COVID-19 Modelling:
A PHASED LIFT OF CONTROL AND OTHER EXIT STRATEGIES

Luc E. Coffeng, MD PhD
Assistant Professor
Department of Public Health
Infectious Disease Control Unit

Webinar, 2 November 2020
Isaac Newton for Mathematical Sciences
Cambridge University
COVID-19 in the Netherlands
COVID-19 in the Netherlands

Jan: Dutch Govt. and RIVM (National Institute for Public Health) feel well-prepared

2-3 Feb: 15 Dutch evacuated from Wuhan and quarantined, no other precautions
9 Feb: another 5 follow
16 Feb: numerous passengers return from a cruise in East Asia, COVID-19 confirmed aboard (none Dutch), no quarantine unless feeling ill
23-25 Feb: Carnaval (R-K tradition in southern part of country, weekend before Lent / Ash Wednesday)
27 Feb: first confirmed infection in a person returning from Lombardia, 2 other family members test positive as well; same night another case reports to ER after returning from skiing holiday in Italy; contact tracing done

1 Mar: 10 confirmed infections so far
3 Mar: first COVID-19 death (86-year old man)
7-12 Mar: outbreak in hospital in Tilburg, Brabant (Carnaval land)
9 Mar: Govt. announces no more shaking of hands, hands hygiene, distance

11 Mar: total number of confirmed infections > 500, Govt. announces “intelligent lockdown”
- Work from home
- Schools, universities, and hospitality services close (take-away still possible)
- Social distancing
- No events

16 Mar.: “stem” speech by PM, imploring people to adhere to measures; “liberal” communication strategy appealing to personal responsibility
18 Mar: cancellation of Eurovision Song Festival in Rotterdam
24 Mar: Govt. announces cancellation of high school final exams (May-June)
COVID-19 in the Netherlands

- **11 March**: Lockdown
- **11 May**: Child care and school for children with special needs reopen
- **2 June**: Schools, universities, and hospitality services reopen (schools: part-time)
- **Sep**: Number of positive cases increases by 40-60% per week
- **28 Sep**: Govt. warns for renewed lockdown
- **14 Oct**: “Semi-lockdown” Hospitality services closed, work from home, schools and universities remain open
COVID-19 modelling

Models provide a glimpse at possible outcomes
COVID-19 modelling in the Netherlands

**RIVM (National Institute of Public Health)**
Current numbers, short-term predictions, advise policy makers

**The “Slack” group / Science vs. Corona Collective (UvA)**
Multidisciplinary exploration of long-term strategies (social + exact sciences)

**Monitoring Consortium (Utrecht University + Erasmus MC and others)**
How good does monitoring need to be to keep things manageable?

**Many parallel initiatives funded by Dutch Research Council (NWO and ZonMw)**
The idea of “flattening the curve” (Feb 2020)

THE LANCET
Volume 395, Issue 10228, 21–27 March 2020, Pages 931-934

Comment

How will country-based mitigation measures influence the course of the COVID-19 epidemic?

Roy M Anderson a, hans Heesterbeek b, Don klinkenberg c, t déirdre Hollingsworth d

https://doi.org/10.1016/S0140-6736(20)30567-5
‘Ik zag de eerste resultaten, en ik dacht: holy fuck, die tijdlijn’

Er is nog geen uitweg bedacht uit deze crisis. Wetenschappers denken nu met het RIVM mee over een exitstrategie voor de pandemie. Die kan zo één tot twee jaar duren. Eén riesz, één hoest en het virus kan weer uitslaan.
EenVandaag

Op1

**Welk land heeft de beste coronastrategie? Vijf lessen over de eerste coronagolf**

Nederland gold internationaal als het land dat fantastisch was voorbereid op pandemieën. Maar toen het coronavirus aanklopte, werden we ook wéér overrompeld. Hoe hebben we, in vergelijking met de landen om ons heen, de eerste slag doorstaan? En is daar wel iets zinnigs over te zeggen? Een vergelijking in vijf lessen.

