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The prevalence of SARS-CoV2 in the US estimated from imperfect testing

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Abstract

4 An accurate estimate of the prevalence and distribution of the novel coron-
5 avirus (SARS-CoV2) in the United States is essential for an effective response
6 to the COVID-19 pandemic. The initial lack of sufficient testing capacity in the
7 United States hinders the effort of stopping the spread of the virus. Furthermore,
8 the US lacks a coherent reporting system where concerned citizens can find ac-
9 curate information. Without an accurate estimation of the prevalence of the
10 infection in the population, we cannot properly determine how likely a positive
11 test result is to be a false positive and how likely a negative result is to be a false
12 negative. Here we present a statistical model for estimating the prevalence of
13 SARS-CoV 2 infection in the nation and in each state by pooling data from all
14 reported state-level testing results. Our results show that accurate reporting (of
15 both positive and negative results) is necessary to properly understand the spread
16 of the virus. The estimated national average of prevalence is about 10% when
17 using all available data. When states without a consistent record of reporting
18 negative results were removed from the analysis, the average is about 6%.

19 Key Words and Terms: Bayesian statistics, binary tests, COVID-19, false
20 negative, false positive, hierarchical model, prevalence

21 **Introduction**

22 Tests with binary outcomes to indicate a binary state of the nature (e.g., presence or
23 absence of a disease agent) are common. Nearly all tests are imperfect: they produce
24 occasional false positive and false negative results. Here we use data of testing for the
25 novel coronavirus (SARS-CoV2) in the United States to demonstrate the use of the
26 Bayesian hierarchical modeling framework to better understand the prevalence of the
27 disease. Our analysis highlights the need for more testing because the test for detecting
28 SARS-CoV2 is imperfect. When a patient is tested we are uncertain whether a positive
29 result is a reliable indicator of the presence of the virus. Likewise, we cannot rule out
30 a negative result being a false negative. The problem of interpreting results from an
31 imperfect test is not new. Recently, Qian et al.¹ provided a summary of the underlying
32 statistical issues of interpreting imperfect test results. The interpretation and use of
33 imperfect test results depend on the purpose of the test. For testing of SARS-CoV2,
34 the purposes of the test are (1) diagnosing individual patients and (2) estimating the
35 prevalence of the virus in a population. For the diagnostic purpose, whether a positive
36 test result is indicative of an infection depends on (1) the quality of the test measured
37 by the rates of false positives and false negatives and (2) the prevalence of the virus
38 in the population. At this point, we do not have a good understanding of these three
39 quantities. They must be estimated from testing data.

40 We present a statistical model to estimate the prevalence of the virus in each state
41 using publicly available data. The quality of the model result depends on (1) our knowl-
42 edge of the test (how well do we know the rates of false positives and false negatives)
43 and (2) the number of people tested (sample size). The better we can characterize the

test and the more people who are tested, the more accurate the estimated population prevalence. A large number of tests allow us better estimate not only the prevalence but also the test's false-positive and false-negative rates. A better understanding of the test and the prevalence makes the test a better diagnostic tool. Using data reported in the public domain (testing results and estimates of rates of false positives and false negatives for similar tests), we developed a computer program to automatically retrieve data from the internet and estimate state-level prevalence. Model estimated prevalence can be readily updated when more data are made available.

Methods

Source of Data

Unfortunately, the US Center for Disease Control and Prevention (CDC) is not publishing complete testing results. We retrieved data from the COVID Tracking Project (covidtracking.com), a joint effort led by by Jeff Hammerbacher of Related Sciences (<https://www.related.vc>) and Robinson Meyer and Alexis Madrigal of *The Atlantic* (theatlantic.com). A full list of the team is on the project's webpage (<https://covidtracking.com/about-team>).

Data quality for each state was evaluated and graded (A-D) by the COVID Tracking Project team based on whether the state reports (1) positive results reliably, (2) negative results reliably, and (3) commercial testing results. All states (except NV) and territories reports positive result reliably. However, many states do not report negative results consistently. For example, the State of Ohio stopped reporting negative results after March 15, 2020. Some states do not report commercial testing results.

