

Preprints are preliminary reports that have not undergone peer review. They should not be considered conclusive, used to inform clinical practice, or referenced by the media as validated information.

Global predictions of short- to medium-term COVID-19 transmission trends : a retrospective assessment

Sangeeta Bhatia (Ss.bhatia@imperial.ac.uk) Imperial College London https://orcid.org/0000-0001-6525-101X Kris Parag Imperial College London https://orcid.org/0000-0002-7806-3605 **Jack Wardle** Imperial College London Natsuko Imai Imperial College London https://orcid.org/0000-0002-4218-9716 Sabine van Elsland Imperial College London Britta Lassmann International Society for Infectious Diseases Gina Cuomo-Dannenburg Imperial College London https://orcid.org/0000-0001-6821-0352 Elita Jauneikaite Imperial College London https://orcid.org/0000-0002-7075-6896 H. Juliette Unwin Imperial College London https://orcid.org/0000-0002-9120-4003 **Steven Riley** Imperial College **Neil Ferguson** Imperial College London https://orcid.org/0000-0002-1154-8093 **Christl Donnelly** Imperial College London https://orcid.org/0000-0002-0195-2463 Anne Cori Imperial College - Faculty of Medicine **Pierre Nouvellet** University of Sussex https://orcid.org/0000-0002-6094-5722

Article

Keywords: COVID-19, SARS-CoV-2, transmission, public health

Posted Date: August 13th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-799162/v1

License: ©) This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License

Global predictions of short- to medium-term COVID-19	
transmission trends: a retrospective assessment $_{3}$	
Sangeeta Bhatia ^{1, *} , Kris V Parag ¹ , Jack Wardle ¹ , Natsuko Imai ¹ , Sabine L Van $$\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ $	
Elsland ¹ , Britta Lassmann ² , Gina Cuomo-Dannenburg ¹ , Elita Jauneikaite ¹ , H. Juliette $\ \ \ $	
T. Unwin ¹ , Steven Riley ¹ , Neil Ferguson ¹ , Christl A Donnelly ^{1, 3} , Anne Cori ¹ , Pierre	
Nouvellet ^{1, 4}	
1 MRC Centre for Global Infectious Disease Analysis, School of Public Health, Imperial	
College London, UK.	
2 ProMED, International Society for Infectious Diseases, Brookline, MA, USA.	
3 Department of Statistics, University of Oxford, Oxford, UK.	
4 School of Life Sciences, University of Sussex, Brighton, UK.	

* s.bhatia@imperial.ac.uk

Abstract

From 8th March to 29th November 2020, we produced weekly estimates of SARS-15 CoV-2 transmissibility and forecasts of deaths due to COVID-19 for 81 countries with 16 evidence of sustained transmission. We also developed a novel heuristic to combine 17 weekly estimates of transmissibility to produce forecasts over a 4-week horizon. We 18 evaluated the robustness of the forecasts using relative error, coverage probability, and 19 comparisons with null models. During the 39-week period covered by this study, both 20 the short- and medium-term forecasts captured well the epidemic trajectory across 21 different waves of COVID-19 infections with small relative errors over the forecast 22 horizon. The model was well calibrated with 56.3% and 45.6% of the observations lying 23 in the 50% Credible Interval in 1-week and 4-week ahead forecasts respectively. We 24 could accurately characterise the overall phase of the epidemic up to 4-weeks ahead in 25 84.9% of country-days. The medium-term forecasts can be used in conjunction with 26

1

13

the short-term forecasts of COVID-19 mortality as a useful planning tool as countries continue to relax public health measures.

Introduction

As of July 2021, more than 4 million deaths have been attributed to COVID-19 with 30 over 180 million cases reported globally [1]. The scale of the current pandemic has led to 31 a widespread adoption of data-driven public health responses across the globe. Outbreak 32 analysis and real-time modelling, including short-term forecasts of future incidence, have 33 been used to inform decision making and response efforts in several past public health 34 challenges including the West African Ebola epidemic and seasonal influenza [2–11]. In 35 the current pandemic, mathematical models have helped public health officials better 36 understand the evolving epidemiology of SARS-CoV-2 [12-14] and the potential impact 37 of implementing or releasing interventions. Short-term forecasts of key indicators such 38 as mortality, hospitalisation, and hospital occupancy have played a similarly important role [15–20], contributing to planning public health interventions and allocation of crucial 40 resources [21-25]. At the same time, the unprecedented level of public interest has 41 placed epidemiological modelling under intense media scrutiny. In light of the prominent 42 role mathematical models have had in policy planning during the COVID-19 pandemic, 43 retrospective assessment of modelling outputs against later empirical data is critical to 44 assess their validity. 45

With the aim of improving situational awareness during the ongoing pandemic, since 46 the 8th March 2020 we have been reporting weekly estimates of transmissibility of 47 SARS-CoV-2 and forecasts of the daily incidence of deaths associated with COVID-19 for countries with evidence of sustained transmission [26]. We have developed three 49 models that are calibrated using the latest reported incidence of COVID-19 cases and deaths in each country. We combined the outputs from the three models into an 51 ensemble and estimates of transmissibility and forecasts were based on the ensemble 52 model. Ensemble models, which combine outputs from different models, are a powerful 53 way of incorporating the uncertainty from a range of models [27, 28] and can produce 54 more robust forecasts than individual models [28–31]. 55

Forecasts are typically produced under the assumption that the trend in growth 56

27

remain the same over the forecast horizon. This is a plausible assumption for the 1-week forecast horizon that we used for our short-term forecasts. However, this assumption is likely to be violated over a long forecast horizon leading to a rapidly increasing uncertainty as the forecast horizon grows. We have developed a novel approach relying on a simple heuristic that combines past estimates of the reproduction number, explicitly accounting for the predicted future changes in population immunity, to produce forecasts over longer time horizons.

