A novel intervention recurrent autoencoder for real time forecasting and non-pharmaceutical intervention selection to curb the spread of Covid-19 in the world

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As the Covid-19 pandemic soars around the world, there is urgent need to forecast the number of cases worldwide at its peak, the length of the pandemic before receding and implement public health interventions to significantly stop the spread of Covid-19. Widely used statistical and computer methods for modeling and forecasting the trajectory of Covid-19 are epidemiological models. Although these epidemiological models are useful for estimating the dynamics of transmission od epidemics, their prediction accuracies are quite low. To overcome this limitation, we formulated the real-time forecasting and evaluating multiple public health intervention problem into forecasting treatment response problem and developed recurrent neural network (RNN) for modeling the transmission dynamics of the epidemics and Counterfactual-RNN (CRNN) for evaluating and exploring public health intervention strategies to slow down the spread of Covid-19 worldwide. We applied the developed methods to the real data collected from January 22, 2020 to May 8, 2020 for real-time forecasting the confirmed cases of Covid-19 across the world.

KEYWORDS AND PHRASES: Covid-19, Recurrent neural networks, Artificial intelligence, Time series, Causal inference, Forecasting.

1. INTRODUCTION

As of May 11, 2020, global confirmed cases of Covid-19 passed 4,152,670 and has spread to 212 countries, causing fear globally (Anastassopoulou et al. 2020). The serious public health threat of Covid-19 has never been seen for more than one century. The government officers and people around the world are desperately trying to slow the spread of Covid-19 (Irfan 2020). We must change our policies to deal with increased mobility of citizens and immediately implement the public health interventions and expanding the virus testing to stop the spread of Covid-19 across the world.

How computer modeling of Covid-19's transmission dynamics could help governments to quickly and strongly move to slow down the spread of Covid-19?

Widely used statistical and computer methods for modeling of Covid-19 simulate the transmission dynamics of epidemics to understand their underlying mechanisms, forecast the trajectory of epidemics, and assess the potential impact of a number of public health measures on curbing the spread speed of Covid-19 (Li et al. 2020, Wu et al. 2020, Zhao et al. 2020, Kucharski et al. 2020, Tuite et al. 2020, Hellewell et al. 2020, Li et al. 2020). Although these epidemiological models are useful for estimating the dynamics of transmission, and evaluating the impact of intervention strategies, they have some serious limitations (Funk et al. 2018, Johansson et al. 2019). First, the epidemiological models consist of ordinary differential equations that have many unknown parameters, and depend on many assumptions. It is difficult to translate public interventions to these parameters. Most analyses used hypothesized parameters, which often lead to fitting data very poor. Health officers desperately want to track the trajectory of epidemics and accurately estimate the peak time and number of cases, duration, and ending time and number of cases of Covid-19 for their health policy plan. However, the forecasting results of using the classical epidemiological models such as Susceptible-Exposed-Infectious-Removed (SEIR) models are highly unreliable. Second, the successful application of public health intervention planning highly depends on the model parameter identifiability. However, overall, the parameters in the complex compartmental dynamic models are unidentifiable (Roosa and Chowell 2019, Roda et al. 2020). The values of parameters cannot be uniquely determined from the real data (Gábor et al. 2017). The variances of the estimators of these parameters are very high.

To overcome limitations of the epidemiological model approach, and assist public health planning and policy making, we formulated the real-time forecasting and evaluating multiple public health intervention problem into off-policy evaluation (OPE) and forecasting treatment response problem where the aim is to estimate the response of a new public health intervention policy, given historical data that

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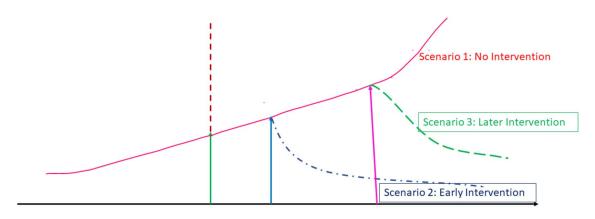


Figure 1. Forecasting intervention response to curbing the spread of Covid-19 under a sequence of interventions.

