www.covid-arg.com

Friday Report: Issue 42

By: John Roberts & Dan Ryan

COVID-19 Actuaries Response Group – Learn. Share. Educate. Influence.

COVID-19 is still one of the hottest topics for scientific papers and articles. The COVID-19 Actuaries Response Group provides a regular Friday update with a summary of key papers and articles.

Vaccination

More Evidence of Transmission Benefits

Two papers published in the last week have highlighted the additional benefit that vaccination brings in terms of reducing onward transmission from an infected person to others. First published was the Oxford study (link) on the effect of vaccination on infection levels.

The primary finding of this study is that the risk of infection is reduced by around 65% after one dose and 70% after two doses of either vaccine. This is consistent with other data, although the confirmation in relation to the now widespread B.1.1.7 variant is reassuring, along with the fact that the results are in relation to a wide post-vaccinated population sample of around 1.3m.

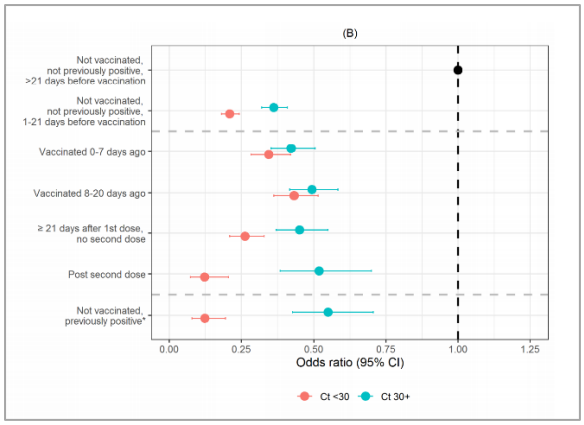
However, of more interest is the fact that the incidence of high viral shedding infectivity, (i.e. a Ct result of under 30) showed a much more substantial decrease of 74% after one dose and 88% after the second dose. This provides good theoretical evidence to suggest that transmission effects may be greater than the headline efficacy figures would suggest.

Supplementary Table 5: Odds ratios (95% confidence intervals) from adjusted models

