Calibrating an Epidemic Compartment Model to Seroprevalence Survey Data

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Abstract

To date, the Covid-19 epidemic has produced tremendous cost and harm. However, to date, many epidemic models are not calibrated to seroprevalence survey(s). This paper calibrates a relatively simple, SIR plus confirmed cases ("SIRX") model against seroprevalence survey data released by the State of New York. The intention of this paper is to demonstrate a potentially new technique of calibration for epidemic models used by scientists, public health officials and governments. The technique can then be incorporated in other more complex models. Open source code is included to assist model developers.

Keywords: Seroprevalence, model, calibration, SIR, compartment, epidemiology

Introduction

The intention of this paper is to provide a calibration technique, applied to a relatively simple SIR plus cases model ("SIRX") using seroprevalence data. This paper is an attempt to communicate to epidemiologists and other modelers within a timeframe that is useful to managing the current epidemic. Numerous simplifications are made to concentrate this communication. Hence additional detail and accuracy are explicitly beyond the scope of this paper.

All code and data are available at [1]. This calibration technique was independently developed by the author. An extensive search for other similar techniques which may have existed in the literature was beyond the time scope of this paper. Such techniques will be credited in subsequent revisions of this paper as they come to the attention of the author.

Generalizing an Antibody Test

As will be explained in detail below, in this paper the New York State "Wadsworth" Antibody Seroprevalence Survey will be used to calibrate a SIRX model.

In the attached appendix, a simplified antibody test is used to demonstrate via linear algebraic manipulations how both sensitivity and specificity would interact with different (perfectly) known seroprevalence time series, assuming that the test is sampled at a fixed time relative to the time series independent variable t. Antibody test sensitivity and specificity curves were rounded from the Wadsworth test in the Appendix so that the arithmetic can be checked by inspection. In the Appendix, and summarized in Figures 1, 2, and 3 below, three different assumed time series are put forward as examples: Figure 1: a cumulative infection growth rate doubling every 3 days (newly infected doubling every 3.64 days), representing an epidemic's typical exponential growth before the introduction of social distancing measures; Figure 2: a flat (constant) infection rate per day; and Figure 3: an exponential decrease in the number of new infections at the same 3.64 halving rate as Figure 1, created by "playing backwards time" from the example Figure 1.

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Figure 1 – Exponential Increase of New Infected Time Series

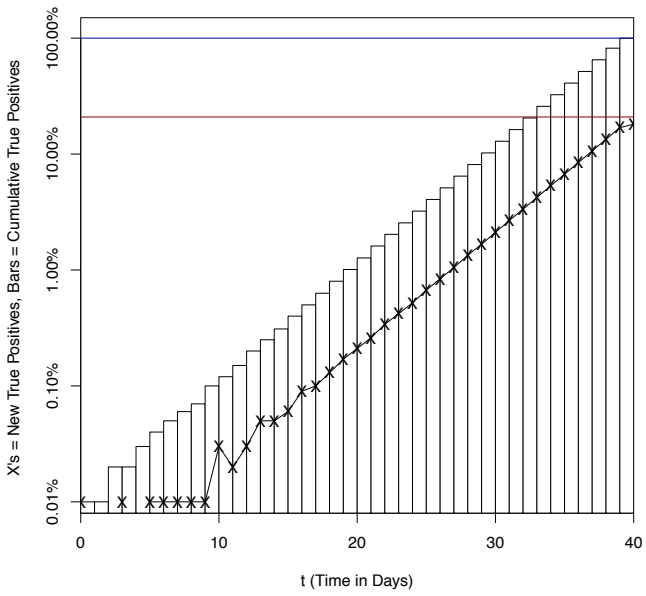


Figure 2 – Flat New Infected Time Series

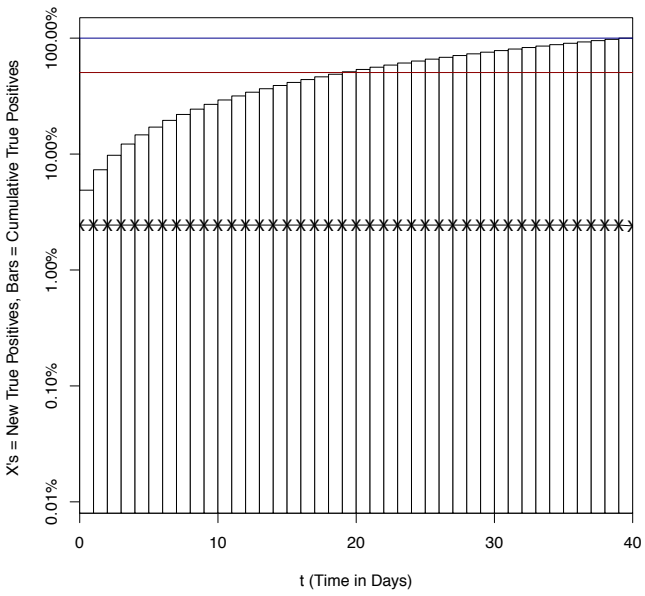
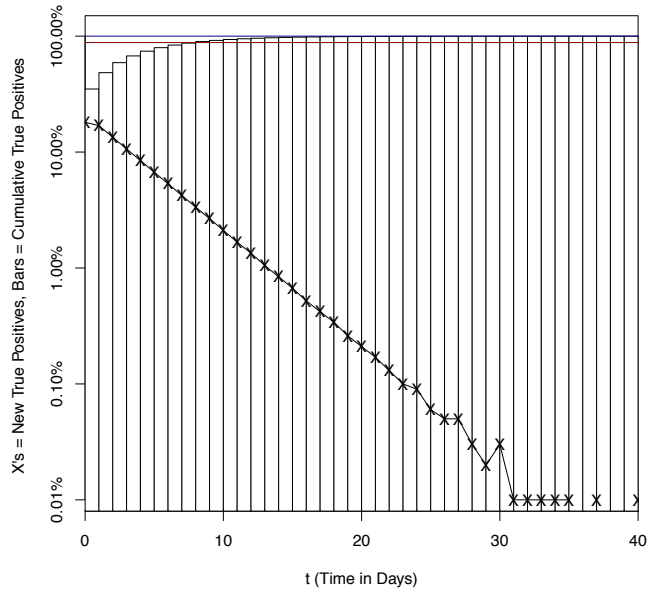


Figure 3 – Exponential Decrease of New Infected Time Series



Infected plus Recovered Time Series Characteristic	Test Positive / True Positive Ratio
Exponential Increase	20.9%
Flat	50.5%
Exponential Decrease	88.0%
Comparison to:	
Naive Use of Test Final Sensitivity and Specificity Instead of Test Curve	89.0%
Naive Assumption of Perfect Test	100%

Table 1
Time Series Characteristic vs Test Positivity

The three different types of new infected time series are shown above.

In each time series chart, the X's connected with the black line represent the number of new infected each day t. The bars represent the cumulative infected. Of note is that once infected, in the time series members of the subpopulation are always counted as positive whether they remain infectious, or have recovered or died and are no longer infectious. The cumulative infected total represents the true total percentage of the tested population who are positive for the condition of ever having been infected.

Given a known true infected time series, using algebra and arithmetic the test results have been computed and presented in Table 1 as the ratio of Test Positive to True Positive. (Please see the Appendix for the calculations.) In the time series charts, these ratios are expressed as the red horizontal line, and compared

to a "perfect" test in the blue horizontal lines. The charts y axis are logarithmic -- and understate the true significance of the undercount. The results clearly show that the ratio of test positive (test infected) to total infected is significantly reduced, in the exponential growth and the flat examples, compared to both (a) the actual number of infected using an accurate calculation; and (b) the naively computed number of infected using a single final sensitivity. This is because the Wadsworth Test, like most antibody tests, increases in sensitivity as the immune system responds to the infection over time. Therefore, if an analysis uses only an antibody test's peak sensitivity (measured three or more weeks after infection), it would significantly underestimate the true infected rate. Further, there is a risk, particularly in test results that do not have their adjustments published, that public health officials, government executives, or the general public will assume naively that seroprevalence test results presented in summary form at press conferences represent an unbiased estimated of the population's true cumulative infection percentage, when instead it is likely significantly higher. Therefore it is clear that care must be taken by the modeler in using test results, particularly those without published detail as to their calculation method or sensitivity and specificity.