may have been generated by a different public health intervention policies (Bibaut et al. 2019). We viewed the interventions as treatments where multiple interventions were administered at different time points. The number of new cases were taken as treatment responses. The ability to accurately estimate effects of public health interventions over time would allow health officers to determine what intervention strategies should be used and the optimal time at which to implement them (Lim et al. 2018). Recurrent Intervention Network (RIN) (Lim et al. 2018) where a recurrent neural network architecture for forecasting a nation's response (number of new cases) to a sequence of planned interventions were used to forecast and evaluate multiple public health interventions for Covid-19 worldwide. Potential outcomes of RIN were trajectory of the spread of Covid-19. Public health interventions including locking down residential buildings and compounds, strict self-quarantine for families, door-to-door inspection for suspected cases, maintaining social distancing, stopping mass gatherings, closure of schools and universities, vacating hotels and university dormitories. To quantify comprehensive intervention strategies, an intervention variable that comprehensively and abstractly measures mobility activities and social distancing was used as an input variable for each block of RIN (detailed description of the intervention measure was summarized in Training Procedures and Loss function Section in the Supplementary Note A, http://intlpress.com/site/pub/files/_supp/sii/ 2021/0014/0001/SII-2021-0014-0001-s001.docx). We cluster all the countries in the world into several groups. For each group, a value (weight) was assigned to each group such that the average prediction error of counterfactual recurrent network (CRN) was small. The RIN is taken as a general framework for investigating how Covid-19 evolves under different intervention plans, how individual nation responds to intervention over time, but also which are optimal timings for assigning interventions. Therefore, this approach will provide new tools to improve public health planning and policy making.

The RIN was applied to the surveillance data of lab confirmed Covid-19 cases in the world up to May 8, 2020. Data

on the number of confirmed, new and death cases of Covid-19 from January 22, 2020 to May 8, 2020 were obtained from John Hopkins Coronavirus Resource Center (https://coronavirus.jhu.edu/MAP.HTML).

2. METHODS

2.1 RIN as a framework for modeling and forecasting the spread of Covid-19 over time with multiple interventions

The RIN uses sequence-to-sequence multi-input/output recurrent neural network (RNN) architectures to model health intervention plan and make multi-step prediction of the response trajectory of Covid-19 over time with multiple interventions (Lim et al., 2018). The RNN can learn the complex dynamics within the temporal ordering of input time series of Covid-19 and use an internal memory to remember. The health intervention plan has multiple intervention regimens. As shown in Figure 1, the RIN determines the intervention response (similar to counterfactual outputs) for a given set of planned interventions and evaluates the impact of different intervention strategies and their implementation times on the curbing the spread of Covid-19 and provides timely selection of optimal sequence of intervention strategies.

The RIN is a RNN autoencoder. It consists of two RNNs: the encoder RNN (vanilla RNN (Figure S1) or long short-term memory (LSTM) (Figure S2) is used as encoder) and the decoder RNN (vanilla RNN or LSTM is used as the decoder). The RNN encoder models input time series (past history of the number of cases of Covid-19 over time) and predicts future response time series (number of cases of Covid-19 in the future with a planned sequence of interventions) (Srivastava et al., 2015). The latent state of the RNN encoder after reading in the entire input time series (past trajectory of Covid-19), is the representation (compressed latent features of the entire input time series) of the input trajectory of Covid-19. Unlike the standard decoder where the decoder reconstructs back the input time series

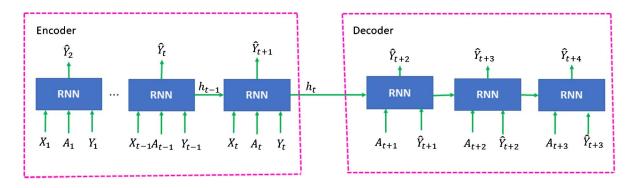


Figure 2. Architecture of recurrent intervention network.

from the latent representation, the RNN decoder uses the learned features of the dynamics of Covid-19 in the RNN encoder to forecast the potential response time series, given a sequence of planned public health interventions as an input to the RNN decoder. The feature vector learned in the RNN encoder is then provided as an input to the RNN decoder which initiate prediction of the future dynamics of Covid-19 under the future interventions (Figure 2). Detailed description of the RIN was listed in Supplementary Note A.

2.2 Training the RIN

RIN training consisted of RNN encoder training and RNN decoder training (Supplementary Note A). We first fitted a model of the system's dynamics of Covid-19 to the data from past experimental interventions to learn representations of the states of the dynamics of Covid-19 (encoder training), and then used the learned fit to extrapolate and forecast the response to the alternative interventions (decoder training).