Maarten Keulemans en Serena Frijters 21 mei 2020, 16:16

Effect van de mate van contact op een tweede coronagolf

Aangegeven is de voorspelling van het aantal besmettingen bij drie scenario’s:

- **bij 30%** van het aantal contacten t.o.v. het aantal van voor de coronaperiode
- **bij 35%**
- **bij 40%**

aantal besmettingen per miljoen inwoners
Characteristics of COVID-19

• Latency: $\sim 5$ days on average (Kissler et al. 2020 Science)

• Infectiousness: $\sim 5$ days on average (Kissler et al. 2020 Science)

• Basic reproduction number $R_0$: $\sim 2.4$ (Kissler et al. 2020 Science, Ferguson et al. 2020)
  • Herd immunity when $\geq 60\%$ of population is immune ($1 - 1/R_0$)

• Doubling time at the start of the epidemic: 5-7 dagen (RIVM)

• Mortality risk about 0.5%-1.0%, strongly increasing with age and co-morbidity (RIVM)
Challenges

- Elimination not feasible as transmission can occur before/without symptoms
- Unclear whether and when a vaccine will be available
- Unknown number of infections
- Unknown how age groups mix and how this affects transmission
- What are the effects of the different components of a full lockdown policy?
- How and where does transmission take place?
  - Statement: “50% of transmission takes place within households”; N.B. this is based on traceable contacts only!!!
- Despite the above, can we think of a way out?
  - An idea: a regionally phased release of the epidemic (“a phased lift”)
Focus of our modelling

- Local, regional, and national transmission and control of infection
- Inter-individual variation in contact rate, disease history, and policy adherence
- Predicted metrics:
  - Case numbers of time (true number of infections, detected and undetected)
  - IC load
  - Herd immunity
- Keeping it simple: no explicit modelling of age or mortality

\[
\beta \frac{I}{N}
\]
Supercluster (province, administrative area)

Cluster (community, neighbourhood)

Population size
- 10000
- 1000
- 100

Exposed: 100
Infectious: 0
Recovered: 0

Assumptions:
- 90% of transmission occurs within clusters
- 5% of transmission occurs in superclusters
- 5% of transmission occurs population-wide
Individual-based SEIR model

\[
\frac{\delta S}{\delta t} = -\lambda S \\
\frac{\delta E}{\delta t} = \lambda S - \rho E \\
\frac{\delta I}{\delta t} = \rho E - \gamma I \\
\frac{\delta R}{\delta t} = \gamma I
\]

\[N = S + E + I + R\]

\[\lambda = \beta \frac{I}{N}\]

\[
\lambda_{ijk} = \varepsilon_{ik} \cdot w_{ijk} \cdot \beta \left( (1 - \theta SC - \theta) \frac{1}{N_{jk}} \sum_{p=1}^{N_{jk}} \Lambda_{pjk} + \theta SC \frac{1}{N_k} \sum_{q=1}^{N_{qk}} \sum_{p=1}^{N_{pk}} \Lambda_{pqk} + \varphi_k \theta \frac{1}{N} \sum_{r=1}^{K} \sum_{q=1}^{N_{qr}} \sum_{p=1}^{N_{qr}} \Lambda_{pqr} \right)
\]

\[
\Lambda_{ijk} = \varepsilon_{ik} w_{ijk} \cdot I(I_{ijk})
\]

\[\varepsilon_{ik}^2 \sim Beta(\mu_k \cdot \tau, [1 - \mu_k] \cdot \tau)\]
Individual-based SEIR model

\[ \lambda_{ijk} = \varepsilon_{ik} w_{ijk} \beta \left( 1 - \theta SC - \theta \right) \frac{1}{N_{jk}} \sum_{p=1}^{N_{jk}} \Lambda_{pjk} + \theta SC \frac{1}{N_k} \sum_{q=1}^{N_{jk}} \sum_{p=1}^{N_{k}} \Lambda_{pqk} + \phi_k \theta \frac{1}{N} \sum_{r=1}^{K} \phi_r \sum_{q=1}^{N_{r}} \sum_{p=1}^{N_{qr}} \Lambda_{pqr} \]

\[ \Lambda_{ijk} = \varepsilon_{ik} w_{ijk} \cdot I(I_{ijk}) \]

\[ \varepsilon_{ik}^2 \sim Beta(\mu_k \cdot \tau, [1 - \mu_k] \cdot \tau) \]

Personal intervention uptake + effect

Personal relative contact rate

Weights for geographic aspects of transmission (90-5-5)

