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Bayesian network analysis of Covid-19 data reveals higher infection prevalence rates and lower fatality rates than widely reported

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ABSTRACT

Widely reported statistics on Covid-19 across the globe fail to take account of both the uncertainty of the data and possible explanations for this uncertainty. In this article, we use a Bayesian Network (BN) model to estimate the Covid-19 infection prevalence rate (IPR) and infection fatality rate (IFR) for different countries and regions, where relevant data are available. This combines multiple sources of data in a single model. The results show that Chelsea Mass. USA and Gangelt Germany have relatively higher IPRs than Santa Clara USA, Kobe, Japan, and England and Wales. In all cases the infection prevalence is significantly higher than what has been widely reported, with much higher community infection rates in all locations. For Santa Clara and Chelsea, both in the USA, the most likely IFR values are 0.3-0.4%. Kobe, Japan is very unusual in comparison with the others with values an order of magnitude less than the others at, 0.001%. The IFR for Spain is centred around 1%. England and Wales lie between Spain and the USA/German values with an IFR around 0.8%. There remains some uncertainty around these estimates but an IFR greater than 1% looks remote for all regions/countries. We use a Bayesian technique called 'virtual evidence' to test the sensitivity of the IFR to two significant sources of uncertainty: survey quality and uncertainty about Covid-19 death counts. In response the adjusted estimates for IFR are most likely to be in the range 0.3–0.5%.

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1. Introduction

Widely reported statistics on Covid-19 across the globe fail to take account of both the uncertainty of the data and possible explanations for this uncertainty (Fenton et al. 2020a, 2020b). In this article, we use a Bayesian Network (BN) model to estimate the Covid-19 *infection prevalence rate* (*IPR*) and *infection fatality rate* (*IFR*) for different countries and regions, where relevant data are available. Unlike other statistical techniques that have been used to interpret Covid-19 data, BNs combine multiple sources of data in a single model that provides statistical estimates that better reflect the uncertainty regarding mechanisms that generate the data, and the amount and type of data that is available.

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The article examines results from recent serological antibody surveys carried out globally. Plainly, any uncertainty about the accuracy of serological testing will influence the estimate of the size of community infected with Covid-19 and this will in turn influence any estimate of the *IFR*. A serological test with low accuracy will tend to poorly estimate the size of the community infected and this, in turn, will lead to a poor estimate of the fatality rate. Also, if the fatality count is itself unreliable the fatality rate will suffer again, because if we do not know how many had the disease and how many have died, we cannot estimate the fatality rate with confidence.

The Bayesian approach is generally recognised as more advanced than classical statistical approaches that are typically applied and can therefore address more complex questions (Pearl 1986, Fenton and Neil. 2018). Unfortunately, while it may seem like there has been a deluge of Covid-19 data, there is a dearth of publicly available data of the type necessary for conducting an unbiased analysis of true infection and death rates. Typically, there is also a lack of transparency surrounding the analysis and use of data, with much of the detail and data remaining secret. Hence, we have gathered data from academic papers (mainly pre-prints), press interviews, and other sources including state archives and the mass media.

The BN model (which is implemented in a commercial, state of the art, probabilistic modelling software application – AgenaRisk; Agena Ltd 2020) provides answers to these questions, even in the presence of such basic uncertainties. Specifically:

- What is the accuracy of serological antibody testing under development and how well does it estimate population infection prevalence?
- What serological testing surveys have been done and what does the data tell us about the prevalence of community infection in different locations.
- If the serological testing surveys are imperfect what effect does this have on our estimated *IPR* s?
- Given our prevalence estimates, how does this compare to the case infection numbers? (those who test positive for Covid-19) that is, how much higher is actual community infection compared to reported infection?
- From reported fatality statistics what is the *IFR*? How does serological test quality affect the reliability of these estimates? Likewise, how does uncertainty about fatality counts affect these estimates?
- How do our estimates of covid-19 IFR compare to influenza IFR?

The article is structured as follows: In Section 2, we discuss Covid-19 testing with a particular focus on serological tests and their accuracy (sensitivity and specificity). In Section 3, we present the data and assumptions used in our analysis. In Section 4, we present the single BN model that provides answers to a series of epidemiological questions about the disease, prevalence and infection, simultaneously, and in such a way that uncertainties about the answers to one question will influence our uncertainties about the other and vice versa. The results are presented in Section 5. Our conclusions are presented in Section 6.

2. Covid-19 serological testing

What is the accuracy of serological antibody tests under development how well does it estimate population infection prevalence?

The Covid-19 *IPR* rate can be deduced from serological antibody testing, which identifies those in the tested population whose body retains an immune response arising from prior infection with Covid-19. As the disease spreads through the population, the proportion of people who develop antibodies increases and the proportion with antibodies depends on exposure and

time since the disease was introduced into the community. Hence, different countries and regions will be at different points in this process and will exhibit different *IPR* rates.

