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Translating Scientific Knowledge to Government Decision Makers Has Crucial Importance in the Management of the COVID-19 Pandemic

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Abstract

In times of epidemics and humanitarian crises, it is essential to translate scientific findings into digestible information for government policy makers who have a short time to make critical decisions. To predict how far and fast the disease would spread across Hungary and to support the epidemiological decision-making process, a multidisciplinary research team performed a large amount of scientific data analysis and mathematical and socioeconomic modeling of the COVID-19 epidemic in Hungary, including modeling the medical resources and capacities, the regional differences, gross domestic product loss, the impact of closing and reopening elementary schools, and the optimal nationwide screening strategy for various virus-spreading scenarios and R metrics. KETLAK prepared 2 extensive reports on the problems identified and suggested solutions, and presented these directly to the National Epidemiological Policy-Making Body. The findings provided crucial data for the government to address critical measures regarding health care capacity, decide on restriction maintenance, change the actual testing strategy, and take regional economic, social, and health differences into account. Hungary managed the first part of the COVID-19 pandemic with low mortality rate. In times of epidemics, the formation of multidisciplinary research groups is essential for policy makers. The establishment, research activity, and participation in decision-making of these groups, such as KETLAK, can serve as a model for other countries, researchers, and policy makers not only in managing the challenges of COVID-19, but in future pandemics as well.

Keywords: COVID-19, mortality, interdisciplinary, ICU capacity, testing, modeling

Introduction

Translational medicine is an enterprise that aims to translate scientific evidence for community benefits in order to elevate the health level of a society.[1] It is essential to find a way to translate scientific findings into digestible information for the general public, health care professionals, insurance companies, leaders of institutions, and government policy makers.[2,3] The latter has particular importance in times of epidemics and humanitarian crises, when government officials

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have a short time to make critical decisions.[4] Foretelling future scenarios and forwarding evidence-based information to policy makers are paramount during pandemics.[5]

Since the beginning of the expansion of COVID-19, epidemiologists, clinical, social and data scientists, mathematicians, and statisticians are working together across the world to understand the spread of this virus.[6] This effort not only led to numerous scientific publications and online resources but also provided data and prediction scenarios for national health agencies and governments to help them make both the urgent daily and most optimal longer term strategic decisions.[7] Unsurprisingly, countries such as Israel, Switzerland, Germany, Canada, and South Korea,[8,9] – where the science level is high and the government listened to scientists – handled the COVID-19 outbreak with regard to better outcomes. In Italy and Spain, where scientific activity is lower,[10] and in the United States, where the government failed to listen to scientists early enough, the initial consequences of the pandemic were more devastating.[11]

In Hungary, the first COVID-19 patient was identified on March 4, 2020. Wisely, the Hungarian government immediately started a conversation with expert scientists and health care professionals to assess the potential future scenarios before decisions about the epidemic were made. The Translational Action and Research Group against Coronavirus – so called KETLAK (Supplementary Document 1) – released and handed 2 documents directly to the National Epidemiological Policy-Making Body, which was led by the Prime Minister of Hungary, to help the decision-making process related to the Easter holidays and gradual normalization of public life. This article summarizes the scientific methodology, results, and suggestions that had a vital impact on the Hungarian government's decisions.

Methods

To support the epidemiological decision-making process, KETLAK members performed several scientific data analyses and formulated them into 3 chapters: (1) results, (2) problems, amd (3) suggestions. Two materials were submitted to the Policy-Making Body on April 9 and 19; and one of the members of KETLAK introduced the conclusions personally.[12]

Modeling intensive care unit (ICU) bed capacity in Hungary

The mathematical model used calculated that at >3000 beds, because of the significant decrease of human capacity (ie, the effectiveness of treatments), the mortality rate will increase significantly as was seen in Wuhan, Italy, or New York.[13,14] Therefore, 30% mortality was calculated for up to 3000 ICU beds, whereas >3000 ICU beds would yield 60% mortality. The details of the calculation can be found in Supplementary Document 1.

Mathematical modeling of the COVID-19 epidemic in Hungary

To predict the possible outcome over time for various R metrics, data were collected on April 8, 2020 from the official Hungarian data resource site (koronavirus.gov.hu). Input parameters of the model included the actual R metric, the total numbers of infected cases up to April 8, and the available and occupied ICU beds. The model was generated both for the whole country and separately for all of the main regions. In the case of Budapest, for example, R was estimated to be 1.25, with 552 reported infected cases and 750 available ICU beds. Additional parameters were set based on available international data such as the number of infected cases that would require ICU admission (2%-4%), the number of days one patient would spend there ($\sim$2 weeks), and the total death rate of ICU patients (30%).[14]

Modeling the regional differences in Hungary: the complex health distance index

To measure regional differences of health status in Hungary, the KETLAK team adopted and restructured the approach of the functional distance index from the economic analyses.[15] The Complex Health Distance Index *(CHDI)* in addition to the availability of health care institutions (physical distance component, PD_i) takes into account the social (SD_i), economic (ED_i), and institutional (DI) characteristics of the regional units analyzed (eg, settlement, district, county) and the main indicators of the health status of the local population. The components are detailed in Supplementary Document 1.[16]

Modeling GDP loss, economic crisis management, and competitiveness

The mathematical model focuses on quantifiable variables, and takes into account data for the previous years and currently available data. This means that it works with the average per-capita gross domestic product (GDP), the population of the given region, and health care data related to morbidities and fatalities. To model the GDP loss for the 5 main Hungarian regions, GDP was corrected and normalized by the estimated death rate, predicted by the first model, for all the main Hungarian regions separately. The details and the mathematical model can be found in Supplementary Document 1.

