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The role of testing and household transmission in the COVID-19 pandemic from the modellers perspective

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Роль тестування та побутових шляхів передачі у пандемії COVID-19 з точки зору моделювання

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Анотація: У цій статті ми описуємо процес моделювання захворювань за допомогою мікромоделювання та агентного моделювання на прикладі COVID-19. Крім того, ми розглядаємо роль побутової передачі захворювання. Наприкінці ми наголошуємо, чому таким важливим є відстеження контактів і як виявлення легких випадків сприяє контролю над епідемією.
Ключові слова: агентна модель, COVID¬19, мережа поширення інфекції.

Abstract: In this article we describe how to model diseases using a microsimulation agent-based model on the example of COVID-19. Moreover we give an insight on the role of household transmission. At the end we emphasize why contact tracing is so important and how the detection of mild cases contributes to the control of the epidemic.
Keywords: Agent-based model, COVID-19, infection network

Introduction. Since its first appearance in Wuhan, China, in December 2019, SARS-CoV-2 became a th, reat worldwide and imposed massive challenges to different societies. In the absence of vaccines and reliable pharmaceutical treatment, non—phar-maceutical interventions (NPIs) were established in almost every country.

Households have long been known to play an important role in disease transmission [1, 2].

Evidence of enhanced risk of infection among family members has been demonstrated for

influenza [3, 4], for pneumococcal [5] and child-related infections [1, 6]. There are many

mathematical models incorporating households, in particular for cocoon vaccinations. They assume theoretical or fit empirical distributions for household sizes. See [7-13] for examples. Household studies during the SARS-CoV-2 pandemic were conducted in various countries of the world [14-18]. Most recent published studies of household transmission of SARS-CoV-2 rely on clinical disease and/or PCR-based viral detection. Serological studies provide an alternative to understand transmission [19, 20]. The tests remain sensitive to detecting past infections beyond the time when the virus is detectable and moreover they give evidence if individuals have ever been infected. Both types of studies have each provided important insights into the transmission patterns of SARS-CoV-2. These include estimates of the household secondary attack rate [21, 22] and evidence of reduced infection rates among young children [23]. Modes on transmission based on age [24, 25, 26] and the determinants of transmission were studied [20, 27, 28, 29] in regional studies. Based on Polish data within the dark figure and the household attack rate for Poland were deduced [22]. Other studies based on testing data can be found in [30, 31]. The effect on vaccination on the household transmission can give an insight into partial immunization of households. A study for this was undertaken in [32]. Mathematical modelling was used to describe the impact of the household sizes [33]. Models based on percolation theory in graphs

were used to describe household bubbles [34, 35]. Closely related to this mathematical approach are branching processes, which were used to analyze contact tracing in the pandemic [36].

In this article we want to give an idea about modelling diseases and how households and contact tracing can be viewed from a modellers perspective.

Problems with Modelling COVID-19. Since the first papers in late 2019 and early 2020, there are more than 300.000 papers about the disease. Especially in the early case of the pandemic, new results were published on a daily basis and made state-of-the-art modelling nearly impossible.

Another major problem is the availability of reliable data. The cases reported are - of course - not the actual cases, but the confirmed cases via a test. In particular in the early phase of the pandemic, RT-PCR machines were not available in all countries on a large scale, such that the testing capacities - in absence of antigen quick tests - were reached quickly. In the early times of the epidemic in the Philippines in 2020, one could follow that the incidences grew linearly. However it shows that the testing capacities are close to the capacity limit, just capturing almost the same amount of new cases daily. The growth in numbers coincides with the enhancement of testing capacities. Also the regional spread of COVID-19 is highly dependent on the locality of the testing centers. In early 2020 there were just a few RT-PCR machines in the Philippines. Almost all cases were close to testing centers. Especially on the island of Mindanao, where the transport of specimen would need up to 8h, cases in proximity to testing centers were often confirmed earlier, while other cases were in some cases not confirmed at all.

