Risk calculators during COVID-19 pandemic. Four innovative examples from Wrocław

Andrzej Jarynowski
Institute for Veterinary Epidemiology and Biostatistics
Freie Universität Berlin,
Königsweg 67, 14163 Berlin, Germany
Interdisciplinary Research Institute
Oriona 15/8, 67-200 Głogów, Poland
E-mail address: a.jarynowski@fu-berlin.de
ORCID: https://orcid.org/0000-0003-0949-6674

Alexander Semenov
Herbert Wertheim College of Engineering,
University of Florida,
1949 Stadium Rd, Gainesville, FL 32611, USA
E-mail address: asemenov@ufl.edu
ORCID: https://orcid.org/0000-0003-2691-4575

Vitaly Belik
Institute for Veterinary Epidemiology and Biostatistics,
Freie Universität Berlin,
Königsweg 67, 14163 Berlin, Germany
E-mail address: vitaly.belik@fu-berlin.de
ORCID: https://orcid.org/0000-0003-3748-0071

Abstract

Aim. The Internet and e-health solutions have become an integral part of daily life due to the pandemic. We are exploring the most impactful and positive innovations such as risk calculators or dashboards with forecasts and current situations aimed at providing information to the public.

Concept. We analysed four innovative, Wrocław-based risk calculators which allow users to better understand transmission dynamics, pathogenesis process or infection control.

Result. Practical application: We show that: 1) Polish COVID-19 symptom checker for self-diagnosis is among the leading products providing similar services around the world; 2) predicting disease course at its beginning is one of the main challenges of future medicine due to the availability of various kinds of data;

3) analysis of spatio-temporal transmission patterns based on digital surveillance for a given community can help with managing infection control locally; and 4) Sputnik V risk calculator enables patients to estimate probabilities of having given adverse events (probably the first app of this kind) following a given individual's variables (age, gender and dose).

Conclusion. There are already thousands of disseminated e-health solutions related to the coronavirus pandemic which will shape medicine for the next decade. Risk calculators can impact both individual decisions as well as community public health service.

Keywords: risk calculator, Adverse Event (AE), Machine Learning (ML), COVID-19, infection probability, risk of severe disease

Introduction

The outbreak and course of the SARS-COV-2 pandemic came as a surprise to the vast majority of countries, as they were unprepared to implement containment measures in the early stages of the epidemic (Jarynowski et al., 2020). However data analysis has been rapidly improving and, both through statistical and analytical means, there is an opportunity to produce high quality dashboards and risk calculators that could become a powerful tool to communicate epidemiological knowledge to the population. Multiple mobile apps have been pushing personalised COVID-related messages in real time and some also allow checking the health status (Tebeje & Klein, 2021). End users can check the probability of coming down with an infection, developing severe symptoms or dying due to COVID-19.

The various COVID-19 risk calculators are intended to help users understand how various conditions interact to determine outcomes: mainly risk of infection and hospitalization related thereto, and even death; they can also map out the risk of adverse events related to vaccination. The idea behind this is that the users can adjust some of the most important parameters to fit their situation. Artificial intelligence and machine learning used in medicine increase the chances of providing patients with better diagnosis as well as managing the healthcare process for instance during pandemic. Implementation of risk calculators for death, acute illness and complications due to SARS-CoV-2 infection gather main attention (as it contributes to curative medicine - treatment of the disease). Hack4Med CRACoV (2021.) medical hackathon took place in 2021 in Cracow where programmers, data scientists, user experience designers, or product managers analysed hospital patients clinical and radiological data to create a tool that would allow for the automation of COVID-19 risk prediction, which organisers referred to as a "COVID risk calculator." Important to note here is that the first and third place in the competition were taken by the teams from Wrocław. The data science revolution is also enabling the development of individual and community models that provide forecasts and risk analysis for infectious disease threats. During the pandemic it became clearer than ever before that complementary methodological approaches need to be combined to understand transmission risks in specific spaces and settings. Thus, human behaviourists have been joined by digital surveillance and machine learning experts. However, as risk calculators of infections and forecasting models are part of preventive medicine, much less resources were allocated thereto and thus there is less competition for Polish projects. A Polish team (from Białystok) found patient's genes which significantly change the prognostic probabilities of the patients (Kwaśniewski et al., 2022). Another group of researchers (form Gdańsk and Olsztyn) built a risk calculator for COVID-19 development based on initial patient signs, symptoms and clinical records, sociodemographic survey and ongoing daily physiological signals with symptomatic surveys (Czekaj et al, 2021; Romaszko-Wojtowicz et al., 2022).

