



Real-time monitoring of prevalence of SARS-CoV-2 antibodies in residual 27<sup>th</sup> week samples from pregnant women



## Background

- COVID-19 pandemic has major impact on health facilities and economies
- Maximum disease burden: the elderly and people with underlying co-morbidity
- Netherlands adopted an *intelligent* or *targeted* lockdown strategy based on the idea of herd-immunity
- ‘Real-time’ monitoring of changes in immunity in relation to lockdown measures of highest priority

## Background

- Case fatality rate (CFR) ~ 3.4% (WHO, March 2020)
- CFR used in modeling and estimations of the impact of the pandemic (e.g. forecasting COVID-19 cases, hospital capacity needs) to guide critical healthcare decisions and political actions
- Uncertain as denominator depends on # patients tested
  - Not everyone has symptoms
  - Shortage of tests
  - Shortage of capacity for contact tracing

## Goal

- To provide (serial) seroprevalence rates of antibodies (IgG/IgM immunity) to SARS-CoV-2 in the Netherlands, and monitor its changes over time in relation to the Dutch intelligent **lockdown** and **open-up measures**, by using 27<sup>th</sup> week residual blood samples of pregnant women

We are doing already much better than other countries → 2 seroprevalence studies

**Blood  
donors**

**Pienter-  
Corona**

## Blood donors



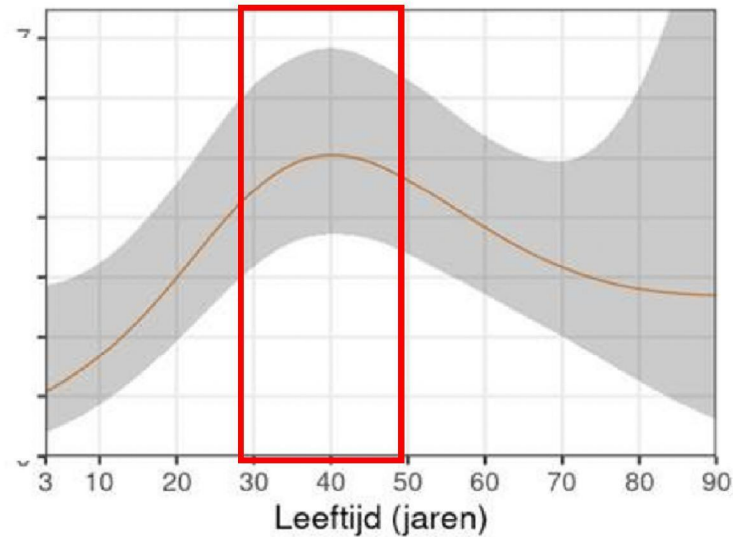
Antistoffen tegen SARS-CoV-2  
bij ~3% Nederlandse bloeddonors

|            |           |      |
|------------|-----------|------|
| 18-30 jaar | 25 / 688  | 3,6% |
| 31-40 jaar | 17 / 494  | 3,4% |
| 41-50 jaar | 26 / 752  | 3,5% |
| 51-60 jaar | 38 / 1234 | 3,1% |
| 61-70 jaar | 29 / 1030 | 2,8% |
| 71-80 jaar | 0 / 10    | (0%) |



Data: 1-15 April: **3.2%**  
Source: Sanquin

## Pieter-Corona



Data: 17 April: **3.6%**  
Source: RIVM

## More insight needed

### **Blood donors**

- \* Healthy people
- \* Overrepresentation Born NL
- \* Underrepresentation women age groups with children
- \* Examples of low rates of other infections diseases

### **Pieter-Corona**

- \* Volunteers. Potential selection certain social-economic groups
  - \* Fear for COVID?
  - \* Costly implementation
  - \* Limited #measuring points

