CONTROL:
COntact TRacing OptimaLization

Projectteam overleg
18 mei 2021

Effectiviteit & optimalisatie van bron- en contactonderzoek om de verspreiding van SARS-Cov-2 te beperken

Agenda

1. **Welkom**
2. Update / stand van zaken
3. Onderzoeksplannen
4. [redacted] Predictoren van een hoog SARS-CoV-2 transmissie risico in Amsterdam en verschillen tussen stadsdelen
5. [redacted] Modellering: hoe kan groepsimmuniteit met zo min mogelijk vaccins worden bereikt?
6. Rondvraag

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1. Welkom
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3. Onderzoeksplannen
4. 5.1.2e Predictoren van een hoog SARS-CoV-2 transmissie risico in Amsterdam en verschillen tussen stadsdelen
5. 5.1.2e Modellering: hoe kan groepsimmuniteit met zo min mogelijk vaccins worden bereikt?
6. Rondvraag

2. Stand van zaken

- Verwerkersovereenkomst / DPIA
  - Concept rondgestuurd
  - Akkoord voor Amsterdam + 1 partner

- Abstracts geaccepteerd
  - Symptoms – 5.1.2e (ECCMID + WEON)
  - Test request delay – 5.1.2e (ECCMID + WEON)
  - Determinants CoronaMelder app use – 5.1.2e (WEON)

- Publiciteit
  - Interview ZonMw
  - 5.1.2e in Webinar Vereniging voor Epidemiologie 24-03
  - SamenSlimOpen 5.1.2e (WUR)

2. Stand van zaken

- CONTROL op GGD site:
  - https://www.ggd.amsterdam.nl/beleid-onderzoek/projecten/control/
  - https://www.ggd.amsterdam.nl/beleid-onderzoek/projecten/control-privacy/

- Vervanging HPZone
  - Nieuw system – datum n.t.b.
  - Data beschikbaarheid?

2. Stand van zaken

- Stages afgerond
  - 5.1.2e Factors associated with a delay in making an appointment to get tested for SARS-CoV-2
  - 5.1.2e COVID in CONTROL door sneltesten

- Lopende stages
  - 5.1.2e Predictoren van een hoog SARS-CoV-2 transmissie risico in Amsterdam en verschillen tussen stadsdelen
  - 5.1.2e Modellering: hoe kan groepsimmuniteit met zo min mogelijk vaccins worden bereikt?
  - 5.1.2e Wat is de toegevoegde waarde van de CoronaMelder app in de bestrijding van SARS-CoV-2?
  - 5.1.2e Doorlooptijden en determinanten van 'indetermined' testuitslag

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3. Onderzoeksplannen

- (bijna) gereed voor submitten bij journal
  - Self-reported symptoms as predictors of SARS-CoV-2 infection
  - Delay between onset of symptoms and test appointment
  - Determinants of CoronaMelder app use

- Vergevorderd
  - Prediction of transmission risk for SARS-CoV-2
  - Time series analysis relation between quality of BCO and R
  - Vaccination strategies to reach herd immunity

- Voorbereiding
  - Determinants of lead times from onset symptoms until end BCO
  - Testing delay and determinants of ‘indetermined’ test results

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GGD
Amsterdam

Predictors of a high SARS-CoV-2 transmission risk and geographical variation in Amsterdam