The SIRX Model

This paper will use a modified SIR model to demonstrate calibration. The model utilized for this example is a simplification of the SIR-X model of Maier and Brockmann [2], itself a generalization of the SIR model. In addition to the three basic SIR compartments of S (susceptible), I (infected), and R (recovered or deceased), there is an additional compartment X (confirmed and reported cases), which allows the model to connect to the confirmed cases reported by public health authorities.[3]

The model is defined by the following differential equations describing the flow between the compartments:

$$dS/dt = -\beta I\, S/N \quad \text{Eq. 1}$$

$$dI/dt = \beta I\, S/N - \gamma I - k_{IX} I \quad \text{Eq. 2}$$

$$dX/dt = k_{IX} I \quad \text{Eq. 3}$$

$$dR/dt = \gamma I \quad \text{Eq. 4}$$

With the constraint:

$$N = S + I + R + X \quad \text{Eq. 5}$$

With definitions:

$S, I, R \equiv$ Susceptible, Infected, or Recovered[4] Population
$X \equiv$ Confirmed Cases Population[5] (assumed quarantined and thus unable to infect Susceptible Population)
$N \equiv$ Total Population
$\beta \equiv$ Transition rate from the Susceptible to the Infected compartment
$\gamma \equiv$ Transition rate from the Infected to the Recovered compartment
$k_{IX} \equiv$ Transition rate from the Infected to Confirmed Cases compartment

[3] Note that Maier and Brockmann provide for a direct transition between the S and the R compartment to explain subexponential growth. This S to R transition is not used in this paper's model.
[4] Note that the Recovered Population includes those who have died. This population had been infected but is no longer infectious.
[5] Similarly the (Confirmed) Case Population includes those who had been confirmed as positive but subsequently died or have recovered, so that they are no longer infectious to the Susceptible population.

$t \equiv$ Time, in units of days for convenience

This model is a SIR model [3] with an extra compartment for the Confirmed cases and where the Confirmed cases are isolated until no longer infectious.

Because this paper's purpose is to demonstrate calibration, for brevity the inherent weaknesses in the SIR model are immaterial and therefore ignored. Regardless, the calibration technique can be applied to more accurate and more complex models, including SEIR models, models that use gamma distributions for compartment distributions vs time, models that use or incorporate directly mortality, models that network individual infections, and so on. Examples include the Imperial College Model [4] and the IHME Model [5]. However, all models would benefit from more accurate calibration with seroprevalence data of which this simplified SIRX model is a mere example.

To simplify this example the γ transition factor has not been calibrated, but is simply assumed to be a constant of 1/8 representing an 8 day mean infectious period. $1/\gamma$ is equivalent to the mean time (in this case 8 days) in an exponential distribution for an infected individual to pass from the Infected compartment to the Recovered compartment (which included mortalities which are assumed to be no longer infectious). The 8 day mean time is both reasonable and sufficient to illustrate calibration to seroprevalence.

Within the SIRX model, as pointed out by Maier and Brockmann, the probability Q_{Prob} of a case ending up in the X Confirmed Cases compartment instead of the R compartment is:

$$Q_{Prob} = k_{IX}/(k_{IX} + \gamma) \qquad \text{Eq. 6}$$

This is roughly equivalent but not the same as the ascertainment fraction, i.e. the ratio of confirmed cases to total infected plus recovered -- differing because of the delay of the infected from entering the Confirmed or Recovered compartments. Regardless, by adjusting Q_{Prob} (or equivalently k_{IX} through the linear relationship in Equation 6 above, the model may be calibrated to match seroprevalence as determined by survey.

The Example Case Data

Daily Confirmed Case data was originally obtained from the New York City Department of Health by manually typing in the data in the daily reports [6], but that has been subsequently discontinued and does not make corrections for past reported data. NYC updated to a time series file [7] which has the advantage that past data are added as delayed reports are processed. The date used in the new NYC time series is the "date of diagnosis" which is presumably the same or slightly delayed from the date of a positive (PCR type) test being received by the medical practitioner. These data are then corroborated against data from the New York State Department of Health [8] by adding up the cases in the 5 counties comprising New York City (Kings, Queens, New York, Bronx, and Staten Island). Of note is that the NYS data's date is "the date the test result was processed by the NYS Clinical Laboratory Reporting System". All three case data sets are contained in the online code and data files for convenience. Visual observation shows that the NYS data are generally one day delayed from the NYC data; and that the NYC data have a larger weekly periodicity "noise" likely due to a relative lack of PCR testing or processing on Saturday and Sunday. The regression technique used in this paper largely averages out such noise, although a more sophisticated technique, based on either day of the week or tests on a day, could correct for the periodic weekly noise. The population for NYC was rounded to 8.623 mm from [9].

The Computational Model

The model was built in the R Programming Language[10]. The SIRX model is encapsulated in a function sirX3() which when given initial conditions of N, $I_{t=t0}$, dI/dt $(at\ t = t0)$, k_{IX}, β, and γ, will solve the differential equations (1) through (4) computationally for any number of days going forward using the Dormond-Prince Runge-Kutta 4th order method R method from the package deSolve as described in Soetaert et al [11]. This computational solution was checked by using a discrete numerical integration where each day is broken into 500 (arbitrarily small) timesteps (i.e. Euler's method) as inspired by Anastassopoulou et al [12]).

The sirX3() function has an optional parameter which linearly changes the initial β_0 by a multiplicative change factor $F_{\beta\Delta}$ (i.e. 0.5) over the fit interval from t_0 to t_1:

$$\beta(t) = (t\ - t_0)/(t_1\ -\ t_0)\ F_{\beta\Delta}\,\beta_0 \qquad \text{Eq. 7}$$

This is useful in fitting the data when a public health policy may have changed social distancing and self-isolation behavior as will be seen below.

Fitting Case Data to Model

A relatively simplistic and (usually) stable method of fitting data is the least squares method. While there are essentially closed form solutions that produce an exact answer for linear models, non-linear models like SIRX cannot be solved using a linear regression. The problem is compounded when when S/N is significantly less than 1 or when a non-constant susceptible to infection transition rate (i.e. β) is assumed. (A changing β is equivalent to a changing effective reproduction number, R_{eff} because $R_{eff} = \beta/\gamma$ in the SIR framework, and must be fit computationally by an algorithm).

Fortunately, Elzhov et al [13] has created within R an excellent Levenberg-Marquant least square fitting within the package minpack.lm called thru the nlsLM() function. The author has been iteratively improving the code algorithmically utilizing these functions for several weeks and has thus experienced and debugged multiple edge cases. In the interest of brevity, the code has been distilled down to a minimum example based around a calling function, runSIRX2, called from the command line.[6] An example of running the code is contained in the function genFiguresAndTables() which will generate the figures and tables used in this paper.

In fitting the data, the algorithm fits the error of the model's estimate against the logarithm of the total cases. This has some desirable computational properties: 1) same weighting of percentage error on large case count data points vs small case counts, i.e. 10,000 vs 500; 2) reducing to the common log-linear least square regression solution if S/N=1. The author has shown (but it is beyond the scope of this paper) that a regression of

$$log(X\ -\ X_0)\ =\ r\,t\ +\ c_0\ +\ \epsilon \qquad \text{Eq. 8}$$

[6] An example of running the code is contained in the function genFiguresAndTables() which will generate the figures and tables used in this paper.

is the general "closed form" symbolic solution when $S/N = 1$ thereby giving the more complex SIRX non-linear least squares optimizer a computationally "nearby" starting set of parameters to bootstrap the regression. Where:

$r \equiv$ the log linear regression's coefficient on t, equivalent to the exponential growth rate
$c_0 \equiv$ the log linear regression's constant
$\epsilon \equiv$ the log linear regression's residual error term
$X_0 \equiv$ the number of cases at t=0 in the regression.

If X_0 is approximately known, for example in the initial growth phase of an epidemic as 1, Equation 8's log-linear regression will produce a reasonable result. However, if X_0 is unknown, for example when an epidemic's new cases are declining exponentially, the regression cannot be formulated in a (log) linear form. In that event, to solve for the parameters X_0, A and r, Equation 8 must be rearranged to a non-linear regression.[7]

$$log(X) = log(X_0 + A\ e^{r(t - t_0)}) + \epsilon \qquad \text{Eq. 9}$$

After this non-linear regression, with X_0, A, and r estimated, the run on the SIRX model has good starting parameters and will normally converge to a solution.