Concept

The paper reviews and discusses the recent results and challenges in the area of innovations in e-health, and focuses on ongoing/finished projects from Wrocław. It assumes these four main pillars of individual risk calculator in infectious disease:

1) Internet self-diagnosis

Large numbers of patients initially turn to various web-based sources for symptoms of health concerns before seeking diagnosis, for instance by referring to Google (Kamiński et al., 2020). Depending on the level of exogenous (social environment) and endogenous (personal characteristics of the user) variables, epidemiological modelling and machine learning could be applied (Munsch et al., 2020). There are a few key factors that increase the difficulty of detecting and isolating cases (infection control in general). The first is the incubation period of the disease, which results in a window of time when patients can infect others before the first solid symptoms appear. A second factor is the high proportion of infected persons passing the disease asymptomatically and mildly symptomatically. However, due to the ease with which the disease is spread, they also become part of the infection chain (virus particles may be present in their exhaled breath) and it is therefore important to be able to classify people at high risk. Diagnostic app could speed up this process.

2) Internet app for prediction of mortality risk and severity

This is probably the biggest category due to availability of clinical (EHR), genetic, sociodemographic data as well as well-resourced fields of curative medicine. Thus, multiple AI-based coronavirus diagnostic programs have been developed. There is hope that solutions developed by software developers with healthcare background will allow a patient with COVID-19 to be quickly assigned to one of main groups: one with a mild course of the disease (no need of aggressive treatment), one with a severe course (decision of including monitoring and available pharmaceutical intervention must be taken as quickly as possible), and one with a high risk of death (monitoring, pharmaceutics with additional support). Such tools primarily aid healthcare professionals in predicting the course of the disease of an individual and most of the solutions are not intended to be used by patients.

3) Interactive dashboards to manage COVID-19 risks for a given region

The main measurable outcome of these apps are models of the influence of dependent, independent and modifiable variables on the probability of people being infected and developing severe symptoms. They may help in estimation of the time of arrivals/re-emergencies (Brockmann, 2018). Tracking with real-time digital spatial surveillance can support local authorities and health workers (Tebeje & Klein, 2021). These models provide rationales and quantitative analysis to support policy-making decisions and intervention plans (testing various scenarios). This allows for deriving new metric for transmission risks and risk contacts at the population level, taking into account small-scale transmission processes in a given POIs (point of interests such as households, schools, workplaces).

4) Predicting individual response to vaccination (effectiveness against infection and safety profile)

This is a relatively new field because it requires individual patient records, but in clinical trials, sponsors and investigators are obliged by FDA, MHRA or EMA to deliver aggregated statistics only. Even with its unique size, in March 2022 Pfizer released over 80,000 pages of vaccine "Comirnaty" documents (Public Health and Medical Professionals for Transparency, 2022); there are no (anonymous) individual patient records which would allow the creation of a personalised calculator.

There are plenty of apps available for COVID-19, but 4 (each for every main pillars of risk calculators) of them were development in Wrocław and they deserve further attention:

- web-based COVID-19 symptom checker done by Infermedica (Infermedica, 2020);
- the individual risk calculator probability of conditional death or hospitalization done by MOCOS group (Mocos, 2021)
- system allowing local authorities and citizens of Wrocław to see various forecasts of spatial distribution of infection probability by Spyrosoft (Spyrosoft, 2021);
- risk calculator for non-severe Adverse Events (AE) of Sputnik V to help people understand reactivity patterns of the vaccine, enabling patients to estimate the probabilities of having given AE by IBI (2021).