CONTROL project

5.1.2e

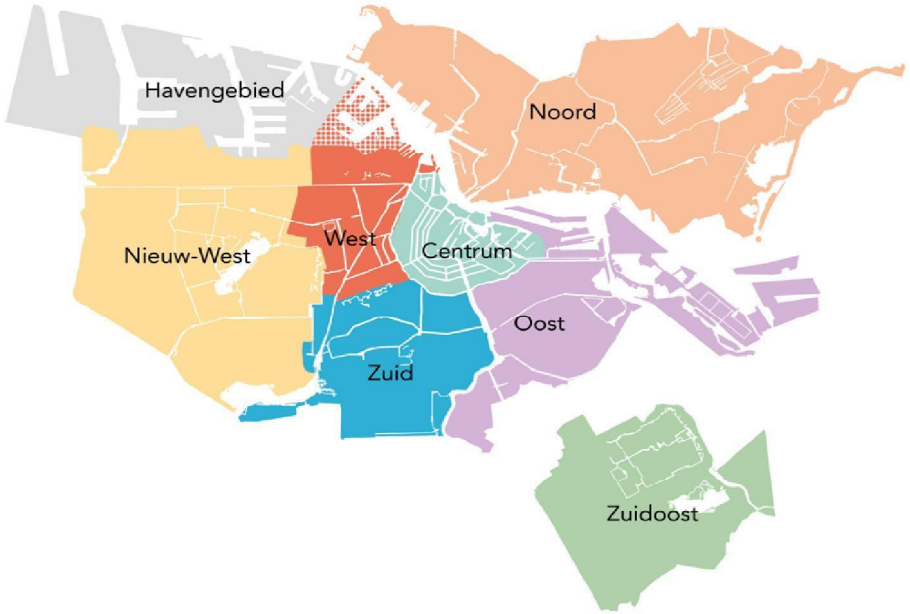
May 18th, 2021

Introduction

- Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has posed a serious threat to global public health
- Source investigation and contact tracing (SICT)
- Demand often greater than can be handled
- Prioritization currently expert-based and focuses on contact characteristics
- Interesting to gain evidence-based insights and focus on case specific factors that can predict high SARS-CoV-2 transmission risk
- Amsterdam: large city and large socio-economic variation between the city districts

Research aim