The RNN encoder training procedures were briefly introduced here. For details, please see the Supplementary Note A. The basic RNN unit in the RIN consisted of input layer, hidden layer and output layer (Figure S1). The input variables in the RNN encoder can include covariates X_t such as density of population, traffic flow, health facility resources, GDP, and social-economic status although this study did not include these quantities, intervention variable A_t and the numbers of cases (potential outcomes) Y_t at the time t. The state in the hidden layer at the time t was denoted by h_t . The output layer had the output variable Y_{t+1} . A nonlinear activation function was exponential linear unit (ELU) (Clevert et al., 2015) which was defined as

$$f(x) = \begin{cases} x & x > 0 \\ \alpha(e^x - 1) & x \le 0 \end{cases},$$

where $\alpha > 0$.

ELU is similar to ReLU when x > 0. ELUs diminish the vanishing gradient effect as ReLUs. The vanishing gradient problem is alleviated because the positive part of these functions is the identity, therefore their derivative is one and not contractive. However, tanh and sigmoid activation functions are contractive almost everywhere.

In contrast to ReLUs, ELUs have negative values (ReLU does not have), which pushes the mean of the activations closer to zero. Mean activations that are closer to zero enable faster learning as they bring the gradient closer to the natural gradient.

The input data were divided into several batches with length of 7 days. Each batch was used to train the RNN encoder which forecasted standard one-step-ahead intervention response Y_{t+1} as close to the observed intervention response Y_{t+1} as possible via the nonlinear mapping (Supplementary note A)

(1)
$$\hat{Y}_{t+1} = f(X_t, A_t, Y_t, h_{t-1}).$$

The mean-squared error was used as loss function for training the RNN encoder. The training was performed via the standard propagation algorithms (Supplementary A). After training was completed, the RNN encoder extracted the hidden state h_t that captured the internal features of the transmission dynamics of Covid-19 via performing a feedforward pass over the training data on the RNN encoder (Supplementary A).

After the RNN encoder training was completed, we began to train the RNN decoder. An RNN unit in the RNN decoder consisted of input layer with intervention variable $A_{t+\tau}$, $(\tau = 1, 2, ...)$, hidden layer with hidden state $Z_{t+\tau-1}$ and output $Y_{t+\tau+1}$. For a given country, observations, intervention A_t and the number of cases Y_t were randomly divided into short batches of up to τ_b time steps. Each batch of short sequence starting at time t and ending at time $t + \tau_b - 1$ consisted of $\{h_t, (A_{t+1}, Y_{t+2}, \dots, A_{t+\tau_b-1}, Y_{t+\tau_b})\}.$ The mean square errors were still used as the RNN decoder loss function. The goal of RNN decoder training is to make its training loss function smallest (Supplementary A).

2.3 Forecasting procedures

After completion of the training, the trained RIN was used to forecast the future number of cumulative cases of

Covid-19 under some planned interventions for each country. During evaluation, we do not have access to groundtruth outcomes. Therefore, we used the trained decoder to make one step ahead forecasting. The outcomes forecasted by the decoder $(\hat{Y}_{t+1}, \dots, \hat{Y}_{t+\tau-1})$ were recursively used as inputs. The recursive multiple-step forecasting involved using a one-step model multiple times where the prediction for the preceding time step and intervention strategy were used as an input for making a prediction on the following time step. For example, for forecasting the number of new confirmed cases for the one more next day, the predicted number of new cases in one-step forecasting would be used as an observational input in order to predict day 2. Repeat the above process to obtain the two-step forecasting. The summation of the final forecasted number of new confirmed cases for each country was taken as the prediction of the total number of new confirmed cases of Covid-19 worldwide under the intended intervention. By running the decoder, we can select starting and ending time of different interventions and the optimal or appropriate interventions to give over time to obtain the best outcomes of controlling the spread of Covid-19 for each country.

3. DATA COLLECTION

The analysis is based on surveillance data of confirmed cumulative and new COVID-19 cases worldwide as of May 8, 2020. Data on the number of cumulative and new cases and COVID-19-attributed deaths across 186 countries from January 22, 2020 to May 8, 2020 were obtained from John Hopkins Coronavirus Resource Center (https://coronavirus.jhu.edu/MAP.HTML).

3.1 Data pre-processing

 \log_2 was used to transform the original data: $X=\log_2(X+1)$. The intervention measure was calculated as follows. Set the intervention measure at the final time $A_{t_f}=1$ for China, $A_{t_f}=0.3$ for South Korea, Switzerland, United Kingdom, Spain, US, Italy, Germany, Iran, and France, and $A_{t_f}=0$ for all other countries. Assume that the intervention measure curve is an exponential function starting at 0 and ends at A_{t_f} . The intervention measure A_t is given by $A_t=\frac{p^t-1}{p-1}*(A_{t_f}-A_0)+A_0$, where $p>0, p\neq 1$ is the curve shape factor and t takes values in evenly sliced numbers of interval [0,1], A_0 is the intervention measure at the initial time t_0 . When p=1, A_t is a linear function $A_t=t*(A_{t_f}-A_0)+A_0$. In this study, we set p=0.01.