Decision making under uncertainty

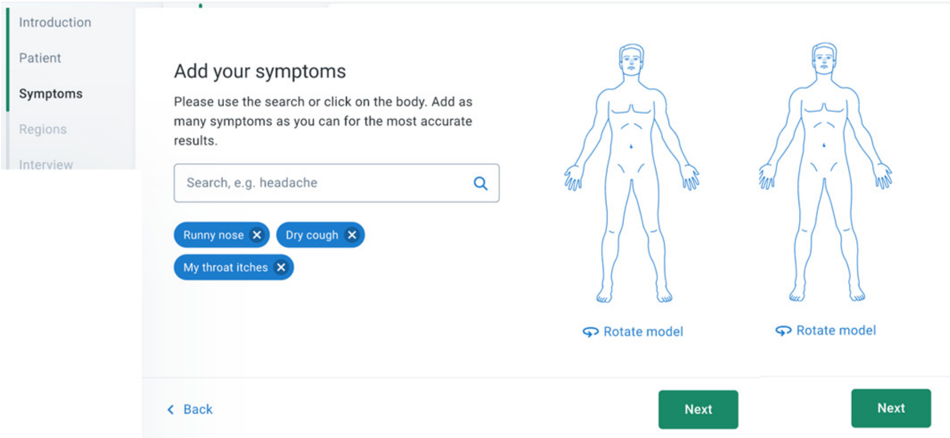
E-health has quickly become a symbol of the democratization of healthcare (when a patient is not only an object but also a subject in the medical process), as well as an opportunity to cope with the epidemic of infectious disease. Disease and adverse event surveillance and risk assessment are the basic tools for improving patient safety and empowerment. Insights to the end-users such as providing risk assessment apps is a standard functionality in business and management, but it is still not very common in evidence-based medicine (Vlassov, 2017). Risk calculators are important instruments for decision making between risk and benefits. Thus, responsive approaches to risk management are recognised in two ways: actual or perceived (Brown, 2014). These kinds of solutions could help improve risk management of individuals (who can make the decision with accurate data, not biased by media induced fear, etc.) and risk communication (by doctors - who could inform a patient with personalised content). Over the course of the pandemic, many people gained knowledge related to the transmissibility of infectious diseases, previously reserved for a small group of specialists, which can be used in multiple ways. E-health literacy (Duplaga, 2020) has increased among citizens in all age groups during the pandemic (it is still a barrier for patients lacking digital skills). These models can work only if accurate and robust epidemiological, clinical, and laboratory data are available, however quality of surveillance and epidemiological data could be questioned (Jarynowski & Belik, 2022). On the other hand, the new generation pays attention to something that has not often been taken into account before—being engaged in a process (patient centric) and aware of their overall wellbeing (Jarynowski & Belik, 2018). Currently, more and more educated people want to calculate and know the risks for their own purposes. Discrete choice experiments of the hypothetical risk of infection or risk of vaccine adverse events suggest possible causation with willingness to vaccinate (Schwarzinger et al., 2021). Thus, unknown and partially understood risks by patients could lead to behavioural changes.

Results

Result 1: web-based COVID-19 symptom checkers by Infermedica (Infermedica, 2020)

Symptom checker (Zagorecki et al., 2013) uses machine learning backed with artificial intelligence to assess symptoms, find dependencies and common patterns in data; it also becomes more effective over time (learning with or without a human teacher). Infermedica company mobilised its resources to respond to the threat of SARS-CoV-2. They set up new API endpoints dedicated solely to COVID-19 risk assessment. Their solution was incorporated into Symptomate as an independent, stand-alone AI-driven tool that provides triage (especially managing COVID-19 risk). It may direct users with initial diagnoses (with a given probability of disease or chance of developing a severe form) to self-care at home, go to a medical consultation (either in-person or via telemedicine), or seek the emergency department. According to Infermedica more than 10 million health check-ups globally have been conducted during the pandemic. In general, patients must fill surveys (dynamic set of questions) which take around 3–5 min (Figure 1).

Figure 1
Screenshot of a triage app



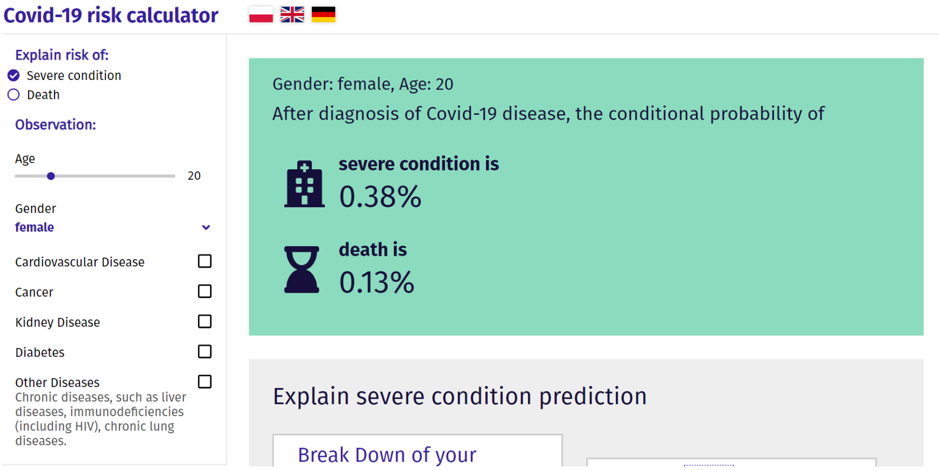
Source: Infermedica (2020).

