**Supplementary Information:** “Citywide serosurveillance of the initial SARS-CoV-2 outbreak in San Francisco”  
Isobel Routledge, Adrienne Epstein, Saki Takahashi et al.

**Contents**

**Supplementary Table 1**: Estimates of test performance characteristics from the overall procedure.

**Supplementary Table 2**: Seroprevalence stratified by demographic group

**Supplementary Table 3**: Seroprevalence stratified by neighborhood

**Supplementary Text 1**: Supplementary Methods

---

**Supplementary Table 1**: Estimates of test performance characteristics from the overall procedure.

| Parameter       | Point estimate and 95% CrI       |
|-----------------|---------------------------------|
| Se_ELISA        | mean = 97.4%, median = 97.6%, 95% CrI = 93.9%, 99.4% |
| Se_Luminex      | mean = 95.0%, median = 95.2%, 95% CrI = 90.9%, 98.0% |
| Sp_ELISA        | mean = 97.5%, median = 97.8%, 95% CrI = 93.7%, 99.6% |
| Sp_Luminex      | mean = 99.2%, median = 99.4%, 95% CrI = 97.0%, 100.0% |
| covariance_Se   | mean = 1.3%, median = 1.0%, 95% CrI = -0.04%, 3.9% |
| covariance_Sp   | mean = 0.4%, median = 0.2%, 95% CrI = 0.0%, 1.7% |
| Se_overall      | mean = 93.7%, median = 94.0%, 95% CrI = 89.0%, 97.2% |
| Sp_overall      | mean = 99.6%, median = 99.8%, 95% CrI = 98.2%, 100.0% |
| adjusted prevalence (overall) | mean = 4.3%, median = 4.2%, 95% CrI = 2.1%, 6.3% |
Supplementary Table 2: Seroprevalence stratified by demographic group

Table showing raw seroprevalence and point estimates and 95% credible intervals for posterior estimates of seroprevalence adjusted for test performance by demographic group.

| Class            | Group       | Positive | Count | Seroprevalence | Adjusted seroprevalence | 2.5% Credible Interval | 97.5% Credible Interval |
|------------------|-------------|----------|-------|----------------|-------------------------|------------------------|------------------------|
| Sex              | F           | 72       | 2491  | 0.0289         | 0.0270                  | 0.0109                 | 0.0361                 |
| Sex              | M           | 119      | 2231  | 0.0533         | 0.0531                  | 0.0373                 | 0.0661                 |
| Age Group        | 0-19        | 11       | 281   | 0.0391         | 0.0410                  | 0.0160                 | 0.0690                 |
| Age Group        | 20-39       | 51       | 1261  | 0.0404         | 0.0399                  | 0.0229                 | 0.0545                 |
| Age Group        | 40-59       | 72       | 1322  | 0.0545         | 0.0546                  | 0.0364                 | 0.0713                 |
| Age Group        | 60-79       | 41       | 1390  | 0.0295         | 0.0281                  | 0.0110                 | 0.0404                 |
| Age Group        | 80+         | 17       | 481   | 0.0353         | 0.0363                  | 0.0155                 | 0.0580                 |
| Insurance Type   | Government  | 120      | 2937  | 0.0409         | 0.0398                  | 0.0232                 | 0.0504                 |
| Insurance Type   | Private or Employer | 50     | 1421  | 0.0352         | 0.0341                  | 0.0157                 | 0.0474                 |
| Insurance Type   | Uninsured   | 16       | 269   | 0.0595         | 0.0634                  | 0.0315                 | 0.0990                 |
| Insurance Type   | Unknown     | 6        | 108   | 0.0556         | 0.0643                  | 0.0228                 | 0.1231                 |
| Hospital Group   | UCSF        | 119      | 3037  | 0.0392         | 0.0379                  | 0.0208                 | 0.0486                 |
| Hospital Group   | ZSFG        | 73       | 1698  | 0.0430         | 0.0419                  | 0.0244                 | 0.0557                 |
| Race/Ethnicity   | Asian       | 30       | 1206  | 0.0249         | 0.0233                  | 0.0079                 | 0.0353                 |
| Race/Ethnicity   | Black or African American | 28    | 591   | 0.0474         | 0.0483                  | 0.0281                 | 0.0696                 |
| Race/Ethnicity   | Hispanic    | 53       | 858   | 0.0618         | 0.0633                  | 0.0437                 | 0.0829                 |
| Race/Ethnicity   | Other       | 14       | 348   | 0.0402         | 0.0422                  | 0.0202                 | 0.0691                 |
| Race/Ethnicity   | White       | 65       | 1675  | 0.0388         | 0.0379                  | 0.0230                 | 0.0506                 |
| Month            | March       | 6        | 192   | 0.0313         | 0.0341                  | 0.0097                 | 0.0655                 |
| Month            | April       | 44       | 959   | 0.0459         | 0.0459                  | 0.0274                 | 0.0631                 |
| Month            | May         | 85       | 2047  | 0.0415         | 0.0404                  | 0.0240                 | 0.0529                 |
| Month            | June        | 56       | 1526  | 0.0367         | 0.0358                  | 0.0189                 | 0.0490                 |
Supplementary Table 3: Seroprevalence stratified by neighborhood