We randomly picked k=64 countries with l=7 length of Covid-19 time series (the number of new cases over time) data staring from the same day to generate k time series with l length for a minibatch to be used for backpropagation training through time. Calculate the mean value of each time series in the batch. The values of each time series were divided by their mean values to normalize the data.

4. RESULTS

4.1 Prediction accuracy of dynamics of Covid-19 using RIN

Accurate prediction of the spread of Covid-19 is important for health intervention plan for the future. To demonstrate that the RIN is an accurate forecasting method, the RIN was applied to confirmed accumulated cases of COVID-19 across 186 countries. Figure 3 plotted reported and onestep ahead predicted time-case curves of Covid-19 where blue dotted curve was the number of estimated cumulative cases after the analysis completion. To further reliably evaluate the forecasting accuracy, we reported 10-step ahead forecasted numbers of cumulative cases and errors of Covid-19 of 8 countries in Table 1 starting with April 29, 2020. The forecasting errors were quite small.

Inputting a sequence of hypothesized public health intervention strategies, the outputs of the RIN decoder were counterfactual numbers of cases of Covid-19 to respond to the intervention strategies. Interventions were measured by number in the interval [0, 1], where 1 indicated the strictest comprehensive public health intervention, 0 indicated no intervention and the values between 0 and 1 indicated the various less strict interventions. To intuitively illustrate the impact of the measure of intervention on the spread of Covid-19, we presented Figure S3. Figure S3 plotted counterfactual numbers of new cases of Covid-19 over time worldwide to respond the interventions with values 0, 0.3, 0.5, 0.7 and 1. We observed that if the measure of intervention was 1, the number of new cases was dramatically deceased to zero. However, when the measure of intervention was 0.3, the number of new cases exponentially increased. The measure of intervention had big effect on the spread of Covid-19.

The number of cases of Covid-19 was a function of the past history and the measure of intervention. Forecasting also depended on the measure of intervention. In Table 1, we also listed the measures of the interventions which provided information on the degrees of current interventions in the country. The measure of interventions in the most countries was 0.6. However, the current measure of interventions in UK was 0.5, the smallest in 8 countries. These results showed that the RIN for forecasting the trajectory of Covid-19 was accurate and reliable. Similar to causal inference, the RIN can be used to evaluate the impact of a sequence of multiple intervention strategies on the curbing the spread of Covid-19 if the interventions were viewed as treatments.

4.2 The number of cases of Covid-19 grows exponentially without additional intensive interventions

To investigate how Covid-19 pandemic surges around the world, we presented Figure 4 that showed the forecasted number of cumulative cases of Covid-19 worldwide over time, assuming that the current intervention measure remains. We observed that the number of cumulative cases

Table 1. Forecasting errors of worldwide and eight countries, where 0.5, 0.55 and 0.6 were intervention measures

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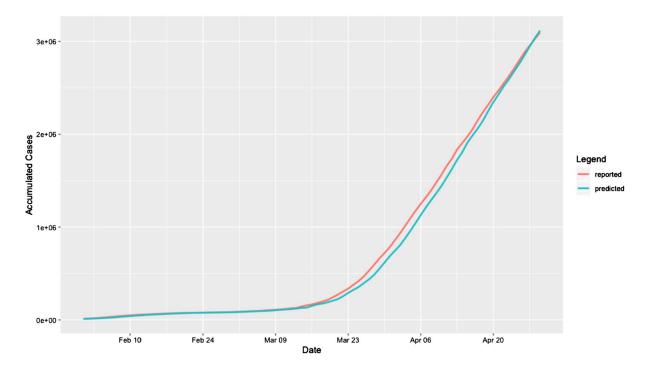


Figure 3. Reported and predicted time-case curves of Covid-19 worldwide where blue dotted curve was the number of reported cumulative cases after the analysis completion.