Here we summarise the key transmission trends from our work on global short-term forecasts between 8th March to 29th November 2020. We provide a rigorous quantitative assessment of the performance of the ensemble model. We also present medium-term forecasts using our approach and retrospectively assess the performance of our method. Our results for medium-term forecasts suggest that we can accurately forecast the trajectory of COVID-19 in several countries for horizons spanning up to 4 weeks.

Results

Methods for estimating transmissibility during epidemics typically rely on the time series 71 of incident cases combined with the natural history parameters of the pathogen [32, 33]. 72 However, in the current pandemic, interpretation and comparison of estimates across 73 countries based on the number of cases was made difficult by the differences in case 74 definitions, testing regimes, and variable reporting across countries as well as over time 75 within each country [34]. We therefore developed three different models that relied on the 76 number of reported deaths to estimate COVID-19 transmissibility and to produce short-77 and medium-term ensemble forecasts of deaths (1- and 4- week ahead respectively). The 78 methods underlying the individual models are illustrated in Figs. 1a to 1c (see Methods 79 and SI Sec. 2 for details). 80

Beginning 8th March 2020, we produced weekly forecasts for every country with evidence of sustained transmission. As the pandemic rapidly spread across the world, the number of countries included in the weekly analysis grew from 3 in the first week (week beginning 8th March 2020), to 94 in the last week of analysis included in this study (week beginning 29th November 2020) (SI2 Fig. 1). Our results are based on the analysis done for 81 countries (see SI Sec. 5 for exclusion criterion) over the 39 week

Short-term forecasts and model performance

Overall, the ensemble model performed well in capturing the short-term trajectory of the epidemic in each country. Across all weeks of forecast and all countries, an average 58.7% (SD 32.4%) of the observations were in the 50% credible interval (CrI) and 89.4% (SD 21.7%) of the observations were in 95% CrI (for a breakdown by country and week of forecast see SI2 Sec. 2.5).

The MRE across all countries and all weeks was 0.4 (SD 0.4) (Fig. 3). That is, on 94 average the model forecasts were 0.4 times lower or higher than the observed incidence. 95 In most countries, the reporting of both cases and deaths through the week was variable, 96 with fewer numbers reported on some days of the week (typically, Saturday and Sunday). 97 The variability in reported deaths strongly influenced the model performance. The MRE 98 scaled linearly with the coefficient of variation (ratio of the standard deviation to the 99 mean) in the reported deaths for the week of forecasting. Thus, the error in forecasts 100 was on average similar to the variability in the reported deaths (SI2 Fig. 3). The MRE 101 of the model scaled inversely with the weekly incidence i.e. the error was relatively large 102 when the incidence was low (SI2 Fig. 3), as estimates of reproduction number when the 103 incidence is low are inherently more unstable [35]. 104

The model performance was largely consistent across epidemic phases (growing, likely 105 growing, decreasing, likely decreasing and indeterminate (SI Sec. 4)) with similar coverage 106 probability and MRE (SI2 Table 1). The slightly larger proportion of observations in 107 the 50% and 95% credible intervals for the 'indeterminate' phase and the larger MRE 108 in this phase together suggest that the model was 'under-confident' with large credible 109 intervals [36]. 110

We compared the performance of the model with that of a null no-growth model. In 111 most instances, the ensemble model outperformed the null model. In 80.9% of the weeks 112 in 'definitely decreasing' phase and 61.4% of weeks in 'definitely growing' phase, the 113 absolute error of the model was smaller than the error made by the null model (Fig. 3, 114 SI2 Sec. 2.2, SI2 Table 2). The null model performed better when the trajectory of the 115 epidemic in a country was relatively stable exhibiting little to no change over the time 116

frame of comparison. This is to be expected as the null model describes precisely this 117 stable dynamic. Indeed, in 68.1% of the weeks in the 'likely growing' phase and 67.1%118 weeks classified as 'indeterminate' phase, the absolute error of the model was larger than 119 the error made by the null model. However, the relative error of the model remained 120 small even in countries and weeks where it did not perform as well as the null model. 121 Similarly, our model performed better than a linear growth model across all phases, 122 specifically in 96.4% of the weeks in 'definitely decreasing' phase and 70.3% weeks in 123 'definitely growing' phase (SI2 Sec. 2.3, SI2 Table 2). 124

Medium-term forecasts and model performance

125

The rapidly changing situation and the various interventions deployed to stem the growth ¹²⁶ of the pandemic make forecasting at any but the shortest of time horizons extremely ¹²⁷ challenging [37]. Despite these challenges, we find that our medium-term forecasts were ¹²⁸ able to robustly capture the epidemic trajectory (Fig. 4) in all countries included in the ¹²⁹ analysis (4). ¹³⁰

Overall, the MRE remained small over a 4-week forecast horizon, with errors increasing ¹³¹ over the projection horizon (SI2 Sec. 3.1). We therefore restricted the projection horizon ¹³² to 4 weeks. The MRE across all countries in 1-week ahead forecasts was 0.4 (SD 0.3), ¹³³ increasing to 2.6 (SD 28.3) in 4-week ahead forecasts (Fig. 5, SI2 Fig. 7). The MRE for ¹³⁴ 1-week ahead forecasts was less than 1 (indicating that the magnitude of the error was ¹³⁵ smaller than the observation) in 91.1% of weeks for which we produced forecasts. The ¹³⁶ corresponding figure for 4-week ahead forecasts was 66.0% (SI2 Table 3). ¹³⁷

The proportion of observations in the 50% CrI remained consistent across the forecast ¹³⁸ horizon and varied from 56.3% (SD 33.4%) in 1-week ahead forecasts to 45.6% (SD ¹³⁹ 40.9%) in 4-week ahead forecasts (SI2 Fig. 8, SI2 Fig. 9). ¹⁴⁰