66 Statistical Methods

67 The basic statistical approach is documented by¹, along with the computational de-
68 tails (github.com/songsqian/imperfect). The basic concept is that the test result
69 is uncertain because of the inevitable false positive and false negative outcomes. To
70 properly interpret the test result, either by a patient or by the state health authority,
71 we must translate the result into the relevant quantity. Because of the inevitable false
72 positive, a positive result cannot be equated to the presence of the virus; likewise, the
73 probability of false negatives makes a negative result less reassuring. As a result, a pos-
74 itive (or negative) result should be interpreted in terms of the probability of infection
75 (or non-infection), specifically, the conditional probability of infection given a positive
76 result. Let $+$ (or $-$) represent a positive (or negative) result, v represent the presence of
77 the virus, and a represent the absence of the virus. When observing $+$ for an individual
78 patient, we want to know $\Pr(v|+)$, which reads “the conditional probability of v given
79 $+$.” This conditional probability is calculated by the Bayes Theorem:

$$\Pr(v|+) = \frac{\Pr(v) \Pr(+|v)}{\Pr(v) \Pr(+|v) + \Pr(a) \Pr(+|a)} \quad (1)$$

80 In other words, to learn about the meaning of a positive result, we need to know three
81 more quantities: $\Pr(+|v)$ (probability of a positive result when the virus is present, or 1
82 minus the probability of a false negative), $\Pr(+|a)$ (the probability of a false positive),
83 and $\Pr(v)$ the prevalence of the virus infection in the population. Interpretation of
84 $\Pr(v)$ depends on the definition of the population¹.

85 Probabilities of false positive and false negative are features of the test and the
86 prevalence of the infection is what we, as a society, want to learn from the repeated
87 testing. At this point, we have no definite knowledge of these three quantities. There-
88 fore, from the perspective of government health authorities, we want to use test results
89 to learn about these quantities so that individual patients can better understand the

90 meaning of their test results.

Following the notation of Qian et al.¹, let θ be the prevalence ($\theta = \Pr(v)$), f_p the false positive rate, and f_n false negative rate, the statistical model for updating the probability distribution of θ is the continuous variable version of the Bayes theorem.

$$\pi(\theta|y, n) = \frac{\pi(\theta)L(\theta|y, n)}{\int \pi(\theta)L(\theta|y, n)d\theta}$$

where y and n are numbers of positive results and total tests and $L(\theta|y, n)$ is the likelihood function (representing the probability of observing y positives out of n tests). The likelihood is derived based on the binomial distribution assumption of y , and it is a function of θ , f_p , and f_n

$$\begin{aligned} p_+ &= \theta(1 - f_n) + f_p(1 - \theta) \\ L(\theta, f_p, f_n|y, n) &\propto p_+^y(1 - p_+)^{n-y} \end{aligned}$$

where p_+ is the probability of observing a positive result. Because we don't know f_p and f_n , we use the Bayes theorem to update them as well:

$$\pi(\theta, f_p, f_n|y, n) = \frac{\pi(\theta)\pi(f_p)\pi(f_n)L(\theta, f_p, f_n|y, n)}{\int_{\theta} \int_{f_p} \int_{f_n} \pi(\theta)\pi(f_p)\pi(f_n)L(\theta, f_p, f_n|y, n)d\theta df_p df_n}$$

91 As the three quantities of interest (θ, f_p, f_n) are probabilities, we use the beta distribu-
 92 tion as their priors. We note that the likelihood function provides information on the
 93 products of θf_p and θf_n . Using independent forms of priors for θ , f_p , and f_n is unlikely
 94 to jointly estimate the three quantities. As a result, providing realistic informative
 95 priors for at least two of the three parameters is necessary.

Prior Specification

As the SARS-CoV2 is a new virus and only a relatively small number of tests are done in the US (only for people with specific symptoms), we don't have a basis for specifying a more informative prior for the prevalence. As a result, we used the hierarchical modeling approach and imposed non-informative prior on the hyper-parameters. For the qPCR test used for detecting SARS-CoV2, we haven't seen studies to quantify f_p and f_n . However, the basic principle of the test is well known. We can use reported f_p and f_n for similar types of tests to develop the priors. We estimate state-level prevalence under three scenarios.