# COVID-Pregnancy-Prevalence-NL - rationale

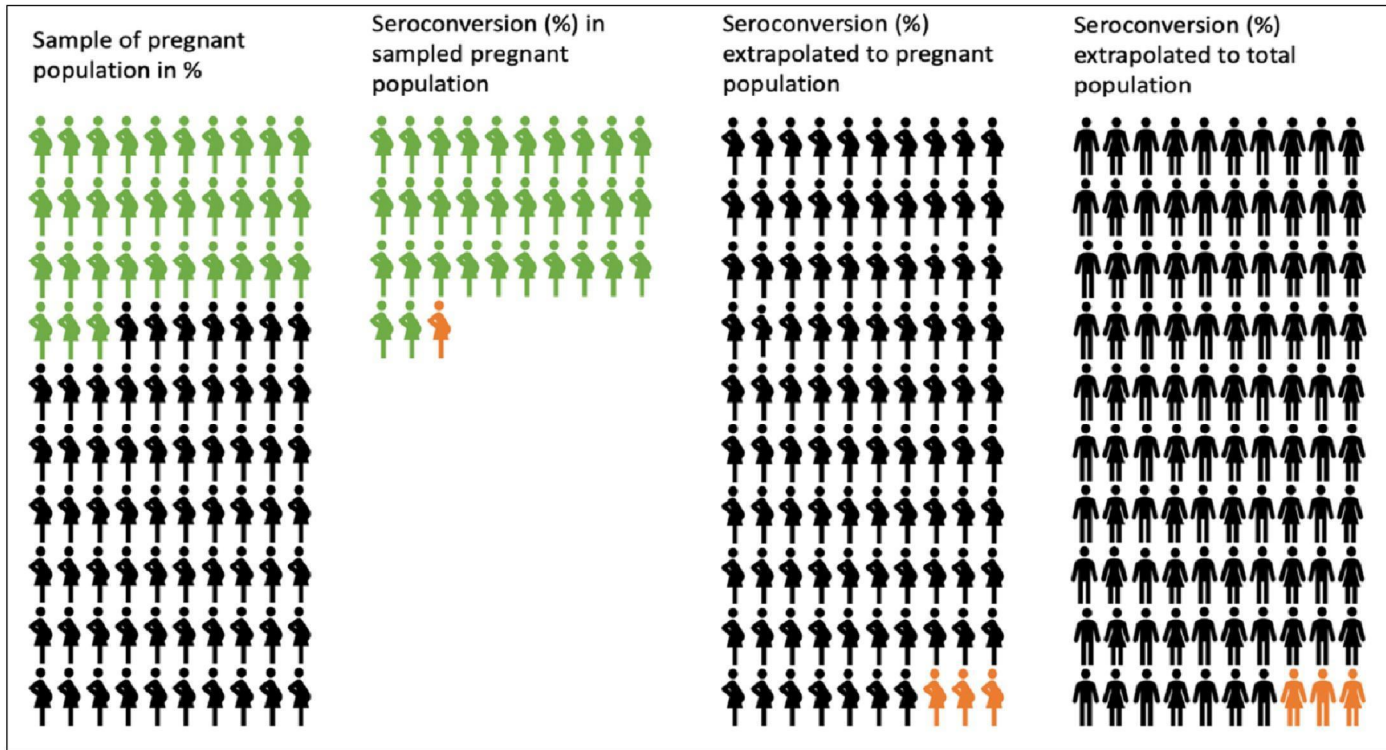
Pregnant women → indicative for general population

- National coverage & less selection on socio-economic groups
- Continuous sample flow
  - Quick insight changes immunity over time
- Quickly feasible and less costly
- Role of children
  - Distinction between women with and without children
  - Additional insight in impact of opening child care/schools
- If more countries implement this, international comparison is possible

