L11, COVID-19

Tom Britton

August, 2020

Preventive measures: homogeneous case – initial phase

Common way of expressing R_0 (Anderson & May, 1991):

$$R_0 = p * k * \ell$$

p is probability of transmission given a "contact" by an infective

k is the rate of "contacts" per unit of time

ℓ is average duration of infectious period

Suppose **preventive measures** (put in place very early) reduce $p * k * \ell$ by a factor c ($c(t)$ if time-varying)

$\Longrightarrow$ new *effective* reproduction number equals $R_E^{(Hom)} = (1-c)R_0$

No outbreak possible if $R_E^{(Hom)} \leq 1$ which is equivalent to $c \geq 1 - 1/R_0$

Stockholm University

Preventive measures and immunity: homogeneous case

If $R_E^{(Hom)} \geq 1$ the epidemic grows and immunity builds up: only infectious contacts with not yet infected individuals result in infection:

$R_E^{(Hom)}(t) = R_0(1-c)s(t)$, where $s(t)$ is *fraction* susceptible

If initially $R_E^{(Hom)} = R_E^{(Hom)}(0) > 1$ then $R_E^{(Hom)}(t)$ decays and for t large enough $R_E^{(Hom)}(t) < 1$ (because $s(t)$ becomes small) and then the epidemic starts declining

Currently $R_E(t) < 1$ in all (?) countries of Europe

Terminology: some use "effective reproduction number" for R_E and others for $R_E(t)$ (i.e. also including immunity). $R_E(t)$ also denoted "current" or "daily" reproduction number

Preventive measures and immunity: heterogeneous case

Let $\mathcal{I}(t)$ represent the composition of individuals that get infected around time t

The effective reproduction number at t (assuming all types of individual reduce spreading by the same fraction c) is then given by

$$R_E^{(Het)}(t) = R_0^{(\mathcal{I}(t))}(1 - c(t))s_{\mathcal{I}(t)}(t)$$

Potential: $R_0^{(\mathcal{I}(t))}$ is the average number of infectious contacts (before prevention) that individuals getting infected around t have,

Preventive measures: $c(t)$ is the cumulative reduction in disease spreading due to preventive measures (really between $\mathcal{I}(t)$ and their contacts)

Immunity: $s_{\mathcal{I}(t)}(t)$ denotes fraction still susceptible among individuals contacted by the $\mathcal{I}(t)$-individuals

Preventive measures and immunity: heterogeneous case

Crude (?) approximation: $s_{\mathcal{I}(t)}(t) \approx s(t)$ (more true with varying social activity – less with assortative mixing)

$$\Longrightarrow R_E^{(Het)}(t) \approx R_0^{(\mathcal{I}(t))}(1-c)s(t)$$

However: nearly **always** is $R_0 = R_0^{(\mathcal{I}(0))} > R_0^{(\mathcal{I}(t))}$!

Reason: Socially active individuals get infected early, later infected have fewer social contacts

$\Longrightarrow$ fewer will get infected in heterogeneous case (true also without preventive measures!)

Incidence over time: homogeneous vs heterogeneous

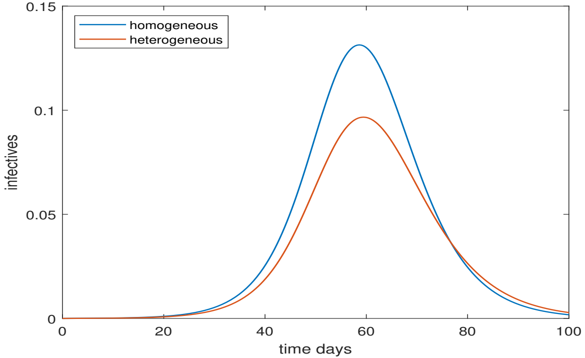

Figure: Incidence over time for a homogeneous model and heterogeneous with age and activity structure. Both have $R_0 = 2.5$ and same $g(s)$.

Also smaller final size: 72% vs 89%

Herd immunity

When $R_E(t) < 1$ the epidemic declines and dies out, so those not yet infected are (soon) protected
(for example $R_E(t) = R_E^{(Het)}(t) = R_0^{(\mathcal{I}(t))}(1-c)s_{\mathcal{I}(t)}(t)) < 1$)

$\Longrightarrow$ given effect of current preventive measures c and given epidemic up until now, there is **sufficient immunity** for epidemic to die out and hence (soon) protecting susceptibles

Herd immunity: refers to the situation without preventive measures: are we safe if we go back to "normality" by setting $c = 0$?