- Estimates assuming a highly accurate test Assuming the test has a false positive probability of 1% and a false negative probability of 1% and both are stable ($f_p \sim \text{beta}(1, 99)$ and $f_n \sim \text{beta}(1, 99)$, with a 95% credible interval of 0.00026-0.036).
- Estimates based on similar tests for other corona-viruses (SARS, MERS, H1N1). Existing studies on tests of similar viruses have a range of false positive and false negative rates. Using a study of the MERS and SARS virus tests²⁻⁵, we constructed a prior distribution for false positive to be $\text{beta}(3, 23)$ (95% credible interval of 0.025-0.26) and false negative $\text{beta}(2, 22)$ (0.01-0.22)
- Estimates assuming the test is as unreliable as the rapid influenza diagnostic test (RIDT)⁶ This test has a high false negative probability and we use $\text{beta}(16, 24)$ (0.26-0.55). The probability of a false positive is relatively low and we used $\text{beta}(4, 45)$ (0.023, 0.17).

A Hierarchical Formulation

We have data from nearly all states and territories. We assumed that f_p and f_n are the same for all states because they use the same test. However, the prevalence can

121 vary by region. But we have no information to separate one state from another other
 122 than the testing data. As a result, we assumed that the prevalence for each state θ_j are
 123 exchangeable and impose a common prior. Advantages of using a hierarchical formu-
 124 lation were explored by Wu et al.⁷, Qian et al.⁸. Expressing the model hierarchically,
 125 we have the following model.

1. At the observational level, data from each state (numbers of positive and negative) are modeled by the binomial distribution

$$y_j \sim \text{Bin}(p_j, n_j)$$

where j represents the j th state, y_j and n_j are the observed number of positive and total number of tests, and Bin represents the binomial distribution. The probability of observing a positive result (p_j) is a function of θ_j , f_p , and f_n :

$$p_j = \theta_j(1 - f_n) + (1 - \theta_j)f_p$$

2. To connect all states together, we used a common prior for state-level prevalence θ_j (after a logit transformation).

$$\text{logit}(\theta_j) \sim N(\mu_0, \sigma_0^2)$$

126 Non-informative priors are used for μ_0 and σ_0^2 .

3. Prior distributions of other parameters

$$f_n \sim \text{beta}(\alpha_n, \beta_n)$$

$$f_p \sim \text{beta}(\alpha_p, \beta_p)$$

127 The hyper-parameter μ_0 is the national average of prevalence (in logit scale) and

σ_0^2 is among state variance of the logit transformed state-specific prevalence.

Results

The estimated state-level prevalence varies by a wide range. Under the best-case scenario, the national mean prevalence is 0.092 (with a 95% credible interval of between 0.058 and 0.132) based on data reported on March 23, 2020. The lowest state-level prevalence is 0.0040 (0.0004-0.011) and the highest is 0.894 (0.879-0.919). For the expected scenario, the national average prevalence is 0.091 (0.056-0.135), and the state-level prevalence ranges from 0.0023 (0.0002-0.0066) to 0.929 (0.889-0.981). Finally, under the worst-case scenario, the national average prevalence is 0.100 (0.0595-0.151), and the state-level prevalence ranging from 0.0019 (0.00014-0.0059) to 0.984 (0.960-0.997) (Figure 1). In all three scenarios, the uncertainty of the estimated prevalence (measured as the width of the 95% credible interval) decreases as the number of tests increases (Figure 2). Because many state did not properly report negative results (e.g., Ohio's number of negative result has stopped at 140 since March 15, 2020 and New Jersey may have changed how it reports negatives on March 16th, 2020), we rerun the model using data from states with data quality grade (from the COVID Tracking Project) of A. The estimated national average is 0.060 (0.043, 0.079) and the state-level prevalence ranges from 0.0093 (0.003, 0.014) to 0.167 (0.149, 0.185) (Figure 3).