The essential functional flow of the algorithm is:

1) Fetch the data;
2) Use simpler linear models (with $S/N = 1$ leaving purely exponential results) to guess initial parameters for the non-linear nlsLM model that will not result in a gradient singularity, thereby causing the model to fail;
3) As desired by the modeler, either use explicit inputs for k_{IX} (equivalent to setting Q_{Prob}) and the beta Change Factor to find the best fit for the current beta from the subset of the data.
4) If the modeler should so desire, the algorithm can find the best fit for k_{IX} and/or the Beta Change Factor $F_{\beta\Delta}$ in addition to β or β_0 (the latter if using the Beta Change Factor $F_{\beta\Delta}$).

Of note is that the constants β and k_{IX} are not constant in the real world over relatively long time periods. This is because social distancing behavior changes the interaction rate between the infected and the susceptible, and hence changes β; and because changes in screening behavior, contact tracing, or reticence to seek healthcare behavior also change with time. This changing of the β and k_{IX} "constants" favors regression over shorter time periods. However, as was shown by the 3 examples based on a real-world seroprevalence test (like the Wadsworth test), a longer period is needed to take into account very significant changes in the test sensitivity. For the purposes of this calibration demonstration, this paper is essentially forced to use at least 30 days preceding the seroprevalence survey. A more accurate model could use more frequent seroprevalence sampling, and perhaps fatality data, to allow a piecewise approximation of the β and k_{IX} regression parameters. This is beyond the scope of this paper.

An example of a calibration model run is in the Calibrating the SIRX to the Seroprevalence Survey section that will follow.

[7] The reader may note that t_0 is not known. It is set by convenience as the start of the data's interval to be analyzed, noting that the regression solved non-linear regression A, and r constants can compensate for any choice of t_0 because $e^{-r\ t_0}$ is also a constant.

The NYS Seroprevalence Data

The seroprevalence data for the example is taken from the Governor of New York, Andrew Cuomo's, press conference prepared slides [14, 15, 16]. The final data used from this paper is taken from the slides (contained in the YouTubes in the references) which differ due to rounding from the Governor's transcript remarks. The data is summarized below:

Table 2 - New York Antibody Survey Results

Date	**22 April**	**27 April**	**1 May**
Total NYS Surveyed	2,933	7,397	15,103
NYC Only Percent	21.2%	24.7%	19.9%
NYC Percent of Total	43%	43%	Not Stated, Assumed 43%

Of note is that the 22 April data, released on 23 April is stated as being "collected over two days". It is assumed it was collected on 20-21 April. The 1 May data, released first on 2 May, is assumed collected 29-30 April. As it is unlikely that the NYC percentage positive test fraction could have declined by 4.8% (from 24.7% to 19.9%) in approximately doubling the sample size over 4 days, it is more likely that there was some unpublished adjustment to the serological survey data[8]. Further, the 2 May press conference indicated that the data was collected "over the past two weeks".

Assuming a constant rate of collection, this paper will use the midpoint, 25 April, for calibration. However, a more accurate estimate could be obtained using the actual collections on each day for the calibration with some type of least squares fit to the data as will be described below. The survey administrator (i.e. a government public health authority), would have available any ex-post corrections made in the unpublished data. This author recommends that government and private survey collectors fully publish all data.

[8] 27 April data: 7,397 x 24.7% x 43%= 786 positive. 1 May data: 15,103 x 19.9% x 43% = 1,292 positive. Therefore, during the 4 day period from 27 April to 1 May, there would only be 1,292 - 786 = 506 new positives out of 43% x (15,103 - 7,397) = 3,314 new tests or 506/3,314=15.3% positives, a decline of 24.7-15.3=9.4% in six days. This is statistically unlikely in such a sample size if the population and test were uniform, and therefore indicates a likely undisclosed adjustment to the data. This paper will use the 19.9% midpoint number is throughout.

The NYS "Wadsworth" Laboratory Antibody Seroprevalence Test

Governor Cuomo described the test as the New York State Department of Health "Wadsworth Center" independently developed antibody test [17]. The author's research, prior to 1 May, did not find published data describing the specificity and accuracy of the Wadsworth Center's test. However, the FDA has described test characteristics for a Wadsworth Center SARS-CoV-2 Antibody test in an Accelerated Emergency Use Authorization ("EUA"), which they released on 1 May 2020 [18, 19]. The tables below, reproduced directly from the EUA, describe the Wadsworth test sensitivity and specificity.[9]

Days from onset	Samples tested (N)	RT-PCR result	NY SARS-CoV MIA Result as Compared to PCR			Sensitivity (95%CI)
			Positive	Indeter.	Negative	
<7	179	Pos	32	30	117	32/179 **17.9%** (12.96% - 24.15%)
7 – 10	67	Pos	21	19	27	21/67 **31.3%** (21.50% - 43.20%)
11 – 15	47	Pos	23	4	20	23/47 **48.9%** (35.28% - 62.76%)
16 – 20	126	Pos	62	19	45	62/126 **49.2%** (40.63% - 57.83%)
>20	334	Pos	265	28	41	265/334 **79.3%** (74.68% - 83.34%)
Total	753					

Table 3 - NYS Wadsworth Test Sensitivity Through ">20 Days from onset" Reproduced from "Table 2" in Reference [18]

Clinical Study	Number of Samples Tested	Results with NY SARS-CoV MIA		
		Positive (> 6SD)	Indeterminate (>3 SD, <6SD)	Negative (<3 SD)
Study 1	44	39	2	3
Study 2	64	56	4	4
Total Samples	108	95	6	7
Sensitivity	**88.0%** (95/108); 95%CI: 80.49% to 92.83%			

Table 4 - NYS Wadsworth Test Sensititivity "for samples collected at least 25 days after symptom onset" Reproduced from "Table 3" in Reference [18]

Note that in both NYS Wadsworth calibration tables above, the time units are days since symptom onset. For purposes of this example, this paper will assume a 5 day incubation period between infection and symptom onset -- thus the sensitivity data need to be adjusted by adding 5 additional days to the left hand

[9] Note that there is a typographical error in the EUA which refers to Table 3 as Table 4..

column. If the model used was a "SEIR" type model (compartments: **S**usceptible, **E**xposed, **I**nfectious, and **R**ecovered), where onset was being used as a proxy for infectious, this could be adjusted directly. Alternatively an additional compartment could be added if infectiousness begins before symptom onset but after infection, i.e. a SEIOR model (compartments: **S**usceptible, **E**xposed, **I**nfectious, **O**nset of symptoms, and **R**ecovered). Additionally, if the model has direct access to the testing results, additional granularity would be available.

The NYS Wadsworth EUA provided sensitivity curve is clearly non-linear between 11 and 20 days after onset. While this could be smoothed out with a curve fitting, if the model has direct access to the underlying data, a more accurate sensitivity curve could be constructed. Such accuracy and confidence interval information is beyond the time scope of this paper.

The specificity data (i.e. 100% less the false positive percentage) are given on page 7 of the EUA for a variety of sample sera and are reasonably assumed by the EUA to not vary with time since infection with SARS-Cov-2. In calibration, the total true positives for all 433 samples in the clinical specificity table (Table 5 of the EUA [18]) is used to calculate an average specificity for all 433 samples: 100% - 5/433 = 98.85%. Taking sensitivity and specificity together, these are used to make a "test calibration table" which is input into the R computational model:

t start	t end	Sensitivity	Specificity
0	11.999...	0.179	0.9885
12	15.999...	0.313	0.9885
16	20.999...	0.489	0.9885
21	25.999...	0.492	0.9885
26	29.999...	0.793	0.9885
>=30		0.880	0.9885

Table 5 - Wadsworth Calibration Test Sensitivity and Specificity

Test Calibration Sample Bias

As an additional caveat, please note that the Wadsworth Test clinical sensitivity tables are calibrated using 753 subjects from "several US clinical collection sites", and using108 samples from Westchester County, collected at undisclosed times in March and April 2020. As the samples were taken from clinical PCR tests at a time when, due to rationing, PCR tests were generally limited to symptomatic individuals who sought out medical care presumably due to severity of illness, and where asymptomatic or mild cases would have difficulty in obtaining a PCR test; it is likely there is a calibration selection bias which increases the relative number of severe cases in the sample. Further, as the age distribution for those with severe disease is clearly biased older as seen in [20] than the general NYC population (seen in [9]), the Wadsworth Test calibration samples are likely biased older. If the model has direct access to the calibration population data, this bias can be eliminated.