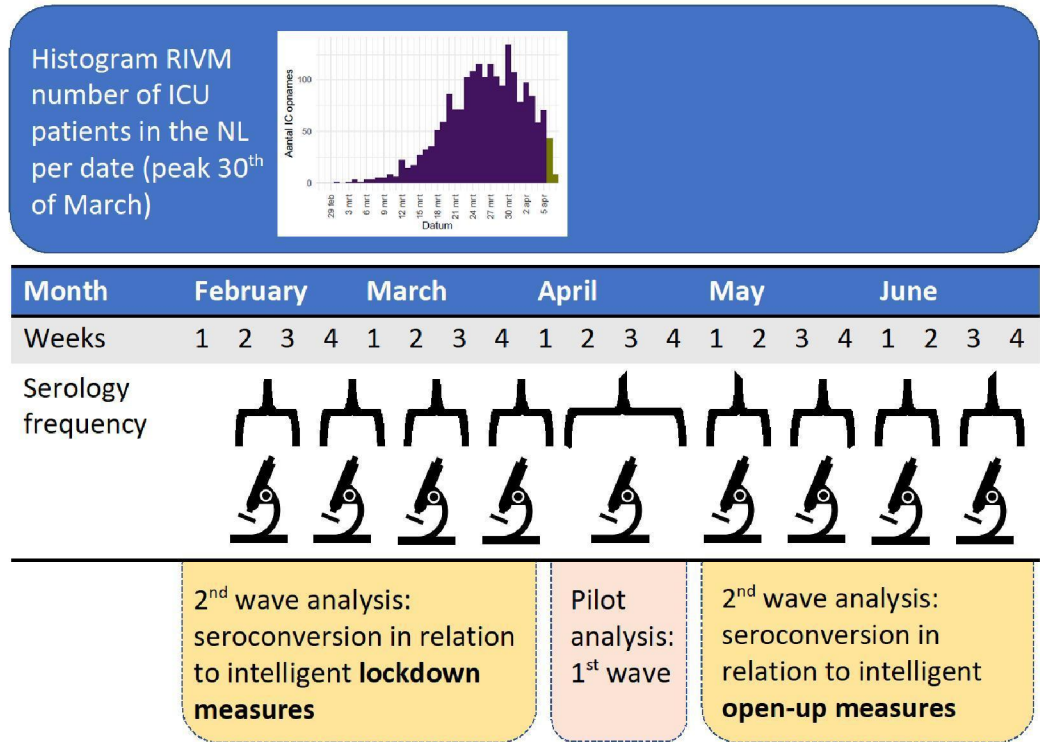
# Design

- Cross sectional study, multiple measurements
- Per year ~ 170,000 pregnant women
- 27th weeks sample: 33% of women (14% Rhesus D-negative, 19% Rhesus c-negative)
- 56,000 = 1,000/week
- Central storage at Sanquin
- Robot testing along with samples blood donors

# Design



# Timeline



## Research question pilot (1<sup>st</sup> wave)

1. Is the seroprevalence of antibodies among pregnant women different from that in other projects (blood donors, Pienter-Corona) in the same time period?
2. Do seroprevalence rates differ between women with and without children?

Research questions  
(2<sup>nd</sup> wave)

3. How does seroprevalence change in relation to the intelligent **lockdown measures** over time? (February/March)
4. How does seroprevalence change in relation to the intelligent **open-up measures** over time? (May/June)
5. How does seroprevalence change over time in women with and without children in relation to childcare/school **lockdown and open-up measures** (Feb/June)

## Sample size (weekly seroprevalence)

**Table 2.** Sample Size for Frequency in a Population

|   |      |
|---|------|
| Population size (for finite population correction factor or fpc)( <i>N</i> ): | 3500 |
| Hypothesized % frequency of outcome factor in the population ( <i>p</i> ):    | 3%±1 |
| Confidence limits as % of 100 (absolute ±%)( <i>d</i> ):                      | 1%   |
| Design effect (for cluster surveys- <i>DEFF</i> ):                            | 1    |

### Sample Size(*n*) for Various Confidence Levels

| Confidence Level(%) | Sample Size |
|---------------------|-------------|
| 95%                 | 848         |
| 80%                 | 421         |
| 90%                 | 643         |
| 97%                 | 986         |
| 99%                 | 1245        |
| 99.9%               | 1659        |
| 99.99%              | 1951        |

### Equation

Sample size  $n = [DEFF * N * p(1-p)] / [(d^2 / Z^2_{1-\alpha/2} * (N-1) + p*(1-p)]$



## Research questions (3<sup>rd</sup> wave)

6. What is the relationship between (detailed) patient characteristics and seroprevalence (age, residential area, ethnicity, SES, number of children).

7. Link with other data sources (Osiris, Perined): what are the maternal and neonatal outcomes in all COVID-19 infected pregnant women compared to non-infected pregnant women?

8. etc.

## Serology – IgG/IgM antibodies to SARS-CoV2

- Sanquin 'in house' antibody test

|                                 |     | PCR confirmed |          |          |
|---------------------------------|-----|---------------|----------|----------|
|                                 |     | pos           | neg      | total    |
| Antibody screen                 | pos | 68            | 2        | 70       |
|                                 | neg | 0             | 305      | 305      |
| total                           |     | 68            | 307      | 375      |
| sensitivity:                    |     | 1             |          |          |
| specificity:                    |     |               | 0.993485 |          |
| diagnostic accuracy:            |     |               |          | 0.994667 |
| *) one case borderline positive |     |               |          |          |