The importance of testing a large number of people and consistently reporting the results is illustrated by comparing the estimation results for four states (Louisiana, Massachusetts, Ohio, and Washington, Figure 4). The State of Washington tested the largest number of people early and reported all test results. The total number of tested people exceeded 1000 on March 9, 2020. Louisiana and Massachusetts had a slow start and were initially inconsistent in reporting negative results. Once their numbers of tests exceed 1000, the estimate prevalence for these two states reached more stable

153 levels. Ohio tested far fewer people compared to the other three states. Furthermore,
154 Ohio stopped reporting negative test results on March 15, 2020. As a result, the steady
155 increase in the estimated prevalence for Ohio is an artifact of the missing negative
156 results.

157 The posterior distributions of f_p and f_n are quite similar to their respective prior
158 distributions (Figure 5). This result suggests that properly characterize the test's rates
159 of false positive and false negative is imperative for proper estimation of the disease
160 prevalence in the population.

161 Discussion

162 Results from a statistical model reflect the population represented by the data. In this
163 case, when testing is highly selective, the estimated prevalence is relevant to the sub-
164 population who meet the screening criteria. The population represented by the data are
165 people who met CDC guidelines. The posted guidelines on CDC web page ([https://](https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-criteria.html)
166 www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-criteria.html) include hos-
167 pitalized patients with COVID-19 symptoms, symptomatic people in high risk groups
168 (older adults and individuals with chronic medical conditions and/or an immunocom-
169 promised state), and healthcare providers with contact with a suspected or confirmed
170 COVID-19 patient. It is unclear whether the SARS-CoV2 prevalence in this sub-
171 population is higher than the prevalence in the general population. To evaluate the
172 effectiveness of the current prevention practices, we need to estimate the prevalence in
173 the general population to monitor the trend.

174 For individual patients, a positive result translates to a probability of true infection
175 of 0.9, 0.52, or 0.146 using equation (1) based on the best-case, expected, or the worst-
176 case scenarios, respectively (Table 1). The difference between the three scenarios is
177 largely represented in the rate of false negative. Under all scenarios, the estimated

178 national average prevalence is relatively stable. The interpretation of the test result
179 in this case lies largely with the quality of the test. If the current test is in par with
180 the qPCR tests used in previous outbreaks of similar viruses, a positive test result to
181 a patient means that the likelihood of infection is only marginally higher than 0.5; a
182 re-test following a positive result is likely necessary.

183 Acknowledgement

184 Supporting Information

185 R code and link to source data are posted at <https://github.com/songsqian/COVID19>.

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216 **Tables**

Table 1: Probability of infection given a positive result

Scenarios	θ_0	$E(f_p)$	$E(f_n)$	$\Pr(v +)$
Best-case	0.092	0.01	0.01	0.90
Expected	0.091	0.12	0.08	0.52
Worst-case	0.100	0.08	0.40	0.15