Modeling the impact of closing and reopening elementary schools

Classic SIR (susceptible-infected-recovered) simulation using EpiFire 3.34 API software was applied to model the contact network of epidemic transmission using the ''small-world-like'' model to compare epidemic scenarios for closing and reopening schools during the current COVID-19 pandemic. This model was developed by Carrat et al and used as a flexible tool to determine interventions during the influenza pandemic.[17] The model captures changing disease transmission dynamics.[18] Details and the mathematical model can be found in Supplementary Document 1.

Modeling the optimal screening strategy in Hungary

A Hungarian-specific model was developed to estimate optimal screening strategies (ie, the number of screening tests needed for recommendations to keep R below a required level). These were calculated for all regions, the individual counties of the region, and the whole country under various scenarios of lifting the socioeconomic lockdown. The calculation was made using R software.[19] Details of calculation can be found in Supplementary Document 1.

Results

Figure 1 shows the impact of previous decisions on the epidemic situation in Hungary and Italy. The first social distancing measures came 15 days earlier in Hungary than in Italy, which resulted in a lower number of daily new cases, suggesting that social distancing measures have great

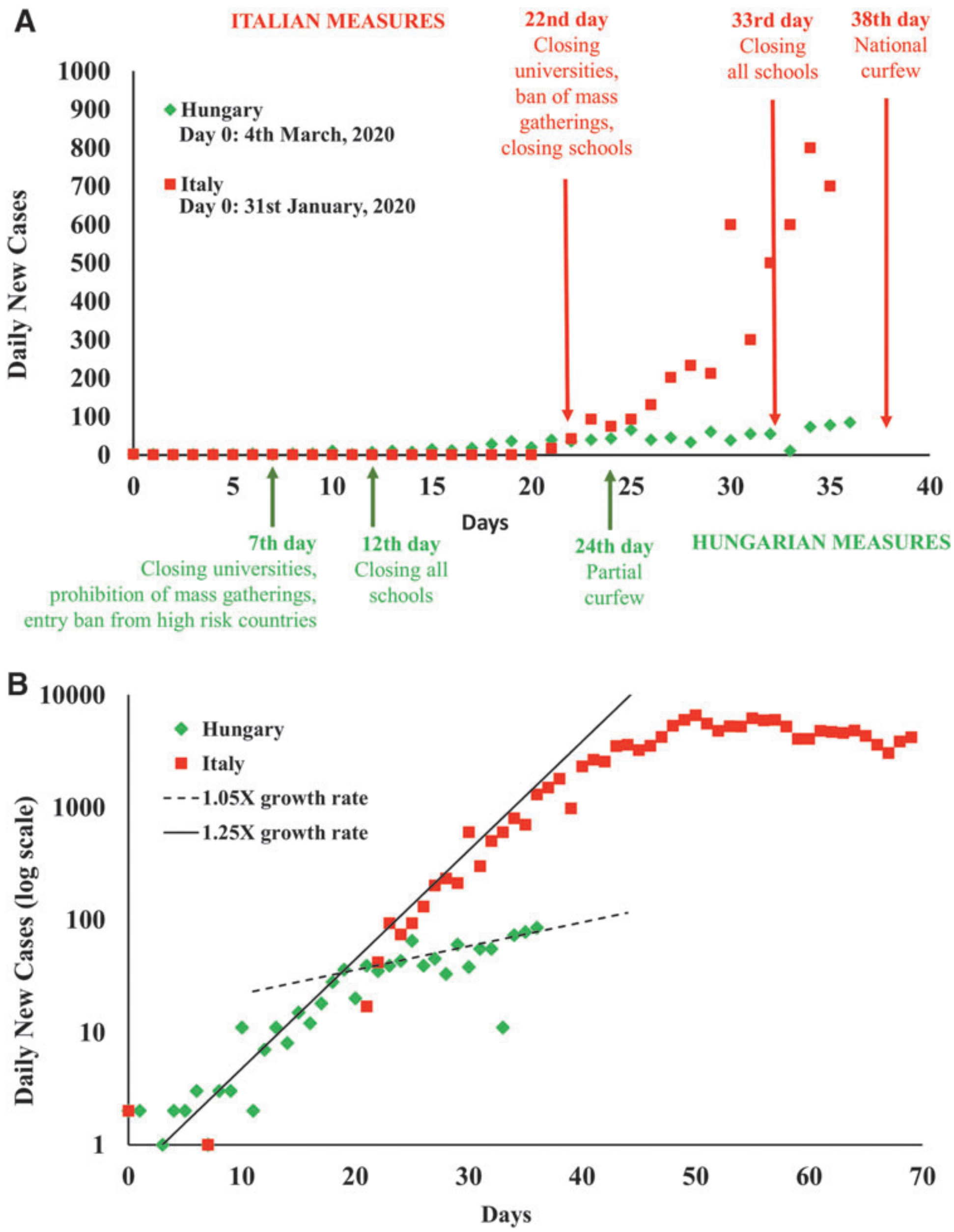

FIG. 1. Impact of previous decisions on the epidemic situation in Hungary. Daily new cases of COVID-19 infection in Italy and Hungary. **(A)** The day of the first case was chosen as day zero for both countries (January 31, 2020 in Italy, and March 4, 2020 in Hungary). Italian measures to control the outbreak and their effective dates are indicated by *black arrows*. Measures by the Hungarian government are indicated by *dashed arrows*. **(B)** Daily new cases depicted on a logarithmic scale. Early day-to-day increase in number of new cases was approximately 1.25x for both countries. For comparison, the growth rate of daily cases decreased to about 1.05x in Hungary after the measures had taken effect.