- Confirmation with CE-marked commercial test

# Challenges

- Final approval needed from CvB
- Financing available for 1<sup>st</sup> wave only
- 1<sup>st</sup> and 2<sup>nd</sup> wave: retrospective anonymous testing → non-detailed data (age range, province, nulliparity (y/n))
- Rough comparison with other data sources (Osiris, Perined) aggregated level
  
- 3<sup>rd</sup> wave: prospective data collection requires Informed Consent
- Individual linkage possible

## Time schedule

- End March Start project group. Brainstorming. Contact CvB
- April Further planning. METC 'niet-WMO plichtig'  
Financing 1<sup>st</sup> wave (pilot).
- May Analysis 1000 pilot samples. Results reported to RIVM.  
First insight added value. ZonMw proposal 2<sup>nd</sup> /3<sup>rd</sup> wave.  
Other financing? RIVM?
- May/June Sampling wave 2 (2x week)
- July Sampling wave 3

# Project working group

## Amsterdam UMC:

- [redacted] (10)(2e)
- [redacted] (10)(2e) (10)(2e) (10)(2e) (10)(2e)
- [redacted] (10)(2e)

## RIVM:

- [redacted] (10)(2e)

## Sanquin:

- [redacted] (10)(2e)
- [redacted] (10)(2e)
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# Project steering committee

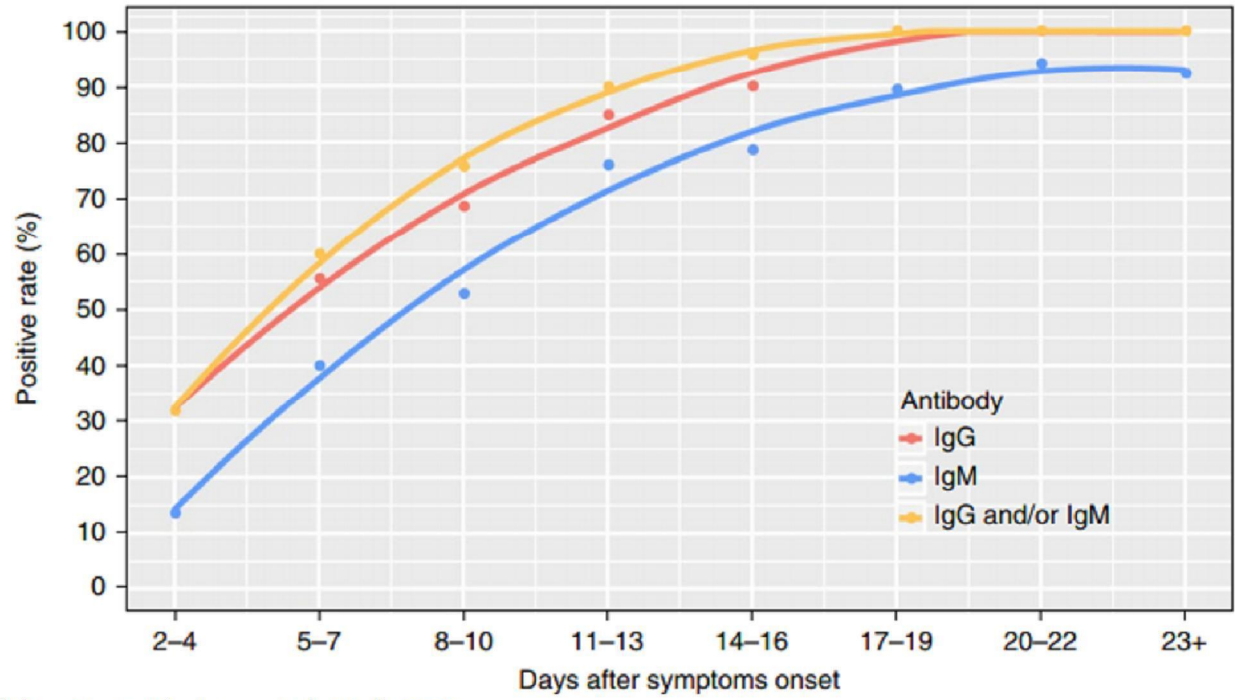
## Stanford University (USA):

-  (10)(2e)

- .....