Using a SIRX run to Estimate a Seroprevalence Test Result

For a given SIRX model run, a table is generated of the true positives, that is the infected plus recovered in the general population that is being sampled in the NYS seroprevalence survey. For a given model run containing infected and recovered in the general population who have not been previously PCR (swab)

tested positive, each such day has a certain number of newly infected on a given date in that population that can be calculated[10] as:

$$C_{+Pop}(t) = I(t) + R(t) \quad \text{Eq. 10}$$

$$C_{+Pop}(t) = N - S(t) - X(t) \quad \text{Eq. 11}$$

where the function at time notation $I(t)$ indicates the value is a time series taken from the SIRX model and

$C_{+\mathrm{Pop}}(t) \equiv$ the cumulative total infected at time *t* in the non "Confirmed-Case" population

Then, a careful application of Equation 33A from the Appendix[11] yields the percentage that is tested positive and presumably reported by the Governor during the press conference. This is done by assuming that the *entire* non-Case Confirmed population is tested at the test date, so that

$$N_{nonX} = N - X_{t=Test} \quad \text{Eq. 12}$$

is used as the denominator in Equation 33A. While $X_{t=Test}$ is typically a small fraction of the total population N, it is somewhat significant. Therefore, Equation 33A becomes:

$$\theta_+ = [\, 1/N_{nonX} \sum_{t=0}^{t_{max}} (p_t + q - 1) C_{t+} \,] + (1 - q) \quad \text{Eq. 13}$$

The θ_+ is thus the fraction that would test positive if the survey encompassed the entire non-Confirmed Population and the test performed precisely as specified in Table 5. Of course, the actual test is a sample and the test is statistically described to have confidence intervals, so that statistical methods could be applied to derive a confidence interval on the test results. The fitting of the case data (using the least squares technique on a limited sample set) is itself subject to statistical estimation errors. But again, this paper is simply demonstrating the technique to derive a mean "point estimate" and the estimation of statistical error is beyond its (already lengthy) scope.

Calibrating the SIRX to the Seroprevalence Survey

As a final step, the modeler flips a switch to get the runSIRX2() algorithm to calculate the seroprevalence; asking the model to adjust inputs for k_{IX} (i.e. Q_{Prob}) and the Beta Change Factor $F_{\beta\Delta}$; or alternatively asking the non-linear least squares algorithm to find a best fit to a seroprevalence that matches the survey data simultaneously with finding the best fit for the daily new cases *X* and the change in daily new cases ΔX. To do this in a single non-linear "regression" the weighting factor is increased for the seroprevalence target least squares error so that it is large enough to act as a constraint -- forcing the least squares algorithm to converge to a solution with seroprevalence very near (within 0.1%) of the survey

[10] This estimate may be slightly inaccurate as some of the $X(t)$ may have a different time series distribution vs. the $I(t) + R(t)$ distribution -- because $R(t)$ and $X(t)$ are delayed compared to $I(t)$. This in turn is due to the fact that the SIRX population must flow thru *I* to get to *R* and *X* compartments. However, to the extent that the ratio of $X(t)/[I(t) + R(t)]$ is small and the percentage variation between ΔX(t)/X(t) is essentially by definition similar to $\Delta R(t)/R(t)$ (because $\Delta X(t)$ is proportion to $I(t)$, as is $\Delta R(t)$), this effect is likely to be small. Calculation of this value is beyond the time scope of this paper.

[11] Please see the Appendix for the variable definitions.

result target. This yields a minimum least squares fit to the case data while simultaneously fitting the seroprevalence data, thereby calibrating the model. An example of this calibration is shown in Figure 4 below.

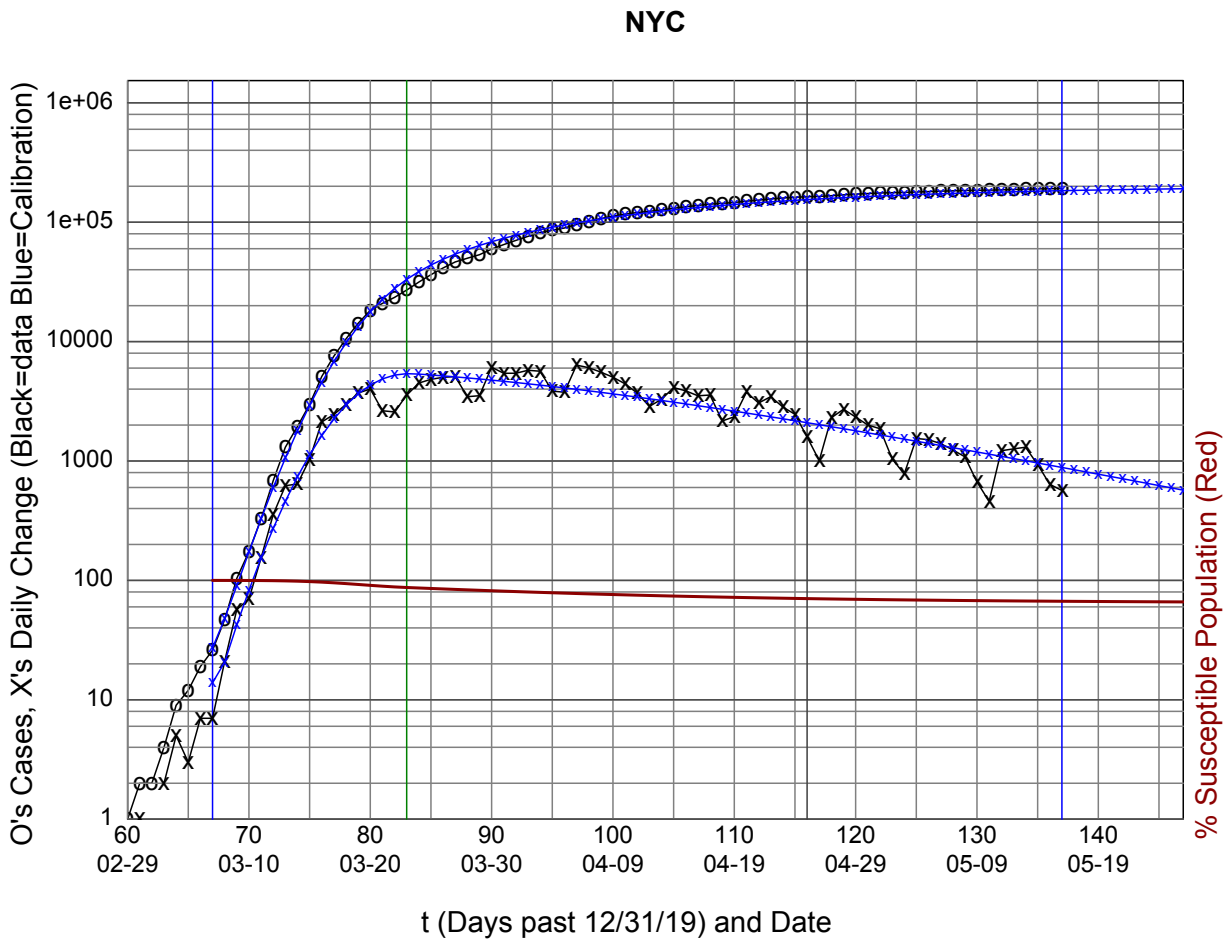


Figure 4 - Calibrated to 19.9% Seroprevalence Survey SIRX using NYC Case Data

The black lines are the actual data with the upper black line (the O's) being the reported cases in the data set (in this case NYC's data from [7]), and the lower black line (the X's) is the daily change in cases. The blue lines are the calibrated fit to the data. The red line is the S/N, i.e. the percentage still susceptible in the population reusing the 1 to 100 scale on the left Y axis.

The calibration needs additional inputs: 1) The mean "effective" date the seroprevalence data are collected (April 25th, the black vertical line), 2) the range of data for which to do the calibration (represented by the vertical blue lines from March 7th to May 16th) -- a section of time for which the data appear to be clean except for the weekly periodic (7 day) variation in tests[12]; and 3) the range of data for which $\beta(t)$ is adjusted as per Equation 7 being also from March 7th and running until March 23rd (16 days = Δt_{chg} from the start of the calibration range). This $\beta(t)$ range brackets the Governor's "lockdown"

[12] The daily data in this NYC test are "by date of diagnosis" which is presumably closer to the date the test is taken than the original (older) NYC data series (total confirmed by NYC DOH as of a certain date), or the NYS data series (total reported to the NYS system as of the date). New York State has total number of PCR tests by County which could be used to adjust the reported NYC data as if testing was done at a constant rate, but this adjustment is beyond the scope of this tutorial.

social distancing order (March 20th). By manually varying Δt_{chg} in integer units, starting at the lockdown date, the minimum residual standard error may be found, so that the optimal Δt_{chg} is that date that has the minimum residual error. This may be done algorithmically, but is beyond the time scope of the code development associated with this paper.