Related question: How much back towards normality can we go (how much can c be reduced) and still have $R_E(t) \leq 1$?

Classical Herd immunity (for vaccination)

Classical question: What fraction h needs to be immunized (by means of vaccination) beforehand, in order to avoid an outbreak without any preventive measures?

Answer when vaccinating uniformly (Anderson & May 1980's, or earlier?): No outbreak if $R_E = R_0(1-h) < 1$. Equivalent to $h \geq h_C = 1 - 1/R_0$ (true for very wide class of epidemic models)

Critical vaccination coverage: $h_C = 1 - 1/R_0$

Answer when vaccinating "optimally": fewer needs to be vaccinated (what fraction depends on model)

Illustration (Pastor-Satorras & Vespignani, 2001): For a scale free social network $h_C \approx 100\%$ when vaccinating uniformly but $h_C < 1\%$ if vaccinating optimally

Disease-induced Herd immunity

Relevant Herd immunity question for Covid-19 (first time ever!): How many must have been infected during a mitigated epidemic outbreak in order to avoid a second epidemic outbreak once all preventive measures are lifted ($c = 0$)?

Scientific scenario: Consider the Covid-19 outbreak in a country with mitigation/lockdown and gradual exit towards normality

Scientific question: When will herd immunity be reached (for no restrictions, $c = 0$) assuming R_0 is known (e.g. $R_0 = 2.5$)?

Disease-induced Herd immunity

Relevant Herd immunity question for Covid-19 (first time ever!): How many must have been infected during a mitigated epidemic outbreak in order to avoid a second epidemic outbreak once all preventive measures are lifted ($c = 0$)?

Scientific scenario: Consider the Covid-19 outbreak in a country with mitigation/lockdown and gradual exit towards normality

Scientific question: When will herd immunity be reached (for no restrictions, $c = 0$) assuming R_0 is known (e.g. $R_0 = 2.5$)?

Answer: When fraction infected equals $h_C = 1 - 1/R_0 = 60\%$?

Main result: Disease-induced herd immunity is lower!

This answer is correct if immunization is uniformly distributed in community (as in vaccination)

But this is **NOT** correct when immunity is achieved from disease spreading

Main result: Disease-induced herd immunity is lower!

This answer is correct if immunization is uniformly distributed in community (as in vaccination)

But this is **NOT** correct when immunity is achieved from disease spreading

Correct answer: Disease-induced herd immunity h_D will occur at a **substantially lower level**, perhaps around 40-45% if $R_0 = 2.5$

Gabriela Gomes et al (2020) indpendently show similar result for a different model: h_D could be as low as 10-20%

Heuristic explanation

In vaccination programs vaccinees are selected "randomly", so immunity is distributed uniformly in the community

But during a disease outbreak immunization is not distributed uniformly – highly active/social individuals are more likely to be infected

$\Longrightarrow$ Immunity is more "efficiently" distributed (still not optimal – cf "optimal vaccination policies")

Earlier knowledge: Well-known that after an outbreak immunity is more efficiently distributed (Diets & Schensle, Anderson & May, Bansal et al, Ferrari et al, ...)

But: No one seem to have realized that this is now "useful" when mitigation/suppression reduces spreading to lower levels ...

Model for illustration

Deterministic multitype model

- 6 age groups and mixing according to Wallinga et al 2006
- Individuals of each age group are divided into 3 "activity levels"
- 50% *Normal* activity, 25% have *Low* (half) activity and 25 % have *High* (double) activity
- Mimics network characterstics a bit

$R_0 =$ dominant eigenvalue of next generation matrix

Final size equations exist

Prevention

Prevention/restrictions: Suppose all mixing rates are reduced by a factor $c = 1 - \alpha$, so $R_E = \alpha R_0$

So if $\alpha < 1/R_0$ epidemic stops

Situation 1: Restrictions from start to end ($\rightarrow$ final size equations)

Our question: What is the smallest α that gives herd immunity after the outbreak is over? What is the overall disease-induced immunity level h_D for this α_*?

By this is meant: Suppose the outbreak with prevention α takes place. Then preventions are lifted. Is the population at risk for a second wave?

Herd immunity levels

Table: Disease-induced herd immunity level h_D and classical herd immunity level $h_C = 1 - 1/R_0$ for different population structures, for $R_0 = 2.0$, 2.5 and 3.0. Numbers correspond to percentages.