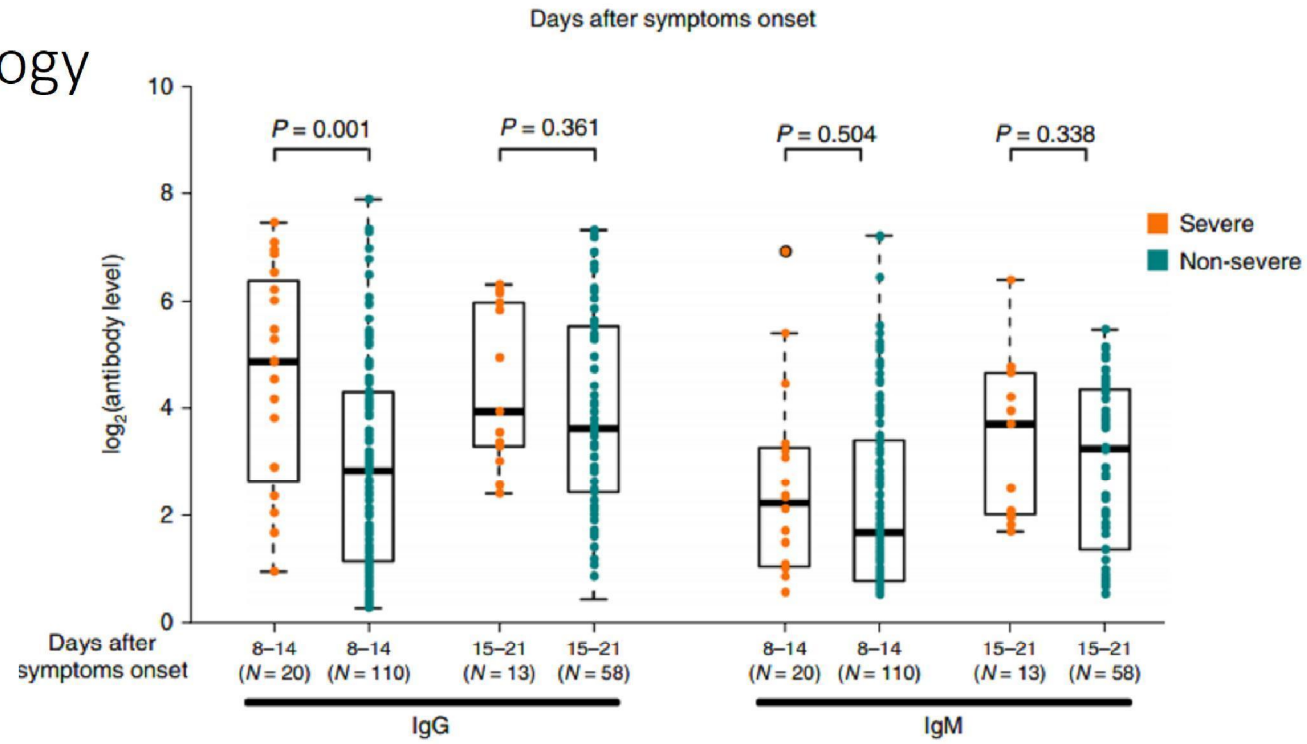
Questions & Suggestions?

# Serology

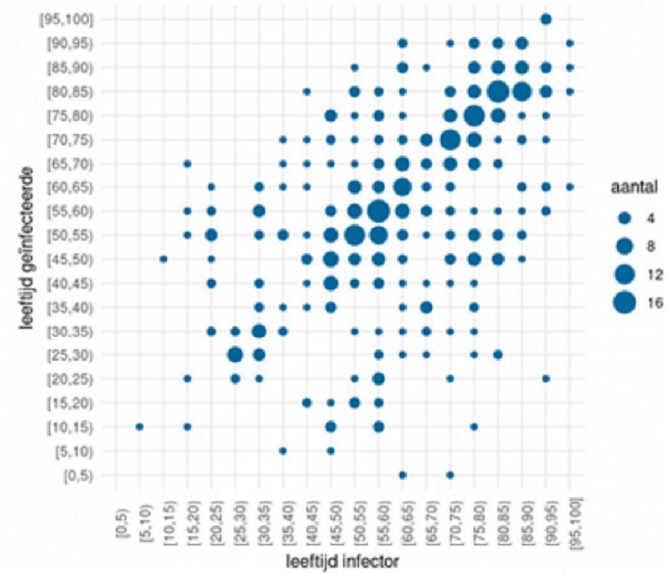


Nature Medicine: Quan-Xin Long et al. April 2020

## Serology



## Role of children in transmission



# Viral load in children