Across the 81 countries and 2210 weeks (15470 days) for which we produced both ¹⁴¹ short- and medium-term forecasts, the phase definition using the reproduction number ¹⁴² estimates from medium-term forecasts, R_t^S (SI Sec. 3 and SI Eq. 11), was consistent with ¹⁴³ that using the estimates from the short-term forecasts (R_t^{curr}) in 87.6% (13559/15470) ¹⁴⁴ of country-days (number of countries X number of days for which we produced forecasts. ¹⁴⁵ The phase definition using reproduction number estimates from medium-term forecasts ¹⁴⁶ was updated each day over the forecast horizon while the short-term forecasts assigned the 147 same phase to all days of a week.) in 1-week ahead forecasts and in 84.9% (13138/15470) 148 of country-days in 4-week ahead forecasts (Fig. 6). When the phase definitions using 149 R_t^S and R_t^{curr} were different, the medium-term estimates most frequently misclassified 150 them as a phase with greater uncertainty. For instance, in 253 weeks when the epidemic 151 phase was identified as 'definitely decreasing' using weekly estimates and incorrectly 152 characterised using medium-term estimates, it was misclassified as 'likely decreasing' 153 in 100% (253/253 weeks) of country-days. Similarly, in the misclassified weeks, when 154 the epidemic phase using weekly transmissibility estimates was 'definitely growing', the 155 medium-term classification was 'indeterminate' in 43.7% (1175/2688) and 'likely growing' 156 in 56.3% (1513/2688) of the country-days. This mis-characterisation is expected as the 157 uncertainty in estimates of R_t^S grows over the forecast horizon. Crucially, none of the 158 weeks where R_t^S misclassified the epidemic phase, the phase using R_t^{curr} indicated the 159 opposite trend (growing classified as decreasing or vice versa). This finding shows that 160 the medium-term transmissibility estimates can be used a reliable indicator of the overall 161 direction of the epidemic trajectory. 162

Discussion

Models used to forecast COVID-19 cases and/or deaths vary in complexity in the data 164 used for model calibration. More complex and/or granular models rely on multiple 165 data streams including data on hospital admissions and occupancy, testing, serological 166 surveys and data on patient clinical progression and outcomes [21]. Such complex 167 location-specific models can provide crucial insights into the ongoing epidemic and 168 inform targeted public health interventions by synthesising evidence from different data 169 streams. However, scaling such analysis to include multiple geographies is challenging 170 because of the variability in availability and reliability of local surveillance data. The 171 computational time needed to fit complex models make scaling them difficult and delays 172 the timely provision of risk estimates. 173

In addition to the variable availability of surveillance data across countries, the widescale societal and behavioural changes brought about by the pandemic impose practical constraints on utilising data that are available for multiple countries. For instance, widely available data on the changes in mobility inferred from mobile phone usage released by Google and Apple were informative of the changes in transmission in the early phase of the COVID-19 pandemic and were used in several modelling studies [38,39]. Although these data continue to be available, recent evidence suggests a decoupling of transmission and mobility in most countries [40,41]. Models that relied on such additional data [39] or assumptions about non-pharmaceutical interventions [42] could not fit the observed trajectory well as the situation continued to change over the course of the epidemic.

Efforts to model and forecast COVID-19 transmission dynamics must therefore meet 184 the challenges of a long and ongoing pandemic spread over an unprecedented scale. 185 Modelling groups around the world have attempted to meet one or both challenges with 186 various analyses conducted at a sub-national scale [43], at a national scale for a specific 187 country [22, 44-46], and for several countries across the globe [47-49]. In contrast to 188 models built for a region or country and calibrated using local data, models that aim to 189 provide a global overview must be sufficiently general to describe the epidemic trajectory 190 in a range of countries/regions using widely available data that are consistently available 191 over time. 192

We have produced short-term forecasts and estimates of transmissibility for 81¹⁹³ countries for more than 65 weeks at the time of writing implementing three simple¹⁹⁴ models that use only the time series of COVID-19 cases and deaths. We have thus¹⁹⁵ traded particularity for generality, to allow us to carry out analysis for a large number¹⁹⁶ of countries over a long period of time. As our methods make few assumptions and use¹⁹⁷ routine surveillance data, they can be easily used during any other future outbreaks.¹⁹⁸

Despite the challenges inherent in forecasting a fast-moving pandemic in the presence 199 of unprecedented public health interventions, our ensemble model was able to successfully 200 capture the short-term transmission dynamics across all countries included in the analysis 201 with small relative error in the weekly forecasts across different COVID-19 waves in 202 each country. The variable performance of our model in weeks and countries with fewer 203 deaths and/or large variability in reported deaths over weeks reflects this trade-off. 204 In the absence of more detailed data, we assumed that epidemiological parameters 205 such as the delay from onset of symptoms to death were the same across all countries 206 and throughout the period of analysis. These parameters are likely to vary over time 207 and between countries and using country-specific parameters could lead to moderate 208 improvements in the model fits and forecast performance.

