To:
 5.1.2e
 5.1.2e
 5.1.2e
 @rivm.nl]

 From:
 5.1.2e
 5.1.2e
 @rivm.nl]

 Sent:
 Wed 2/10/2021 3:07:29 PM
 Subject:
 Re: next generation matrices

 Received:
 Wed 2/10/2021 3:07:30 PM
 AZ Vaccine Allocation (1).docx

## Hi 5.1.2e

Here are the updated results assuming lockdown interventions for the whole period. Predictably, the code for the changing contact matrices broke, so I'm trying to fix that. I can send the results when I have them, but I don't know how long it will take.

Best,

5.1.2e

From:5.1.2eSent:5.1.2eSent:Wednesday, 10 February 2021 11:28:16To:5.1.2eSubject:RE:next generation matrices

Hi 5.1.2e The factor 8 was a rough estimate for months ago. I learned from 5.1.2e yesterday that he estimates 32% ascertainment now. So a factor 3 is the most recent guess we have. Best 5.1.2e From: 5.1.2e 5.1.2e < 5.1.2e @rivm.nl> Sent: woensdag 10 februari 2021 11:14 To: 5.1.2e 5.1.2e < 5.1.2e @rivm.nl>

Subject: Re: next generation matrices



I'm playing with my initial conditions using OSIRIS and NICE data and remember you saying that number of infections is something like 8 \* number of cases. Do you have a simple multiplier on number of cases that roughly equals the number infectious and number infected (latent) that I could use? Let me know if 5.1.2e would be better people to ask.

Thanks,

## 5.1.2e

From:5.1.2eSent:Wednesday, 10 February 2021 09:15:45To:5.1.2eSubject:RE:nextgeneration matrices

Hi 5.1.2e

Great to see these results! The results look ok. I was wondering how large the differences would be, and this is very small. Best

 5.1.2e

 From:
 5.1.2e
 5.1.2e
 @rivm.nl>

 Sent:
 dinsdag 9 februari 2021 19:58

 To:
 5.1.2e
 5.1.2e
 @rivm.nl>

 Subject:
 Re:
 next generation matrices

## Hi 5.1.2e

Thanks for the explanation of next generation matrices. Your way of thinking about it makes sense to me. I'll try to implement it in the coming days.

I managed to produce some results! I need to work on the initial conditions because they're not quite right, but I wanted to have a look at the different strategies when the model had the correct behaviour (see attached).

There was very little difference between the 3 strategies, but young to old did result in the lowest cumulative incidence. I want to try to implement a changing contact matrix because that may make the strategies differ by more (young people will have proportionally more contacts compared to elderly, which will drive transmission, resulting in a larger effect of vaccination in this group)

Let me know if you think these look ok.

Best,

5.1.2e

From:5.1.2eSent: Tuesday, 9 February 2021 08:21:28To:5.1.2eSubject: next generation matrices

## Hi 5.1.2e

Here is my way of thinking about next generation matrices.

As long as contact rates are symmetrical, which they are for covid-19 (if I contact you, you contact me), the largest eigenvalue is the reproduction number, the associated right eigenvector of the next generation matrix is proportional to the number of cases in each age group, the associated left eigenvector is proportional to the force of infection in each age group. This also holds for an "effective next generation matrix" when the proportion of susceptibles is smaller than one: the largest eigenvalue is effective reproduction number, etc.

This can be used to check whether the parameterization of the contactmatrices makes sense: if you take initial conditions that are representative of say three weeks ago, you simulate the number of cases per age group and the force of infection per age group. The distribution of observed cases per group and the observed distribution of force of infection over age should match these observations. The growth rate in number of cases should reflect the actual growth rate.

When you can show these similarities, we know that the largest eigenvalue and associated eigenvectors are properly encoded in the model, and this suffices to get the right outcomes for all kinds of perturbations such as vaccination.

Hope that this is useful for you? Some of this is published in the attached publication, just as a proof that it is true, don't feel pressured to read it. Best

5.1.2e