217 **Figure**

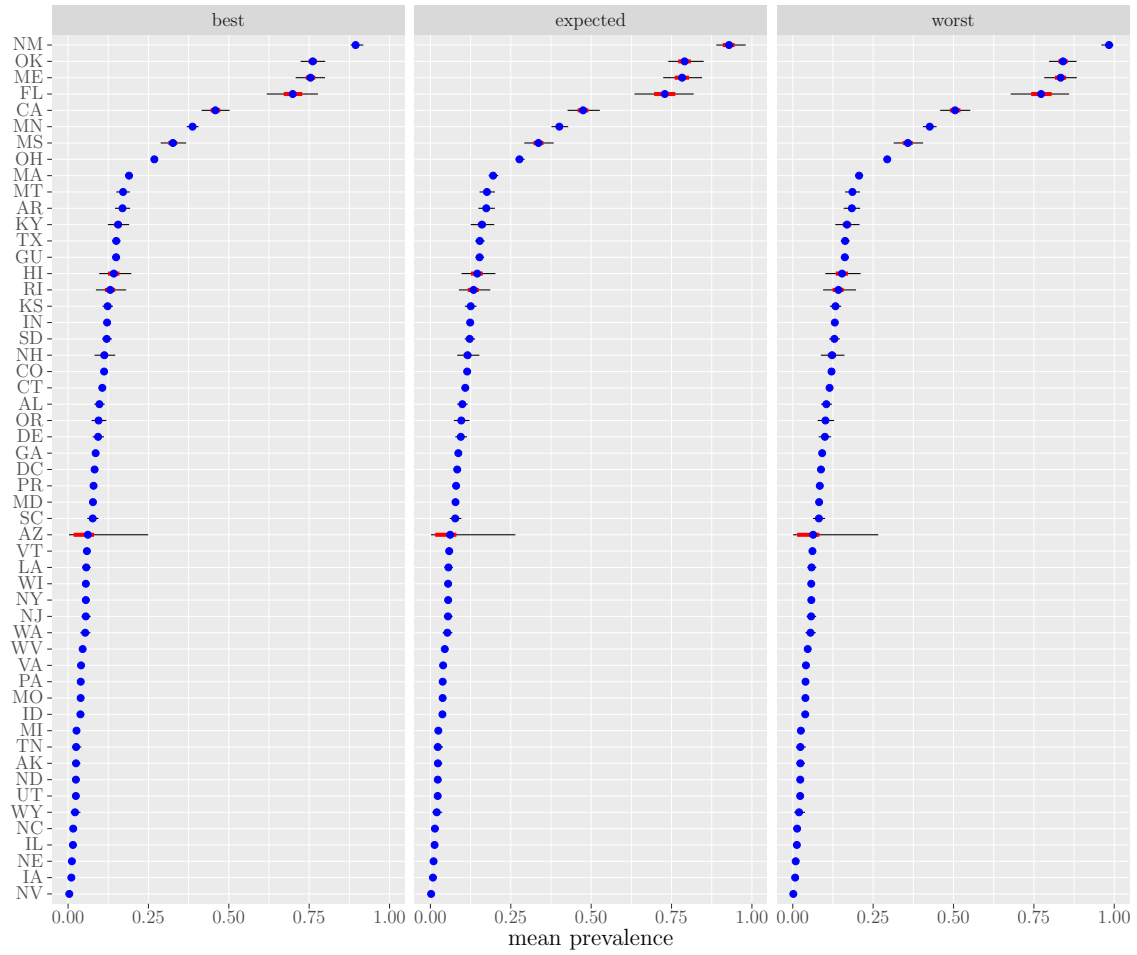


Figure 1: Hierarchical model estimated state-level SARS-CoV2 prevalence based on data reported by March 23, 2000. The blue dots are the estimated means, the red thick bars are the 50% credible intervals, and the thin black lines are the 95% credible intervals.

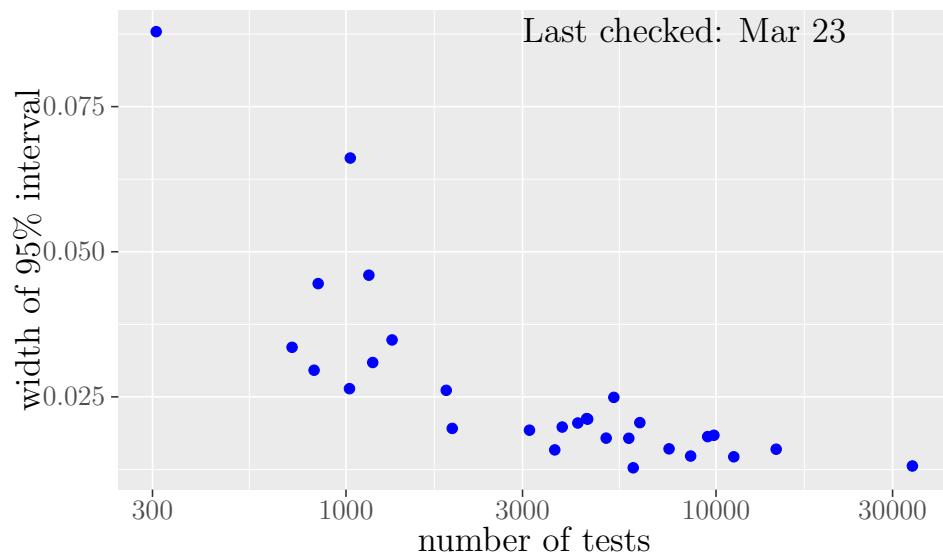


Figure 2: Uncertainty of the estimated state-level prevalence, measured as the width of the 95% credible interval (estimated using data from states with reliable data reporting system, see Figure 3), is a inversely related to the total number of tests performed.