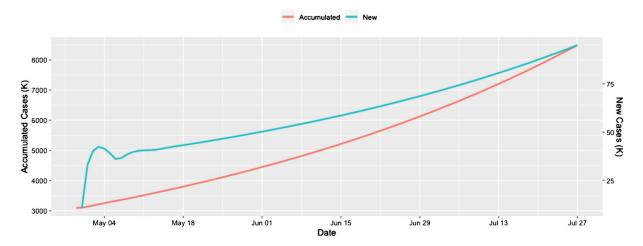


Figure 4. The numbers of cumulative and new cases of Covid-19 worldwide over time, assuming the current intention remains unchanged. The curves in blue color and red color represented the number of cumulative cases and the number of new cases, respectively.

of Covid-19 exponentially grown and would reach extremely high number 8,491,301 on July 1, 2020 if none of additional comprehensive public health intervention was implemented. Similarly, Figure 5 and Figure S3 plotted time-case curves of Covid-19 of eight countries: Italy, Spain, Iran, Germany, USA, France, Belgium and UK, and worldwide with unchanged intervention strategies in the future, respectively. We also observed exponentially growth of the numbers of cases of Coid-19 for many countries without additional intervention.

4.3 We are in the eve to successfully curb the spread of Covid-19

As Covid-19 Accelerates and exponentially grows, how to slow down the spread of Covid-19 is an urgent task for every country around world. To demonstrate that when the additional intervention was implemented, the number of new cases of Covid-19 would decrease, we presented Figures 6 and 7. Figures 6 and 7 plotted the number of cumulative case and new case curves of Covid-19 over time for 12 countries:

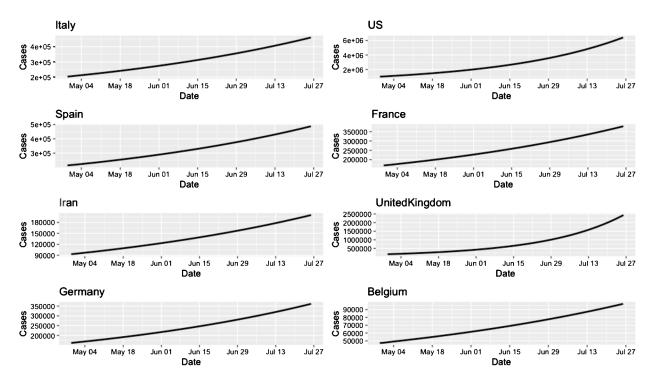


Figure 5. Forecasted number of cumulative cases of Covid-19 of eight countries Italy (A), Spain (B), Iran (C), Germany (D), USA (E), France (F), UK (G) and Belgium (H) over time without additional interventions.

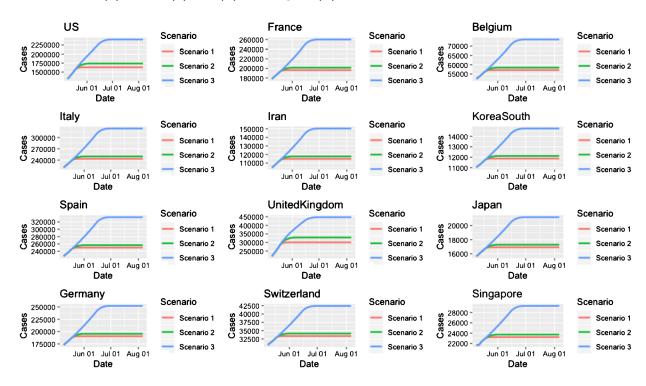


Figure 6. Number of cumulative case curves of Covid-19 over time for 12 countries under three invention scenarios. (A) Time-case plot for US, (B) Time-case plot for Italy, (C) Time-case plot for Spain, (D) Time-case plot for Germany, (E) Time-case plot for France, (F) Time-case plot for Iran, (G) Time-case plot for UK, (H) Time-case plot for Switzerland, (I) Time-case plot for Belgium, (J) Time-case plot for South Korea, (K) Time-case plot for Japan, and (L) Time-case plot for Singapore.

