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Long-term forecasting of the COVID-19 epidemic

Dynamic Causal Modelling, UCL, UK

- The next peak of about 1.8% should be in summer (12 July 2023). The effective population immunity should remain at 96% for the foreseeable future. This suggests an endemic equilibrium with seasonal fluctuations in prevalence between 0.8% and 1.8% over the next year.
- The real-time estimate of the R-number is 0.81 (credible interval from 0.65 to 0.98) on 7 April 2023 and should continue to fall.
- The 7-day average of daily (certified) deaths may peak at just over 100 per day this week and then fall to around 50 per day for the remainder of the year.
- These predictions include prevalence-dependent behavioural changes: contact rates should continue to fluctuate between 85% and 95% of prepandemic rates, for the foreseeable future.
- The basic reproduction number R₀ is estimated to be 8.1. This reflects an 61% increase in transmission risk, relative to the average since 1 Jan 2020. This estimate includes viral mutation and seasonality effects.
- · Current estimates of the vaccination efficacy are:

preventing infection: 21.2% (CI 18.6 to 23.8)

preventing transmission following infection 63.9% (CI 62.3 to 65.4)

preventing serious illness when symptomatic (age 15-34) 74.3% (Cl 73.7 to 75.0)

preventing serious illness when symptomatic (age 35-70) 61.2% (CI 60.2 to 62.2)

preventing fatality when seriously ill 83.8% (CI 82.9 to 84.7)

• The corresponding cumulative (vaccinated vs. unvaccinated) risks are:

relative risk of infection 78.8%

relative risk of mild illness 48.4%

relative risk of severe illness 16.6%

relative risk of fatality 2.7%

For example, full vaccination reduces the risk of being infected and subsequently developing a severe illness to 16.6% of the risk prior to vaccination. The risk then increases slowly until the next vaccination.

- The average serial interval is 4.2 days
- · The average period between exposure and becoming infectious is 2.4 days
- · The average asymptomatic period is currently 2.4 days

• (Symptomatic) IFR: likelihood of dying from COVID-19 (%)

Age group		0-14	15-34	35-69	70+	
recent vaccination:		0.000	0.000	0.000	0.007	
no vaccine protection:		0.000	0.000	0.004	0.084	
For reference, the probability of dying from flu is about						
Age group	5-17	18-49	50-64		65+	
	0.000	0.002	0.009		0.022	

These headlines furnish a national picture of the epidemic and obscure regional variations. A more detailed picture — at the level of lower tier local authorities — can be found in the accompanying local dashboard. Please see the national dashboard for the data fits upon which the long-term forecasts are based and accompanying confidence intervals.

These long-term forecasts are based upon a dynamic causal model (DCM) of viral transmission and mitigated responses. This particular (age-stratified) model is equipped with a vaccination state that affords immunity of various kinds (i.e., reduces the risk of infection, transmission, developing serious illness and dying when seriously ill).

The DCM generates various data that quantify the progression of the epidemic, including the number of reported (first) vaccinations. These data are used to estimate model parameters controlling contact rates, transmission risk and periods of infectiousness using standard variational procedures. Crucially, these variables are themselves time-dependent and depend upon mitigating responses, modelled as the (prevalence-dependent) probability of moving from low to high contact rate locations (e.g., from home to

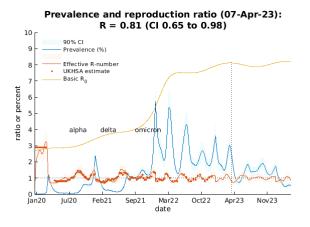
the workplace). The data include daily positive tests, reported deaths within 28 days of a positive PCR test, certified deaths disaggregated by age and place of death, hospital admissions, contact rate proxies, such as car use and Google mobility data, and so on.

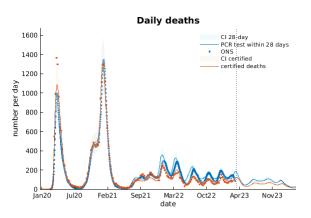
Much like weather forecasts, the ensuing predictions should not be overinterpreted because there is an inherent (although quantified) uncertainty about underlying epidemiological and sociobehavioural variables. These reports are released on a weekly basis so that people can see how the predictions change — and uncertainty resolves — as time progresses and more data are assimilated.

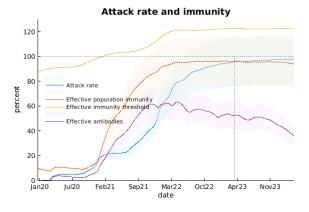
Because the DCM combines an epidemiological model with an agent-based behavioural (and testing) model, it can predict mitigating responses to changes in community transmission. These predictions are the **most likely outcomes** given population responses to date. In other words, DCM does not rely on information about future scenarios (e.g., roadmaps for unlocking). This complements — and contrasts with — SPI-M projections of **reasonable worst-case scenarios** that assume a particular schedule of interventions and epidemiological parameters. Generally, the most likely predictions of mitigated responses — i.e., what is likely to happen — are more optimistic than worst-case projections of unmitigated responses—i.e., what could happen.

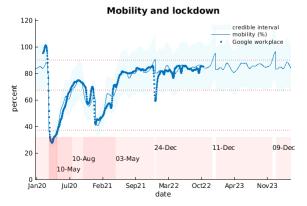
Summary graphs

In the summary graphs below, the lines and shaded intervals correspond to predictions and 90% credible intervals, while the dots are (smoothed) data upon which the estimates are based.