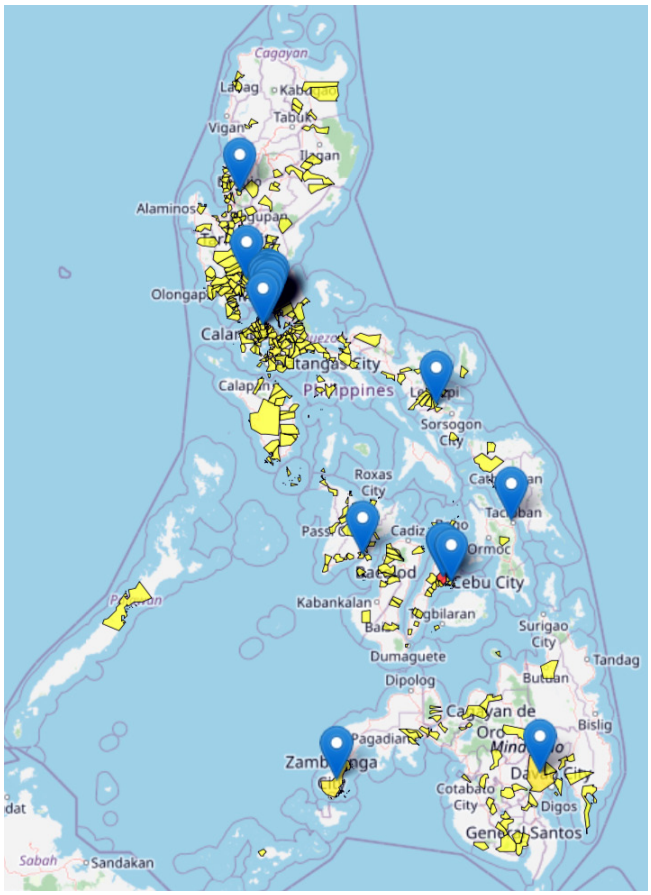

Figure 1 – Testing facilities (blue) and areas with COVID-19 cases in the Philippines early 2020

This misleading data however is used for models which provide results for decision makers. Especially in the local distribution of intensive care units, testing and vaccination centers, a wrong input can lead to a catastrophic output.

How to model diseases – Differential equations vs. Agent-based models. There are many different models for diseases and especially in the COVID-19 pandemic, all classes of models were studied. The easiest class of models are the standard differential equation compartmental models, which divide the population in different subcategories, which interact with each other. Such models go back to the classical McKendrick model from 1927. Due to the easy structure of the equations, the analysis of such dynamical systems is in many cases straight forward and long-time behaviour and critical points, as well as the basic reproduction number can be deduced directly.

The drawback of these models is, that it is indeed very hard to embrace local heterogeneous structures, such as age-dependent contacts, household structures or working networks. In the classical differential equation models, the society is averaged and subsidised under the attribute of the corresponding compartment. This leads to the fact that susceptible individuals have the same probability to be infected by a far away infected than an infected in their direct surrounding. The more different attributes, such as age specific progression and contacts, quarantine and disease status etc. one wants to include, the more compartments one needs. This makes the model more complicated and can lead to overfitting or into systems which can not cope with the accessible data. The advantage of differential equation models is that they are well scalable and very fast in simulation and implementation. Because of this they can be used easily to obtain global optimization strategies.

Another class of models, which can cope both with individual contact structure as well as a contact based non-pharmaceutical intervention strate-

gy are agent based models. In agent-based models every individual has certain attributes, which contribute to their disease progression. Moreover, again, the individuals are assigned certain states of the disease. One hence tries to reflect the infection process „as it may happen" in a computer simulation, based on a stochastic system. The infection is modelled via probabilities of an infectious contact and the transmission. The contacts are dependent on age, gender, household or workspace groups, etc., while the transmission probability is also dependent on age but also other factors such as comorbidites, natural immunities or other effects could be modelled as attributes to the individual agents. The basis of the model is hence a synthetic population which reflects the entity one wants to consider in a realistic way. During the time an individual is infected, it will progress through different stages, such as being infectious, having a severe disease progression, being hospitalised and being cured or dead. All of these progression dates and also the case that the status is reached at all are encoded in probabilities one can obtain from state-of-the-art medical data.