The Covid-19 *IPR* rate will also be crucially dependant on our ability to accurately measure whether an individual has antibodies. Typically, serological tests of blood or other body fluids are used to detect antibody levels and hence determine either infection (IgM antibodies) or potential immunity (IgG antibodies). Presence of the latter identifies whether patients have previously had the disease, independent of whether they exhibited symptoms. Leaving aside concerns about whether immunity is temporary or indeed absent, our uncertainty about whether a patient has had Covid-19 depends on the accuracy of the serological testing process. A patient who has tested positive using a Covid-19 serological test can do so for two reasons—they genuinely have antibodies at detectable levels (these are called 'true positives'), or the testing process falsely identifies them as antibody positive (these are called 'false positives'). Hence, accuracy of the test is determined by its sensitivity¹ and specificity, where:

Sensitivity = True positive rate = 1 - (False negative rate)Specificity = 1 - (False positive rate)

As false positive and false negative rates rise, the greater our uncertainty will be about any diagnosis of Covid-19 for an individual and across a population.

Serological testing processes, kits and machines are presently being assessed for accuracy using samples drawn from patients who are known to have the disease or are disease free. Pharmaceutical companies and academic researchers use these known samples to determine the sensitivity and specificity. At the time of writing a number of pharmaceutical serological tests have been made available in the marketplace and indeed some have received FDA emergency authorised approval for use (FDA 2020). Accuracy for many of these tests is presently being debated.

The Covid-19 *IFR* rate is simply the number of fatalities up to some point in time divided by the size of the community infected with the virus. The number of infected will include those who test positive for antibodies, which includes those who tested positive (IgM antibodies) and those who currently test negative, but show an immune response (IgG antibodies) identifying that they were infected with Covid-19 sometime in the past. Likewise, the number of community infected cases will include those who are asymptomatic and symptomatic, whether hospitalized or not, those who finally die with (or of) the disease, and those who were infected but have fully recovered. We can estimate the number of community infected from the serological testing, and as we have said, this depends on the accuracy of the testing process. If the serological tests are inaccurate estimates of the number of fatalities, and any uncertaint, leading to less reliable estimates for *IFR*. Similarly, the number of fatalities, and any uncertainty about the true number of fatalities, also influences the *IFR*. For example, overestimation of causalities by certifying Covid-19 deaths where patients died as a result of some pre-existing condition while infected with Covid-19, rather than only those where Covid-19 was the direct cause of their death (Fenton et al. 2020a) will lead to greater uncertainty about the fatality rate.

3. Data and assumptions

What serological testing surveys have been done and what does the data tell us about the prevalence of community infection in different locations?

We use serological antibody survey data from these sources:

- Santa Clara County, California, USA (Bendavid et al. 2020)
- Kobe, Japan (Doi 2020)
- Gangelt, Germany (Streeck et al. 2020)
- Chelsea, Massachusetts, USA (Saltzman 2020)

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- NHS England and Wales serological survey, UK (Blanchard 2020)
- Spain (Carlos 2020)

We have also gathered and used publicly available data on serological antibody test accuracy for each of these test sources from the FDA (2020), manufacturer websites and research papers:

- Roche, as hypothetical for England and Wales UK (FDA 2020)
- Kurabo Inc, for Kobe, Japan (Karubo Ltd 2020)
- Premier Biotech, for Santa Clara, California, USA (Bendavid et al. 2020)
- EUROIMMUN for Gangelt (FDA 2020)
- BioMedomics for Chelsea, Massachusetts, USA (BioMedomics 2020)
- Orient Gene Biotech, for Spain (Carlos 2020)

It is important note that the sensitivity and specificity values are normally calculated using simply arithmetic ratios; so if the sample tested had zero false positives or false negatives then the sensitivity and specificity would be reported to be perfect (100%), no matter how many were tested. However, if you run one, and only one, test and confirm it positive, would you believe the test to be perfect on such a small experiment? This issue is addressed by the BN model. Some tests identify early or existing infection through detection of IgM antibodies. Other tests can identify patients who at some point in the past were infected with and successfully fought off the disease through detection of IgG antibodies. Many antibody tests are developed that can detect both, and where a test has this capability the regulated clinical trial and test validation process generally identifies different sensitivity and specificity values for that test for each antibody. Many of the Covid-19 antibody tests receiving emergency clearance can detect two or three antibodies but are only reporting one sensitivity and specificity value. More often this is for IgM antibodies, creating further uncertainty when we use that test to identify those who previously had the disease.

To illustrate our uncertainties about the results of serological testing we look at the false positive and false negative rates for the various serological test sources, used to estimate population infection prevalence, as shown in Table 1.

UK fatality data and Covid-19 infection rates were collected from the UK Office for National Statistics (ONS) (ONS 2020a) and from the worldometers website (Worldometers 2020).

All available data are taken from the mid-April to early May 2020 snapshot. Thus, different countries and regions within countries will have different *IPRs* as these will be a determined by when the virus was first introduced and the time elapsed. For data we assume the time from infection to recovery (or fatality) is sufficient to ensure that any anyone infected will have detectable traces of antibodies in their blood.