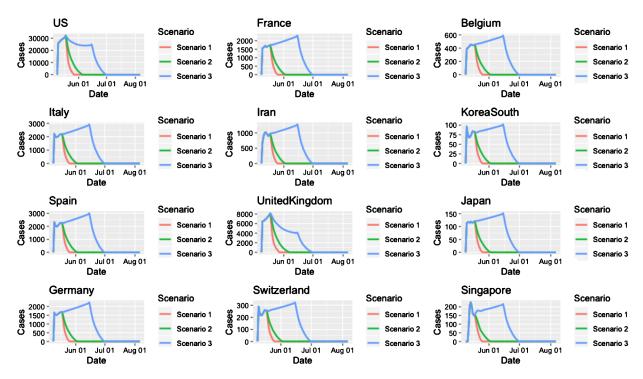


Figure 7. Number of new case curves of Covid-19 over time for 12 countries under three invention scenarios. (A) Time-new case plot for US, (B) Time-new case plot for Italy, (C) Time-new case plot for Spain, (D) Time-new case plot for Germany, (E) Time-new case plot for France, (F) Time-new case plot for Iran, (G) Time-new case plot for UK, (H) Time-new case plot for Switzerland, (I) Time-new case plot for Belgium, (J) Time-new case plot for South Korea, (K) Time-new case plot for Japan, and (L) Time-new case plot for Singapore.

US, Italy, Spain, Germany, France, Iran, UK, Switzerland, Belgium, South Korea, Japan and Singapore under three invention scenarios, respectively. Scenario 1 started with the intervention measure of 0.50 for one week, then transitioned to the intervention with a measure of 0.70 in two weeks. The scenario 2 started with the intervention measure of 0.5 for the first week, and then transitioned to the intervention with a measure of 0.70 in three weeks. The scenario 3 started with the intervention measure for one week, changed to 0.60 in three weeks and finally transitioned to the intervention with a measure of 0.70 in three weeks. Figures 6 and 7 showed that when the countries moved to intervention with measure of 0.70, the spread of Covid-19 in all 12 countries was curbed. Now the measures of interventions in the most of 12 countries were closer to 0.60 (Table 1). These countries were closing to stopping the spread of Covid-19 if additional interventions such as wearing face masks were implemented.

Next we investigated how various intervention strategies reduced the peak time and cumulative case numbers, and the final total number of cases. Table 2 showed the forecasted results of COVID-19 worldwide and in 11 countries under three sequences of interventions (Scenarios 1-3). Figure S4 plotted the time-case curves of Covid-19 worldwide under three invention scenarios. We can see that under all three scenarios, the peak times worldwide and in all 11 countries were May 18, 2020 and April 24 or before April 24,

2020, respectively; and the spread of COVID-19 worldwide and in all 11 countries would be stopped by the end of June, 2020.

5. CONCLUSION/DISCUSSION

As an alternative to the epidemiologic transmission models, we formulated the real-time forecasting and evaluating multiple public health intervention problem into a novel causal inference problem. We viewed the interventions as treatments where multiple interventions were administered at different time points. The number of new cases were taken as treatment responses. The RIN uses sequence-to-sequence multi-input/output recurrent neural network as a tool for modeling the real-time trajectory of the transmission dynamics of Covid-19, health intervention planning and making multi-step prediction of the response trajectory of Covid-19 over time with multiple interventions. The RNN can learn the complex dynamics within the temporal ordering of input time series of Covid-19 and use an internal memory to remember the hidden features.

This AI and causal inference-inspired approach allows us to address three important questions. The first question is the prediction accuracy. Unlike other dynamic systems where the parameters in the systems and control variables