Note that there may be timing differences of a few days between reporting of the PCR Swab Test data represented by the NYC times series data (the black lines) and the seroprevalence test dates which reported in the during the Governor's press conferences. Also note that the change in $\beta(t)$ is fit as if it is linear in the Δt_{chg} time interval and that this is an approximation to the hidden underlying process. Additional code could add a start date immediately before and after the lockdown date.

What can be seen is that 1) the SIRX model visually does a good job of fitting both the daily change in cases (lower blue line) and the cumulative daily cases (the upper blue line); and 2) the percent still susceptible is around 70% compared with the serological survey showing around 80%. The actual numbers can be seen in Table 6 below.

The model text output in Table 6 shows that a perfect seroprevalence test would show 28% positive[13] in the total population on April 25th, and with 163,000 PCR reported infected (about 2%, presumed not in the seroprevalence survey) there are only about 71% remaining susceptible in the population. This continues to decrease slowly to around 67%.

Table 6 - Model Run Data and Calibration

	Date	t	C(Cases)	ΔC	I(Model)	X(Model)	ΔX(Model)	S%(Model)
1	2020-02-29	60	1	NA	NA	NA	NA	NA
2	2020-03-01	61	2	1	NA	NA	NA	NA
3	2020-03-02	62	2	0	NA	NA	NA	NA
4	2020-03-03	63	4	2	NA	NA	NA	NA
5	2020-03-04	64	9	5	NA	NA	NA	NA
6	2020-03-05	65	12	3	NA	NA	NA	NA
7	2020-03-06	66	19	7	NA	NA	NA	NA
8	2020-03-07	67	26	7	1556.4	27.2	13.9	99.98
9	2020-03-08	68	47	21	3275.0	47.9	20.7	99.95
10	2020-03-09	69	104	57	6567.3	90.2	42.3	99.91
11	2020-03-10	70	174	70	12547.5	172.9	82.6	99.82
12	2020-03-11	71	328	154	22834.3	326.6	153.7	99.68
13	2020-03-12	72	684	356	39563.7	598.9	272.3	99.44
14	2020-03-13	73	1304	620	65229.9	1058.2	459.3	99.06
15	2020-03-14	74	1947	643	102272.0	1795.3	737.1	98.50
16	2020-03-15	75	2980	1033	152387.4	2919.9	1124.6	97.72
17	2020-03-16	76	5103	2123	215676.0	4550.5	1630.6	96.71
18	2020-03-17	77	7557	2454	289882.2	6796.4	2245.9	95.45
19	2020-03-18	78	10534	2977	370090.3	9734.9	2938.5	94.01
20	2020-03-19	79	14241	3707	449146.0	13388.9	3654.0	92.46
21	2020-03-20	80	18251	4010	518806.8	17711.6	4322.8	90.90
22	2020-03-21	81	20886	2635	571301.3	22583.9	4872.2	89.44
23	2020-03-22	82	23461	2575	600808.1	27824.8	5240.9	88.18
24	2020-03-23	83	27019	3558	604447.0	33214.3	5389.5	87.20
25	2020-03-24	84	31514	4495	594742.4	38557.7	5343.4	86.38
26	2020-03-25	85	36348	4834	584540.7	43812.3	5254.6	85.59
27	2020-03-26	86	41371	5023	573901.2	48974.1	5161.8	84.81
28	2020-03-27	87	46463	5092	562870.7	54039.3	5065.2	84.05
29	2020-03-28	88	49919	3456	551495.4	59004.6	4965.3	83.32
30	2020-03-29	89	53442	3523	539820.6	63867.1	4862.6	82.61
31	2020-03-30	90	59543	6101	527890.6	68624.5	4757.4	81.92
32	2020-03-31	91	64971	5428	515748.4	73274.6	4650.1	81.25

[13] These figures in this paragraph are arbitrarily rounded to 1%. Also note that the precise calculation of a perfect seroprevalence test requires both the numerator and denominator be adjusted, i.e. $(\Sigma I - X) / (\mathrm{N} - \mathrm{X})$ where ΣI is the total cumulative infected. $S = S_{pct}\, N$ and $\Sigma I = N - S$. For NYC $N \cong$ 8,623,000. In numbers carrying extra precision to make the arithmetic clear $(\Sigma I - X) / (\mathrm{N} - \mathrm{X}) \cong$ 2599527/8468394 ≅ 28% for April 25th.

	Date	t	C(Cases)	ΔC	I(Model)	X(Model)	ΔX(Model)	S%(Model)
33	2020-04-01	92	70403	5432	503435.2	77815.7	4541.1	80.60
34	2020-04-02	93	76156	5753	490990.9	82246.4	4430.8	79.97
35	2020-04-03	94	81803	5647	478453.2	86565.8	4319.4	79.37
36	2020-04-04	95	85651	3848	465858.2	90773.2	4207.4	78.78
37	2020-04-05	96	89420	3769	453239.9	94868.3	4095.1	78.21
38	2020-04-06	97	95773	6353	440630.0	98850.9	3982.6	77.66
39	2020-04-07	98	101822	6049	428058.4	102721.3	3870.4	77.13
40	2020-04-08	99	107374	5552	415552.7	106480.0	3758.7	76.62
41	2020-04-09	100	112403	5029	403138.4	110127.6	3647.6	76.13
42	2020-04-10	101	116833	4430	390839.0	113665.1	3537.5	75.66
43	2020-04-11	102	120540	3707	378675.9	117093.5	3428.5	75.20
44	2020-04-12	103	123406	2866	366668.6	120414.3	3320.8	74.76
45	2020-04-13	104	126693	3287	354834.4	123628.8	3214.5	74.34
46	2020-04-14	105	130813	4120	343189.0	126738.7	3109.9	73.93
47	2020-04-15	106	134681	3868	331746.2	129745.7	3007.0	73.54
48	2020-04-16	107	138199	3518	320518.1	132651.7	2906.0	73.17
49	2020-04-17	108	141767	3568	309515.1	135458.7	2806.9	72.80
50	2020-04-18	109	143930	2163	298746.2	138168.6	2709.9	72.46
51	2020-04-19	110	146277	2347	288218.9	140783.7	2615.0	72.12
52	2020-04-20	111	150046	3769	277939.2	143306.0	2522.3	71.80
53	2020-04-21	112	153106	3060	267912.2	145737.9	2431.9	71.49
54	2020-04-22	113	156565	3459	258141.3	148081.5	2343.6	71.20
55	2020-04-23	114	159396	2831	248629.3	150339.2	2257.7	70.92
56	2020-04-24	115	161858	2462	239377.8	152513.3	2174.1	70.64
57	**2020-04-25**	**116**	**163447**	**1589**	**230387.4**	**154606.2**	**2092.8**	**70.38**
58	2020-04-26	117	164455	1008	221657.9	156620.1	2013.9	70.13
59	2020-04-27	118	166759	2304	213188.5	158557.4	1937.3	69.90
60	2020-04-28	119	169472	2713	204977.5	160420.3	1862.9	69.67
61	2020-04-29	120	171806	2334	197022.8	162211.2	1790.9	69.45
62	2020-04-30	121	173809	2003	189321.5	163932.4	1721.2	69.24
63	2020-05-01	122	175674	1865	181870.3	165586.1	1653.7	69.03
64	2020-05-02	123	176722	1048	174665.7	167174.4	1588.4	68.84
65	2020-05-03	124	177499	777	167703.4	168699.7	1525.2	68.66
66	2020-05-04	125	179043	1544	160979.1	170164.0	1464.3	68.48
67	2020-05-05	126	180552	1509	154488.1	171569.3	1405.4	68.31
68	2020-05-06	127	181951	1399	148225.4	172917.9	1348.6	68.15
69	2020-05-07	128	183191	1240	142186.0	174211.7	1293.8	67.99
70	2020-05-08	129	184276	1085	136364.5	175452.6	1240.9	67.84
71	2020-05-09	130	184944	668	130755.6	176642.6	1190.0	67.70
72	2020-05-10	131	185403	459	125353.7	177783.5	1140.9	67.56
73	2020-05-11	132	186622	1219	120153.2	178877.3	1093.7	67.43
74	2020-05-12	133	187885	1263	115148.6	179925.5	1048.2	67.31
75	2020-05-13	134	189189	1304	110334.2	180930.0	1004.5	67.19
76	2020-05-14	135	190123	934	105704.4	181892.4	962.4	67.08
77	2020-05-15	136	190761	638	101253.5	182814.4	922.0	66.97
78	2020-05-16	137	191327	566	96976.0	183697.5	883.1	66.86
79	2020-05-17	138	NA	NA	92866.4	184543.2	845.7	66.76
80	2020-05-18	139	NA	NA	88919.2	185353.0	809.8	66.67
81	2020-05-19	140	NA	NA	85129.0	186128.4	775.4	66.58
82	2020-05-20	141	NA	NA	81490.5	186870.7	742.3	66.49
83	2020-05-21	142	NA	NA	77998.4	187581.2	710.5	66.41
84	2020-05-22	143	NA	NA	74647.8	188261.2	680.0	66.33
85	2020-05-23	144	NA	NA	71433.6	188911.9	650.8	66.25
86	2020-05-24	145	NA	NA	68350.8	189534.6	622.7	66.18
87	2020-05-25	146	NA	NA	65394.8	190130.5	595.8	66.11
88	2020-05-26	147	NA	NA	62738.0	190717.6	569.2	65.90