4. The Bayesian network (BN) model

A BN is a graphical model consisting of nodes and arcs where the nodes represent variables and an arc between two variables represents a dependency. The strength of each dependency, as

Table 1. Sensitivity a	Table 1. Sensitivity and specificity tests.							
Test source	Number of FP tests	False positives	Specificity (%)	Number of FN tests	False negatives	Sensitivity (%)		
Roche	5272	10	99.8	29	0	100.0		
Kurabo ^a	521	0	100.0	500	100	80.0		
Premier Biotech	371	2	99.5	160	7	95.6		
EUROIMMUN	80	0	100.0	30	3	90.0		
BioMedomics	128	12	90.6	397	45	88.7		
Orient Gene Biotech ^a	500	0	100.0	500	75	85.0		

Table 1. Sensitivity and specificity tests

a Note the Karubo and Orient Biotech test sources are inferred from published sensitivity and specificity statics and total sample sizes.

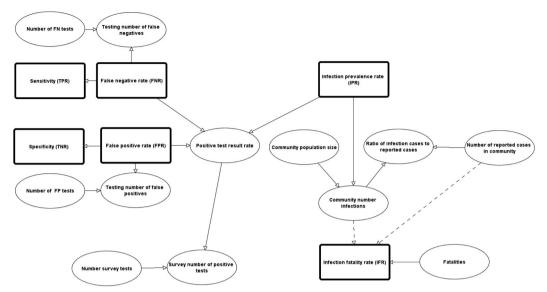


Figure 1. Bayesian Network Model to estimate Covid-19 IPR and IFR.

well as the uncertainty associated with these, is captured using probabilities and statistical distributions. When observed data are entered into the model for specific variables all the probabilities for, as yet unknown, unobserved or latent variables, are updated by Bayesian inference.

The BN model used for our analysis is shown in Figure 1 for the joint probability density function below:

$$f(TPR, FNR, \dots, IFR) = f(TPRFNR)f(FNn_{FN}, FNR) \times f(TNRFPR)f(FP|n_{FP}, FPR)f(P|IPR, FNR, FPR) \times f(PS|n_{S}, P)f(CZ, P)f(R|C, RCC)f(IFR|F, C) f(IPR)f(Z)f(RCC)$$

This represents the conditional and prior probability functions for these variables, as shown in Table 2. The statistical distributions and conditional probability densities are given in the Appendix.

Bayesian inference is performed in AgenaRisk (Agena Ltd 2020) which uses the dynamic discretization algorithm (Neil, Tailor, and Marquez 2007).

The goal of a mass serological antibody survey is to estimate the *IPR* of the virus in the population. If we knew the *IPR*, the false negative rate (*FNR*), and false positive rate (*FPR*) then we can determine the probability, *P*, of a positive test result as:

$$P = IPR(1 - FNR) + (1 - IPR)FPR$$

This is because there are two ways to test positive. The first is where someone is infected (probability *IPR*) and correctly test positive (probability (1 - FNR)), giving $(1 - FNR) \times IPR$. The second is where someone is *not* infected, (1 - IPR), but they falsely test positive, *FPR* and this gives us (1 - IPR)FPR.

Here we use the BN to solve the 'inverse problem', where we estimate the *IPR* given information about *FNR*, *FPR*, and *P*, that is, the test accuracy (sensitivity and specificity) and the number of positive tests from a given serological survey. Again, poor test accuracy will lead to poorer estimates of the *IPR* and, again, the size of the survey, in terms of samples taken, will determine the confidence in our estimates, with bigger samples translating to better information.

Once the BN model estimates the distribution for *IPR* this is used to estimate community infections, *C*, and ultimately the infection fatality rate, *IFR*.

TPR	True positive rate (sensitivity)	IPR	Infection Prevalance Rate
TNR	True negative rate (specificity)	PS	Survey number of positive tests
FN	False negatives in testing	ns	Number of survey tests
FP	False positives in testing	IFR	Infection fatality rate
n _{FN}	Number of false negative tests	С	Community number of infections
n _{FP}	Number of false positive tests	Ζ	Community population size
FPR	False positive rate	R	Ratio of infection cases to reported cases
FNR	False negatve rate	RCC	Number of reported cases in community
Ρ	Positive test result rate	F	Number of fatalilites

Table 2. Variables in Bayesian Network model.

5. Results using available data

5.1. Infection prevalence rates

If the serological testing surveys are imperfect what effect does this have on our estimated *IPR* s?

To date very few serological surveys have been carried out and where they have been, some results have been difficult to obtain given the secrecy involved. The survey data and sources are listed below in Table 3. Note that here we are using raw data unadjusted for demographic or other population features.

*Note that the positive test results for England and Wales is inferred from public announcements made by the UK Government's Chief Medical Officer (Blanchard 2020) about the UK ONS antibody survey (ONS 2020b).

We have the serological test results from the Santa Clara County, California USA, study (Biomedomics 2020) and Gangelt, Germany (FDA 2020). However, for the Kobe, Japan, study we only had specificity and sensitivity point values and total sample sizes from Kurano (Karubo Ltd 2020) and had to infer the likely values. Also, we do not know what serological tests were applied in England and Wales. The UK government have, however, announced they were choosing Roche as one of their serological antibody test suppliers, and so we assume a test with equivalent accuracy was used (FDA 2020).