Due to the variability in testing and reporting of cases across different countries and 210 over time within countries, using the reported number of cases to estimate transmissibility 211 and produce forecasts is difficult without using more complex models. For these reasons, 212 we primarily used deaths to estimate the reproduction number as we assumed that 213 reporting of COVID-19 deaths was more complete and consistent over time and across 214 different country surveillance systems. Although this assumption is unlikely to hold for 215 many countries [50-52], our methods are robust to a constant rate of under-reporting 216 over time as this would not alter the overall epidemic trends. A limitation of our work is 217 that our estimates reflect the epidemiological situation with a delay of approximately 19 218 days (the delay from an infection to a death [42]). Nevertheless, our short-term forecasts 219 and transmissibility estimates provide a valuable global overview and continuous insights 220 into the dynamic trajectory of the epidemic in different countries. They also provide 221 indirect evidence about the effectiveness of public health measures. Future research 222 could investigate integrating more data streams into the models. In addition to the 223 weekly reports that we publish, our work has also contributed to other international 224 forecasting efforts [22, 36, 44]. 225

We developed a simple heuristic to combine past estimates of transmissibility and a 226 decline in the proportion of susceptible population to produce medium-term forecasts. 227 We were able to achieve good model performance in forecasting up to 4 weeks ahead. 228 Consistent with findings from other modelling studies [22], we found that the model 229 error was unacceptably high beyond 4 weeks, suggesting that forecasting beyond this 230 horizon is difficult. Importantly, our characterisation of the epidemic phase using 231 weighted estimates of transmissibility were largely in agreement with that using short-232 term transmissibility estimates. Thus, our method was successful at capturing the 233 broad trends in transmission up to 4 weeks ahead. The medium-term forecasts can 234 therefore serve as a useful planning tool as governments around the world plan further 235 implementation or relaxation of non-pharmaceutical interventions. 236

Our method incorporates the depletion of susceptible population and hence can in ²³⁷ principle be extended to account for increasing population immunity as vaccination is ²³⁸ rolled out across the world. However, inclusion of vaccine induced immunity depends ²³⁹ on the availability of reliable data on vaccination coverage. Further, even if such data ²⁴⁰

were available, teasing apart the impact of vaccination on transmission and mortality 241 could be non-trivial. In light of these issues, it might be challenging to extend our 242 approach to rigorously assess the effect of vaccination on epidemic trajectory on a global 243 scale. However, our latest estimates of transmissibility indirectly reflect the impact of 244 vaccination on transmission, allowing for the delay from vaccination to full immunity, 245 and from infection to death. As we continue to track COVID-19 transmissibility globally, 246 any temporal changes in transmissibility would implicitly account for the changes due to 247 differential vaccination coverage. 248

Mathematical modelling and forecasting efforts have supported data-driven decision 249 making throughout this public health crisis. Our work has aimed to improve global 250 situational awareness. Using relatively simple approaches, we were able to produce 251 robust forecasts for COVID-19 in 81 countries and provide crucial and actionable insights. 252 This effort is being continued [26] as the world continues to grapple with renewed waves 253 of COVID-19 cases. 254

Methods

The instantaneous reproduction number is frequently used to quantify transmissibility. 256 It is defined as the average number of secondary cases that an individual infected at 257 time t would generate if conditions remained as they were at time t [53]. When applied 258 to the incidence of deaths (rather than cases), the instantaneous reproduction number 259 R_t^D represents the average number of secondary deaths "generated by" the death of a 260 primary case at time t. We developed three different models, each of which estimated 261 transmissibility in the recent past and produced forecasts of COVID-19 deaths (SI Sec. 2.1 262 to 2.3). We then combined the outputs of these models to build an unweighted ensemble 263 (SI Sec. 2.4). We produced short-term forecasts (i.e. 1-week ahead), for which changes 264 in the population immunity level could be ignored. Over the course of the epidemic, the 265 effect of the potential depletion of the susceptible population on the trajectory of the 266 epidemic may become more pronounced. Inherently, by estimating transmissibility in 267 real-time, our models account for any general decrease in the proportion of population 268 being susceptible. However, the forecasts produced do not account for any further 269 decrease in this proportion, which may become substantial when forecasting over a 270

2021

medium- to long-term time horizon.

We also produced medium-term forecasts (up to 4-weeks ahead) accounting for 272 the depletion of the susceptible population due to the increased levels of natural host 273 immunity. In order to estimate transmissibility for medium-term forecasts, we combined 274 past estimates of transmissibility into a single weighted estimate as follows. Let T denote 275 the last time point in the existing incidence time series of cases or deaths and let R_T^{curr} 276 refer to the most recent estimate of reproduction number for a given model. Starting 277 with the transmissibility estimates of R_T^{curr} from the ensemble model, we went back one 278 week at a time, for as long as the 95% credible interval (CrI) of $R_{T'}^{curr}$ (where T' < T) 279 overlapped the 95% CrI of R_T^{curr} . We then sampled from the posterior distribution 280 of $R_{T'}^{curr}$ in each of those weeks, with a probability that decays exponentially in the 281 past to favour the more recent estimates (Fig. 1d). Each week, the rate of decay β was 282 optimised by minimising the relative error in the predictions for the previous week. As 283 the weighted reproduction number R_t^{w} already accounts for the population immunity at 284 time t, we first estimated an effective reproduction number defined as the reproduction 285 number if the entire population were susceptible (SI Eq. 10). We then estimated the 286 reproduction number R_t^S accounting for the effect of population immunity at time t due 287 to infection (SI Eq. 11). 288

Forecast horizon

The short-term forecast horizon was set to be 1 week. We produced forecasts for the 200 week ahead (Monday to Sunday) using the latest data up to (and including) Sunday. 201 We did not model the potential changes in the population immunity levels as any such 202 change is not expected to affect the trajectory of the epidemic over this short time 203 horizon. 204

The medium-term forecasts were made over a 4-week horizon using R_t^S . Since 295 estimates of the weighted reproduction number could only be obtained once we had 296 sufficient weekly estimates to combine, medium-term forecasts were produced from 29th 297 March to 29th November 2020. 298

Epidemic Phase

Assessing model performance

The model forecasts were validated against observed deaths as these became available. 305 To quantitatively assess the performance of the model for both short- and medium-term 306 forecasts, we used the mean relative error (MRE) and the coverage probability i.e. the 307 proportion of observations that are in a given credible interval of the distribution of 308 forecasts (SI2 Sec. 2). We compared the absolute error of the model (the absolute 309 difference between the forecasts and observations averaged across simulated trajectories) 310 with the error of a model that used (i) the average of the last 10 observations as a 311 forecast for the week ahead (no growth) [54], and (ii) forecasted using a linear model 312 fitted to the last 10 observations (linear growth). 313