The drawback of agent-based models is, that they are very slow compared to differential equation models. Moreover due to the stochastic nature, not every outcome in every run is the same. One hence has to perform several parallel simulations and average these to obtain a result. This effort makes it also very costly to search of optimal strategies. One hence is more interested in more structural questions, which can than be tuned tailor-fit after the system-intrinsic mechanisms are understood better.

MOCOS-Microsimulation model. For the spread of COVID-19 we use an individual based SIR model. The infection process is modeled by a non-Markov process with infection probabilities of susceptible individuals after contact with infected individuals which are time-dependent. As described above such microsimulations can resolve the heterogeneity of epidemiologically relevant characteristics of the population better than classical differential equation models. The individual description allows a moreover a more detailed study of the effect of counter measures to the pandemic.

Population structure. The sample population is a synthetic reproduction of the considered entity. It consists of age and household composition. More detailed structures like spatial assignment, gender, profession or comorbidity relevant health status are not taken into consideration. For the simulations here we used the census data from the Philippines [37].

Disease progression within patients. The disease progression is modelled according to the present medical knowledge. The incubation time is assumed to follow a lognormal distribution with median 3.92 and variance 5.516 [38]. The time till hospitali-zation from the onset of symptoms is assumed to be Gamma distributed with median 1.67 and variance 7.424 [38]. Patients with non severe progression possibly stay at home and the time from onset of symptoms till staying at home is also assumed to be Gamma distributed with median 2.31. and variance 8.365 [38]. The maximal duration of the infectious period is assumed to be 14 days [38].

Contact Structure and Infection Transport. Within the households we assume a clique contact structure. A large fraction of secondary infections is due to household contacts [38]. The probability of a household member to become infected by an already infected household member, who is infectious within a time interval of length T, scales as 1-exp(-T/L), where L+1 is the household size [38]. Outside of the households infected individuals create on average c T secondary infections, given that all contacts of these individuals are susceptible. Here c is an intrinsic parameter. According to Adamik et al. [38], the out-reproduction number R* is defined as the expectation of c T, which is according to the parameters chosen in our model equal to 2.34c. The number of secondary infections of an individual outside the household is modeled to be Poisson distributed with mean (c T). Severe progression is more likely for older patients as will be shown also in the results that follow. The contact structure was intentionally chosen to be simple in order to have only one relevant and easily to interpreted parameter in the model.

Testing and quarantine. We included additional model features to study the effect of testing followed by household quarantine in case the testing was positive. We assume that individuals with severe symptoms will always be detected and individuals with mild symptoms will be detected with probability q within D days after onset of symptoms. A detection is followed up by quarantine of the corresponding household with the effect that all out-household contacts by members of those households are stopped. The parameter q can be interpreted as the likelihood that a person with characteristic mild symptoms will be tested for COVID-19.

Contact tracing. In our model, the tracking of contacts is described the probability of finding a second infected person from an index patient and mean time from finding a second infected person

to a positive test result. A priori, it is not clear if the probability of finding the source of an index patient is the same as the probability of finding a second infected patient. We assume the two probabilities are approximately equal, which is why we use only probability b in the simulations.

Since contact tracing always starts with a first index patient who is found by means of a general test, the effectiveness of contact tracing is closely related to the a priori probability of finding a patient with a mild course. The higher the detection rate of individuals with a mild course, the more effective the effect of contact tracing. We will explain this effect in more detail below.

The role of households. The role of households can actually be divided in two major mechanisms. First the households, since they consist of many individuals, have interlinks within each other. For example a family and friendship network can lead to a large household cluster, in which many contacts can occur. This household contact network hence is a strongly connected part of the whole interaction network. If one individual within this network is infected, this infection may spread quickly within the whole household network, due to the large number of contacts.

Secondly the sizes of households play a keyhole in the number of possible contacts within but also in between two households. While one individual has just one link to another one, a household of three has already 6 possible links to another household of three. One can assume that the disease spread within a household is, due to the high number of contacts of people living together, very quick. Hence the size of the household plays a catalytic effect in the disease spread.