Population structure	$R_0 = 2.0$		$R_0 = 2.5$		$R_0 = 3.0$	
	h_D	h_C	h_D	h_C	h_D	h_C
Homogeneous	50.0	50.0	60.0	60.0	66.7	66.7
Age structure	46.0	50.0	55.8	60.0	62.5	66.7
Activity structure	37.7	50.0	46.3	60.0	52.5	66.7
Age & Activity structure	34.6	50.0	43.0	60.0	49.1	66.7

Prevention: Situation 2 – restrictions and exit during outbreak

$\Longrightarrow$ We need to model time evolution of epidemic

Model: Deterministic SEIR

- February 15: start
- March 15: Restrictions put in place (4 different α)
- June 30: All restrictions lifted

Incidence over time

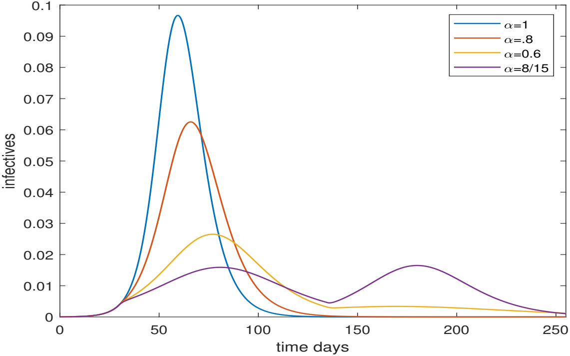

Figure: Incidence over time for the age+activity structure with $R_0 = 2.5$. Four different preventive levels inserted March 15 (day 30) and lifted June 30 (day 135). The blue, red, yellow and purple curves corresponds to no, light, moderate and severe preventive measures, respectively.

Cumulative fraction infected over time

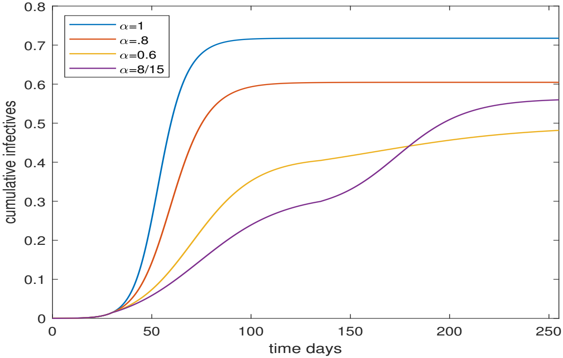

Figure: Plot of the cumulative fraction infected over time for age+activity structure and $R_0 = 2.5$. Four different preventive levels inserted March 15 and lifted June 30. The blue, red, yellow and purple curves corresponds to no, light, moderate and severe preventive measures, respectively.

Cumulative: Gradual exit during summer

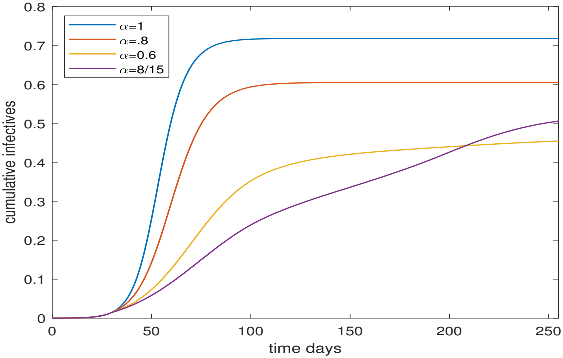

Figure: Same as above but: Preventive measures inserted March 15 and lifted gradually between June 1 and August 30. The blue, red, yellow and purple curves corresponds to no, light, moderate and severe preventive measures, respectively.

Conclusion and discussion

Main result: Disease-induced herd immunity h_D is substantially lower than classical $h_C = 1 - 1/R_0$

How much lower? Needs to be investigated (Gabriela Gomes studied a model with continuously variable susceptibility)

Additional heterogeneities: Household, schools, work places, spatial, ... Most (all?) of these will make difference bigger!

"Non-proportional" restriction/prevention: isolation of elderly, school closing, ... Some will make difference bigger, others unclear

If socially active change behavior more $\Longrightarrow$ difference becomes smaller

Important unsolved research questions for COVID-19

Recall

$$R_E(t) = R_0^{(\mathcal{I}(t))}(1 - c(t))s_{\mathcal{I}(t)}(t)$$

Potential, preventive measures and immunity

Important research questions for a particular community:

- What is the current potential $R_0^{(\mathcal{I}(t))}$?
- What is the effect of various preventive measures and how do they add up?
- What is the current immunity level (as well as susceptibility levels for those not yet infected)?