Data

We used the number of COVID-19 cases and deaths reported by the World Health ³¹⁵ Organisation (WHO) [1]. Any data anomalies were corrected using data published by ³¹⁶ the European Centre for Disease Prevention and Control [55], or other sources. All ³¹⁷ data used in the study are available at the github repository associated with this article ³¹⁸ (https://github.com/mrc-ide/covid19-forecasts-orderly). ³¹⁹

Code

All analysis was carried out in R version 4.0.2. The code for the analysis is available as orderly [56] project at https://github.com/mrc-ide/covid19-forecasts-orderly. DeCa model is available as an R package at https://github.com/sangeetabhatia03/ ascertainr. The accompanying R package https://github.com/mrc-ide/rincewind contains utility functions for creating the figures and processing model outputs.

11/25

320

304

Supporting information

334

S1 1. Supplementary Methods. The supplementary file contains a description of the methods and details on data, epidemiological parameters, and code.

S1 2. Supplementary Results. The supplementary file contains additional results 329 on model performance. 330

S1 3. Web tool. An interactive web-tool available at https://shiny.dide.imperial. ³³¹ ac.uk/covid19-forecasts-shiny/ presents both short- and medium-term forecasts, ³³² and reproduction number estimates for all countries included in the analysis. ³³³

Acknowledgements

The authors acknowledge funding from the MRC Centre for Global Infectious Disease 335 Analysis (reference MR/R015600/1), jointly funded by the UK Medical Research Council 336 (MRC) and the UK Foreign, Commonwealth & Development Office (FCDO), under the 337 MRC/FCDO Concordat agreement and is also part of the EDCTP2 programme supported 338 by the European Union. JW acknowledges research funding from the Wellcome Trust 339 (grant 102169/Z/13/Z). SB acknowledges funding from the Wellcome Trust (219415). 340 This study is partially funded by the National Institute for Health Research (NIHR) 341 Health Protection Research Unit in Modelling and Health Economics, a partnership 342 between Public Health England, Imperial College London and LSHTM (grant code 343 NIHR200908); and acknowledges funding from the MRC Centre for Global Infectious 344 Disease Analysis (reference MR/R015600/1), jointly funded by the UK Medical Research 345 Council (MRC) and the UK Foreign, Commonwealth & Development Office (FCDO), 346 under the MRC/FCDO Concordat agreement and is also part of the EDCTP2 programme 347 supported by the European Union. The views expressed are those of the author(s) and 348 not necessarily those of the NIHR, Public Health England or the Department of Health 349 and Social Care. 350

Contributions

S.B. developed and implemented the methods and led the analysis. K.V.P. and J.W. contributed to development of code. P.N. designed the study, developed the methods and supervised the study. C.A.D and A.C. supervised the study and helped with revising the manuscript. All authors contributed to writing the manuscript.

References

- WHO Coronavirus Disease (COVID-19) Dashboard; 2021. https://covid19. 357 who.int.
- Lipsitch M, Finelli L, Heffernan RT, Leung GM, Redd; for the 2009 H1N1 Surveil lance Group SC. Improving the evidence base for decision making during a
 pandemic: the example of 2009 influenza A/H1N1. Biosecurity and Bioterrorism:
 Biodefense Strategy, Practice, and Science. 2011;9(2):89–115.
- WHO Ebola Response Team. Ebola Virus Disease in West Africa The First
 9 Months of the Epidemic and Forward Projections. New England Journal of
 Medicine. 2014;371:1481–1495. doi:10.1056/NEJMoa1411100.
- The Ebola Outbreak Epidemiology Team. Outbreak of Ebola virus disease in the Democratic Republic of the Congo, April & May, 2018: an epidemiological study.
 The Lancet. 2018;392:213–221. doi:10.1016/S0140-6736(18)31387-4.
- 5. Nsoesie Ε, J. Peaks Mararthe Μ, Brownstein Forecasting 369 of Seasonal Influenza Epidemics. PLoS Currents. 2013;5. 370 doi:10.1371/currents.outbreaks.bb1e879a23137022ea79a8c508b030bc. 371
- Bogoch II, Brady OJ, Kraemer MU, German M, Creatore MI, Kulkarni MA, et al. Anticipating the international spread of Zika virus from Brazil. The Lancet. 2016;387(10016):335–336.
- WHO Ebola Response Team. West African Ebola Epidemic after One Year Slowing but Not Yet under Control. New England Journal of Medicine. 2015;372(6):584– 587. doi:10.1056/NEJMc1414992.