The full probability distributions that the BN model computes *IPR* for all cases are shown in Figure 2 and the associated summary statistics are listed in Table 4.

From Figure 2 and Table 4 we can see that Chelsea Mass. USA and Gangelt Germany have relatively higher *IPRs* than Santa Clara USA, Kobe, Japan and England and Wales.

5.2. Estimates of community infections

Given our prevalence estimates, how does this compare to the case infection numbers? (those who test positive for Covid-19) that is, how much higher is actual community infection compared to reported infection?

Now we have an estimate of the *IPR* we can use this to estimate the number of community infections, *C*, in a region or country, given the relevant community population size. We can also compare this estimate with the number of reported cases of Covid-19 in the community, to determine the extent to which Covid-19 is more or less widespread than thought and also to determine proportion of cases likely to be symptomatic/asymptomatic and severe/slight.

Source data on the actual number of Covid-19 infection cases have been taken from the relevant research papers or other sources, and in the case of the UK from worldometers, for mid-April, where it reported to be circa. 100,000 (Worldometers 2020). The summary statistics form the distributions calculated from the BN of the number of community infections are given in Table 5.

Table 5 shows that the estimated community prevalence is much higher than reported prevalence. Figure 3 and Table 6 show the results from the model of the ratio of estimated to

Table 3. Serological surveys.

Test source	Samples	Positive tests
Santa Clara	3330	50
Kobe	521	22
Gangelt	500	75
Chelsea	200	64
England and Wales	1000	50*
Spain	50983	3049

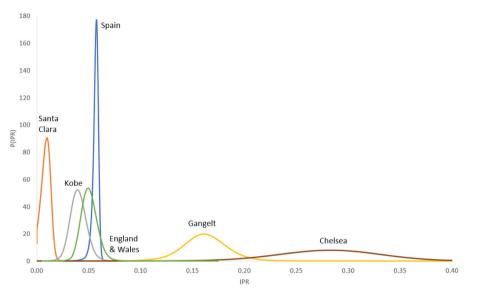


Figure 2. Posterior marginal distribution of Infection prevalence rate (IPR) for country/region cases.

Case	Test source	Assumption	Mean	95% CI
Santa Clara	Premier Biotech	Actual source	0.00879 (0.88%)	(0.0009, 0.0165)
Kobe	Kurabo	Actual source	0.040 (0.4%)	(0.0254, 0.0562)
Gangelt	EUROIMMUN	Actual source	0.162 (16.2%)	(0.1162, 0.0208)
Chelsea Mass.	BioMedomics	Actual source	0.28 (28.1%)	(0.1795, 0.3780)
England and Wales	Roche	Hypothesised source	0.0506 (0.51%)	(0.0368, 0.0670)
Spain	Orient Gene Biotech	Actual source	0.05663 (0.56%)	(0.0496, 0.0617)

Table 4. Summary statistics for IPR.

reported cases and the effect that unreliability in survey testing has on the result. Clearly in all cases the extent of community prevalence is much higher than reported. There is however considerable uncertainty about the ratio distribution for Kobe and Santa Clara, given their confidence interval is so wide.

5.3. Infection fatality rates

From reported fatality statistics what is the Covid-19 IFR?

The final piece of the jigsaw puzzle is our estimation of *IFR*, for each of the countries and regions where we have data available, and here this includes, England and Wales and Chelsea Mass. USA, Santa Clara USA, Kobe Japan, Spain, and Gangelt, Germany.

The reported fatalities up to mid-April in the UK is 23,554 (ONS 2020b). The reported fatality count for Chelsea, Massachusetts is 39 (Saltzman 2020) and for Santa Clara, California is 94 (Ioannidis 2020). For Gangelt, Germany it is 7 (Streeck et al. 2020). For Spain, the fatality count is

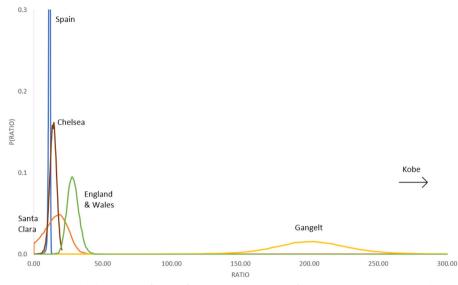


Figure 3. Posterior marginal distribution of Ratio of estimated community infections (*R*) to cases to reported cases by country/region cases (excluding Kobe, Japan).