- Investigate predictors of a high SARS-CoV-2 transmission risk in Amsterdam
- Explore how these predictors differ between Amsterdam's city districts
- Contribute to optimization and effective prioritization of SICT practices



Methods (1)

Study design

- Contact Tracing Optimization (CONTROL) study
- Data collection: context of regular infectious disease control
- Occurred in 2 parts:
  - Questions when requesting SARS-CoV-2 test (telephone/ internet)
  - Telephone semi-structured interviews for confirmed cases
- CoronIT, HPZone

Methods (2)

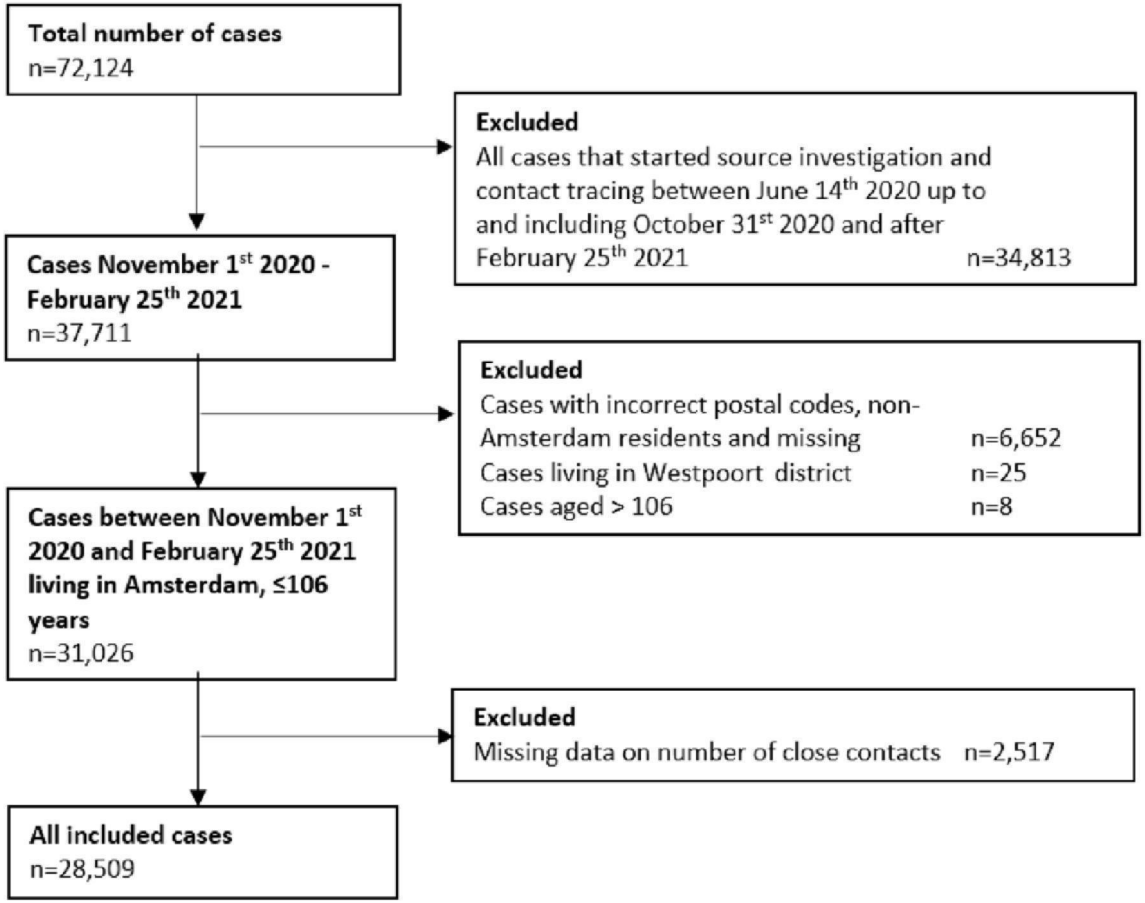
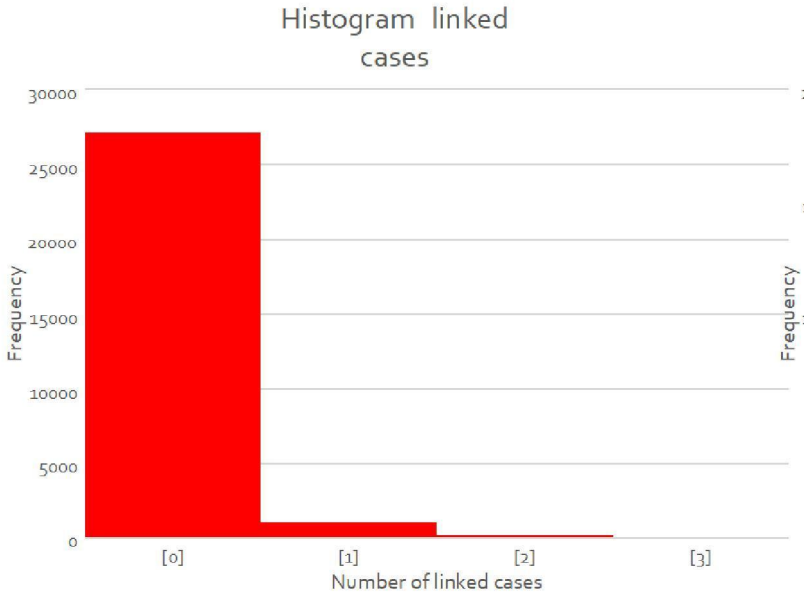
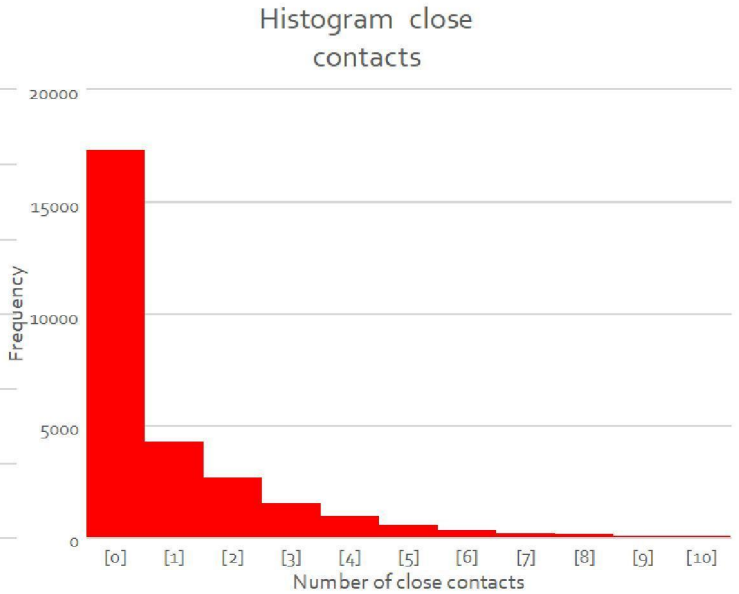