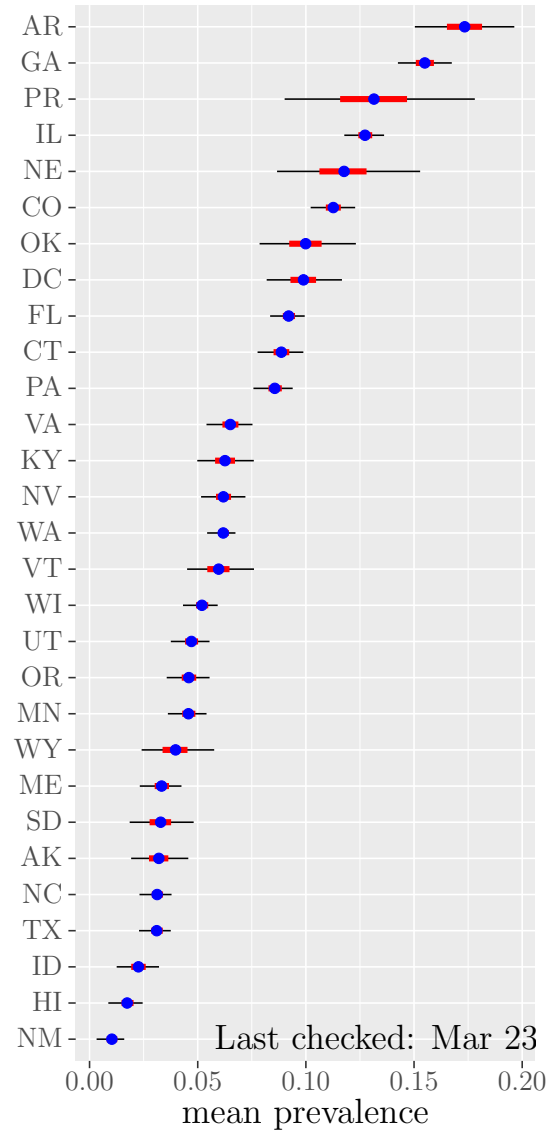


Figure 3: Estimated state-level prevalence using data from states with reliable data reporting system