The application allows to see the details and review the arguments for and against the diagnosis. Authors implemented CDC and WHO guidelines with information how to proceed for triage for COVID-19. According to benchmark (Munsch et al., 2022), Symptomate has the highest sensitivity and specificity among other self-diagnostic tools for provided validation sets (without taking into account the model which was partially trained on this particular dataset).

Results 2: COVID-19 Individual Risk Assessment by MOCOS (Mocos, 2021)

People may be interested in estimating the individual probability of conditional death or hospitalisation. MOCOS members have built a risk model based on the data from the first wave of epidemic in Poland and delivered it to the public (Adamik et al., 2020). The model is built on a sample of over 52 thousand cases surveyed by NIZP-PZH. For this tool, case fatality rate (CFR) and hospitalization rates were calculated according to the registered cases in the first and partially second wave of infections, which was known to have a specific geographical pattern (Jarynowski, Wójta-Kempa, & Krzowski, 2020). Out of all available features that are sociodemographic (age, gender, spatial resolution up to the voivodeship level), related to symptoms (cough, fever, lack of taste, etc.), and related to medical conditions (comorbidities), the authors selected features that have high predictive power. All modelling calculations are done in R. This tool is also able to provide visualizations to communicate key performance features, that are interesting indicators which summarise some elements of the analysis. Thanks to the visualizations, it can minimise the amount of presented text and make the web app more intuitive and more readable.

Figure 2
Screenshot of risk of severe conduction or death



Source: Mocos (2021).

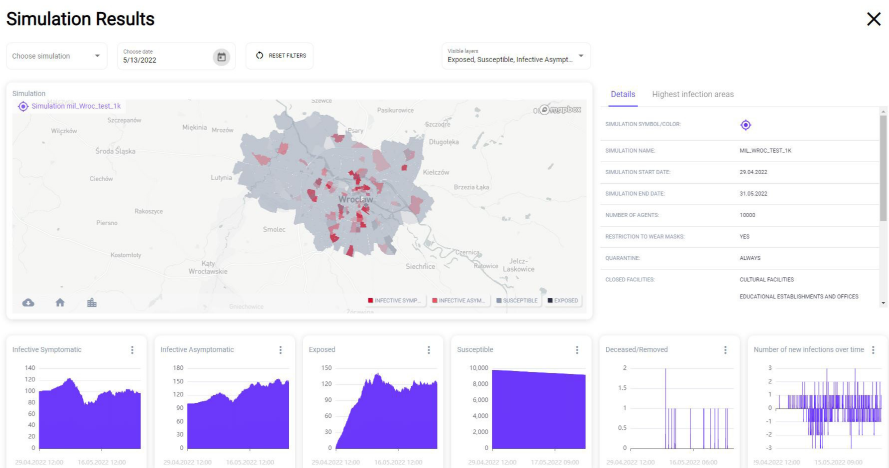
This app is not only delivering risk probabilities (Figure 2) but it is trying to answer questions such as “What influences the calculated mortality? How does mortality depend on age? What influences the hospitalization risk? How does the risk of hospitalization depend on age?”. This way the app is also educating the user. As for the interactive webpage, authors foresee to include boxplots, density functions and Kaplan-Meier curves for the more statistically prepared users.

Results 3: Mobility modelling for simulation of spatial spread of infectious diseases on example of Wrocław by Spyrosoft

With the system developed by Spyrosoft, local authorities can track how (possibly adjustable) parameters affect the risk of infection in the city (Knop et al., 2021). Users are able to simulate scenarios to assess the effectiveness of various restrictions. Authors propose an agent-based mobility model (spatial resolution ~500m, temporal resolution ~1h). They use mathematical modelling to determine mobility patterns close to reality. During the COVID-19 pandemic, aggregated mobility data based on mobile devices became freely available from technology companies (e.g., Selectivv in Poland only or Google/Apple COVID-19 Community Mobility Reports, the Facebook COVID-19 Mobility Data available globally, but also in Poland). During the synthetic trajectory generation process, these agents act as an equivalent of commuters from Wrocław. Authors integrated a mobility model with virus spread simulation, using an agent's interaction schema where pathogens can be transmitted in POIs (the points-of-interest such as schools, homes, working places, etc.). Indicating risk spaces could help in spatial infection control with different hygiene requirements such as disinfection/decontamination or separation up to isolation (Jarynowski & Skawina, 2020). Disease transmission between agents will occur with some probability depending on the duration of exposure, susceptibility of the individual, location of the interaction, and some other factors. It is worth stressing that localisation of interaction may change the probability of infection.