Table 6 - Model Run Data and Calibration (Continued)

```
Country/State: NYC      Data Source: NYC
---------------Log-Linear Bootstrap Model DC----------------
lm(formula = log(dC) ~ t, data = six[iData & six$dC > 0, ])
      Min       1Q   Median       3Q      Max
 -5.16660 -0.64413  0.45806  0.84863  1.37365
                  Estimate Std. Error t value  Pr(>|t|)
 Intercept        6.4423764  0.7791232  8.2688 6.445e-12 ***
 r  from dC       0.0100020  0.0074888  1.3356    0.1861
 ---
 Residual standard error: 1.2932 on 69 degrees of freedom
 Multiple R-squared:  0.025201, Adjusted R-squared:  0.011073
 F-statistic: 1.7838 on 1 and 69 DF,  p-value: 0.18607
---------------Log-Linear Bootstrap Model DC3---------------
lm(formula = C ~ I(sign(rDC) * exp(rDC * (t - tMin))), data = six[iData,
     ])
      Min       1Q   Median       3Q      Max
 -40301.8 -15257.9  -1676.1  17422.4  24536.2
                  Estimate Std. Error t value  Pr(>|t|)
 Co from dC       -222728.8    10551.8 -21.108 < 2.2e-16 ***
 A  from dC        225595.8     7134.2  31.622 < 2.2e-16 ***
 ---
 Residual standard error: 17782 on 69 degrees of freedom
 Multiple R-squared:  0.93545,  Adjusted R-squared:  0.93451
 F-statistic: 999.94 on 1 and 69 DF,  p-value: < 2.22e-16
---------------Closed Form Solution Exponential Model-------
Formula: log(C) ~ logOrNA(A * sign(r) * exp(r * (t - tMin)) + Co)
       Estimate  Std. Error t value  Pr(>|t|)
 r   5.2479e-02  6.5355e-03  8.0299 1.933e-11 ***
 Co -1.1680e+04  3.5215e+03 -3.3169  0.001464 **
 A   1.1702e+04  3.5210e+03  3.3235  0.001434 **
 ---
 Residual standard error: 0.84497 on 68 degrees of freedom
 Number of iterations to convergence: 22
 Achieved convergence tolerance: 1.4901e-08
---------------SIRX Model Bootstrap W/Preset Qprob-----------
Formula: log(C * isC + dC * isDC) ~ log(sirX3(retX = isC, retDX = isDC,
     tABtest = dTABcal, ABcurve = ABcurve, Tmax = dTmax, kIX = kIX,
     N = N, errorRetVal = (isC * C + isDC * dC), tChg = tChg,
     gamma = gamma, X0 = X0, dX0 = dX0, beta = beta, betaChgFact = betaChgFact))
               Estimate Std. Error t value  Pr(>|t|)
 X0           25.4161165  7.6503598  3.3222  0.001141 **
 dX0          18.3063212  2.4859080  7.3640 1.431e-11 ***
 beta          0.8070939  0.0190606 42.3435 < 2.2e-16 ***
 betaChgFact   0.1774649  0.0065004 27.3006 < 2.2e-16 ***
 ---
 Residual standard error: 0.34113 on 139 degrees of freedom
 Number of iterations to convergence: 30
 Achieved convergence tolerance: 1.4901e-08
---------------SIRX Model Calibration Run-----------
Formula: log(C * isC + dC * isDC) ~ log(sirX3(retX = isC, retDX = isDC,
     tABtest = dTABcal, ABcurve = ABcurve, Tmax = dTmax, N = N,
     errorRetVal = (isC * C + isDC * dC), tChg = tChg, gamma = gamma,
     X0 = X0, dX0 = dX0, beta = beta, kIX = kIX, betaChgFact = betaChgFact))
               Estimate Std. Error t value  Pr(>|t|)
 X0           2.7233e+01 5.4125e+00  5.0315  1.49e-06 ***
 dX0          1.3869e+01 1.3579e+00 10.2136 < 2.2e-16 ***
 beta         9.0210e-01 1.5296e-02 58.9773 < 2.2e-16 ***
 kIX          8.9110e-03 2.1672e-04 41.1178 < 2.2e-16 ***
 betaChgFact 1.5034e-01 4.0232e-03 37.3672 < 2.2e-16 ***
 ---
 Residual standard error: 0.23429 on 138 degrees of freedom
 Number of iterations to convergence: 30
 Achieved convergence tolerance: 1.4901e-08
------------------------
Calibration Run Summary:
Location=NYC N=8.623e+06 tMin=67 tMax=137 tBetaChange=83 tSeroTest=116 CasesDataSource=NYC
Gamma=0.125000 Beta0=0.902095 BetaChgFactor=0.150338 Beta1=0.135619 kIX=0.008911 Qprob=0.066544
Perfect/Predicted Test Results = 0.283305 / 0.199044 vs Calibration Target=0.199000
```

Run 1 - R Model Run Output[14]

[14] The statisticians and R programmers will recognize that the Model Run Output includes output of the summary() function applied on nlsLM() and lm() functions. The statistical estimates (i.e. standard errors, t-values and probabilities) have not been reviewed in this paper and their use may cause the user to draw non-factual conclusions about accuracy.

Discussion and Conclusion

Why is the model's estimate of true infected plus recovered 40% higher than in the reported data?

The difference is due to a calibration with the FDA's published sensitivity table from the NYS Wadsworth Lab test against a modelled slowly growing total number of infected plus recovered in the general population. While it is not known if this seroprevalence data were already calibrated (i.e. adjusted to present the population true infected plus recovered percentage) when presented by the New York Governor, it is important for modelers to ask the question. It is important to ask for full disclosure of the method of calibrating the test. If the test was not calibrated, a large underestimation of the seroprevalence would result, and hence getting to and achieving so called herd immunity would appear to be a more difficult task that must be more slowly approached.

Further, this implies that the infection fatality ratio (the IFR) may be overestimated by a similar factor of around 40% if the calibration is accurate. It is important for our public health leadership to have such information to make accurate estimates of the effects of various strategies. As other models use IFR as an input together with mortality data to estimate the current state and future evolution of the epidemic, it is important to estimate more accurately these data, suitably adjusted for delayed sensitivity, so as to draw more accurate conclusions from those models.

This paper does not purport to be an accurate estimate of seroprevalence, true cumulative infected or IFR. It serves to technically assist other modelers who may incorporate its techniques to understand the epidemiological situation. This paper's seroprevalence calibration technique, especially after refinement, checking for inaccuracies, and integration into more advanced models, is applicable in cities, smaller states, and smaller countries where seroprevalence data is available, and where the epidemiological parameters like social interaction are fairly uniform. Epidemiologically heterogenous geographic units would necessarily need to be subdivided into more homogenous subunits for analysis.

As of the date of this writing, in the opinion of the author, it is of utmost urgency to continue seroprevalence survey collection and to use it for model calibration, so that we can better understand, collectively, where we are now, and where the epidemic will likely take us.