importance in a national strategy. First, the KETLAK team modeled different scenarios for the decision makers in which the number of deaths were estimated in relation to the predicted number of new cases (number of people infected by COVID-19 virus) together with the modeled numbers of available and occupied ICU beds. The best-case scenario for the whole country, using R metrics estimated on April 8, shows that maintaining the restriction would result in a total of 20,000 new cases at the peak, that there would still be an adequate number of ICU beds to cover the needs for the most serious cases, and therefore, the total number of deaths would be <1500 (Figure 2A). The worst-case scenario was modeled for higher R metrics (R = 2.2) (ie, what would happen for the whole country if all restrictions were removed). The numbers indicate that within 3 weeks there would not be enough ICU beds, as there would have been ∼40,000 at the peak, the number of infected cases would have reached 550,000, and the number of deaths was predicted to be 70,000 (Figure 2B).

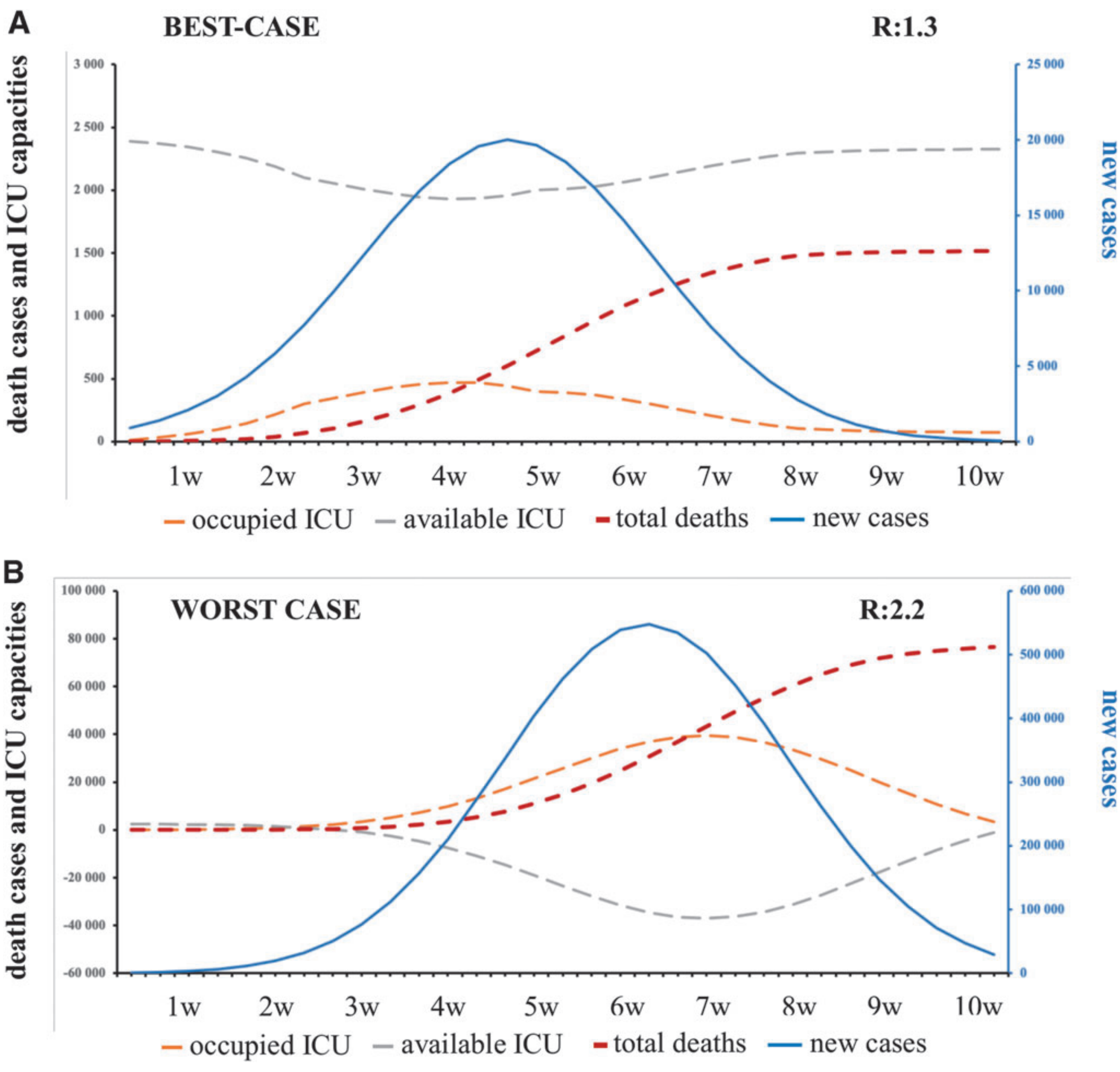

FIG. 2. Mortality scenarios for the whole country with 2 different R metrics. **(A)** Best-case scenario with R set to 1:3. **(B)** Worst-case scenario with R set to 2.2. In both cases, the left side of the y-axis stands for numbers presented by the *dashed-line curves*, such as the total death, occupied and available ICU beds (in *red*, *orange* and *gray*, respectively), the right side of the y-axis stands for the numbers presented by the single *normal line curve* (ie, the predicted new cases [in *blue*]). The numbers of available and occupied ICU beds are in close connection and if one is decreasing, the other is increasing by the same number. When no more ICU beds are available, the number will go to less than zero, showing the lack of ICU beds. ICU, intensive care unit

