Points arising from 1st COVID-19 group meeting

*Sanity checks*

There are a set of things one could do to validate Karl’s framework. I work up from those that are most simple to most complex.

1. Sensitivity to priors: One would explore different settings of the priors to see how stable the inferences from the model are to adjustments of the priors, either means or variances. My understanding is that this approach moves into the realm of Bayesian robustness analysis.
2. Out-of-sample tests: perform more out-of-sample tests, similar to what Karl did for Italy. Although, we would need to confirm exactly what he did in the case of Italy, but essentially one would be model fitting on the early time-series from a country and testing that it can predict what follows.
3. Recoverability approaches: Bayesian generative models are particularly well set-up for testing recoverability, since, at their heart, they give a recipe for generating data. In my mind, one would sample from the priors of a generative model to seed a data generation, in which the model would be run forward to generate data sets. The data sets we would generate would be time-series, potentially for many countries.

For example, one could take the model that Karl has fit to the data, i.e. the parameter settings, and generate data sets from it. I know that for “standard” DCMs there is code to do this relatively automatically, although I am not sure where to find the code.

1. Parameter recoverability: in this approach, one would generate many data sets, fit the generating model to all of them. This would give an optimum parameter setting and credibility interval (Bayesian version of a confidence interval) for each parameter, for each synthetically generated data set. One can then see how often the (ground) truth parameter setting sits in the credibility intervals of the parameter of the generated data. If the true parameters tend not to fall in these credibility intervals, there is a problem with the model fitting, i.e. the true parameters cannot be recovered. (Bonkhoff et al (in press), see below, is a new paper of ours that uses this approach, but in a much simpler setting. Anna, the first author, may be able to join our next meeting – she is the expert with this method.)
2. Model recoverability: you can do the same basic thing, but with respect to model comparison. This approach is particularly useful for assessing whether complexity penalisations are accurate. Say you have two models (perhaps both fit to the same data set), one would sample from the priors to generate many data sets from both models. Then, you cross-fit, i.e. fit both models to \*all\* the synthetic data sets. Then, you can do model comparison for each data set (e.g. using Bayes factors or comparison of free energies), and determine which model wins for each data set. The question then is does the generating model always win? If it does not, there is a problem, and typically the problem is in the complexity penalisation.
3. One issue with these recoverability approaches is that you really want to run the fitting algorithm many times. So, if fitting is very expensive and time consuming, they become hard. So, this is something we would have to determine.
4. One could also compare what one obtains with Karl’s variational Bayes algorithm and with Monte-Carlo Markov Chain (MCMC) algorithms. Although, it will be a pretty complex MCMC algorithm, since it will need to fit time-series data. [Again, Anna is the expert with these.]

*Social isolation*

There was general agreement that Karl’s finding that social-isolation has little impact in the UK is surprising and worth investigating The following are some points on this issue.