- Meltzer MI, Atkins CY, Santibanez S, Knust B, Petersen BW, Ervin ED, et al. 378
 Estimating the future number of cases in the Ebola epidemic–Liberia and Sierra 379
 Leone, 2014–2015. 2014;. 380
- Barry A, Ahuka-Mundeke S, Ali Ahmed Y, Allarangar Y, Anoko J, Archer BN, et al. Outbreak of Ebola virus disease in the Democratic Republic of the Congo, April–May, 2018: an epidemiological study. The Lancet. 2018;392(10143):213–221.
 doi:10.1016/S0140-6736(18)31387-4.
- Biggerstaff M, Johansson M, Alper D, Brooks LC, Chakraborty P, Farrow DC, et al.
 Results from the second year of a collaborative effort to forecast influenza seasons
 in the United States. Epidemics. 2018;24:26–33. doi:10.1016/j.epidem.2018.02.003.
- for the Influenza Forecasting Contest Working Group, Biggerstaff M, Alper D,
 Dredze M, Fox S, Fung ICH, et al. Results from the Centers for Disease Control and
 Prevention's predict the 2013–2014 Influenza Season Challenge. BMC Infectious
 Diseases. 2016;16(1):357. doi:10.1186/s12879-016-1669-x.
- Verity R, Okell L, Dorigatti I, Winskill P, Whittaker C, Imai N, et al. Estimates of the severity of coronavirus disease 2019: a model-based analysis. Lancet Infectious Diseases. 2020;doi:10.1016/S1473-3099(20)30243-7.
- Nishiura H, Linton NM, Akhmetzhanov AR. Serial interval of novel coronavirus (COVID-19) infections. International Journal of Infectious Diseases. 396 2020;doi:10.1016/j.ijid.2020.02.060. 397
- Ali ST, Wang L, Lau EH, Xu XK, Du Z, Wu Y, et al. Serial interval of SARS-CoV-2 was shortened over time by nonpharmaceutical interventions. Science.
 2020;369(6507):1106–1109. doi:10.1126/science.abc9004.
- Massonnaud C, Roux J, Crépey P. COVID-19: Forecasting short 401 term hospital needs in France. medRxiv. 2020; p. 2020.03.16.20036939. 402 doi:10.1101/2020.03.16.20036939. 403
- 16. Ahmadi A, Fadaei Y, Shirani M, Rahmani F. Modeling and forecasting trend of 404
 COVID-19 epidemic in Iran until May 13, 2020. Medical Journal of the Islamic 405
 Republic of Iran. 2020;34:27. doi:10.34171/mjiri.34.27. 406

- Ferstad JO, Gu A, Lee RY, Thapa I, Shin AY, Salomon JA, et al. A model to forecast regional demand for COVID-19 related hospital beds. medRxiv. 2020; p.
 2020.03.26.20044842. doi:10.1101/2020.03.26.20044842.
- Reno C, Lenzi J, Navarra A, Barelli E, Gori D, Lanza A, et al. Forecasting 410
 COVID-19-Associated Hospitalizations under Different Levels of Social Distanc-411
 ing in Lombardy and Emilia-Romagna, Northern Italy: Results from an Ex-412
 tended SEIR Compartmental Model. Journal of Clinical Medicine. 2020;9(5):1492. 413
 doi:10.3390/jcm9051492. 414
- IHME COVID-19 health service utilization forecasting team and Murray, Christopher JL. Forecasting COVID-19 impact on hospital bed-days, ICU-days, ventilatordays and deaths by US state in the next 4 months. medRxiv. 2020; p. 417 2020.03.27.20043752. doi:10.1101/2020.03.27.20043752.
- 20. Goic M, Bozanic-Leal MS, Badal M, Basso LJ. COVID-19: Short-term 419 forecast of ICU beds in times of crisis. PLOS One. 2021;16(1):e0245272. 420 doi:10.1371/journal.pone.0245272. 421
- Knock ES, Whittles LK, Lees JA, Perez-Guzman PN, Verity R, FitzJohn RG, et al. Key epidemiological drivers and impact of interventions in the 2020 SARS-CoV-2 epidemic in England. Science Translational Medicine. 2021; p. eabg4262.
 doi:10.1126/scitranslmed.abg4262.
- 22. Ray EL, Wattanachit N, Niemi J, Kanji AH, House K, Cramer EY, et al. Ensemble Forecasts of Coronavirus Disease 2019 (COVID-19) in the U.S. medRXiv.
 2020;doi:10.1101/2020.08.19.20177493.
- 23. Roosa K, Lee Y, Luo R, Kirpich A, Rothenberg R, Hyman J, et al. Real-time 429
 forecasts of the COVID-19 epidemic in China from February 5th to February 24th, 430
 2020. Infectious Disease Modelling. 2020;5:256–263. doi:10.1016/j.idm.2020.02.002. 431
- IHME COVID-19 Forecasting Team. Modeling COVID-19 scenarios for the United
 States. Nature Medicine. 2020;doi:10.1038/s41591-020-1132-9.
- 25. Chintalapudi N, Battineni G, Amenta F. COVID-19 disease outbreak forecasting of registered and recovered cases after sixty day lockdown in Italy: A data 435

driven model approach. Journal of Microbiology, Immunology and Infection. 436 2020;doi:10.1016/j.jmii.2020.04.004. 437

- 26. Short-term forecasts of COVID-19 deaths in multiple countries; 2021. https: 438 //mrc-ide.github.io/covid19-short-term-forecasts/. 439
- 27. Dormann CF, Calabrese JM, Guillera-Arroita G, Matechou E, Bahn V, Barton K,
 et al. Model averaging in ecology: a review of Bayesian, information-theoretic, and
 tactical approaches for predictive inference. Ecological Monographs. 2018;88(4):485–
 504. doi:10.1002/ecm.1309.
- Buckee CO, Johansson MA. Individual model forecasts can be misleading, but together they are useful. European Journal of Epidemiology. 2020;35(8):731–732.
- Johansson MA, Apfeldorf KM, Dobson S, Devita J, Buczak AL, Baugher B, et al. An open challenge to advance probabilistic forecasting for dengue epidemics.
 Proceedings of the National Academy of Sciences. 2019;116(48):24268-24274.
 doi:10.1073/pnas.1909865116.
- Reich NG, McGowan CJ, Yamana TK, Tushar A, Ray EL, Osthus D, 450
 et al. Accuracy of real-time multi-model ensemble forecasts for seasonal 451
 influenza in the US. PLoS Computational Biology. 2019;15(11):e1007486. 452
 doi:10.1371/journal.pcbi.1007486. 453
- Viboud C, Sun K, Gaffey R, Ajelli M, Fumanelli L, Merler S, et al. The RAPIDD 454
 Ebola forecasting challenge: Synthesis and lessons learnt. Epidemics. 2018;22:13– 455
 21. doi:10.1016/j.epidem.2017.08.002. 456
- Wallinga J, Teunis P. Different epidemic curves for severe acute respiratory syndrome reveal similar impacts of control measures. American Journal of Epidemiology. 2004;160(6):509–516.
- 33. Cori A, Ferguson NM, Fraser C, Cauchemez S. A new framework and software to
 estimate time-varying reproduction numbers during epidemics. American Journal
 of Epidemiology. 2013;178(9):1505–1512. doi:10.1093/aje/kwt133.