Figure 3

Screenshot of Spyrosoft user view



Source: own communication.

Author's main contribution to the field is the incorporation of non-home-work related activities. The dashboard (Figure 3) summarises the most important features from the developed model. The tool enables local authorities to calculate the infection risk of citizens in a given context (for instance commuting or attending gatherings) and compare it with the background risk of infection in everyday life. In addition, the tool provides information for the population mobility to manage the risk of maintaining the organizational process, and in the event of an outbreak will help in its elaboration by the epidemiological surveillance.

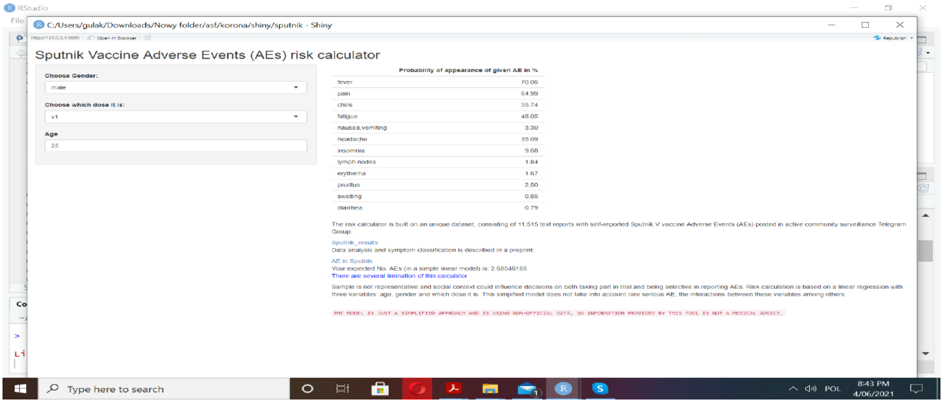
Results 4: Vaccine safety app by IBI (2021)

Efficacy in protecting from severe COVID-19 outcomes and statistics on severe adverse events (AEs) were the targeted endpoints of Sputnik V Moscow's clinical trial published in the Lancet (Logunov et. al., 2021). Thus, no serious adverse events were detected (on the same level as placebo with the incidence of 0.3%). Sputnik V researchers mentioned 7,485 common AEs but described severe and rare ones only. 12,296 patients were enrolled for all (including non-severe) adverse events. Unfortunately, for non-severe adverse events data from only 1029 of > 60 y.o. patients were included in the Lancet paper (who are expected to present less symptoms than average). The authors claimed a delay in obtaining full information, and the underlying ground truth prevalence of AEs (at least according to clinical trials) for Sputnik V was not known to the general audience. Thus, one must wait for results from ongoing clinical trials (for instance in UAE – NCT04656613) or registration process (for instance by European Medical Agency (EMA, 2021)) as well as partially from post registration passive surveillance such as the one done in Argentina (Ministerio Salud, 2021). Allegations were concerned with issues of safety of Sputnik V that were voiced not only by the Russian citizens but were also raised by multiple researchers and agencies. Thus, some activists started community-based surveillance/participatory epidemiology in social media, i.e., Telegram (Semenov et al., 2019; Statista, 2021). The considered risk calculator is built on a unique dataset, consisting of 11,515 text messages with self-reported Sputnik V vaccine AEs posted in active community surveillance Telegram Group (Telegram, 2021). An active surveillance of Sentinel-like properties was applied, so users could report cases even if no symptoms were observed, which would make them more comparable with clinical trials than typical AEs registries such as VAERS (North America) or ARR (European Union). Data analysis and symptom classification is described in the reference (Jarynowski et al., 2021). This is a huge advantage of our database which could allow us to calculate absolute probabilities and it could be compared with active surveillance systems such as "V-safe" after-vaccination health checkers in the US (Shimabukuro et al., 2021). After constructing the most relevant symptom set (fever, pain, chills, fatigue, nausea/vomiting, headache, insomnia, lymph node enlargement, erythema, pruritus, swelling, and diarrhoea), the next step was to build and train a machine learning model to classify posts into classes of symptoms. Specifically, BERT ANN architecture was used to perform the classification. Since self-reported symptoms may contain multiple adverse events, the problem was modelled as multi-label classification. To compare the performance, additional machine learning methods such as shallow ANN or simple keyword set search may be applied. There are clear co-occurrence patterns, so systemic, local and gastric symptoms usually appear together. The results showed that the AE profile of Sputnik V was comparable with other COVID-19 vaccines (more to vector than mRNA type). Moreover, by retrospective analysis, we found that females reported more AEs than males (1.2-fold, $P<.001$), there are more AEs in the first than the second dose (1.13-fold, $P<.001$) and the number of AEs decreases with age ($\beta=.05$ per year, $P<.001$) (Jarynowski et al., 2021). These dependencies (also known to exist in other COVID vaccines) can help people (with given demographics) understand which short-term possible adverse events to expect.