Table 5. Summar	y statistics	for Community	y number infections, C.	
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Case	Test source	Assumption	Mean	95% CI	Reported cases
Santa Clara	Premier Biotech	Actual source	15,668	(1617, 29529)	956
Kobe	Kurabo	Actual source	60,839	(38428, 85499)	69
Gangelt	EUROIMMUN	Actual source	2,015	(1443, 2595)	10
Chelsea Mass.	BioMedomics	Actual source	16,131	(12821 19637)	803
England and Wales	Roche	Hypothesised source	2,839,500	(2057300, 3753600)	100,000
Spain	Orient Gene Biotech	Actual source	2,600,100	(2274700, 2804900)	230,000

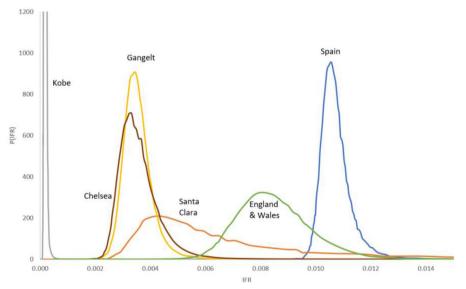


Figure 4. Posterior marginal distribution of Infection fatality rate (IFR) for country/region cases.

27,888 (Worldometers 2020) and for Kobe Japan it is 10 (loannidis 2020). Figure 4 shows the predicted distributions from the BN model for each *IFR*, while Table 7 shows the summary statistics.

The most likely (modal) *IFR* values are grouped for Santa Clara and Chelsea, both in the USA, with mode values of 0.3–0.4%. However, for Santa Clara there is higher uncertainty giving a long

Case	Test source	Test source Assumption		95% CI
Santa Clara	Premier Biotech	Actual source	16	(1.68, 30.98)
Kobe	Kurabo	Actual source	881	(556.93, 1240.5)
Gangelt	EUROIMMUN	Actual source	201	(144.24, 259.7)
Chelsea Mass.	BioMedomics	Actual source	14	(8.95, 18.92)
England and Wales	Roche	Hypothesised source	28	(20.3, 37.5)
Spain	Orient Gene Biotech	Actual source	11	(9.88, 12.19)

 Table 6.
 Summary statistics for ratio of estimated community infections, R, to reported cases.

tail in the data hence the mean value is significantly higher at 1.02%. This shows the estimate for Santa Clara is less informative. Kobe, Japan is very unusual in comparison with the others with values an order of magnitude less at 0.001%. The *IFR* for Spain has a low variance, which is unsurprising given the very large survey conducted, with a mean and mode rate close to each other centred around 1%. England and Wales lie between Spain and the USA/German values with a mode and mean of 0.8%.

5.5. Sensitivity to uncertainty

How does serological test quality affect the reliability of the above estimates of the *IFR*? Likewise, how does uncertainty about fatality counts affect these estimates?

The preceding analysis has simply used the available 'raw' data without any adjustment for demographics or to take account of differences between countries and regions. In this section, we choose two sources of uncertainty that have not been covered by other researchers and which strongly determine the sensitivity of results, especially for *IFR*. These concern fatality counts and the quality of the serological surveys themselves.

There is some controversy over UK fatality counts (Fenton et al. 2020a) and there appear to be many reasons not to trust the fatality count, including:

- Ambiguity and confusion about diagnostic criteria for Covid-19
- Care home deaths not certified by a qualified medical practitioner
- Hospital and other deaths signed off as 'caused by' Covid-19 when they are 'with' Covid-19
- The number of excess deaths could be much higher because of cases that remain undiagnosed

Similar concerns apply to Spain and potentially elsewhere. Given that these uncertainties work in both directions we must be careful to include under and over-estimates and not chose one to suit our prejudices or political outlook.

The Santa Clara study has been heavily criticised by some statisticians in a popular blog (Stats Blog 2020), mainly because subjects were recruited using Facebook and perceived issues with sample sizes and other aspects of the analysis undertaken. Similar observations and comments have been made about the Chelsea study because subjects were chosen for convenience and availability rather than at random.

Typically, experimenters would design their study to address the sensitivity of the results to uncertainties, using relevant and, potentially, causal classifications such as demographic stratification of the relevant population. However, given that we have observational rather than experimental data we can only perform a post hoc evaluation of the sensitivity of the results. Hence, in this section we address these major uncertainties, using our BN model. The lack of controls in these observational studies translates into less informative estimates and more variability.

We use the notion of 'virtual' evidence to assess how different observations might affect our results. In this way we view the observations not as 'facts' but as random variables, bounded by possible ranges of value. This enables us to ask hypothetical questions such as: What would the

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Table 7. Summary statistics for the IFR rate.

Case	Test source	Fatality count	Mode	Mean	95% CI
Santa Clara	Premier Biotech	94	0.004 (0.4%)	0.0102 (1.02%)	(0.0031, 0.0595)
Kobe, Japan	Kurabo	10	0.00015 (0.001%)	1.7271E – 4 (0.0002%)	(1.16E – 4, 2.60E-4)
Chelsea Mass.	BioMedomics	39	0.003 (0.3%)	0.0029 (0.29%)	(0.0025, 0.0054)
Gangelt, Germany	EUROIMMUN	7	0.003 (0.3%)	0.0036 (0.36%)	(0.0026, 0.0048)
England and Wales	Roche	23,554	0.008 (0.8%)	0.0085 (0.85%)	(0.0062, 0.0114)
Spain	Orient Gene Biotech	27,888	0.010 (1.0%)	0.0107 (0.107%)	(0.0099, 0.0122)

Table 8. Virtual evidence scenarios.