* Is the formulation of the equation that calculates P in slide 6 going to lead to some odd outcomes?
* What is the meaningful range of the theta\_sde parameter, which Karl shows has little, if any, impact on the data in a sensitivity analysis; see slides 23 and 24. In particular, the top right panel of slide 24 suggests there are other ranges of the theta\_sde parameter in which there could be more sensitivity.
* Does sde have little effect, simply because the parameter explains the same variability as one or more other parameters?
* Note, in one sense, the Bayesian model reduction should prune parameters that are strongly correlated, since throwing one out would not change accuracy much, but would reduce complexity. So, one might think that the remaining parameters after model reduction would be more orthogonal in their influence. THIS IS SOMETHING IT MIGHT BE WORTH DISCUSSING, BECAUSE IT RELATES TO A NUMBER OF THE ISSUES WE DISCUSSED, E.G. THE CAPACITY FOR THE AT-RISK POPULATION SIZE VARIABLE TO SWEEP UP VARIABILITY THAT MAY BE EXPLAINED IN OTHER WAYS. THIS SAID, DOES THE 2ND ORDER SENSITIVITY ANALYSIS ACTUALLY REVEAL THAT THERE ARE DEPENDENCIES BETWEEN REMAINING VARIABLES?
* I have added slide 7, which more fully explores the form of the P parameter as you change theta\_sde. One point to note, is that the curve changes less and less as you increase theta\_sde, with biggest changes as theta\_sde increases from zero. This pattern of change would be consistent with the top right panel in slide 24.
* One thing to explore is different initial settings of the theta\_sde parameter, even with narrow priors to prevent it moving much from that setting during fitting. Although this may be pretty much what Karl has in slide 24.
* Karl’s argument is that the reason that social distancing has little impact in the UK is because there is less different between the number of people in homes and at work than there is in other countries. So, it would be interesting to see how different the sensitivity analysis would be for a country that does not have this property. For example, slide 19 suggests that China has quite the opposite pattern, with very many more contacts at work than the UK and less at home than the UK.
* Other issues we discussed included,
  + Whether age needs to be modelled, since the lock-down can be thought of as forcing younger people, who do not feel at risk, to socially isolate.
  + There was also discussion of whether Karl’s P equation on slide 7 makes sense with theta\_sde below one. Interestingly, if you look at slide 19, the social distancing panel, shows that there are actually quite a lot of countries where this is indeed the case, i.e. they show a convex pattern, rather than concave.
* New idea: looking more carefully at Karl’s equations, it strikes me that there could be another very important thing that Karl is not modelling. It reflects that the government’s specific social distancing policy is to ask people to stay at home. A key property of staying at home is that the people you are with does not change from day to day. These are the people that you can get infected by. In contrast, if you are at work, you will be mixing with some \*new\* people.

When you look at Karl’s slide 8, “Am I Infected?”, the probability of going from susceptible to infected is 1-(1-trn-Pinfectious)\_Rin. Critically, this probability does not change from day to day. However, surely it should change, i.e. if you have been at home with, say, three other people for 14 days and you have not yet been infected, the probability of being infected will be extremely low. This is essentially because you are with the \*same\* people you have been with for the previous 14 days. That is, if they have not infected you within 14 days, they are very unlikely to be infectious.

I think Karl needs a further parameter that quantifies the probability that you meet somebody \*new\*, because for those people, the probability of infecting you is much higher than for people who are not new, given you are currently uninfected.

An interesting idea from Su Li

Just had another thought about the social distancing formula. Another issue with the equation is that the probability of transitioning from Home to Work (which I assume includes other social activity outside home such as shopping) should be determined by clinical symptoms rather than infection status.

In other words, without enforcing a blanket social distancing rule, you will only ask for a self-certified sick leave if you have a more than moderate level of symptoms or your GP advices you to stay at home or tested positive for COVID-19. Unauthorised absence from work is often not allowed in workplace. So, even one is infected but showed no symptoms or only very mild symptom, the person is likely to either go to work or go to shops as normal.

This is a reasonable assumption for COVID-19 as many infected people have no or very mild symptoms while SARS or ebola make people get very sick very quickly, so once infected, most people won’t be able to leave their beds.

So, if the social distancing parameter is initially set to 1, the probability of people going out to work should be 1-p(clinical symptoms), i.e. only the non-symptomatic go out. Of course, a more accurate model would build symptom severity into the parameters.

*Inference of at-risk population size*

* Could force this to have a particular value, perhaps much larger (e.g. the population of London) than fitting currently finds and see what changes?

*Further issues*

* We have to be aware that we currently lack expertise in the area of epidemiology. We either need to read some relevant papers or enlist somebody with that expertise.

Bonkhoff, A. K., Hope, T., Bzdok, D., Guggisberg, A. G., Hawe, R. L., Dukelow, S. P., ... & Bowman, H. (in press at Brain). Bringing Proportional Recovery into Proportion: Bayesian Hierarchical Modelling of Post-Stroke Motor Performance. *medRxiv*, 19009159.