In addition to these two points, households also contribute to the inter-age contacts. While in the outer-household transmission contact networks are often very age specific and only restricted to certain age groups (e.g. school contacts, workspace contacts, contacts due to hobbies), in households often more than one generation lives with each other. Hence it is likely that the disease can be transmitted from a grand child to the grand mother, while children have usually not many contacts in the age group of their grand parents apart from their family. The infected age group is then carrying the infection in their own contact network. By this effect the households are interlinks between different contact networks.

Why testing and contact tracing is important.

In the absence of vaccines and reliable pharmaceutical treatment, non--pharmaceutical interventions (NPIs) were established in almost every country and are since the objective of intensive studies [43, 44]. In Germany and many other countries, NPIs consist of lockdown measures, i.e. the reduction of contacts or the entire country or different groups and contact tracing in all of its variants. While severe lockdown measures are threatening the local economy, contact tracing has no direct implications on the economy except the individuals who are taken to quarantine. Our simulations show that effective contact tracing with testing and household quarantine can make the epidemic undercritical, hence controllable.

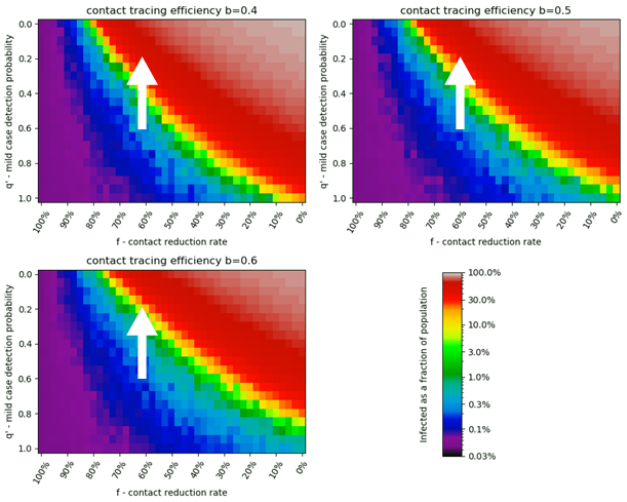

Figure 2 – Behaviour of epidemic based on the mild case detection and contact reduction for the Philippines.

This is due to the fact that not only symptomatic cases are found but also pre- and asymptomatic cases. Indeed every positive tested individual serves as a multiplier for new identified contacts. For this, after an individual is tested positive, its contacts are traced and tested also, while the positive case is set to household quarantine and hence is not anymore inside the infection network.

For any other found contact which is positive, this procedure is repeated. While the contacts

are informed and tested, they stay also in household quarantine until the test result arrives.

It is clear that not every contact is found. In many cases the contacts are traced based on the memory of the index patient and its family. Most of the sporadic contacts such as contacts in public transport or during shopping are unknown. However new technologies such as the CORONA-WarnApp, a smart phone App used in Germany for contact tracing could enhance the number of sporadic contacts found.

As it is known for COVID-19, many infections are transmitted by patients without symptoms or

mild symptoms. Contact tracing is one of the major keystones to find such mild cases. If a symptomatic case is found and all of its contacts are tested, the asymptomatic cases are found and then set to quarantine and their contacts are tested. One hence reduces the number of infectious people and makes the epidemic less critical.

How the backtracking rate b, the mild case detection probability q and the contact reduction rate f are influencing the epidemic can be seen in Figure 2. The contact reduction rate here is benchmarked to the contacts in February 2020 (0 %). A contact reduction of 100 % means that only inner household transmission takes place. The colours of the heat map indicate which part of the population will be infected after the end of the epidemic. Note that there is only a small region between less than 1 % and more than 30 % of the population being infected. The three pictures show a different contact tracing efficiency. The arrows are indicating that a change of testing strategy can make an epidemic critical. This can for example happen if due to capacity limits, just cases with severe symptoms are tested. In this case the mild case detection rate declines and as the error indicates, with the same contact reduction, the epidemic turns critical. In this setting then, one needs severe lockdown measures to gain again control over the disease, since a massive raise of incidences usually comes with an overwhelming of the contact tracing system.

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