Case	Virtual evidence		
Santa Clara	Observed positives $PS_{obs} \sim Uniform(1, 50)$		
Chelsea Mass.	Observed positives $PS_{obs} \sim Uniform(1, 64)$		
England and Wales	Fatalities $F_{obs} \sim Triangular(5000, 10000, 30000)$		
Spain	Fatalities $F_{obs} \sim Triangular(6000, 12000, 35000)$		

results have been had fatalities been exaggerated or the number of positives from a study been fewer?

For the Santa Clara $PS_{obs} = Binomial(n_{s_1}, P) = 50$, meaning we have 50 positive results from the binomial model. Virtual evidence allows us to place a likelihood over the distribution for PS_{obs} that reflects our uncertainty about the study design. Here we use $PS_{obs} \sim Uniform(1, 50)$ representing a sceptical belief that any value between one and fifty is equally likely from this study because the study design was such that it made it more likely that prior infected subjects would volunteer. Once we enter this virtual evidence into the BN it will compute the posterior probability distribution using this likelihood instead of a single point observation. Bayesian inference then computes the posterior distribution using this 'sceptical' likelihood along with other evidence in the model. Clearly, the resulting posterior will not necessarily match the likelihood provided, and indeed may contradict it, perhaps demonstrating the scepticism was unwarranted. We can apply the same process to the fatality counts and apply 'virtual evidence' that reflects deeper uncertainties about whether people 'died because of' Covid-19 as opposed to 'with' Covid-19.

We applied virtual evidence in four cases, as shown in Table 8. Uncertainties about the study design are represented for Santa Carla and Chelsea, Mass., USA. Uncertainties about the true fatality count are represented for England & Wales and Spain.

The sensitivity of IFR to these changes to the evidence is shown with the full distributions in Figure 5 and summary statistics in Table 9.

The effect of virtual evidence is to increase the variability of the results, as one would expect. For the Santa Clara and Chelsea studies where we adjusted the observed survey positives the mean fatality rate estimates increase. However, the modal values do not change much at all, remaining around 0.3–0.5%, suggesting that the BN model is balancing the sceptical explanations against other evidence in the model and discounting any virtual evidence that is perhaps too sceptical. Figure 6 shows the posterior marginal distributions that result from the application of virtual evidence on the number of positive tests for these studies. Clearly any strong scepticism that the number of genuine positives must be close to zero is not warranted and in the case of Chelsea observations less than 30 are difficult to justify. The model clearly 'believes' the survey results are credible.

After the adjustment, distributions of the IFR across the USA, Spain and the UK look very similar; the most likely range for IFR is between 0.2 and 1%, with values beyond this looking less likely.

5.6. Comparison with influenza

How do our estimates of covid-19 IFR compare to influenza IFR?

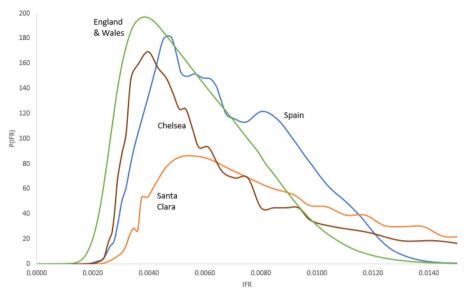


Figure 5. Posterior marginal distribution of Infection fatality rate (IFR) for country/region cases in virtual evidence scenarios.

Case	Test source	Fatality count	Mode	Mean	95% CI
Santa Clara	Premier Biotech	94	0.005 (0.5%)	0.0217 (2.17%)	(0.0038, 0.0968)
Chelsea Mass.	BioMedomics	39	0.003 (0.3%)	0.0124 (1.24%)	(0.0030, 0.0485)
England and Wales	Roche	23,554	0.004 (0.4%)	0.0056 (0.56%)	(0.0024, 0.0106)
Spain	Orient Gene Biotech	27,888	0.004 (0.4%)	0.0107 (1.07%)	(0.0032, 0.0118)
0.04					
0.04					
		Santa Clara			
0.03		Clara			
0.03					
P(POSITIVE TESTS)					
VITIS0.02			Chelsea		
P(PC					
0.02					
0.01					
0.01					
0.00	15.00	30.00		5.00	60.00
0.00	15.00	POSITIVE		5.00	00.00

Table 9. Summary statistics for IFR in virtual evidence scenarios.

Figure 6. Posterior marginal distribution of Infection for the number of positive tests for the Santa Clara and Chelsea cases.

For comparison, the fatalities in England and Wales for the 'higher than seasonal average' in the year 1999/2000 were 21,290 excess deaths attributed to influenza like illness (Crofts et al. 2004), from an infected population of 440,440 (influenza like illness reports) (ONS 2015). With a population of approximately 52 m this is an *IPR* of just over 0.8% and a case fatality rate *CFR* of

4.8%. However, it should be noted that the equivalent of population level serological antibody testing is not routinely performed for influenza hence the *IPR* is likely to be underestimated and the *IFR* significantly less than the *CFR*.