Through stratified data (Gender, age and dose information), by concatenating the filters of the dashboard, the user can create customised specific situations or compare scenarios across different ages or genders. Risk calculation is based on a linear regression with three variables: age, gender and vaccination shot number (Figure 4).

Figure 4

Screenshot of the Risk Calculator using Shine APP (for R language)



Source: own research based on IBI (2021).

The risk level is the estimated probability (0-100%) that an individual suffers from a given symptom. First predictive linear models were run to estimate regression coefficients for each symptom separately: fever, pain, chills, fatigue, nausea/vomiting, headache, insomnia, lymph node enlargement, erythema, pruritus, swelling, and diarrhoea. The linear regression is a mathematical model which makes it possible to describe the impact of variables to be provided by a patient (Figure 4) on the probability of appearance of AE. The regression coefficients and the parameters of the independent variables (age, dose and gender) give an individual risk estimation for each AE for the patient being examined. Thus, we used estimated coefficients such as Intercept, Age (continuous numeric variable), Gender (nominal variable with the levels "male" and "female"), and Dose (nominal variable with levels "v1" and "v2") in a function with data provided by patient to obtain probability of manifestation of a given AE. The results, i.e., probabilities for given parameters, are provided in a tabular format (Figure 4). There are some limitations. Sample (from Telegram) used to train the model is not representative and social context could influence decisions on both taking part in trial and being selective in reporting AEs. Moreover, many very important aspects of susceptibility for AE are either unknown (such as comorbidities) or estimated with large uncertainty. Frequencies of rare AEs were not included in this analysis. Reports were provided by individuals >18 y.o. only, so extrapolation to younger groups must be interpreted with extreme caution. The model only projects risk into probability domain, no sensitivity on linking function was provided, does not take into account nonlinear relations and the interactions between these variables.

Conclusions and further research

The use of technology in medicine may relate to computer-aided procedures, and e/m-health has widely been used in the pandemic. Solutions from Wrocław have been competitive with big tech and well-known research institutes. There are hundreds (or even thousands) of risk calculators of COVD-19's severity and mortality or prediction of infection dynamics in local areas (Clift et al., 2021). However, up to our knowledge, there is no other responsive risk calculator for COVID-19 vaccines' adverse events, thus the last example of Sputnik V is a unique innovation on the worldwide level. Broad COVID immunization programs induced discourse on the risks (such as discomfort of non-severe adverse events) and benefits (such as efficacy) of vaccination. Mild adverse effects became an important issue for many people as it also has an economic component due to possible sick leaves and reorganization of life among people suffering with not life-threatening, but still annoying AE. This online calculator for estimating individual chances of AEs could be used by both doctors and patients and should help in managing vaccination.

We demonstrate the value of Data Analysis to create web-based risk calculators – a new tool to facilitate the control of infectious diseases spread. Investigation of various underlying models such as regressions, Bayesian approaches, Machine Learning, etc. could be applied to risk calculators based on the available data. Moreover, visualization techniques could be verified for better presentation of results. Issues like communicating the probabilistic outcome of a calculator to a patient should be accompanied by e-health (Duplaga, 2020) and mathematical (Gigerenzer & Edwards, 2003) literacy assessment if this solution was to be used in campaigns targeting the general population.

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