Table showing raw seroprevalence and point estimates and 95% credible intervals for posterior estimates of seroprevalence adjusted for test performance by neighborhood and for individuals experiencing homelessness. Adjusted seroprevalence was not estimated for neighborhoods with sample sizes below 50 samples from unique individuals.

| Neighborhood               | Positive | Count | Seroprevalence | Adjusted seroprevalence | 2.5% Credible Interval | 97.5% Credible Interval |
|----------------------------|----------|-------|----------------|-------------------------|------------------------|------------------------|
| Bayview                    | 15       | 206   | 0.0728         | 0.0809                  | 0.0456                 | 0.1232                 |
| Bernal Heights             | 2        | 103   | 0.0194         | 0.0287                  | 0.0040                 | 0.0734                 |
| Castro/Upper Market        | 3        | 102   | 0.0294         | 0.0393                  | 0.0089                 | 0.0826                 |
| Chinatown                  | 2        | 42    | 0.0476         | NA                      | NA                     | NA                     |
| Crocker Amazon             | 4        | 49    | 0.0816         | NA                      | NA                     | NA                     |
| Diamond Heights            | 1        | 14    | 0.0714         | NA                      | NA                     | NA                     |
| Downtown/Civic Center      | 14       | 277   | 0.0505         | 0.0571                  | 0.0305                 | 0.0900                 |
| Excelsior                  | 15       | 200   | 0.0750         | 0.0834                  | 0.0450                 | 0.1280                 |
| Financial District         | 1        | 51    | 0.0196         | 0.0387                  | 0.0023                 | 0.1053                 |
| Glen Park                  | 3        | 37    | 0.0811         | NA                      | NA                     | NA                     |
| Golden Gate Park           | 0        | 1     | 0.0000         | NA                      | NA                     | NA                     |
| Haight Ashbury             | 2        | 95    | 0.0211         | 0.0310                  | 0.0034                 | 0.0796                 |
| Inner Richmond             | 4        | 144   | 0.0278         | 0.0340                  | 0.0089                 | 0.0721                 |
| Inner Sunset               | 8        | 157   | 0.0510         | 0.0580                  | 0.0240                 | 0.0988                 |
| Lakeshore                  | 3        | 105   | 0.0286         | 0.0383                  | 0.0095                 | 0.0857                 |
| Marina                     | 1        | 63    | 0.0159         | 0.0309                  | 0.0019                 | 0.0902                 |
| Mission                    | 11       | 342   | 0.0322         | 0.0327                  | 0.0139                 | 0.0550                 |
| Nob Hill                   | 1        | 80    | 0.0125         | 0.0245                  | 0.0016                 | 0.0685                 |
| Noe Valley                 | 2        | 115   | 0.0174         | 0.0256                  | 0.0028                 | 0.0656                 |
| North Beach                | 4        | 80    | 0.0500         | 0.0615                  | 0.0187                 | 0.1282                 |
| Ocean View                 | 5        | 140   | 0.0357         | 0.0431                  | 0.0125                 | 0.0841                 |
| Outer Mission              | 5        | 127   | 0.0394         | 0.0469                  | 0.0160                 | 0.0875                 |
| Outer Richmond             | 7        | 166   | 0.0422         | 0.0485                  | 0.0192                 | 0.0919                 |
| Outer Sunset               | 8        | 273   | 0.0293         | 0.0326                  | 0.0121                 | 0.0574                 |