Figure 1. Flowchart of in- and exclusion criteria of the study sample

Methods (3)

- Outcome: Transmission risk
  1. Whether cases had 'linked cases' (dichotomous)
  2. Number of close contacts cases had (count, excess zero's)
- Distribution number of linked cases and close contacts





0 linked cases	≥1 linked case
n=27,157 (95.3%)	n=1,352 (4.7%)

0 close contacts	≥1 close contacts
n=17,306 (60.7%)	n=11,203 (39.3%)

Methods (3)

- Potential predictors
  - Age (≤14/ 15-24/ 25-34/ 35-44/ 45-54/ 55-64/ 65-74/ ≥75)
  - Sex (male/ female)
  - Occupation (healthcare/ education/ other high-risk/ other lower-risk sectors/ unemployed)
  - Travel history in past 14 days (yes/ no)
  - Notified by 'CoronaMelder app' (yes/no/ does not know or does not have the app)
  - Country of birth (The Netherlands/ other Western countries/ non-Western countries)
  - Time between symptom onset and start of SICT (0-3/3-7/>7 days)
  - Socioeconomic status on neighbourhood level
  - Population density on neighbourhood level
- Cases linked to city district based on postal code of current residence

Methods (5)

Statistical analysis (1)

- Two prediction models
- Stratified for city districts

- Linked cases
- Multivariable logistic regression analysis
- Stepwise backward selection (P<0.05)
- Odds ratios (OR) and their 95% confidence intervals (CI) were estimated
- Model predictive accuracy: area under the ROC curve (AUC)
  - 0.5: no discriminative power ; 1.0: perfectly discriminating model
- SPSS version 26

Methods (5)

Statistical analysis (2)

- Number of close contacts
- Zero-Inflated Negative Binomial (ZINB) regression analysis
  - Negative binomial 'count' part: non-excess zeros and non-zero values in the over-dispersed count distribution
  - Zero-inflated part: excess zero values
- Stepwise backward selection (P<0.05)
- Incidence risk ratios (IRR) and their 95% CIs were estimated
- Relative quality of the model: Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC)
  - Decrease in AIC and BIC indicated improved fit
- STATA version 15

Results (1)

Table 1. Characteristics of SARS-CoV-2 cases in Amsterdam, the Netherlands, November 1st, 2020 – February 25th, 2021.