6. Conclusion

Widely reported statistics on Covid-19 across the globe fail to take account of both the uncertainty of the data and possible explanations for this uncertainty. In this article, we have used a BN model to estimate the Covid-19 *IPR* and *IFR* for different countries and regions, where relevant data are available. This combines multiple sources of data in a single model.

We used this model, and available data on serological surveys, fatality counts and test accuracy, to answer the following questions: What is the accuracy of serological antibody tests under development and will it be sufficient to estimate population infection prevalence? What serological testing surveys have been done and what does the data tell us about the prevalence of community infection in different locations? If the serological testing surveys are imperfect what effect does this have on our estimated *IPR* s? Given, our prevalence estimates, how does this compare to the case infection numbers? From reported fatality statistics what is the *IFR*? How does serological test quality affect the reliability of these estimates? Likewise, how does uncertainty about fatality counts affect these estimates? How do our estimates of Covid-19 *IFR* compare to influenza *IFR*?

The results show that Chelsea Mass. USA and Gangelt Germany have relatively higher IPRs than Santa Clara USA, Kobe, Japan and England and Wales. In all cases the infection prevalence is significantly higher than has been widely reported, with much higher community infection rates in all locations. For Santa Clara and Chelsea, both in the USA, with most likely IFR values of 0.3-0.4%. Kobe, Japan is very unusual in comparison with the others with values an order of magnitude less than the others at, 0.001%. The IFR for Spain has a low variance, which is unsurprising given the large survey conducted, with an IFR centred around 1%. England and Wales lie between Spain and the USA/German values with an IFR around 0.8%. There remains some uncertainty around these estimates but an IFR greater than 1% looks remote. We used a Bayesian technique called 'virtual evidence' to test the sensitivity of the IFR to two significant sources of uncertainty: survey quality and uncertainty about death rates. In response the adjusted estimates for IFR that are most likely to be in the range 0.3–0.5%. The unadjusted and adjusted Covid-19 IFR s calculated may be significantly less than that from the 1999/2000 UK influenza season, which had an IPR of just over 0.8% and a case fatality rate CFR of 4.8%. However, the influenza *IPR* is likely to be underestimated and the *IFR* significantly less than the *CFR* due to the absence of routine serological surveillance.

It is worth emphasising the significant problems facing any researcher with objectives like ours. There is a severe lack of transparency and important data sets are inaccessible. To support open debate these should be treated as a public good and shared openly throughout the scientific community in a timely manner.

Note

1. Note that these rates can either be presented as percentages (ranging from 0 to 100%) or as probabilities (ranging from 0 to 1) as done in the formulas here.

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References

Agena Ltd. 2020. "AgenaRisk". http://www.agenarisk.com.

- Bendavid, E., B. Mulaney, N. Sood, S. Shah, E. Ling, R. Bromley-Dulfano, C. Lai, et al. 2020. COVID-19 Antibody Seroprevalence in Santa Clara County, California. *medRxiv*. https://www.medrxiv.org/content/ doi:10.1101/2020. 04.14.20062463v2..2020. doi:10.1101/2020.04.14.20062463.
- Biomedomics. 2020. COVID-19 IgM/IgG Rapid Test. Biomedics Inc. https://www.biomedomics.com/products/infectious-disease/covid-19-rt/
- Blanchard, S. 2020. Comments made in press report by Whitty, C., Chief Medical Officer, UK Government. How many people in London have REALLY had coronavirus? *Daily Mail newspaper*. Accessed 24 April 2020. https:// www.dailymail.co.uk/news/article-8250371/How-people-REALLY-caught-coronavirus.html.
- Carlos. 2020. Instituto de Salud, Carlos III. Estudio ENE-Covid-19: Estudio nacional de seor-epidemiologia de la infection por SARS-Cov-2 en Espana. May 2020. https://portalcne.isciii.es/enecovid19/documentos/ene_covid19_res.pdf
- Crofts, J. P., C. A. Joseph, M. Zambon, J. Ellis, D. M. Fleming, and J. M. Watson. 2004. "Influenza Surveillance in the United Kingdom: October 2002 to May 2003." Communicable Disease Report. CDR Supplement 14: 1–9.
- Doi, A., K. Iwata, H. Kuroda, T. Hasuike, S. Nasu, A. Kanda, T. Nagao, et al. Seroprevalence of novel coronavirus disease (COVID-19) in Kobe, Japan. *medRxiv* https://www.medrxiv.org/content/10.1101/2020.04.26.20079822v2.
- FDA. 2020. U.S. Food and Drug Administration. EUA Authorized Serology Test Performance. Accessed 22 April 2020. https://www.fda.gov/medical-devices/emergency-situations-medical-devices/eua-authorized-serology-testperformance.
- Fenton, N., and M. Neil. 2018. *Risk Assessment and Decision Analysis with Bayesian Networks*. Boca Raton, FL: CRC Press.
- Fenton, N. E., M. Neil, M. Osman, and S. McLachlan. 2020a. "COVID-19 Infection and Death Rates: The Need to Incorporate Causal Explanations for the Data and Avoid Bias in Testing." *Journal of Risk Research* 1–4. doi:10. 1080/13669877.2020.1756381.
- Fenton, N., M. Osman, M. Neil, and S. McLachlan. 2020b. Coronavirus: Country comparisons are pointless unless we account for these biases in testing. *The Conversation*. https://theconversation.com/coronavirus-country-comparisons-are-pointless-unless-we-account-for-these-biases-in-testing-135464
- loannidis, J. 2020. The infection fatality rate of COVID-19 inferred from seroprevalence data. *medRxiv*. https://www. medrxiv.org/content/10.1101/2020.05.13.20101253v1. doi:10.1101/2020.05.13.20101253.
- Karubo Ltd. 2020. Products and Technology. https://www.kurabo.co.jp/bio/English/index.html.
- Neil, M., M. Tailor, and D. Marquez. 2007. "Inference in Hybrid Bayesian Networks Using Dynamic Discretization." Statistics and Computing 17 (3): 219–233. doi:10.1007/s11222-007-9018-y.
- ONS. 2015. UK Office for National Statistics. Highest number of excess winter deaths since 1999/2000. Accessed 25 November 2015. https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/ articles/highestnumberofexcesswinterdeathssince19992000/2015-11-25
- ONS. 2020a. Deaths involving COVID-19, England and Wales. *UK Office for National Statistics*. https://www.ons.gov. uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/datasets/ deathsinvolvingcovid19englandandwales.
- ONS. 2020b. ONS jointly leading government's large-scale virus infection and antibody test study. *UK Office* for National Statistics. Accessed 22 April 2020. https://www.ons.gov.uk/news/news/ onsjointlyleadinggovernmentslargescalevirusinfectionandantibodyteststudy