| Pacific Heights            | 6        | 89    | 0.0674         | 0.0800                  | 0.0309                 | 0.1471                 |
| Parkside                   | 5        | 144   | 0.0347         | 0.0413                  | 0.0138                 | 0.0833                 |
| Potrero Hill               | 5        | 88    | 0.0568         | 0.0699                  | 0.0243                 | 0.1318                 |
| Presidio                   | 0        | 18    | 0.0000         | NA                      | NA                     | NA                     |
| Presidio Heights           | 0        | 39    | 0.0000         | NA                      | NA                     | NA                     |
| Russian Hill               | 0        | 49    | 0.0000         | NA                      | NA                     | NA                     |
| Sealiff                    | 0        | 15    | 0.0000         | NA                      | NA                     | NA                     |
| South of Market            | 13       | 346   | 0.0376         | 0.0405                  | 0.0197                 | 0.0654                 |
| Twin Peaks                 | 3        | 46    | 0.0652         | NA                      | NA                     | NA                     |
| Visitacion Valley          | 4        | 121   | 0.0331         | 0.0410                  | 0.0114                 | 0.0835                 |
| West of Twin Peaks         | 5        | 141   | 0.0355         | 0.0427                  | 0.0144                 | 0.0855                 |
| Western Addition           | 5        | 305   | 0.0164         | 0.0221                  | 0.0064                 | 0.0434                 |
| Homeless                   | 16       | 157   | 0.1019         | 0.1078                  | 0.0614                 | 0.1652                 |
Supplementary Text 1: Supplementary Methods

Estimating test performance and positivity cutoffs for the serological assays

Selecting samples for confirmatory testing: All 5,244 SCALE-IT laboratory samples (corresponding to 4,735 unique patients) were first screened on the ELISA platform. In addition, 117 positive control samples from the LIINC cohort and 93 negative control samples were tested on this platform. The antibody concentration of each sample was calculated from the ELISA OD value using a plate-specific standard curve from serial dilutions of a pool of positive control samples. Based on the distributions of concentration values among these control samples, SCALE-IT samples with a concentration value above 0.049 were selected for confirmatory testing, corresponding to test performance characteristics of 98.3% sensitivity and 97.8% specificity.

Determining seropositivity of SCALE-IT samples: Based on the above, 653 SCALE-IT samples were selected for confirmatory testing on the Luminex platform, on which we included three SARS-CoV-2 antigens (one preparation each of the S, RBD, and N proteins). In addition, 260 positive control samples from the LIINC cohort and 114 negative control samples were tested on this platform. The antibody concentration of each antigen of each sample was calculated from the Luminex MFI value using a plate-specific standard curve from serial dilutions of a pool of positive control samples.

We then fit a multiple logistic regression model to the control samples and their Luminex concentration values for the three antigens. We used this model to classify each SCALE-IT sample as seropositive or seronegative; samples with a predicted probability value which corresponded to a specificity of 100.0% and sensitivity of 95.8% (AUC: 0.983) were classified as seropositive. The five-fold cross-validated sensitivity of this algorithm, fixing specificity at 100.0%, was estimated to be 95.4%. Given the relatively low expected seropositivity in the population, we chose to maximize the specificity of this classifier.