- 34. Pullano G, Di Domenico L, Sabbatini CE, Valdano E, Turbelin C, Debin M,
 et al. Underdetection of cases of COVID-19 in France threatens epidemic control.
 ⁴⁶⁴
 Nature. 2021;590(7844):134–139. doi:10.1038/s41586-020-03095-6.
 ⁴⁶⁵
- Parag KV. Improved estimation of time-varying reproduction numbers at low 466
 case incidence and between epidemic waves. Epidemiology; 2020. Available from: 467
 http://medrxiv.org/lookup/doi/10.1101/2020.09.14.20194589. 468
- 36. European Covid-19 Forecast Hub: Weekly reports; 2021. https:// 469 covid19forecasthub.eu/reports. 470
- 37. Castro M, Ares S, Cuesta JA, Manrubia S. The turning point and end of an expanding epidemic cannot be precisely forecast. Proceedings of the National Area Academy of Sciences. 2020;117(42):26190–26196. doi:10.1073/pnas.2007868117.
- 38. Vollmer MAC, Mishra S, Unwin HJT, Gandy A, Mellan TA, Bradley V, et al. A 474 sub-national analysis of the rate of transmission of COVID-19 in Italy. Public 475 and Global Health; 2020. Available from: http://medrxiv.org/lookup/doi/10. 476 1101/2020.05.05.20089359. 477
- Unwin HJT, Mishra S, Bradley VC, Gandy A, Mellan TA, Coupland H, et al. 478
 State-level tracking of COVID-19 in the United States. Nature Communications. 479
 2020;11(1):1–9. 480
- 40. Nouvellet P, Bhatia S, Cori A, Ainslie KEC, Baguelin M, Bhatt S, et al. Reduction
 481
 482
 483
 484
 484
 484
 485
 485
 486
 486
 486
 487
 487
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488
 488</
- Ainslie KEC, Walters CE, Fu H, Bhatia S, Wang H, Xi X, et al. Evidence of initial success for China exiting COVID-19 social distancing policy after achieving containment. Wellcome Open Research. 2020;5:81. doi:10.12688/wellcomeopenres.15843.2.
- Flaxman S, Mishra S, Gandy A, Unwin HJT, Mellan TA, Coupland H, et al. 487
 Estimating the effects of non-pharmaceutical interventions on COVID-19 in Europe. 488
 Nature. 2020;584(7820):257–261. doi:10.1038/s41586-020-2405-7. 489
- 43. Mishra S, Scott J, Zhu H, Ferguson NM, Bhatt S, Flaxman S, et al. A COVID-19 490
 Model for Local Authorities of the United Kingdom. medRxiv. 2020;. 491

44.	Bracher J, Wolffram D, Deuschel J, Goergen K, Ketterer JL, Ullrich A, et al.	492
	Short-term forecasting of COVID-19 in Germany and Poland during the second	493
	wave–a preregistered study. med Rxiv. 2020; doi:10.1101/2020.12.24.20248826.	494
45.	COVID-19 Austria; 2021. https://www.covid19model.at.	495
46.	Hawryluk I, Mellan TA, Hoeltgebaum H, Mishra S, Schnekenberg RP, Whittaker	496
	C, et al. Inference of COVID-19 epidemiological distributions from Brazilian	497
	hospital data. Journal of the Royal Society Interface. 2020;17(172):20200596.	498
47.	Abbott S, Hellewell J, Thompson RN, Sherratt K, Gibbs HP, Bosse NI, et al.	499
	Estimating the time-varying reproduction number of SARS-CoV-2 using national	500
	and subnational case counts. Wellcome Open Research. $2020;5(112):112$.	501
48.	COVID-19 LMIC Reports; 2020. https://mrc-ide.github.io/	502
	global-lmic-reports/.	503
49.	COVID-19 Daily Epidemic Forecasting: 2021. https://renkulab.shinyapps.	504
-	io/COVID-19-Epidemic-Forecasting.	505
50	Alves THE de Souze TA de Almeide Silve S Demos NA de Oliveire SV	
50.	Inderreporting of death by COVID 10 in Brazil's second most populous state	506
	Eventions in Dublic Health, 2020.8	507
	Fiontiers in Fublic fieattii. 2020;8.	508
51.	Angulo FJ, Finelli L, Swerdlow DL. Estimation of US SARS-CoV-2 infections,	509
	symptomatic infections, hospitalizations, and deaths using seroprevalence surveys.	510
	JAMA Network Open. 2021;4(1):e2033706–e2033706.	511
52.	Mwananyanda L, Gill CJ, MacLeod W, Kwenda G, Pieciak R, Mupila Z, et al.	512
	Covid-19 deaths in Africa: prospective systematic postmortem surveillance study.	513
	British Medical Journal. 2021;372.	514
53.	Fraser C. Estimating individual and household reproduction numbers in an	515
	emerging epidemic. PloS One. 2007;2(8). doi:10.1371/journal.pone.0000758.	516
54.	Gu Y. COVID-19 projections using machine learning.; 2021. https://	517
	covid19-projections.com.	518
	-	