Then the team investigated regional differences in Hungary (Fig. 3). The mathematical models clearly indicated that Hungary could not be handled as a whole, but rather regional differences should be taken into account. When each region was examined separately, the regional distribution of people older than age 65 years (Figure 3A), the differences between ICU capacities (Figure 3B), the estimated GDP loss from lack of labor force (Figure 3C), and the inequalities in the CHDI (Figure 3D) could be clearly seen.

Therefore, the best-case scenario that was modeled earlier also was modeled for each region separately. Although there are large differences between the regions, there would be enough hospital capacity in case of maintaining the socioeconomic lockdown (Supplementary Fig 1). The worst-case scenario for each region separately indicates that none of the regions would have enough ICU bed capacity. Moreover, clear differences can be seen in how many weeks a region can survive with the available number of ICU beds. As expected, regions where these numbers reach the limits earlier would suffer the most in mortality (Supplementary Fig 1).

Next, the KETLAK team provided disease transmission simulations to help with crucial decisions about closing and reopening elementary schools. The disease transmission simulation model of Budapest can be seen in Figure 4 whereas the county seat urban models are displayed in Supplementary Figs 2 and 3. According to the calculations for Budapest in the case of R = 2.2 or higher, large epidemic-size classes are prone to face fast disease transmission with relatively high frequency. In this case, the chance for an effective health policy intervention to suppress or mitigate the epidemic cycle is very low. Therefore, the team does not suggest early or complete release of school closures; moreover, the team supports a prolonged and stepwise opening of contact education in elementary schools. The epidemic size estimations for the county seats demonstrate that smaller subgroups develop the epidemic outbreak with higher frequency than even in the baseline R = 2.2 scenario.

Because it was suggested earlier that a higher number of tests results in a lower rate of mortality, the KETLAK team compared the number of tests performed in different countries. This examination revealed that the amount of daily

