w_{1,i}w_{2,i}$. The remaining vector of 5000 population-weighted samples was summarized to a mean, lower quantile (2.5%) and upper quantile (97.5%). This summarization procedure was done separately for different subpopulations: either the entire sample, the sample split into the three periods, or the CLI and non-CLI arms separately.

9. SCAN acknowledgements

This technical report was drafted based on SCAN data by Roy Burstein, Karen Cowgill, Michael Famulare and Jay Shendure. SCAN is a partnership between the team behind the Seattle Flu Study (SFS) and Public Health — Seattle & King County (PHSKC). SCAN is being executed by the Brotman Baty Institute for Precision Medicine (BBI).

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