Prevalence and reproduction ratio: this panel provides a forecast of (i) the prevalence of infection and (ii) the reproduction ratio or R-number (blue and orange lines, respectively) with their accompanying confidence intervals (shaded areas). These forecasts are based upon parameters estimated from data up until the reporting date (the vertical line). The data include GOV.UK estimates of the R-number, which are shown for comparison with the DCM estimates. The **basic reproduction ratio** (R0 – yellow line) can be read as the R-number in the absence of any mitigating reductions in contact rates. This reflects fluctuations in transmission risk due to seasonality effects and viral mutations. The 'alpha', 'delta' and 'omicron' indicate when the corresponding variants were introduced to the UK. The current DCM does not model the multiple strains or variants separately: it assumes viral spread can be approximated with a mixture, whose epidemiological parameters (e.g., transmission risk) change smoothly over time.

The DCM estimate of the effective R-number is based upon a generative model (i.e., a real-time estimate using data assimilation). The corresponding consensus estimates from the UKHSA are based upon retrospective (e.g., Bayesian regression) analysis of recent data and are therefore treated as a lagged estimator. The black dots correspond to the UKHSA estimates moved backwards in time by 16 days from their date of reporting.

Attack rate and immunity: this panel shows long-term forecasts of attack rate, population or herd immunity and the percentage of people who have seroconverted following vaccination (in blue, red and purple, respectively). In addition, an estimate of the effective immunity threshold is provided under simplifying (SIR) assumptions (yellow lines).

The attack rate corresponds to the number of people who have been infected since the onset of the outbreak (blue line). This can be supplemented with a small proportion of the population that have pre-existing immunity (e.g., mucosal immunity or cross immunoreactivity with other SARS viruses). The combination underwrites herd or population immunity, read here as the proportion of people with seropositive or seronegative (e.g., T cell) immunity.

The effective immunity threshold is based upon the effective reproduction ratio under pre-pandemic contact rates, adjusted for vaccine efficacy. The reproduction ratio corresponds to the product of the contact rate, transmission risk and mean infectious period. Note that the effective immunity threshold fluctuates. This reflects the fact that transmission risk changes with time. In this model, transmission risk is modelled as a seasonal fluctuation multiplied by smooth (increasing) function of time. A fluctuating

transmission risk accommodates changes in transmissibility (e.g., due to viral evolution) that is contextualised by seasonal variations in transmission (e.g., due to changes in temperature, humidity, socialising outdoors and the propensity for aerosol transmission).

Based upon the changes in testing, death rate and other data, one can estimate the efficacy of vaccination at several points in the chain from infection to death. This DCM is equipped with two infection states: infected (i.e., exposed) versus infectious (i.e., contagious) and two clinical states: mildly symptomatic versus systemic illness. The efficacy of vaccination is modelled in terms of the relative risk of (i) becoming infected, (ii) becoming infectious after exposure to the virus (i.e., being able to transmit the virus), (iii) becoming seriously ill when mildly symptomatic, and (iv) dying when seriously ill. The relative risk of becoming infected subsumes contact rates and transmission risk. These relative risks can be expressed in terms of conditional efficacies or composed to evaluate the cumulative risk of morbidity and mortality, relative to not being vaccinated. Note that parameterising vaccine efficacy in this way means that a loss of protection is modelled by moving—with a small probability—to a non-vaccinated state (c.f., waning immunity).

Daily deaths: this panel shows fatality rates as assessed by patients who died within 28 days of positive PCR test and people who died from certified COVID-19. The former represents an underestimate of COVID-related mortality, where the degree of underestimation depends upon testing rates. The discrepancy is modelled by evaluating the probability of succumbing to COVID-19 and having had a positive PCR test within 28 days.

Mobility and lockdown: a long-term forecast of mitigating (i.e., protective) sociobehavioural responses, based upon car use as quantified by the Department of Transport and—in this graph — Google workplace and retail activity. These measures of mobility are expressed in terms of the percentage of pre-pandemic levels. The expected mobility has been thresholded at three levels to illustrate different levels of lockdown. The dates on the lower (graded pink) bar annotate a transition from a more protective level of mobility to a less protective level. Forecasts of mobility are based upon underlying contact rates that depend upon the prevalence of infection, which are then modulated with a smooth function of time.

This dynamic causal model includes age-stratification into four groups (below the age of 15, between 15 and 35, between 35 and 70, and over 70 years of age). The contact rates within and between the groups (for high and low contact rate locations) are estimated from the data, under mildly informative lognormal shrinkage priors. Please see the following technical report for further technical details.

Changes since last report:

· Linear increase in T-Cell immunity half-life over time.

Software note: The figures in this report can be reproduced using annotated (MATLAB) code available as part of the free and open source academic software SPM (https://www.fil.ion.ucl.ac.uk/spm/), released under the terms of the GNU General Public License version 2 or later. The routines are called by a demonstration script that can be invoked by typing >> DEM_COVID_UK4 at the MATLAB prompt.

Data sources: (also available as CSV files)

https://coronavirus.data.gov.uk

https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/datasets/coronaviruscovid19infectionsurveydata https://covid.ioinzoe.com/data#levels-over-time

https://www.gov.uk/guidance/the-r-number-in-the-uk#contents

https://www.gov.uk/government/statistics/transport-use-during-the-coronavirus-covid-19-pandemic https://www.google.com/covid19/mobility/

Peer-reviewed references [1-6] and archival papers [7-14]

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- 13. Friston, K.J., et al., Viral mutation, contact rates and testing: a DCM study of fluctuations. medRxiv, 2021: p. 2021.01.10.21249520.

14. Friston, K.J., et al., Tracking and tracing in the UK: a dynamic causal modelling study. arXiv, 2020

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