Potential isolation of entire superclusters

Indicator function for whether someone is infectious
Data

• Hospital admission among known cases: 19% (RIVM, 4-22 April 2020)
• IC admission among hospital admissions: 22% (RIVM, 4-22 April 2020)
• Duration of IC admission: 20 days (95%-CI 1-60 days) (RIVM)
• Trend in IC admissions (NICE)
• Seroprevalence (85% sensitivity, 99% specificity)
  • Day 21 since lockdown: ~3.0% in blood donors (Sanquin)
  • Day 36 since lockdown: 3.6% in general population (PIENTER)
Model calibration

* Discrepancy possibly due to special risk profile of first cases and/or rapid increase in cases due to large scale event (e.g., carnaval).
Model calibration

190,000 cases cumulatively in NLD (1.1%)
Estimated effect

- Case detection rate:
  - ~ 1 / 200 (898 known cases up to 12 March 2020 where 191,000 predicted by model)
  - ~ 1 / 10 (4 till 22 April 2020)

- Effect of lockdown
  - Week 1: transmission reduced to 30% (i.e. the square of individual contact reductions)
  - After week 1: transmission reduced to 15%

- IC admission probability: ~ 1 / 182

- Maximum number of prevalent infectious cases that Dutch IC capacity can cope with (108 beds per 1 million population):
  - 0.6% (6,000 per 1 miljoen)
What if we...

- Implement a phased lift of control, region by region?
Assumptions:

- 2 million population in 2,000 clusters in 20 superclusters
- Introduction of infection in a few superclusters (bottom left)
- Simulate lockdown (until "Day 0") such that Dutch national trends in number of cases is reproduced until 1 May 2020
- From "Day 0" onwards: phased lift of control
- Final immunity prevalence: ~75%
  - Epidemic overshoot
- IC capacity not overburdened
- Duration of epidemic: ~2 years (with optimal timing of phased lift, like here)
Epidemic overshoot
Final immunity prevalence: ~75%
IC capacity not overburdened
Duration of epidemic: ~2 years (with optimal timing of phased lift, like in previous slide, 2.5 years with regular schedule like here)
Sensitivity analysis

Crucial:
• Number of phases
• Time interval between phases
• Policy adherence in region that have yet to lift control

No very important:
• Isolation of regions where control is lifted
• Mismatch between regional boundaries and actual geographical transmission units
• Fraction of population does not participate in lift (≤25%)
• Heterogeneity (effects can be compensated with top three factors)
Considerations for a phased lift

- Infrastructure required to move patients between hospitals throughout the country
- Sufficient policy adherence in areas that have yet to lift control
- Shield off vulnerable groups

- Price: more infections = more mortality (although far less than during an uncontrolled epidemic)
Predicting the impact of exit strategies

- Phased lift of control
- Stop all interventions
- Flattening the curve
- Lightswitch (intermittent lockdown)
- Test, trace, isolate (contact tracing)
Stop all interventions

Number of infectious cases per million

Number of cases in IC per million

Percentage recovered (%)

Time since start of strategy (days)
Flattening the curve

Transmission reduced to: 35% 55% 90%
Flattening the curve

Transmission reduced to: 30% 55% 90%

Number of infectious cases per million

Number of cases in IC per million

Percentage recovered (%)

Time since start of strategy (days)
Light switch (intermittent lockdown)
Complete lift of measures
Detection of Infectious cases within 3 days (average)
10% of exposed contacts successfully quarantined
90% reduction in individual contact rate
Test, trace, isolate

Complete lift of measures
Detection of Infectious cases within 5 days (average)
10% of exposed contacts successfully quarantined
90% reduction in individual contact rate
Test, trace, isolate

Complete lift of measures
Detection of Infectious cases within 5 days (average)
50% of exposed contacts successfully quarantined
90% reduction in individual contact rate
Concluding notes

• Practice has shown that contact tracing alone is not sufficient
• Dutch Govt. seems to respect the need for time to let effects become clear (before changing policy again)

• Open challenge: what are the effect of components of lockdown strategies?
  • People respond differently to the same policy over time

• Need for more explicit modelling of geographical aspects (COVID-19 Monitoring Consortium)
  • Mobility data from mobile phones
  • Social network data from Statistics Netherlands

• Need to incorporate population dynamics of behavior
  • Social science input needed

• Recent development: “Red Team” of independent scientists positioning themselves as an independent advisor besides (opposing) the RIVM via public media offensive
  • Call for short intense lockdown and then management through contact tracing
THANK YOU FOR YOUR ATTENTION

Blog:

Online app:
https://scienceversuscorona.shinyapps.io/covid-exit/

l.coffeng@erasmusmc.nl