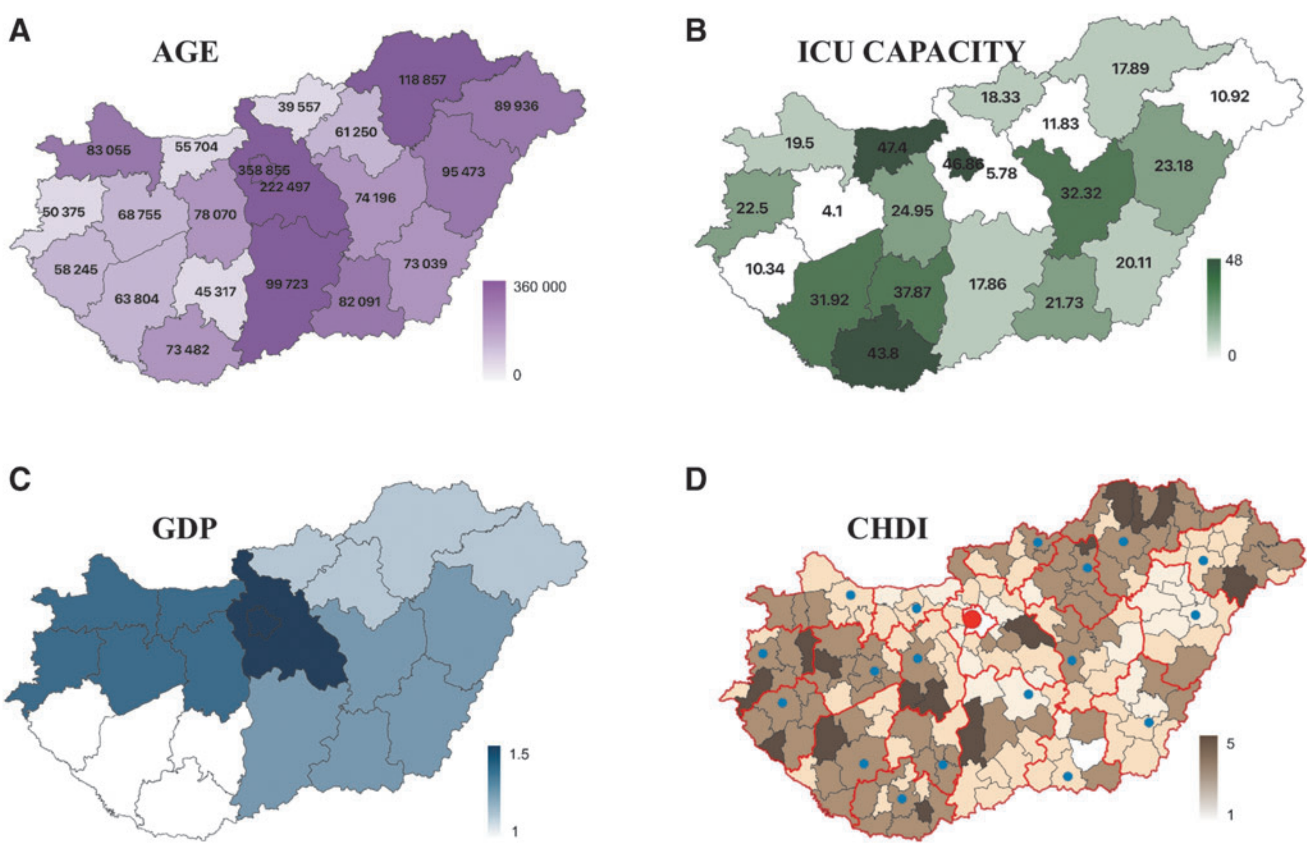

FIG. 3. Regional differences in Hungary. **(A)** The number of people older than age 65 years. **(B)** The number of available ICU beds for the different counties, calculated for 100,000 people. The most beds are available in regions where the 4 medical universities are located (Budapest, Debrecen, Szeged and Pécs). **(C)** The estimated GDP loss related to lack of labor force (infection, mortality). The values are normalized and then scaled between 1 and 1.5 to illustrate the differences among the 5 main Hungarian regions. The biggest economic loss is expected to be suffered in the greater Budapest region and Northern Transdanubia. **(D)** The calculated CHDI for the different regions. Higher values represent poor health conditions of the local population and barriers in access to health care. The territorial location of the most disadvantaged districts can be found in inner and geographic peripheries of the country. Districts where county seats are standing (*blue points; red* for Budapest) have the best health conditions and access to health care institutions with outpatient care. CHDI, Complex Health Distance Index; GDP, gross domestic product; ICU, intensive care unit

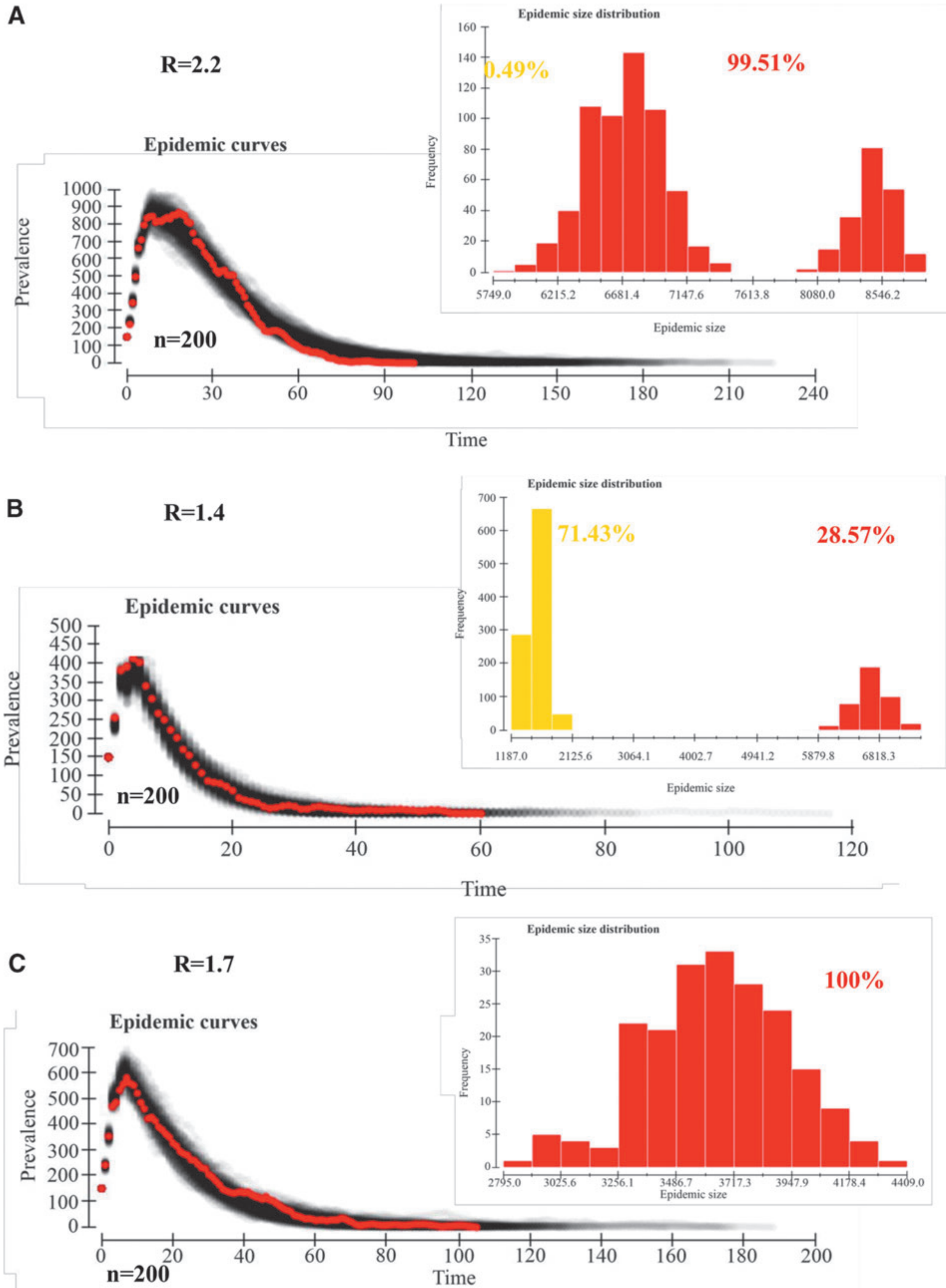

FIG. 4. Impact of closing and reopening elementary schools in Budapest. Simulation models of disease transmission dynamics to demonstrate the COVID-19 outbreak in Hungary with the reproduction rate (R) = 2.2 **(A)** and the effect of closing (R = 1.4) **(B)** and reopening (R = 1.7) **(C)** elementary educational institutions in Budapest. (n = 200 simulations were run for each R scenario.)