Weaknesses

1) Instability of k_{IX} and β over time.
2) There is bias in the sample used to produce the seropositivity test compared to the survey population.
3) Too many degrees of freedom in the regression may require additional seroprevalence data points, or incorporation of mortality data to determine both k_{IX} and β.
4) Inaccurate estimation of sensitivity and specificity increases error.
5) Non-uniform subpopulations would need to be subdivided into multiple uniform analyses.
6) Noise in the case data, for example from different rates of testing, needs to be mitigated further
7) Lack of confidence intervals would allow naive application of this model to draw significantly inaccurate conclusions.
8) This paper was written by one person and published without peer review -- there may be significant errors.
9) ***This paper should not be used directly to support any epidemiological conclusion without professional review. It is designed to be an element that can be incorporated into other professional models.***

Math Appendix:
Calculating Test Results from the 3 S's: Seropositivity, Sensitivity and Specificity

Let

N ≡ Total number tested
x ≡ Number of tested positives that are condition positive (true positives)
y ≡ Number of tested negatives that are condition negative (true negatives)
x' ≡ Number of tested positive that are condition negative (false positives)
y' ≡ Number of tested negative that are condition positive (false negatives)
p ≡ Sensitivity of the test
q ≡ Specificity of the test
T_+ ≡ Total number tested positive (regardless of the true condition)
T_- ≡ Total number tested negative (regardless of the true condition)
S_+ ≡ Fraction of tested who are (true condition) seropositive
C_+ ≡ number of tested who are condition positive (regardless of the test result)
C_- ≡ number of tested who are condition negative (regardless of the test result)

By definition:

$$T_+ = x + x' \quad \text{Eq. 1A}$$

$$T_- = y + y' \quad \text{Eq. 2A}$$

$$C_+ = x + y' \quad \text{Eq. 3A}$$

$$C_- = y + x' \quad \text{Eq. 4A}$$

$$p = x/C_+ \quad \text{Eq. 5A}$$

$$q = y/C_- \quad \text{Eq. 6A}$$

$$N = x + y + x' + y' = T_+ + T_- = C_+ + C_- \quad \text{Eq. 7A}$$

Combining the definitions in Eq. 3A and 4A with 5A and 6A:

$$(x + y')\,p = x \quad \text{Eq. 8A}$$

$$(1 - p)\,x = p\,y' \quad \text{Eq. 9A}$$

$$(x + y')\,p = y \quad \text{Eq. 10A}$$

$$(1 - q)\,y = q\,x' \quad \text{Eq. 11A}$$

Combining Eq. 2A and 9A; and 1A and 11A respectively:

$$T_- = y + (1/p - 1)\,x \quad \text{Eq. 12A}$$

$$T_+ = x + (1/q - 1)\,y \quad \text{Eq. 13A}$$

Rearranging Eq. 12A:

$$y = T_- + (1 - 1/p)\,x \quad \text{Eq. 14A}$$

Substituting Eq. 14A into 13A and then expanding, simplifying, rearranging and solving for x:

$$T_+ = x + (1/q - 1)\,[\,T_- + (1 - 1/p)\,x\,] \quad \text{Eq. 15A}$$

$$T_+ = x + (1/q - 1)(1 - 1/p)\,x + (1/q - 1)\,T_- \quad \text{Eq. 16A}$$

$$x + (1/q + 1/p - 1/pq - 1)\,x = T_+ + (1 - 1/q)\,T_- \quad \text{Eq. 17A}$$

$$(1/q + 1/p - 1/pq)\,x = T_+ + (1 - 1/q)\,T_- \quad \text{Eq. 18A}$$

$$x = [T_+ + (1 - 1/q)\,T_-] / (1/p + 1/q - 1/pq) \quad \text{Eq. 19A}$$

By symmetry:

$$y = [T_- + (1 - 1/p)\,T_+] / (1/p + 1/q - 1/pq) \quad \text{Eq. 20A}$$

Eq. 21A

By rearranging Eq. 9A to solve for y' and substituting the definition of C_+ from Eq. 3A, and then simplifying:

$$C_+ = x + (1/p - 1)\,x \quad \text{Eq. 22A}$$

$$C_+ = x/p \quad \text{Eq. 23A}$$

Substituting Eq. 19A into 23A and multiplying through by 1/p:

$$C_+ = [T_+ + (1 - 1/q)\,T_-] / (1 + p/q - 1/q) \quad \text{Eq. 24A}$$

Noting the definition of $N = T_+ + T_-$ and rearrange the definition to substitute for T_+ in Eq, 24A :

$$C_+ = [N - T_- + (1 - 1/q)\,T_-] / (1 + p/q - 1/q) \quad \text{Eq. 25A}$$

$$C_+ = (N - T_-/q) / (1 + p/q - 1/q) \quad \text{Eq. 26A}$$

Using again the definition $N = T_+ + T_-$ and substituting for T_- :

$$C_+ = [N - (N - T_+)/q] / (1 + p/q - 1/q) \quad \text{Eq. 27A}$$

Simplifying and then solving for T_+

$$C_+ = [T_+ + N(q - 1)] / (q + p - 1) \quad \text{Eq. 28A}$$

$$C_+(q + p - 1) = T_+ + N(q - 1)] \quad \text{Eq. 29A}$$

$$T_+ = (p + q - 1)C_+ + N(1 - q)] \quad \text{Eq. 30A}$$

Thus, if one knows with certainty the specificity and sensitivity for any test population and the number who have been tested and are actually positive, the number that are tested positive are known[15].

This can be used to illustrate the difference between naively taking the positive antibody percentage of a test as an estimate of the true positive antibody percentage of the same test population. It can also be compared to the assumption of a single sensitivity against an actual calibrated test that has increasing sensitivity dependent on the number of days since infection.

Note that if the sum of the sensitivity and specificity is less than 1 (i.e. their sum is less than 100%), the antibody test is unusable (i.e. bad) as the coefficient on C_+ is negative, so that a higher condition positive result would impossibly create a lower test positive result. This corresponds to a receiver operating

[15] For purposes of this paper, which is an example demonstration of the effects of known sensitivity and specificity on the naive results, no calculation is made of the inaccuracy due to small sample size (i.e. confidence interval or distribution); and no adjustments are made for the known spread or distribution of specificity or sensitivity measurements. They exist and can be statistically computed if the information is available at the cost of added complexity.

characteristic (ROC) point in the lower right hand half of the plot that is worse than a random guess [21], i.e. more wrong than right.

Also note ***if the specificity is a perfect 100%*** Eq. 30A reduces to simplified forms:

$$T_+ = p\, C_+ \qquad \text{Eq. 31A}$$

Equation 31A is occasionally useful, but for example in the cases where specificity is even just 5% below 100% (i.e. 95%), this simplified equation yields significant errors.

A simple example will show how this information can be used to calculate the test results from known seropositivity:

Assumption: Specificity is known precisely as 0.99 and does not vary with time. Sensitivity is exactly according to this table of the time post infection:

Days Since Infection Interval Start	Days Since Infection Interval End	Sensitivity
0	11.999...	0.20
12	20.999...	0.30
21	25.999...	0.50
26	29.999...	0.80
30	No end	0.90

Table 7A - Simplified (Rounded) Sensitivity Table

This is a rounded to the nearest 10% version of the NY Wadsworth Test (see this paper's Table 5 - Wadsworth Calibration Test Sensitivity and Specificity). When the tested subjects consists of a pool with different infection dates, Equation 30A cannot be used to compute the tested positive for the test in aggregate. Instead, each "vintage" of infection must be used to individually calculate the tested positive for that vintage, with the total of tested positive for each vintage then summed up to get the total tested positive for the survey. Additionally, the false positives must be included for the cohort of the test that has never been infected. Let

$\theta_+ \equiv$ The percentage of the entire test population that is test positive (of all vintages)
$S_+ \equiv$ The percentage of the entire test population that is condition (truly) positive (of all vintages)

By definition

$$\theta_+ = 1/N \sum_{t=0}^{t_{max}} T_{t+} \qquad \text{Eq. 32A}$$

Or by substitution of Eq. 30A into Eq. 32, and then expanding and simplifying:

$$\theta_+ = [\, 1/N \sum_{t=0}^{t_{max}} (p_t + q - 1) C_{t+} \,] + (1 - q) \qquad \text{Eq. 33A}$$

The formula in 33A is easy to apply. 1) Use a model to estimate the true infected at each time (in days) C_{t+}. i.e. at the 25 day vintage say there are 4 infected. 2) Multiply that by the coefficient which is the sum of the sensitivity p_t for that 25 day vintage, plus the specificity, less 1. 3) Sum that up for all

vintages. Note that for those beyond the maximum (in the table above, 30 or more days), they can be included all together. 4) Divide that sum by the total number of tested (regardless of test result or true infected or not infected state. 5) Add to the result 1 minus the specificity (which is assumed to be the same at all vintages. The result is the percentage of the entire test population that is expected to test positive assuming the specificity and sensitivity is exactly correct.