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- Pearl, J. 1986. "Fusion, Propagation, and Structuring in Belief Networks." Artificial Intelligence 29 (3): 241–288. doi:10. 1016/0004-3702(86)90072-X.
- Saltzman, J. 2020. Nearly a third of 200 blood samples taken in Chelsea show exposure to coronavirus, *Boston Globe*. Accessed 17 April 2020. https://www.bostonglobe.com/2020/04/17/business/nearly-third-200-blood-samples-taken-chelsea-show-exposure-coronavirus/
- Stats Blog. 2020. Concerns with that Stanford study of coronavirus prevalence. Statistical modelling, causal inference and social science blog. 2020. https://statmodeling.stat.columbia.edu/2020/04/19/fatal-flaws-in-stanfordstudy-of-coronavirus-prevalence/

Streeck, H., B. Schulte, B. Kuemmerer, E. Richter, T. Höller, C. Fuhrmann, E. Bartok, et al. 2020. Infection fatality rate of SARS-CoV-2 infection in a German community with a super-spreading event. *medRxiv*. https://www.ukbonn. de/C12582D3002FD21D/vwLookupDownloads/Streeck_et_al_Infection_fatality_rate_of_SARS_CoV_2_infection2. pdf/\$FILE/Streeck_et_al_Infection_fatality_rate_of_SARS_CoV_2_infection2.pdf.

Worldometers. 2020. COVID-19 Coronavirus Pandemic. https://www.worldometers.info/coronavirus/.

Appendix: Bayesian network model

 $f(TPR, FNR, \ldots, IFR) = f(TPRFNR)f(FNn_{FN}, FNR) \times$

 $f(TNRFPR)f(FP|n_{FP}, FPR)f(P|IPR, FNR, FPR) \times$

 $f(PS|n_{S}, P)f(CZ, P)f(R|C, RCC)f(IFR|F, C) f(IPR)f(Z)f(RCC)$

False Positive Rate : $FPR \sim Uniform(0, 1)$

False Negative Rate : $FNR \sim Uniform(0, 1)$

Specificity (FPR) = 1 - FPR

Sensitivity (TPR) = 1 - FNR

Testing number of false positives : $FP \sim Binomial(n_{FP}, FPR)$

Number of FP tests : n_{FP}

Testing number of false negatives : $FN \sim Binomial(n_{FN}, FNR)$

Number of FN tests : n_{FN}

Infection prevalence rate : $IPR \sim Uniform(0, 1)$

Positive test result rate : P = IPR(1 - FNR) + (1 - IPR)FPR

Number of survey tests : n_s

Survey number of positive tests : $PS \sim Binomial(n_S, P)$

Community population size : $Z \sim Uniform(1, 1E10)$

Number of reported Covid19 cases in the community : RCC

Community number of infections : $C \sim max(RCC, Binomial(Z, IPR))$

Ratio of infected cases to reported cases : $R = \frac{C}{RCC}$

Fatalities : F

Infection Fatality Rate : IFR = F/C

Virtual evidence for England and Wales: *Fatalities* : $F_{obs} \sim Triangular(5000, 10000, 30000)$ Virtual evidence for Spain: *Fatalities* : $F_{obs} \sim Triangular(6000, 12000, 35000)$ Virtual evidence for Santa Clara, USA study: $PS_{obs} \sim Uniform(1,50)$ Virtual evidence for Chelsea, USA study: $PS_{obs} \sim Uniform(1,64)$