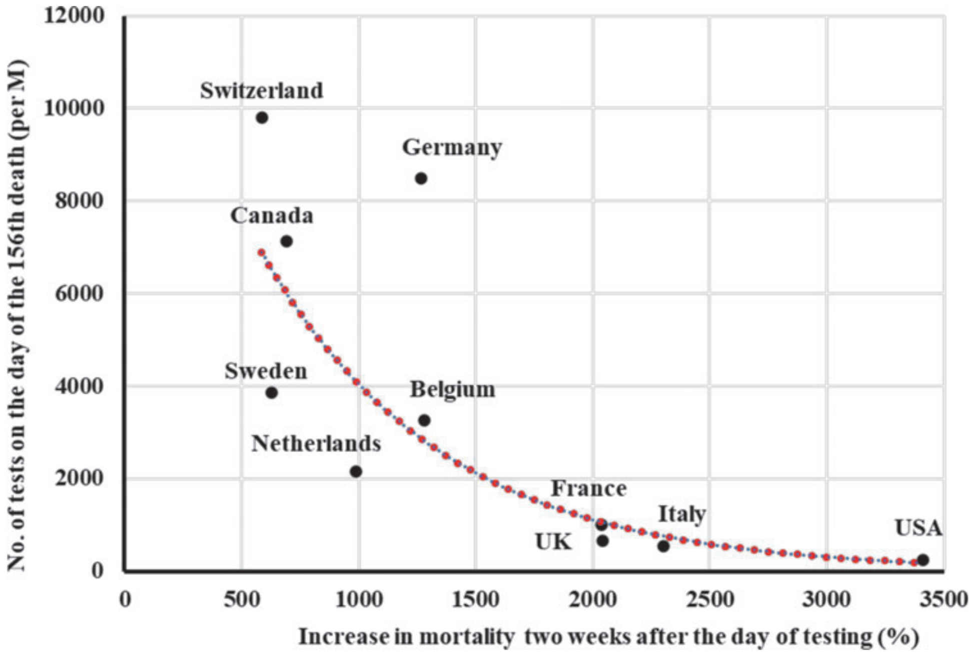

FIG. 5. Association between the number of tests and mortality. Percentage increase in the number of deaths in different countries 2 weeks after the day of testing.

testing highly determines the rate of subsequent mortality (Figure 5). Figure 6A shows that the amount of tests are very low in Hungary. Internationally available data show that Germany is one of the most efficient European countries at keeping the mortality rate low. Using this number as a reference point, the team estimated the optimal number of tests needed in Hungary (Figure 6B).

After that, numbers from Figure 6B were corrected for each county by regional hospital capacities, such as ICU beds, GDP, and the CHDI index (Figure 6C). Using these parameters, Figures 6D and 6E show how many tests would be needed in the case of easing restrictions by reopening the primary schools and completely reopening the whole country, respectively. Details of the results can be found in Supplementary Document 2.

Discussion

The tasks of the scientific community include recognizing challenges in specific circumstances, conducting high-quality research based on scientific methodology, preparing evidence-based summaries of scientific results, and communicating them in understandable language to the target groups who can use the knowledge. The latter includes 2-way communication between the scientific community and government decision makers as well. An excellent example of this is the European Commission's Scientific Advice Mechanism system, in which the High Level Group of Scientific Advisors[20] and Academies provide timely, independent scientific advice to the highest policy level in Europe and for the wider public to support their decision-making.[21,22] This is especially important in situations where there is a short time to make key decisions that affect the daily lives and health of the population. This article presents the preparation and summary of 2 important scientific materials and their effects in Hungary.

The first scientific summary reviewed the international situation and then modeled the course and dynamics of the COVID-19 epidemic. These approaches took into account the crucial R metric, which refers to the average number of people that one sick person goes on to infect in a group that has no immunity.[23] The results clearly showed that epidemiological decisions could be of great significance to the outcome of an epidemic. A detailed summary of the problems identified and suggested solutions can be found in Supplementary Document 3.

There were recent epidemics caused by members of the coronavirus family. These epidemics had different dynamics and characteristics. The deadly outbreak of Severe Acute Respiratory Syndrome[24] in 2003 in Toronto, which claimed 43 lives among 253 infected patients, was successfully contained by a rapid and efficient response by scientists and politicians fighting it shoulder to shoulder.[25,26] The successful strategy against the current SARS-CoV-2 pandemic in South Korea stemmed from their recent bitter experience with the Middle East respiratory syndrome (MERS) outbreak. They learned the lesson that only scientific evidence could guide political decisions in an epidemic.[27]

As was mentioned in the introduction, several challenges must be faced during the COVID-19 pandemic. This paper shows direct evidence that there is a large difference between the territorial patterns and the economic, social, and health care structures in Hungary, which can have an impact on the spread of the pandemic.

