The risk for a second wave - and how it depends on R_0, current immunity level and current restrictions

Tom Britton, Stockholm University

November 2020

with Frank Ball and Pieter Trapman (MedRxiv, October 9, 2020)

Continuation of Britton et al (2020), *Science*

Stockholm University

Things happen fast ...

Perhaps title should be changed to

The risk for a third wave - and how it depends on ...

Advertisement: 2 post doc positions

We will soon be advertising two post doc positions:

One in **Statistical modelling of Covid-19**: Collaboration with Norway and Finland and financed by NordForsk

One in **Stochastic and statistical modelling of infectious disease outbreaks**: Slightly more theoretical, financed by the Swedish Research Council

Both will be announced on www.math.su.se shortly (or send me an e-mail)

Deadline to apply: December 9, 2020 (for both)

Reality

Empirical evidence that Covid-19 is strongly affected by various heterogeneities

(At least) four **types** of individual heterogeneities:

– Age

– Susceptibility (risk of being infected upon exposure): biological

– Social activity (affects both risk of getting infected and infecting others): sometimes modelled using networks, households, categorizing social activity groups, ...

– Infectivity (some individuals excert more virus than others): biological

Epidemic models with heterogeneities

Compared with a more homogeneous model (having the same initial growth and R_0) a heterogeneous epidemic model results in:

– smaller fraction getting infected

– the peak of incidence is delayed

But: also affects how infected (and later immune) individuals are distributed in community, which in turn affects risk for a 2nd wave

Todays topic: What **effect of preventive measures** is required in a region having some given R_0 and current immunity level $\hat{i}$, and how is this affected when acknowledging heterogeneities

Notation:

p: relative reduction of infectious contacts – "effect of prev meas"

$\hat{i}$: community fraction immune

Homogeneous epidemic model: the first wave

Consider an SIR epidemic model in a community of **identical individuals** that **mix homogeneously**

Key parameter: $R_0 =$ average number of infectious contacts a *typical* infected individual during *early stage* of the outbreak

"Early stage": All contacts lead to infections + No prevention

Key result: A big outbreak is impossible if $R_0 < 1$

Preventive measures: Suppose *early* preventive measures reduce R_0 by factor p (no prevention: $p = 0$, all individuals completely isolated: $p = 1$, "lock-down": $p = 0.6 - 0.8$)

$$\Longrightarrow R_0^{(Prev)} = R_0(1 - p)$$

No outbreak if $R_0^{(Prev)} < 1 \iff p > p_{Min} := 1 - 1/R_0$

$p_{Min}^{(Start)} =$ minimal amount of prevention in beginning

Homogeneous epidemic model: a second wave

Suppose a suppressed or mitigated outbreak took place resulting in a fraction $\hat{i}$ becoming immune

Without prevention: $R = R_0(1 - \hat{i})$

Effective reproduction number: taking current immunity $\hat{i}$ and current preventive measures p into account :

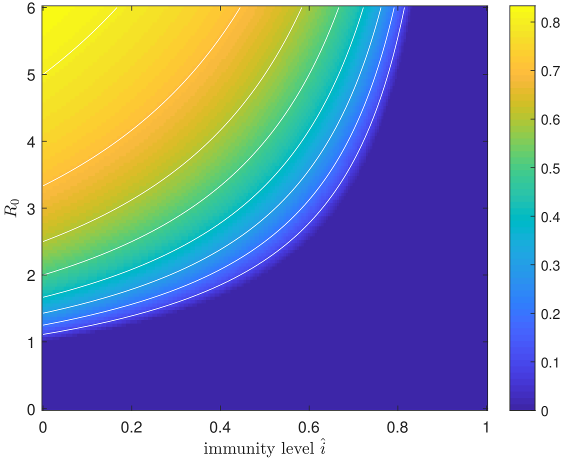
$$R_t = R_0(1 - p)(1 - \hat{i})$$

No outbreak if $R_t < 1 \iff p > p_{Min} = 1 - 1/(R_0(1 - \hat{i}))$

Same value on p_{Min} if immunity comes from vaccination, hence denoted $p_{Min}^{(Vac)}$

Stockholm University

Heatmap of $p_{Min}^{(Vac)} = 1 - 1/(R_0(1 - \hat{i}))$



An epidemic model allowing for (some) heterogeneities

SIR epidemic, but now four types of heterogeneities:

- **Age cohorts**: with mixing and community fractions taken from empirical study (Wallinga et al, 2006)
- **Variable social activity**: assumed independent of other heterogeneities
- **Variable susceptibility**: assumed independent of other heterogeneities
- **Variable infectivity**: assumed independent of other heterogeneities

Simple model for social activity, susceptibility and infectivity:

50% have medium level, 25% have low (=half this level) and 25% have high (=double) this level

Stockholm University

An epidemic model allowing for heterogeneities, cont'd

Model of heterogeneity quite arbitrary but conservative:

no left or right tails, and coefficient of variation $= 0.48$

Heterogeneity of infectivity has no effect (on deterministic model) $\Longrightarrow$ variable immunity left out

Multitype epidemic: $6 * 3 * 3 = 54$ types

Deterministic epidemic model: individuals are gategorized by age group, social activity class and susceptibility class (which affect risk of getting infected and infecting others)

$R_0 =$ largest eigenvalue to 54*54 next generation matrix

Final size equations exist

Stockholm University

Prevention and vaccination for Multitype epidemic

Consider preventive measures such that **all** contacts are reduced with the same factor p (restrictive assumption!)