Table 2. Covid-19 dynamics in 11 countries and worldwide for three scenarios

Scenario	Country	US	Italy	Spain	Germany	France	Iran
Scenario 1	Peak Time	4/24/2020	3/21/2020	3/25/2020	3/27/2020	4/12/2020	3/30/2020
	Peak Number (New)	36188	6557	9630	6933	26849	3186
	Peak Number (Cumulative)	905358	53578	49515	50871	121712	41495
	End Time	5/27/2020	5/26/2020	5/26/202	5/26/202	5/26/202	5/26/202
	End Cases	1633438	243198	249919	190450	196231	114863
	Duration		116	115	120	123	97
Scenario 2	Peak Time	4/24/2020	3/21/2020	3/25/2020	3/27/2020	4/12/2020	3/30/2020
	Peak Number (New)	36188	6557	9630	6933	26849	3186
	Peak Number (Cumulative)	905358	53578	49515	50871	121712	41495
	End Time	6/6/2020	6/3/2020	6/3/2020	6/3/2020	6/3/2020	6/3/2020
	End Cases	1738794	249776	256694	195499	201447	117782
	Duration	134	124	123	128	131	105
Scenario 3	Peak Time	4/24/2020	3/21/2020	3/25/2020	3/27/2020	4/12/2020	3/30/2020
	Peak Number (New)	36188	6557	9630	6933	26849	3186
	Peak Number (Cumulative)	905358	53578	49515	50871	121712	41495
	End Time	7/1/2020	7/1/2020	7/1/2020	7/1/2020	7/1/2020	7/1/2020
	End Cases	2402819	323821	332980	252159	259993	150317
	Duration	159	152	151	156	159	133
:	Country	UK	Belgium	Korea South	Japan	Singapore	Worldwide
Scenario 1	Peak Time	4/10/2020	4/15/2020	3/3/2020	4/17/2020	4/20/2020	5/18/2020
	Peak Number (New)	8733	2454	851	1161	1426	200938
		74005	99579	F100		0011	5685045
	Peak Number (Cumulative)	74605	33573	5186	9787	8014	3063043
	Peak Number (Cumulative) End Time	74605 $7/1/2020$	$\frac{33573}{7/1/2020}$	$\frac{5186}{7/1/2020}$	9787 $7/1/2020$	8014 $7/1/2020$	5/28/2020
	End Time	7/1/2020	7/1/2020	7/1/2020	7/1/2020	7/1/2020	5/28/2020
Scenario 2	End Time End Cases	7/1/2020 300936	7/1/2020 57109	7/1/2020 11875	7/1/2020 16927	7/1/2020 23228	5/28/2020 6116772
Scenario 2	End Time End Cases Duration	7/1/2020 300936 118	7/1/2020 57109 112	7/1/2020 11875 123	7/1/2020 16927 121	7/1/2020 23228 123	5/28/2020 6116772 125
Scenario 2	End Time End Cases Duration Peak Time	7/1/2020 300936 118 4/10/2020	7/1/2020 57109 112 $4/15/2020$	7/1/2020 11875 123 3/3/2020	7/1/2020 16927 121 $4/17/2020$	7/1/2020 23228 123 4/20/2020	$ \begin{array}{r} 5/28/2020 \\ 6116772 \\ 125 \\ \hline 5/18/2020 \end{array} $
Scenario 2	End Time End Cases Duration Peak Time Peak Number (New)	7/1/2020 300936 118 4/10/2020 8733	7/1/2020 57109 112 4/15/2020 2454	7/1/2020 11875 123 3/3/2020 851	7/1/2020 16927 121 4/17/2020 1161	7/1/2020 23228 123 4/20/2020 1426	5/28/2020 6116772 125 5/18/2020 203456
Scenario 2	End Time End Cases Duration Peak Time Peak Number (New) Peak Number (Cumulative)	7/1/2020 300936 118 4/10/2020 8733 74605	7/1/2020 57109 112 4/15/2020 2454 33573	7/1/2020 11875 123 3/3/2020 851 5186	7/1/2020 16927 121 4/17/2020 1161 9787	7/1/2020 23228 123 4/20/2020 1426 8014	5/28/2020 6116772 125 5/18/2020 203456 5687563
Scenario 2	End Time End Cases Duration Peak Time Peak Number (New) Peak Number (Cumulative) End Time	7/1/2020 300936 118 4/10/2020 8733 74605 6/7/2020	7/1/2020 57109 112 4/15/2020 2454 33573 6/3/2020	7/1/2020 11875 123 3/3/2020 851 5186 6/3/2020	7/1/2020 16927 121 4/17/2020 1161 9787 6/3/2020	7/1/2020 23228 123 4/20/2020 1426 8014 6/3/2020	5/28/2020 6116772 125 5/18/2020 203456 5687563 6/7/2020
Scenario 2 Scenario 3	End Time End Cases Duration Peak Time Peak Number (New) Peak Number (Cumulative) End Time End Cases	7/1/2020 300936 118 4/10/2020 8733 74605 6/7/2020 329467	7/1/2020 57109 112 4/15/2020 2454 33573 6/3/2020 58472	7/1/2020 11875 123 3/3/2020 851 5186 6/3/2020 12117	7/1/2020 16927 121 4/17/2020 1161 9787 6/3/2020 17285	7/1/2020 23228 123 4/20/2020 1426 8014 6/3/2020 23737	5/28/2020 6116772 125 5/18/2020 203456 5687563 6/7/2020 6843077
	End Time End Cases Duration Peak Time Peak Number (New) Peak Number (Cumulative) End Time End Cases Duration	7/1/2020 300936 118 4/10/2020 8733 74605 6/7/2020 329467 128	7/1/2020 57109 112 4/15/2020 2454 33573 6/3/2020 58472 120	7/1/2020 11875 123 3/3/2020 851 5186 6/3/2020 12117 131	7/1/2020 16927 121 4/17/2020 1161 9787 6/3/2020 17285 129	7/1/2020 23228 123 4/20/2020 1426 8014 6/3/2020 23737 131	5/28/2020 6116772 125 5/18/2020 203456 5687563 6/7/2020 6843077 135
	End Time End Cases Duration Peak Time Peak Number (New) Peak Number (Cumulative) End Time End Cases Duration Peak Time	7/1/2020 300936 118 4/10/2020 8733 74605 6/7/2020 329467 128 4/10/2020	7/1/2020 57109 112 4/15/2020 2454 33573 6/3/2020 58472 120 4/15/2020	7/1/2020 11875 123 3/3/2020 851 5186 6/3/2020 12117 131 3/3/2020	7/1/2020 16927 121 4/17/2020 1161 9787 6/3/2020 17285 129 4/17/2020	7/1/2020 23228 123 4/20/2020 1426 8014 6/3/2020 23737 131 4/20/2020	5/28/2020 6116772 125 5/18/2020 203456 5687563 6/7/2020 6843077 135 5/18/2020
	End Time End Cases Duration Peak Time Peak Number (New) Peak Number (Cumulative) End Time End Cases Duration Peak Time Peak Number (New)	7/1/2020 300936 118 4/10/2020 8733 74605 6/7/2020 329467 128 4/10/2020 8733	7/1/2020 57109 112 4/15/2020 2454 33573 6/3/2020 58472 120 4/15/2020 2454	7/1/2020 11875 123 3/3/2020 851 5186 6/3/2020 12117 131 3/3/2020 851	7/1/2020 16927 121 4/17/2020 1161 9787 6/3/2020 17285 129 4/17/2020 1161	7/1/2020 23228 123 4/20/2020 1426 8014 6/3/2020 23737 131 4/20/2020 1426	5/28/2020 6116772 125 5/18/2020 203456 5687563 6/7/2020 6843077 135 5/18/2020 202443
	End Time End Cases Duration Peak Time Peak Number (New) Peak Number (Cumulative) End Time End Cases Duration Peak Time Peak Number (New) Peak Number (Cumulative)	7/1/2020 300936 118 4/10/2020 8733 74605 6/7/2020 329467 128 4/10/2020 8733 74605	7/1/2020 57109 112 4/15/2020 2454 33573 6/3/2020 58472 120 4/15/2020 2454 33573	7/1/2020 11875 123 3/3/2020 851 5186 6/3/2020 12117 131 3/3/2020 851 5186	7/1/2020 16927 121 4/17/2020 1161 9787 6/3/2020 17285 129 4/17/2020 1161 9787	7/1/2020 23228 123 4/20/2020 1426 8014 6/3/2020 23737 131 4/20/2020 1426 8014	5/28/2020 6116772 125 5/18/2020 203456 5687563 6/7/2020 6843077 135 5/18/2020 202443 5686550