Therefore, in addition to using available international data, the KETLAK team included major influencing factors such as age differences, ICU bed availability, and the differences in CHDI separately in the later analysis. Because a pandemic is not only a health crisis but also a socioeconomic crisis, the team took regional GDP differences into account as well. It was also important because the socioeconomic

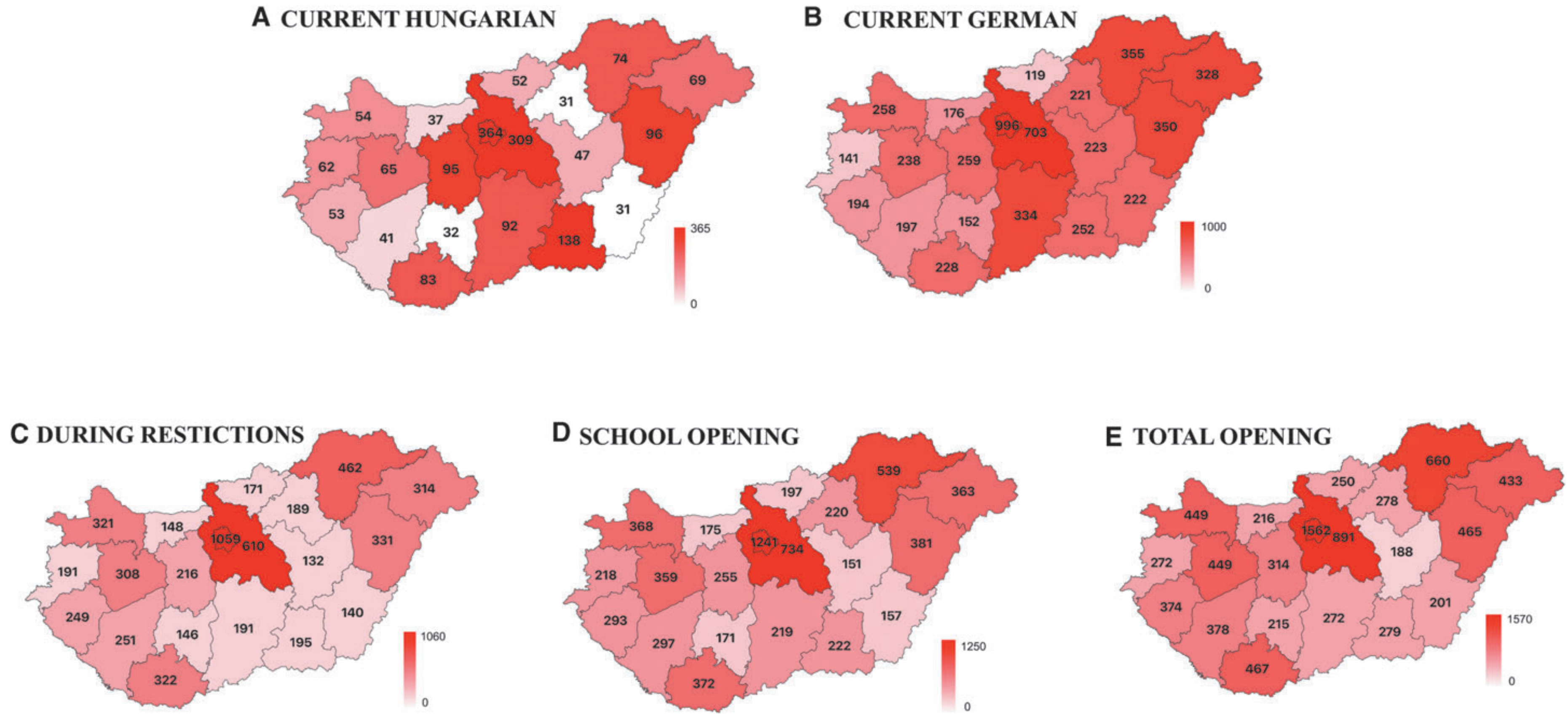

FIG. 6. Current testing in Hungary and in Germany. **(A)** Number of tests for all counties (for 100,000 people) in Hungary on April 8, 2020. **(B)** Required number of tests for the regions if the German testing rate (50,000 tests per day) is taken as a reference. Suggested testing in Hungary calculated from the German testing number modified by the Hungarian ICU capacity, GDP and CHDI. The optimal number of tests based on the German testing rate, corrected by ICU capacity, GDP, and CHDI, in case of maintaining the restrictions **(C)**, reopening primary schools **(D)**, and removing all the restrictions except for the elderly **(E)**. All numbers are corrected to the population of the given county. CHDI, Complex Health Distance Index; GDP, gross domestic product; ICU, intensive care unit.

crisis structures that evolve after the pandemic ends also will display various patterns deriving from pre-crisis specificities and the dynamic variables observed during the crisis. The former can be changed with a slow process, while the latter, once understood, may play a key role in spatial organization. Importantly, Pearson's correlation of the aforementioned factors showed clear association between the parameters (Supplementary Fig 4).

In the second part of the material released on April 9, the team used disease transmission model simulations for different urban models to support decision-making on institutional closures and management practices in response to the COVID-19 pandemic. A detailed summary of the problems identified and suggested solutions can be found in Supplementary Document 3.