	Total (n=28,509)
Age (in years), median [IQR]	37.0 [25.0-52.0]
Sex, Female n(%)	15,107 (53.0)
Country of birth	
The Netherlands	18,217 (69.5)
Other Western countries	1,333 (5.1)
Non-Western countries	6,673 (25.4)
Missing	*2,286*
Occupation, n(%)	
Health care	2,706 (10.0)
Education	1,600 (5.9)
Other high-risk sector	1,835 (6.8)
Other (lower-risk) sector	10,899 (40.1)
Unemployed	10,110 (37.2)
Missing	*1,359*
City district, n(%)	
Centrum	2,234 (7.8)
Nieuw-West	6,116 (21.5)
Noord	3,598 (12.6)
Oost	4,562 (16.0)
West	4,440 (15.6)
Zuid	4,166 (14.6)
Zuidoost	3,393 (11.9)

Abbreviations: *IQR* interquartile range

Results (2)

Table 2. Final multivariable prediction model for having linked SARS-CoV-2 cases in Amsterdam, the Netherlands, November 1st, 2020 – February 25th, 2021 (n=23,916).

	OR (95% CI)	*P* value
Age (in years)		
25-34		**<0.001**
0-14	0.97 (0.75-1.25)	0.810
15-24	**1.40 (1.17-1.66)**	**<0.001**
35-44	**0.79 (0.64-0.98)**	**0.028**
45-54	0.85 (0.69-1.05)	0.137
55-64	1.09 (0.88-1.35)	0.440
65-74	**1.60 (1.24-2.07)**	**<0.001**
≥75	**1.82 (1.36-2.44)**	**<0.001**
Sex		
Male	**0.88 (0.79-0.99)**	**0.039**
Country of birth		
The Netherlands		**0.001**
Other Western countries	**0.71 (0.52-0.96)**	**0.026**
Non-Western country	**0.77 (0.65-0.90)**	**0.001**
Time between symptom onset and start SICT (in days)		
0-3		**<0.001**
4-7	**0.83 (0.73-0.95)**	**0.005**
>7	**0.43 (0.32-0.58)**	**<0.001**
Population density [a] (scale 1:3500)	**1.03 (1.00-1.06)**	**0.043**
Socioeconomic status [a]	**1.15 (1.08-1.22)**	**<0.001**

AUC: 0.61 (95%CI=0.60-0.63)

Abbreviations: *OR* odds ratio; *CI* confidence interval; *SICT* source investigation and contact tracing.

[a] On neighborhood level

Results (3)

Table 3. Overall P-values of final multivariable prediction model for having linked SARS-CoV-2 cases, stratified for Amsterdam city districts, the Netherlands, November 1st, 2020 – February 25th, 2021.

	Centrum (n=1,767)	Nieuw-West (n=5,210)	Noord (n=3,111)	Oost (n=3,896)	West (n=3,593)	Zuid (n=3,461)	Zuidoost (n=2,878)
	Overall P value						
Age (in years)	**0.020**	**0.001**	0.388	**<0.001**	0.074	**0.007**	0.503
Sex	0.302	0.171	0.866	0.924	0.257	0.230	**0.033**
Country of birth	0.450	0.772	0.147	0.089	0.084	0.432	0.240
Time between symptom onset and start SICT (in days)	0.063	**0.002**	0.299	**0.037**	0.222	**0.033**	0.130
Population density [a] (scale 1:3500)	0.353	0.414	0.825	0.560	0.857	0.768	0.135
Socioeconomic status [a]	0.240	**<0.001**	0.741	0.566	0.805	0.622	0.728
AUC (95% CI)	0.65 (0.60-0.70)	0.67 (0.63-0.70)	0.59 (0.55-0.64)	0.64 (0.60-0.68)	0.61 (0.57-0.64)	0.63 (0.58-0.67)	0.63 (0.58-0.68)

Abbreviations: *CI* confidence interval; *SICT* source investigation and contact tracing; *AUC* area under the receiver operating characteristic curve [a] On neighborhood level

Statistically significant results (p<0.05) are presented in bold.

