Evaluating and optimizing COVID-19 vaccination policies: a case study of Sweden

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We evaluate the efficiency of vaccination scenarios for COVID-19 by analysing a data-driven mathematical model. Healthcare demand and incidence are investigated for different scenarios of transmission and vaccination-schemes. Our results suggest that reducing the transmission rate affected by invading virus strains, seasonality and the level of prevention, is most important. Second to this is timely vaccine deliveries and expeditious vaccination management. Postponing vaccination of antibody-positive individuals reduces also the disease burden, and once risk groups have been vaccinated, it is best to continue vaccinating in a descending age order. (Joint work with Henrik Sjödin and Joacim Rocklöv, MedRxiv, https://doi.org/10.1101/2020.04.15.20066050).

Analysing the Effect of Test-and-Trace Strategy in an SIR Epidemic Model

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An important reason for modelling the spread of infectious disease lies in better understanding the effect of various preventive measures. One such preventive measure which has received a lot of attention during the ongoing Covid-19 pandemic is the so-called Test-and-Trace strategy. By this we mean that testing (of suspected cases and/or randomly chosen individuals) is increased with the hope that finding infected individuals quicker will reduce transmission. The tracing part of this strategy is that individuals who are tested positive, are quickly asked for their recent contacts, and such contacts are then localized and also tested. Those contacted who give positive test results are then contact traced and so on.

Here we consider a Markovian SIR epidemic model with the rate of infectious contacts λ and the rate γ at which infectious individuals naturally recover. To this model we add a Test-and-Trace (TT) strategy, where individuals are tested at rate δ and once tested positive (diagnosed) each of their contacts are immediately traced independently with some fixed probability p. If such a traced individual is infected, the contact tracing is iterated.

This model is analysed using large population approximations, both for the early stage of the epidemic, where it behaves like a certain branching process of the to-be-traced components, and for the main phase of the epidemic where the process of to-be-traced components converges to a deterministic process defined by a system of differential equations. Then, we use these approximations to quantify the effect of testing and of contact tracing on the effective reproduction numbers, the probability of a major outbreak and the final fraction of infected individuals. In particular, the branching process approximation is derived not for the true individuals but by treating the to-be-traced components as "macro" individuals. So, we first find the component reproduction number, namely the average number of new components generated by one component before diagnosed, and then we derive the reproduction number for individuals from this component reproduction number. The main conclusions are that the reproduction number for the to-be-traced components is *not* monotonically decreasing with the reporting fraction $\delta/(\delta+\gamma)$ and tracing probability p, however the individual reproduction number which is derived from the component reproduction number, turns out to be monotonically decreasing with the reporting fraction and tracing probability, and especially the reporting fraction appears to play a bigger role in reducing the individual reproduction number.

A discrete time filtered counting process model

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Counting process models are often used for describing longitudinal events and failure time data, typically by defining states that determine the possible transitions and their hazards. In medical applications, the events can be *diseased*, *receiving treatment*, *death due to disease* or *death due to other causes*, and *no event* (e.g. staying alive). We consider a multivariate counting process in discrete time, counting mutually exclusive discrete events, that may depend arbitrarily on the entire history of the process. A multi-state model can be imposed on it, if desired, where the current state is a function of the history of the counting process. For example, the current state can be identified with the last event occurred, possibly excluding *no event*, and else simply *alive*.

Occasionally, in particular in retrospective register based studies, some of the events may be observed or registered only at a subset of points in time, for example biomarkers that are sampled at regular intervals, or hospital visits triggered by symptomatic signs of disease progression, or because data collection on some types of events only occur during parts of the study period due to external reasons. Therefore, we allow events of non-absorbing type may be filtered, meaning that they might not be observed, at random or deterministic times, while absorbing events are only not observed due to right censoring (e.g dropout, end of study) or because of prior absorption.

We compare methods for estimating model parameters within the maximum likelihood framework, including direct maximization of the latent likelihood and Monte Carlo Expectation Maximisation. The performance of the estimators, including bias and coverage probabilities of confidence intervals, are compared in a series of simulations studies.

Bland-Altman plots for more than two observers

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In clinical agreement studies the Bland-Altman plot [1] is a common tool to visualize and assess agreement between two methods or two observers of numerical measurements, and the plot will often be reported in the resulting scientific papers.

To increase power and extern validity of studies, one would in most cases recommend carrying out agreement studies with more than two distinct observers, preferably at least 3-5. This works quite well in the mixed effects models that most often will be used to numerically analyse the study, but challenges the applicability of Bland-Altman plots for visualization; the latter is especially of concern as Bland-Altmann plots typically are quite familiar for clinicians who have to translate results of agreement studies to clinical practice. In the literature [2] a suggestion in this situation often is to report multiple pairwise Bland-Altman plots and to add lines or varying symbols to the plot, but this gets quickly unhandy.

We propose a generalization of the classical Bland-Altman plot to an arbitrary number of observers by replacing the pairwise differences in the classical plot by the observed intra-individual standard deviation, plotting the points

$$(\bar{x}_i, s_i) = \left(\frac{1}{m} \sum_{j=1}^{m} x_{ij}, \sqrt{\frac{1}{m-1} \sum_{j=1}^{m} (x_{ij} - \bar{x}_i)^2} \right).$$

based on the measurements x_{ij} of n individuals by m observers.

By distribution considerations we suggest that the 95% limit of agreement line be placed at

$$Quantile_{\chi(m-1)}(0.95) \frac{1}{\sqrt{m-1}} s$$

with $s = n^{-1} \sum_i^n s_i$. We examined by means of a simulation study that this choice is reasonable also in the finite sample case.

References

[1] J. M. Bland and D. G. Altman, Statistical methods for assessing agreement between two methods of clinical measurement, Lancet 327 (1986), no. 8476, 307–310.

[2] Carstensen, B., Comparing Clinical Measurement Methods, Wiley (2010)

Regression discontinuity and survival analysis

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In this talk I present work on the regression discontinuity design when applied to right-censored survival data. The regression discontinuity design is a design used to evaluate the effect of treatment (a 0-1 random variable) on some outcome, when the data are observational. Assignment to the treatment group is determined by the value of an observable covariate lying on either side of a fixed threshold. The idea is that the individuals whose value of this covariate is in a small interval around the threshold are alike, so that by basing inference on these individuals one is controlling for unobserved confounders.