Previous modeling studies from the 2003 SARS outbreak in mainland China, Hong Kong, and Singapore, the 2009 H1N1 influenza pandemic in Taiwan, as well as limited information from clinical reports about the 1957 Asian influenza pandemic, where R was estimated to be similar to COVID-19, provide different results and divergent aspects of effect estimation.[28–30] Even using mathematical models for the very same SARS outbreak in 2005, the estimated effect of school closure was calculated to be very different from the disease transmission reduction.[31] Studies modeling the COVID-19 pandemic[32–34] support the restriction measures including the closure of educational institutions at national levels; however, there are gaps in the literature on the estimation of school closure intervention separately from other strict and general social distancing control.

Here the team could conclude that educational institution closure cannot be estimated as a homogenous effect on disease transmission. Different urban models with differing school population size, contact density, and dynamics, and different inhabitant populations can shape infection transmissibility and its impact on epidemic progression significantly.

In addition to the results gained from modeling the mitigation and suppression-based strategies and the disease transmission network dynamics, the first (April 9) material had a dire message, too. If the R value cannot be reducted, there is no chance of finding a good solution to restart the lives of the population. Therefore, in the second material the KETLAK team concentrated on the methods that can help to decrease the R value. In the first analysis the team revealed that the amount of screening and testing could have a large effect on mortality. Data showed that Germany is one of the most efficient European countries at keeping the mortality rate low. Therefore, the German data were used as a reference point to estimate the optimal number of tests needed in Hungary.

However, in order to be specific to the conditions of the regions, the number of tests likely to be required was corrected for each county by regional hospital capacities, such as ICU beds, GDP, and the CHDI index. The team admits that the CHDI will need further modifications in the future. It can be expanded with new indicator systems and individual indices (eg, number of population, aging index population density, incomes, health human and material capacity in health care). Modification of the CHDI also is suitable to analyze these indicators at different territorial levels (eg, in urban areas in the context of a city and its neighborhoods).[35]

These further possible indicators based on applying diversified territorial levels can be summarized in a risk matrix to define the most important socioeconomic and health risks and their vulnerability groups, especially during a pandemic. However, given the limited time available to compile the material, the team did not have the time to incorporate the changes into the current model. Therefore, a call for a dynamic organization of health care service is crucially needed, details of which can be found in Supplementary Document 4.

In the final analysis, to provide the most detailed assistance to decision makers, the KETLAK team also analyzed the numbers of tests required to resolve the restrictions by region. In the current phase of the COVID-19 pandemic, the proper diagnostic tool to identify individuals who can potentially communicate the infection is the polymerase chain reaction (PCR)-based molecular assay, which detects ribonucleic acid target regions of the SARS-CoV-2 pathogen's nucleic acid.[36,37] The national operative protocol in Hungary specifies on-site upper respiratory tract sampling (nasopharyngeal and oropharyngeal or buccal swab) and PCR testing,[38] which is in accordance with the World Health Organization recommendations.

Considering the capacities available for PCR, 4000–6000 testing is the maximum limit of the successful feasibility calculated on April 18, 2020. During the elaboration of a complex testing and screening strategy, the team aimed to fit it close to the accessibility rather than aiming to reach perfection. However, it should be noted that a continuous effort should be made to strategically enhance the throughput of COVID-19 PCR testing and screening at this stage. Serological testing also should be a testing issue as COVID-19 begins to subside to detect the immunized state of the population. Therefore, the team recommended testing approaches for symptomatic patients and health care professionals and highlighted the importance of residential base representative screening. Details can be found in Supplementary Document 5.

Similar to the European Commission, 4–5 high-level groups of scientific advisors help the decision makers in Hungary, so it is challenging to judge which analysis has a decisive impact on the final decisions. There were several similarities and differences in the analyses of the research groups. For example, although the ITM Network Mathematical Epidemiology Group was unique in the analysis of contact numbers, the multidisciplinary KETLAK consortium highlighted (1) the need for regional thinking and (2) calculation of the effect of real health capacities on mortality scenarios.

Importantly, it seems that the analyses described in this article and presented to the National Epidemiological Policy-Making Body could have a major impact on governmental decision-making because several of these suggestions had already taken effect before the submission of this article for publication. For example:

(1) Previous considerations of the possible lifting of restrictions during the Easter holidays were rejected and lifting the restrictions was postponed for approximately a month[39];
(2) Regional variations of the epidemic have been introduced; restrictions will be eased in less densely populated areas while Budapest and the surrounding area will remain under a more strict control;
(3) The importance of increasing the amount of testing has been recognized by the authorities;

(4) A representative population screening study was recently initiated that involves more than 10,000 volunteers and the concerted effort of the country's 4 medical universities.[40]

Further improvement of the KETLAK models and more precise identification of target groups for testing is a must. For example, in addition to health care workers and workers of essential companies (eg, power plants, food processing factories), nursing homes and chronic patients in hospitals should be tested. There also is a need to concentrate on the health care of the non-COVID-19 population, and calculation of the effect of commuting workers in neighboring countries.

Conclusion

In conclusion, in times of epidemics, formation of interdisciplinary research groups is essential for policy makers, as none of the disciplines can model the complex problems that arise during an epidemic alone. The establishment, research activity, and participation in decision-making of the KETLAK group can serve as a model for other countries, researchers, and policy makers not only in managing the challenges of COVID-19, but in future pandemics as well.

Author Disclosure Statement

The authors declare no conflict of interest.

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Supplementary Material

Supplementary Document 1
Supplementary Document 2
Supplementary Document 3
Supplementary Document 4
Supplementary Document 5
Supplementary Fig 1
Supplementary Fig 2
Supplementary Fig 3
Supplementary Fig 4

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