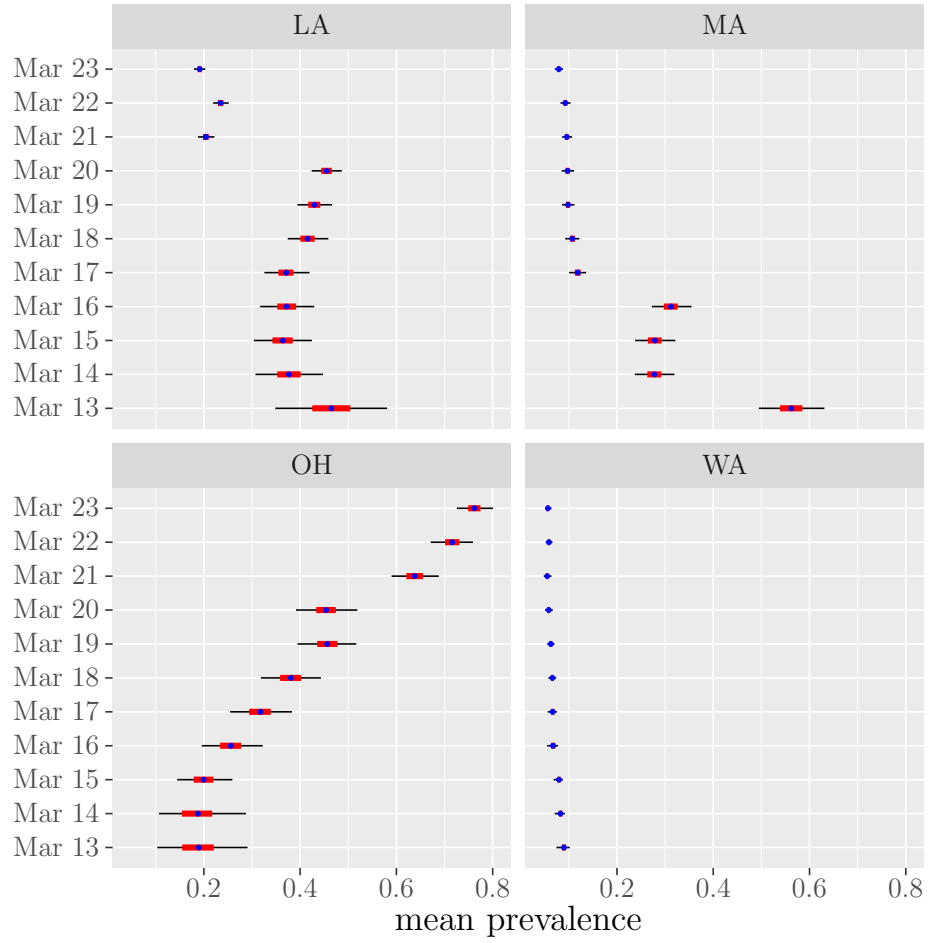


Figure 4: Estimated state-level prevalence for four states from March 13 to March 23, 2020

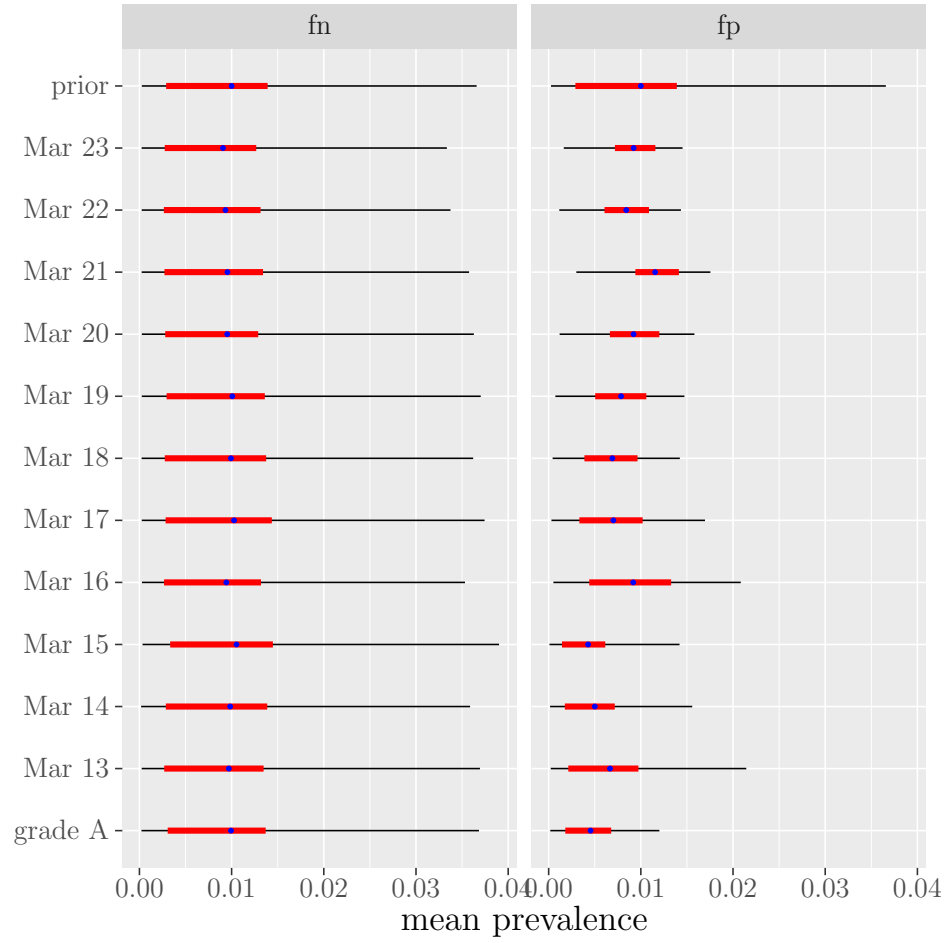


Figure 5: Comparison of priors and posteriors of f_p and f_n based on data from March 13 to 23, 2020