- 55. Situation updates on COVID-19; 2021. https://www.ecdc.europa.eu/en/ 519 covid-19/situation-updates. 520
- 56. FitzJohn R, Ashton R, Hill A, Eden M, Hinsley W, Russell E, et al.. orderly: 521
 Lightweight Reproducible Reporting; 2021. Available from: https://github. 522
 com/vimc/orderly. 523

Figures



Fig 1. Schematic of the models (a) Model 1 assumes a single value for $R[T-\tau+1, T]$. The model is fitted using only the data in this window $(T - \tau + 1 \text{ to } T)$ to jointly estimate the initial incidence of deaths and $R[T - \tau + 1, T]$. For details, see SI Sec. 2.1. (b) Model 2 optimises the window over which R_t is assumed to be constant by minimising the cumulative predictive error over the entire epidemic time series. Estimates from $R[T-\tau^*+1,T]$ are used to forecast into the future, with τ^* the window of optimal length. See also SI Sec. 2.2. (c) Model 3 uses data from both cases and deaths (SI Sec. 2.3). The dashed blue curve represents the incidence of reported cases weighted by the case-report to death delay distribution, where μ is the mean delay. ρ_t is the ratio of the observed deaths and the weighted cases at time t and is analogous to an observed case fatality ratio. Forecasts of deaths are obtained by sampling from a binomial distribution using the most recent estimate of ρ_T . See also SI2 Fig. 3. (d) To obtain medium-term forecasts, we combine the most recent transmissibility estimate R_T^{curr} (shown in dark blue) with estimates of transmissibility in the previous weeks to produce a weighted estimate of transmissibility R_T^w (filled in pink) at time T. Estimates from previous weeks are combined with the most recent estimates if the 95% CrI of estimates in week k, R_{T-7k}^{curr} overlaps the 95% CrI of R_T^{curr} . Estimates for weeks where the 95% CrI overlap are shown in light purple, and where the 95% CrI do not overlap in grey. The dashed horizontal lines represent the 2.5th and 97.5th quantile of R_T^{curr} . We combine the estimates by sampling from the posterior distribution of R_{T-7k}^{curr} with probability proportional to $e^{-\beta *k}$, where β is a rate at which the probability decays as we go back in time.



Fig 2. Short-term forecasts. The short-term forecasts and observed deaths for six countries: Brazil, India, Italy, South Africa, Turkey and the United States of America (USA). For each country, the top panel shows the observed deaths in gray; the solid green line shows the median forecast. The shaded interval represents the 95% CrI of forecasts. The forecasts were produced using the most recent estimates of R_T^{curr} assuming that the transmissibility remains constant. The bottom panel for each country shows the effective reproduction number (R_T^{curr}) used to produce the forecasts. The solid green line in the bottom panel for each country is the median estimate of R_T^{curr} while the shaded region represents the 95% CrI. The dashed red line indicates the $R_T^{curr} = 1$ threshold. Note that the y-axis is different for each subfigure. See SI 3 for results for all other countries.



Fig 3. Short-term forecasts MRE and comparison with null model (a) The mean relative error of the ensemble model for each week of forecast (x-axis) and for each country (y-axis). Dark blue cells indicate weeks where the relative error of the model was greater than 2. (b) The ratio of the absolute error of the model to the absolute error of a no-growth null model that uses the average of the last 10 days as a forecast for the week ahead. Shades of green show weeks for a given country where the ratio was smaller than 1 i.e., the ensemble model error was smaller, and weeks where the ratio was greater than 1 i.e. the ensemble model error was larger than the null model error are shown in shades of red (yellow to red). Dark blue indicates weeks when the ratio was larger than 2. In order to present a representative sample, we first ranked all countries by the percentage of weeks in which ensemble model error was smaller than the null model error. We then selected every third country from the top 75 countries in this list. Results for the selected 25 countries are shown here. See SI2 Fig. 1 for the results for other countries. Ordering of countries in the figure reflects the order in the ranked list i.e. countries with the highest percentage of weeks with model error smaller than null model error are shown on the top.



Fig 4. Medium-term forecasts. The medium-term forecasts and observed deaths for six countries: Brazil, India, Italy, South Africa, Turkey and the United States of America (USA). For each country, the top panel shows the observed deaths in grey; the solid green line shows the median the 4-weeks ahead forecast. The shaded interval represents the 95% CrI of forecasts. The bottom panel for each country shows the median (solid black line) and the 95% CrI (grey shaded area) of weekly estimate of R_t^{curr} from the short-term forecasts and the median (green line) and the 95% CrI (shaded green area) of R_t^S i.e. the reproduction number accounting for depletion of susceptible population from the medium-term forecasts over a 4-week horizon (Methods). The dashed red line indicates the $R_t^S = 1$ threshold. Note that the y-axis is different for each subfigure. The forecasts were produced every week over a 4-week forecast horizon. The figure shows all non-overlapping forecasts over the course of the pandemic. See SI 3 for results for all other countries and weeks.



Fig 5. Relative error of medium-term forecasts. The mean relative error of the model in 1-week, 2-week, 3-week and 4-week ahead forecasts for each week when a forecast was made (x-axis) and for each country (y-axis). Blue cells indicate weeks where the relative error of the model was greater than 2. For ease of presentation, results are shown for the same 25 countries as Fig. 2. See SI2 Sec. 2 for the results for other countries.



Fig 6. Characterisation of the epidemic phase. For a given classification of epidemic phase using the weekly estimates of the reproduction number from the short-term forecasts(x-axis), the figures in the cell show the percentage of days for which the characterisation was consistent using the medium-term reproduction number estimates (show on the y-axis)

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- globalforecastsSI1.pdf
- globalforecastsSI2.pdf
- globalforecastsSI1.pdf
- globalforecastsSI2.pdf
- nrsoftwarepolicy.pdf
- nrreportingsummary.pdf