Determining the test performance characteristics of the two-assay procedure: The test performance characteristics of a single assay (i.e., sensitivity and specificity) can be determined from a 2x2 table of positive/negative control samples and their binary classification on that assay using a binomial model. For a two-assay scenario, the binomial model can be extended to a multinomial framework where each control sample has two test results: their binary classification on each of the two assays. Importantly, there may be conditional dependence between assays, where conditional on the true disease status of a given sample, the test performance of one assay may vary depending on the result on the other assay. The magnitude of this conditional dependence between two assays can be directly estimated based on the results of control samples that have been tested on both assays.

Here, of our 266 unique positive control samples, 111 were tested on both platforms (108 classified as positive by both, 1 classified as positive by ELISA and negative by Luminex, and 2 classified as negative by both), 149 were tested only on Luminex (141 classified as positive, 8 classified as negative), and 6 were tested only on ELISA (all 6 classified as positive). Of our 119 unique negative control samples, 88 were tested on both platforms (87 classified as negative by both, 1 classified as positive by ELISA and negative by Luminex), 26 were tested only on Luminex (all 26 classified as negative), and 5 were tested only on ELISA (4 classified as negative, 1 classified as positive).

We employed a modeling framework that jointly estimates assay-specific sensitivities (Se_ELISA and Se_Luminex), assay-specific specificities (Sp_ELISA and Sp_Luminex), correlation between sensitivities (covariance_Se), correlation between specificities (covariance_Sp), and seroprevalence. We allowed control samples that were tested only on one assay to contribute to the estimation of that assay’s performance characteristics using the standard binomial model.

As the SCALE-IT samples were tested in a serial procedure that required a sample to be positive on the two assays to be classified as seropositive, we estimated the overall sensitivity of the approach as: Se_overall = Se_ELISA * Se_Luminex - covariance_Se, and the overall specificity of the approach as: Sp_overall = 1 - (1 - Sp_ELISA)*(1 - Sp_Luminex) - covariance_Sp. Using these estimates of overall sensitivity and specificity, we obtained adjusted estimates of seroprevalence as: adjusted prevalence = (raw prevalence + Sp_overall - 1) / (Se_overall + Sp_overall - 1). The posterior estimates of these parameters are provided in Supplementary Table 1. The code to implement this model is included in our GitHub repository.
Calculating under-ascertainment

We compared our seroprevalence estimates to the weighted average of weekly cumulative incidence of reported cases up until June 14 2020 from the San Francisco Department of Public Health\(^3\) and using the estimated population size of 881,549 in San Francisco according to the 2019 American Community Survey\(^4\). To estimate the proportion of overall infections that are ascertained, we weighted the weekly cumulative case counts by the proportion of our sample sampled in the corresponding week, lagged by two weeks collection to reflect the approximate time to sero-conversion among newly infected individuals\(^5\).

**Supplement References**

1. Rogan, W. J., & Gladen, B. Estimating prevalence from the results of a screening test. *American journal of epidemiology*, **107**(1), 71–76 (1978). doi:10.1093/oxfordjournals.aje.a112510

2. Gardner, I. A., Stryhn, H., Lind, P. & Collins, M. T. Conditional dependence between tests affects the diagnosis and surveillance of animal diseases. *Prev. Vet. Med.* **45**, 107–122 (2000).

3. [Data] City and County of San Francisco. *COVID-19 Cases and Deaths*. Available at: https://data.sfgov.org/stories/s/dak2-gvuj.

4. [Data] United States Census Bureau. *American Community Survey Data Releases*. Available at: https://www.census.gov/programs-surveys/acs/news/data-releases.html.

5. Long, Q.-X. *et al.* Antibody responses to SARS-CoV-2 in patients with COVID-19. *Nat. Med.* **26**, 845–848 (2020).