are, in general, independent, the epidemic systems have intervention and system dependent parameters. We designed the intervention variable that quantified comprehensive intervention strategies and had close relationships with the parameters in the epidemic systems. Therefore, the RINs could take the parameters in the epidemic dynamic systems as input control variables that can be estimated in the RIN training. The RIN models were closer to real epidemic dynamic systems than the epidemiological models. Therefore, our results showed that the RIN substantially improved the accuracies of prediction and subsequently multiple-step forecasting.

The second question is how important is the intervention time. Since interventions are complicated and are difficult to quantify, we designed three intervention scenarios to represent the degrees and delays of interventions. Since

the proposed methods combine the real data and models, they allowed us to evaluate the consequences of multiple intervention strategies, while maintaining the analysis as close to the real data as possible. The RIN investigated the impact of multiple public intervention plans and intervention measures on the size, duration and time of the virus outbreak and recommended the appropriate intervention times.

We estimated the duration, peak time and ending time, peak number of new cases and cumulative cases, and maximum number of cumulative cases of COVID-19 under three intervention scenarios for 184 countries in the world. We observed that the number of cumulative cases of Covid-19 would exponentially grow and reach extremely high number 199,554,596 on July 6, 2020 if none of additional comprehensive public health intervention was implemented. However, we also found that top 12 countries with the largest number

of the lab confirmed cumulative cases of COVID-19 were closing to stopping the spread of Covid-19 if additional interventions such as wearing face masks were implemented. We can see that under all three scenarios, the peak times were before April 15, 2020 and the spread of COVID-19 would be stopped before the end of May, 2020.

CONFLICT OF INTEREST

We have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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