Results (4)

Table 4. Final multivariable prediction model for close contacts in Amsterdam, the Netherlands, November 1st, 2020 – February 25th, 2021 (n=15,508)*.

	IRR (95% CI)	*P* value
Age (in years)		
25-34	*Ref*	
0-14	**1.40 (1.11-1.76)**	**0.005**
15-24	1.09 (0.98-1.21)	0.104
35-44	0.95 (0.85-1.07)	0.427
45-54	**0.82 (0.72-0.93)**	**0.003**
55-64	**0.80 (0.70-0.91)**	**0.001**
65-74	**0.81 (0.68-0.97)**	**0.020**
≥75	0.88 (0.69-1.12)	0.309
Country of birth		
The Netherlands	*Ref*	
Other Western countries	**0.78 (0.66-0.91)**	**0.002**
Non-Western country	0.97 (0.86-1.09)	0.646
Occupation		
Unemployed	*Ref*	
Health care	**1.61 (1.37-1.90)**	**<0.001**
Education	**1.32 (1.11-1.56)**	**0.001**
Other high risk sector	**1.24 (1.07-1.44)**	**0.005**
Other (lower risk) sector	1.09 (0.99-1.20)	0.083
Travel history		
Yes	**1.37 (1.14-1.64)**	**0.001**
Socioeconomic status [a]	**1.06 (1.01-1.10)**	**0.014**

	AIC	BIC
Full model	44,533	44,877
Final model	44,528	44,826

Abbreviations: *IRR* incidence rate ratio; *CI* confidence interval; *SICT* source investigation and contact tracing; *Ref* Reference category. [a] On neighborhood level. *Only count part of the model is shown

Results (5)

Table 5. P-values of final multivariable prediction model for close contacts, stratified for Amsterdam city districts, the Netherlands, November 1st, 2020 – February 25th, 2021.

	Centrum (n=1,767)	Nieuw-West (n=5,210)	Noord (n=3,111)	Oost (n=3,896)	West (n=3,593)	Zuid (n=3,461)	Zuidoost (n=2,878)
	P value						
Age (in years)							
25-34	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
0-14	0.530	0.122	0.314	0.091	0.968	0.171	0.197
15-24	0.326	0.701	0.629	0.776	0.569	0.163	0.108
35-44	0.309	**0.003**	0.639	0.203	0.653	0.205	0.969
45-54	0.963	**0.007**	0.391	0.503	0.130	0.170	**0.020**
55-64	0.920	0.169	0.587	0.122	**<0.001**	**<0.001**	0.195
65-74	0.129	0.570	0.517	0.886	0.226	0.219	0.308
≥75	0.459	0.384	0.958	0.653	0.544	0.082	0.201
Country of birth							
Netherlands	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
Other Western countries	**0.015**	0.342	**0.020**	0.444	0.525	0.432	0.931
Non-Western countries	**0.002**	0.396	0.086	0.574	0.752	0.362	0.068
Occupation							
Unemployed	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
Health care	**0.003**	**<0.001**	0.204	0.741	0.074	**0.027**	**0.004**
Education	0.331	**0.008**	0.188	0.418	**0.033**	0.708	**0.006**
Other high risk sector	0.810	**<0.001**	0.665	0.835	0.348	0.070	0.470
Other (lower risk) sector	0.114	**0.010**	0.882	0.565	0.460	0.408	0.100
Recent travel Yes	0.495	0.551	0.306	0.197	0.316	**0.014**	0.880
Socioeconomic status [a]	0.750	0.248	0.112	0.094	0.846	0.665	0.195

Abbreviations: *SICT* source investigation and contact tracing; *Ref* Reference category [a] On neighborhood level

- AIC & BIC decreased for every city district

Discussion (1)

Interpretation

- Age
  - Older cases had higher odds on linked cases, but less close contacts
    - More susceptible contacts?
    - More accurate/ complete answers during SICT?
  - Younger cases had more close contacts, but lower odds on linked cases
    - School?
    - Lower contribution to SARS-CoV-2 transmission?
- Occupation and travel history
  - More close contacts
  - Not a predictor of linked cases
    - Prevention measures

Discussion (2)

Strengths

- First study to analyze case-specific predictors of SARS-CoV-2 transmission risk
- Large study sample

Limitations

- Limited number of cases with linked cases
- Number of linked cases and close contacts potentially underestimated
  - E.g. recall bias, social desirability, inaccurate execution of SICT

Conclusions

- Preliminary insights into predictors of SARS-CoV-2 transmission risk
- Informative for decision-making regarding prioritization of SICT
- Predictors of having linked cases and close contacts: age, country of birth, neighborhood SES
- Predictors of linked cases: sex, time between symptom onset and start SICT, neighborhood population density
- Predictors of close contacts: occupation, recent travel history

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4. Sophie Campman: Predictoren van een hoog SARS-CoV-2 transmissie risico in Amsterdam en verschillen tussen stadsdelen
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6. Rondvraag

VACCINATION STRATEGY TO REDUCE THE REPRODUCTION NUMBER

A SIMULATION MODEL

Project Group 18/05/2021
PRESENTED BY
5.1.2e

WHO AM I?