$\Longrightarrow R^{(Prev)} = R_0(1-p) < 1 \iff p_{Min}^{(Start)} = 1 - 1/R_0$

$\Longrightarrow$ same $p_{Min}^{(Start)}$ as in homogeneous case

Suppose a fraction $\hat{i}$ are immunized from (uniform) vaccination

Effective reproduction number

$$R_t^{(Vac)} = R_0(1-p)(1-\hat{i}) \quad \Longrightarrow \quad p_{Min}^{(Vac)} = 1 - 1/(R_0(1-\hat{i}))$$

$\Longrightarrow$ same $p_{Min}^{(Vac)}$ as in homogeneous case

Prevention and disease-induced immunity

Suppose instead that a fraction $\hat{i}$ are immunized from a suppressed or mitigated outbreak

Then immunity is **not** uniformly distributed: socially active and highly susceptible individuals are over-represented

$\Longrightarrow$ This immunity is more "effective"

$$\Longrightarrow R_t^{(Dis)} < R_0(1-p)(1-\hat{i}) \Longrightarrow p_{Min}^{(Dis)} < p_{Min}^{(Vac)} = 1-1/(R_0(1-\hat{i}))$$

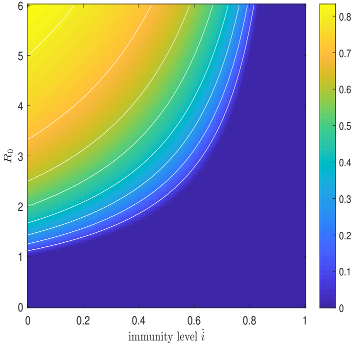
$\Longrightarrow$ The minimal amount of preventive measures is lower:

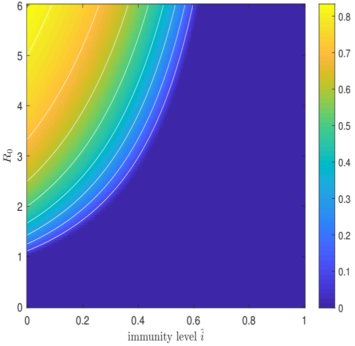
a) if immunity comes from disease spreading cf vaccination

b) if acknowledging heterogeneities cf homogeneous model

Heatmap of p_{Min}

Left: Vaccine-induced immunity and/or homogeneous model
Right: Disease-induced immunity + heterogeneous model





Example: $R_0 = 2.5$, $\hat{i} = 25\%$: $p_{Min}^{(Vac)} = 47\%$ and $p_{Min}^{(Dis)} = 29\%$

Herd immunity

Herd immunity: If $p_{Min} = 0$ (blue in heat map).

$\hat{i}_{Herd}$ quantifies the minimal herd immunity level

Illustration: Suppose $R_0 = 2.5$, then

$\hat{i}^{(Dis)}_{Herd} \approx 39\%$, whereas

$\hat{i}^{(Vac)}_{Herd} \approx 60\%$

Minimal preventive measures

Illustration: Country estimates of R_0 taken from Flaxman et al (2020) and tweeked within country from country specific analyses

Region	R_0	Deaths/100k	$\hat{i}$ (%)	$p_{Min}^{(start)}$ (%)	$p_{Min}^{(Dis)}$	$p_{Min}^{(Vac)}$
Madrid	4.7			78.7		
Cataluna	4.5			77.8		
Lombardy	3.4			70.6		
Lazio	3.4			70.6		
New York	4.9			79.6		
Wash D.C.	2.5			60.0		
Stockholm	3.9			**74.4**		
Copenhagen	3.5			**71.4**		
Oslo	3.0			**66.7**		

Illustration: Immunity estimates taken from case fatality numbers and assuming the **same** $ifr = 0.5\%$ in all regions.

Region	R_0	Deaths/100k	$\hat{i}$ (%)	$p_{Min}^{(start)}$ (%)	$p_{Min}^{(Dis)}$	$p_{Min}^{(Vac)}$
Madrid	4.7	145	29.0	78.7	58.3	70.0
Cataluna	4.5	77.4	15.5	77.8	68.9	73.7
Lombardy	3.4	168	33.6	70.6	34.7	55.7
Lazio	3.4	16.2	3.2	70.6	68.6	69.6
New York	4.9	169	33.8	79.6	54.4	69.2
Wash D.C.	2.5	89.4	17.9	60.0	40.8	51.3
Stockholm	3.9	102	20.4	**74.4**	**59.7**	67.8
Copenhagen	3.5	20.0	4.0	**71.4**	**69.0**	70.2
Oslo	3.0	11.4	2.3	**66.7**	**65.1**	65.9

Conclusions

Main conclusions

- Disease-induced immunity reduces R_t more than vaccine-induced immunity
- All regions need preventive measures (no herd immunity)
- Regions with moderat R_0 and low immunity may now require more prevention than regions with higher R_0 and some immunity

Important extensions towards realism: waning immunity, more realistic prevention (different for different groups), non-uniform vaccination, other heterogeneities