In the following examples, it will be convenient computationally to split T_+ in Eq. 30A into a left and right half, i.e.

$$T_+ = T_{+Left} + T_{+Right} \quad \text{Eq. 34A}$$

$$T_{+Left} = (p + q - 1)C_+ \quad \text{Eq. 35A}$$

$$T_{+Right} = N(1 - q) \quad \text{Eq. 36A}$$

By inspection one can see that T_{+Left} is the component of the positive tests due to actual condition positive, and that T_{+Right} is the component of the positive tests due to (imperfect) specificity without regard for condition.

Similarly, it is convenient to split the percentage test results in Equation 33A into left and right component:

$$\theta_+ = \theta_{+Left} + \theta_{+Right} \quad \text{Eq. 37A}$$

$$\theta_{+Left} = 1/N \sum_{t=0}^{t_{max}} (p_t + q - 1)C_{t+} \quad \text{Eq. 38A}$$

$$\theta_{+Right} = 1 - q \quad \text{Eq. 39A}$$

An example is below for a cumulative infected population doubling every 3 days arbitrarily cutoff at 10000 total infected, tested at 40 days since Day 0:

t	Δt	p_t	$\sum_{t=0}^{t} C_{t+}$	C_{t+}	T_{+Left}
0	40	0.9	1	1	0.89
1	39	0.9	1	0	0.00
2	38	0.9	1	0	0.00
3	37	0.9	2	1	0.89
4	36	0.9	2	0	0.00
5	35	0.9	3	1	0.89
6	34	0.9	4	1	0.89
7	33	0.9	5	1	0.89
8	32	0.9	6	1	0.89
9	31	0.9	8	2	1.78
10	30	0.9	10	2	1.78
11	29	0.8	12	2	1.58
12	28	0.8	16	4	3.16
13	27	0.8	20	4	3.16
14	26	0.8	25	5	3.95
15	25	0.5	32	7	3.43
16	24	0.5	40	8	3.92
17	23	0.5	50	10	4.90
18	22	0.5	64	14	6.86
19	21	0.5	80	16	7.84
20	20	0.3	101	21	6.09
21	19	0.3	128	27	7.83
22	18	0.3	161	33	9.57
23	17	0.3	203	42	12.18
24	16	0.3	256	53	15.37
25	15	0.3	322	66	19.14
26	14	0.3	406	84	24.36
27	13	0.3	512	106	30.74
28	12	0.3	645	133	38.57
29	11	0.2	812	167	31.73
30	10	0.2	1024	212	40.28
31	9	0.2	1290	266	50.54
32	8	0.2	1625	335	63.65
33	7	0.2	2048	423	80.37
34	6	0.2	2580	532	101.08
35	5	0.2	3250	670	127.30
36	4	0.2	4096	846	160.74
37	3	0.2	5160	1064	202.16
38	2	0.2	6501	1341	254.79
39	1	0.2	8191	1690	321.10
40	0	0.2	10000	1809	343.71
			Subtotal	10000	1989.00
			θ_{+Left}		19.9%
			θ_{+Right}		1.0%
			θ_{+}		20.9%

Table 8 - Infections Doubling Every 3 Days Example

As can be noted, the calculated total test positives $\theta_{+}$is only 20.89%, whereas the total true positives is 100%. This ratio, of approximate 5x the true positives to test positives is exaggerated because 1) the number of infections is rapidly growing; and 2) in the end 100% of this hypothetical test population is infected.

t	Δt	p_t	$\sum_{t=0}^{t} C_{t+}$	C_{t+}	T_{+Left}
0	40	0.9	244	244	217.16
1	39	0.9	488	244	217.16
2	38	0.9	732	244	217.16
3	37	0.9	976	244	217.16
4	36	0.9	1220	244	217.16
5	35	0.9	1464	244	217.16
6	34	0.9	1708	244	217.16
7	33	0.9	1952	244	217.16
8	32	0.9	2196	244	217.16
9	31	0.9	2440	244	217.16
10	30	0.9	2684	244	217.16
11	29	0.8	2928	244	192.76
12	28	0.8	3172	244	192.76
13	27	0.8	3416	244	192.76
14	26	0.8	3660	244	192.76
15	25	0.5	3904	244	119.56
16	24	0.5	4148	244	119.56
17	23	0.5	4392	244	119.56
18	22	0.5	4636	244	119.56
19	21	0.5	4880	244	119.56
20	20	0.3	5124	244	70.76
21	19	0.3	5368	244	70.76
22	18	0.3	5612	244	70.76
23	17	0.3	5856	244	70.76
24	16	0.3	6100	244	70.76
25	15	0.3	6344	244	70.76
26	14	0.3	6588	244	70.76
27	13	0.3	6832	244	70.76
28	12	0.3	7076	244	70.76
29	11	0.2	7320	244	46.36
30	10	0.2	7564	244	46.36
31	9	0.2	7808	244	46.36
32	8	0.2	8052	244	46.36
33	7	0.2	8296	244	46.36
34	6	0.2	8540	244	46.36
35	5	0.2	8784	244	46.36
36	4	0.2	9028	244	46.36
37	3	0.2	9272	244	46.36
38	2	0.2	9516	244	46.36
39	1	0.2	9760	244	46.36
40	0	0.2	10000	240	45.60
			Subtotal	10000	4950.00
			θ_{+Left}		49.5%
			θ_{+Right}		1.0%
			θ_{+}		50.5%

Table 9 - Flat New Cases Example

In this example, daily new infections are constant with the exception of the final day, where they are reduced from 244 to 240 to make the example equal exactly 10,000 for the period. Note that the percentage infected detected by the test θ_{+} is half the true infected rate.

t	Δt	p_t	$\sum_{t=0}^{t} C_{t+}$	C_{t+}	T_{+Left}
0	40	0.9	1809	1809	1610.01
1	39	0.9	3499	1690	1504.10
2	38	0.9	4840	1341	1193.49
3	37	0.9	5904	1064	946.96
4	36	0.9	6750	846	752.94
5	35	0.9	7420	670	596.30
6	34	0.9	7952	532	473.48
7	33	0.9	8375	423	376.47
8	32	0.9	8710	335	298.15
9	31	0.9	8976	266	236.74
10	30	0.9	9188	212	188.68
11	29	0.8	9355	167	131.93
12	28	0.8	9488	133	105.07
13	27	0.8	9594	106	83.74
14	26	0.8	9678	84	66.36
15	25	0.5	9744	66	32.34
16	24	0.5	9797	53	25.97
17	23	0.5	9839	42	20.58
18	22	0.5	9872	33	16.17
19	21	0.5	9899	27	13.23
20	20	0.3	9920	21	6.09
21	19	0.3	9936	16	4.64
22	18	0.3	9950	14	4.06
23	17	0.3	9960	10	2.90
24	16	0.3	9968	8	2.32
25	15	0.3	9975	7	2.03
26	14	0.3	9980	5	1.45
27	13	0.3	9984	4	1.16
28	12	0.3	9988	4	1.16
29	11	0.2	9990	2	0.38
30	10	0.2	9992	2	0.38
31	9	0.2	9994	2	0.38
32	8	0.2	9995	1	0.19
33	7	0.2	9996	1	0.19
34	6	0.2	9997	1	0.19
35	5	0.2	9998	1	0.19
36	4	0.2	9998	0	0.00
37	3	0.2	9999	1	0.19
38	2	0.2	9999	0	0.00
39	1	0.2	9999	0	0.00
40	0	0.2	10000	1	0.19
			Subtotal	10000	8700.80
			θ_{+Left}		87.0%
			θ_{+Right}		1.0%
			θ_{+}		88.0%

Table 10 - Infections Decreasing at 3 days Half-Life Example

Even in an example where infections are decreasing at an exponential rate, with a 100% true infection rate, the antibody test only gets an 88% total tested positives. However, the amount of underestimation is only 100-88=12% in this case, vs. 100-21=79% in the growing case or 100-50=50%% in the flat case.

This stark difference in underestimation of the true infected percentage depending on the growth or decline of the true infected population time series demonstrates that calibration requires an estimation of the rate of growth or the decline in growth of the true infected time series.

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