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*

ORIGINAL RESEARCH TOPIC

* Optimising vaccination distribution for herd immunity, based on the basic reproduction number of different age-groups.

* Main problem:
  * Determining R_0
    * Generally hard to estimate
    * Really hard to estimate due to the non-pharmaceutical measures and different variants.

* Changed approach to prevent many assumptions.

RESEARCH TOPIC

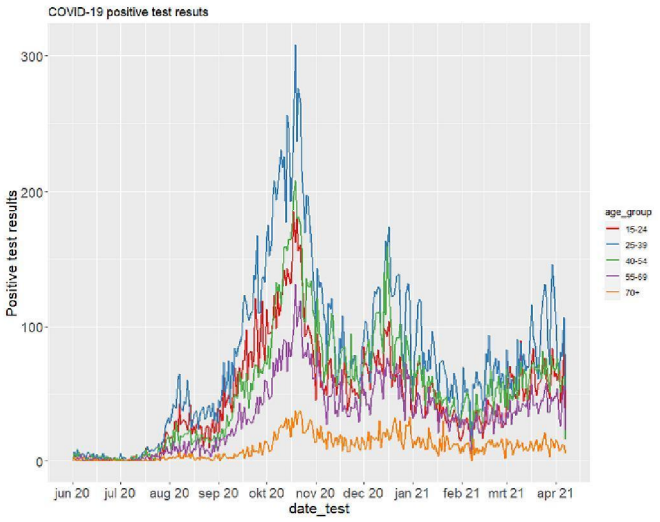
* Finding the best vaccination strategy to lower the spread of COVID-19 with the use of a simulation model.

* Research question:
  * Which age based vaccination strategy would lower the COVID-19 reproduction number most?
    * What effect does each vaccination strategy have on the reproduction number of different age-groups?
    * What are the critical vaccination levels, where the reproduction number falls below 0, per vaccination strategy?
    * Are there vaccination levels where the effect of vaccination starts to increases or decreases?
    * To what extent does the simulation perform similarly to reality since vaccination has begun?

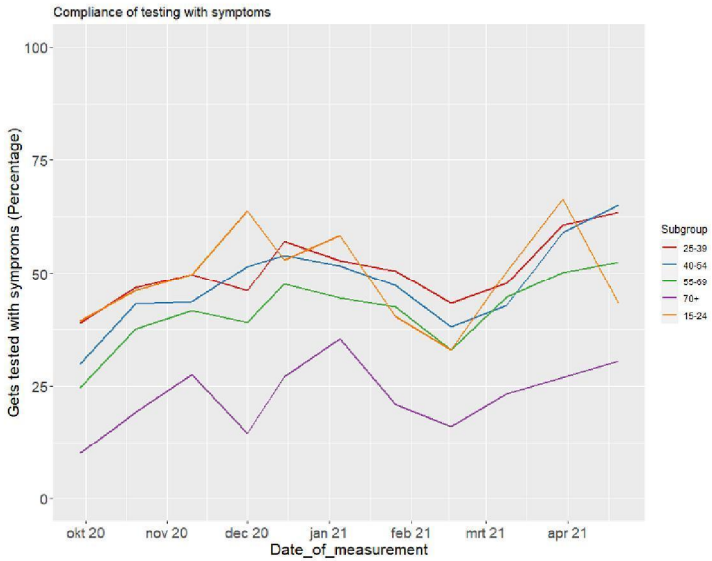
METHOD

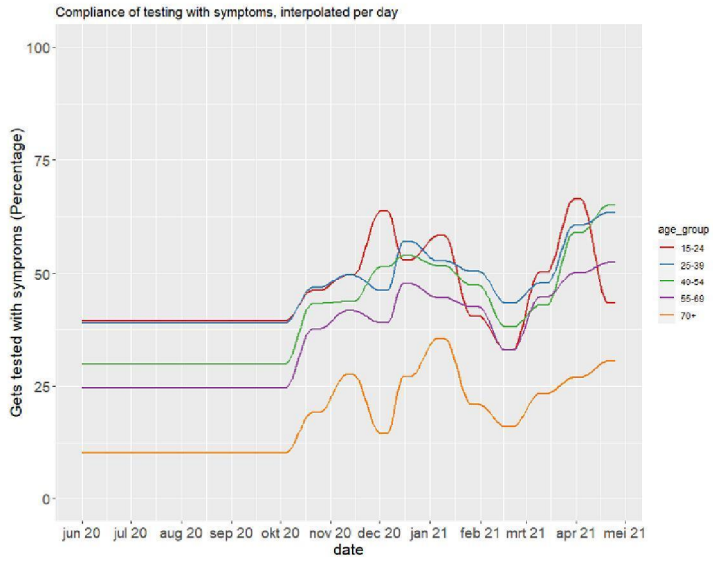
* Scale positive test results using RIVM behaviour data on compliance to get tested if they have symptoms.
  * Assumption: Same distribution of negative/positive
  * The RIVM behaviour data is interpolated to get a compliance score per day.
* Determine the R-effective per age group using the Attack Rate (AR) method.
  * Takes population size into account
  * Proportional sum of R for all age-groups equals R for all.
* Simulations *(work in progress)*

* Data



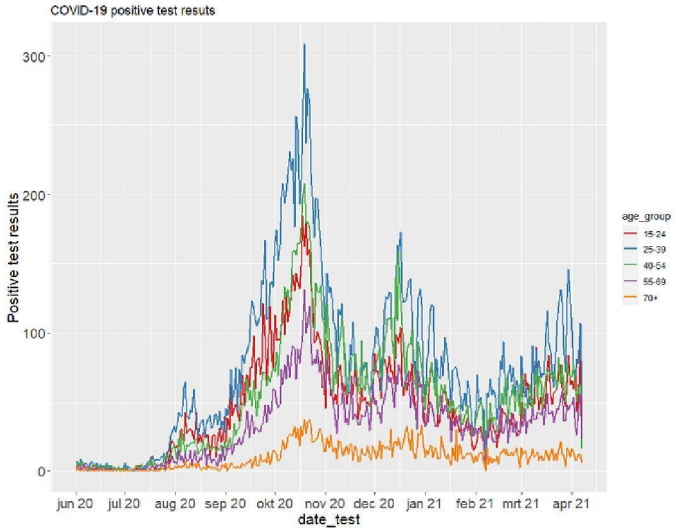
INTERPOLATE RIVM COMPLIANCE DATA



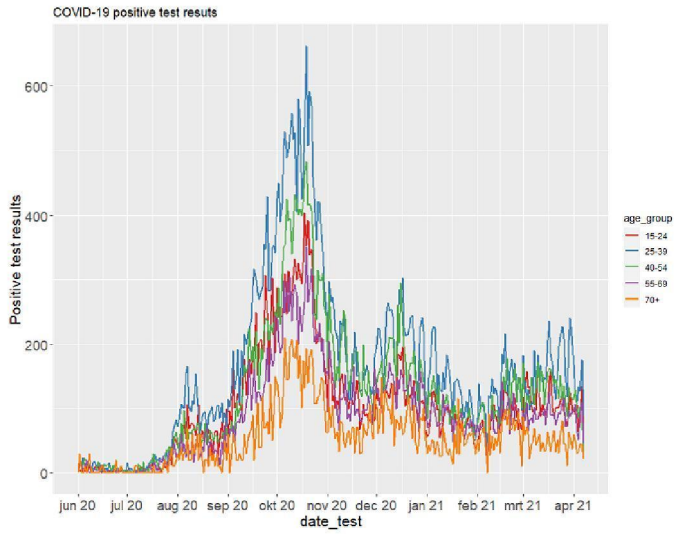


SCALING TESTING DATA

Non-Scaled Data

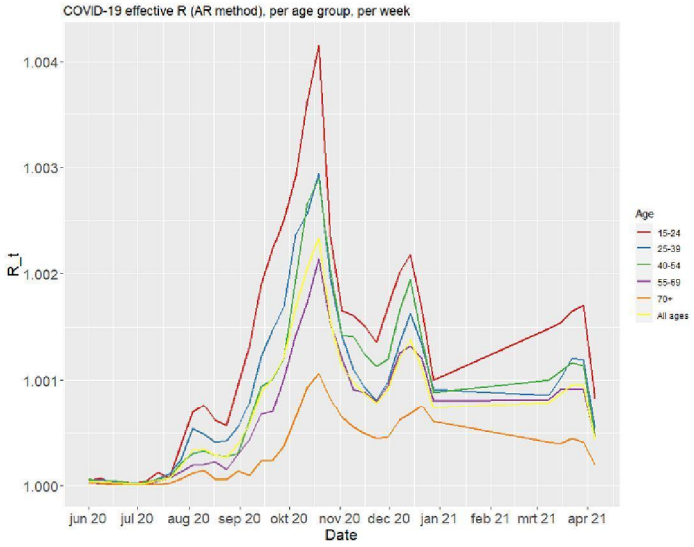


Scaled Data

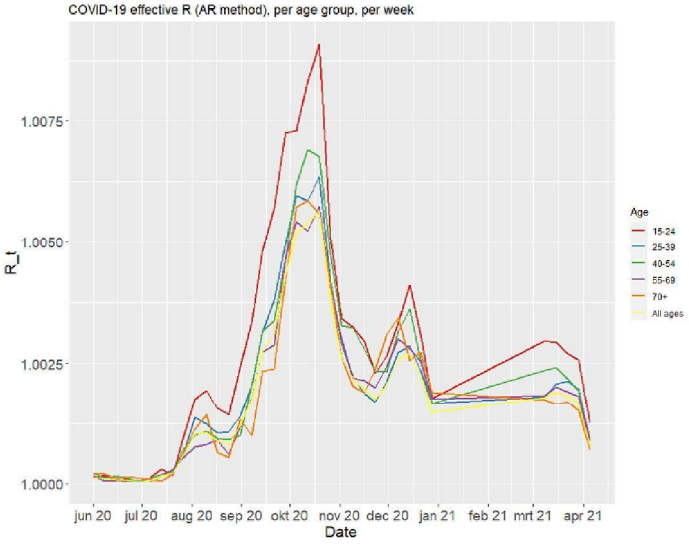


EFFECTIVE REPRODUCTION NUMBERS

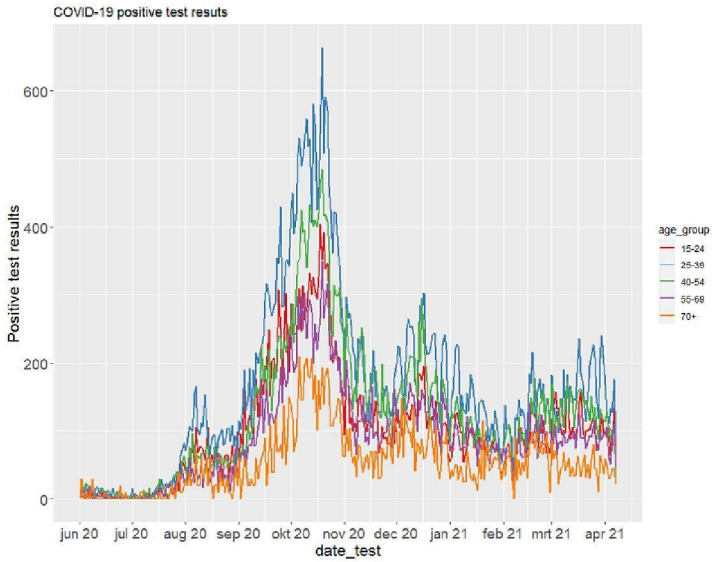
Non-Scaled data

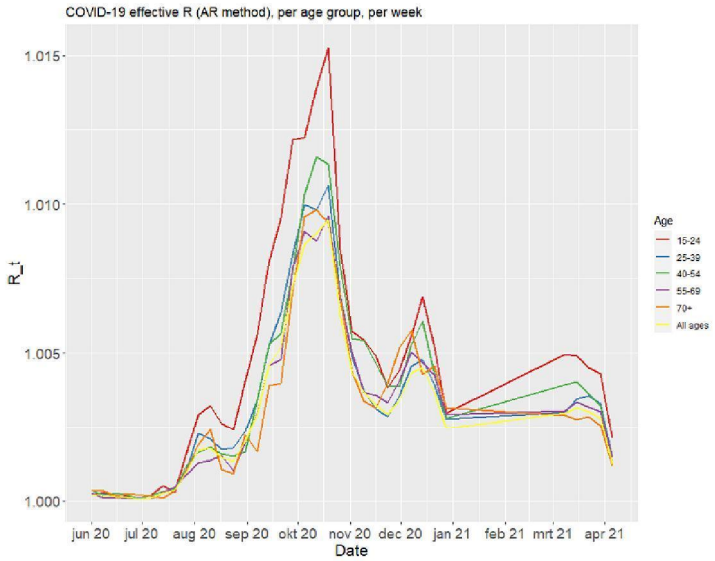


Scaled data



TAKING ASYMPTOMATIC CASES INTO ACCOUNT





SIMULATION *(WORK IN PROGRESS)*

* Initial reproduction number per age-group determined from test data.
* Determine new effective reproduction number, per age-group, per week.
* Implement contact matrices[1], available for “all locations”, “home”, “school”, ”work”, and “other”.
* Implement availability of the different vaccinations.
* Implement capacity to vaccinate.
* Scale down the amount of infected using the RIVM behaviour data on compliance to get tested, for an expected value of positive test results.

[1] https://journals.plos.org/ploscompbiol/article?rev=2&id=10.1371/journal.pcbi.1005697

QUESTIONS?

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