Model	Not vaccinated, no prior positive, 1-21 days before vaccination		Vaccinated 0-7 days ago			Vaccinated 8-20 days ago			≥21 days after 1st dose, no second dose			Post second dose			Not vaccinated, previously positive		
	OR (95% CI)	P-value vs baseline	OR (95% CI)	P-value vs baseline	Pairwise p-value	OR (95% CI)	P-value vs baseline	Pairwise p-value	OR (95% CI)	P-value vs baseline	Pairwise p-value	OR (95% CI)	P-value vs baseline	Pairwise p-value	OR (95% CI)	P-value vs baseline	Pairwise p-value
All positives																	
Unadjusted	0.34 (0.31, 0.37)	<0.001	0.36 (0.32, 0.40)	<0.001	0.995	0.36 (0.33, 0.40)	<0.001	1.000	0.18 (0.16, 0.20)	<0.001	<0.001	0.22 (0.17, 0.27)	<0.001	0.716	0.31 (0.25, 0.38)	<0.001	0.258
Adjusted	0.28 (0.26, 0.31)	<0.001	0.38 (0.33, 0.43)	<0.001	0.001	0.45 (0.40, 0.51)	<0.001	0.204	0.35 (0.30, 0.40)	<0.001	0.004	0.30 (0.23, 0.38)	<0.001	0.889	0.30 (0.24, 0.38)	<0.001	1.000
Ct value																	
Mean Ct <30	0.21 (0.18, 0.24)	<0.001	0.35 (0.28, 0.42)	<0.001	<0.001	0.43 (0.36, 0.51)	<0.001	0.408	0.26 (0.21, 0.33)	<0.001	<0.001	0.12 (0.07, 0.20)	<0.001	0.050	0.12 (0.08, 0.19)	<0.001	1.000
Mean Ct ≥30	0.36 (0.32, 0.41)	<0.001	0.42 (0.35, 0.50)	<0.001	0.671	0.49 (0.42, 0.58)	<0.001	0.731	0.45 (0.37, 0.55)	<0.001	0.965	0.52 (0.38, 0.70)	<0.001	0.962	0.55 (0.43, 0.71)	<0.001	1.000
Symptoms																	
Symptoms reported	0.25 (0.21, 0.28)	<0.001	0.30 (0.25, 0.37)	<0.001	0.521	0.41 (0.34, 0.49)	<0.001	0.122	0.28 (0.22, 0.35)	<0.001	0.012	0.10 (0.06, 0.18)	<0.001	0.012	0.13 (0.08, 0.21)	<0.001	0.992
No symptoms reported	0.32 (0.29, 0.37)	<0.001	0.47 (0.39, 0.56)	<0.001	0.002	0.52 (0.44, 0.61)	<0.001	0.961	0.43 (0.36, 0.53)	<0.001	0.539	0.51 (0.38, 0.69)	<0.001	0.902	0.51 (0.40, 0.65)	<0.001	1.000
Ct pattern																	
ORF1ab+N+S, N+S, ORF1ab+S	0.23 (0.18, 0.30)	<0.001	0.28 (0.18, 0.44)	<0.001	0.984	0.32 (0.20, 0.50)	<0.001	1.000	0.29 (0.16, 0.51)	<0.001	1.000	0.18 (0.06, 0.51)	0.001	0.975	0.25 (0.13, 0.47)	<0.001	0.998
OR+N	0.29 (0.26, 0.33)	<0.001	0.36 (0.30, 0.43)	<0.001	0.335	0.45 (0.38, 0.53)	<0.001	0.335	0.34 (0.28, 0.41)	<0.001	0.084	0.22 (0.15, 0.32)	<0.001	0.225	0.21 (0.14, 0.29)	<0.001	1.000

*Pairwise p-value: p-value testing whether the OR for each vaccine status group is different to the vaccine status group below; so respectively "Vaccinated 0 to 7 days ago, 1 dose" vs "Not vaccinated, no prior positive, 1-21 days before vaccination", "Vaccinated 8 to 20 days ago" vs "Vaccinated 0 to 7 days ago", "Vaccinated ≥ 21 days ago, 2 doses" vs "Vaccinated ≥ 21 days ago, 1 dose" and "Not vaccinated, but swab or antibody positive >45 days ago" vs "Vaccinated ≥ 21 days ago, 2 doses".

Note: all odds ratios are compared to the reference category of **Not vaccinated, no prior positive (>45 days ago), >21 days before vaccination.** Results shown graphically in **Figure 3**.

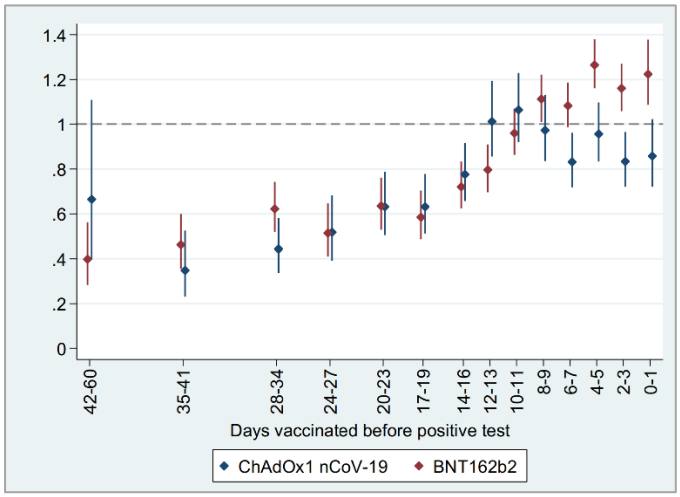


This was followed by a large population study (link) by Public Health England which tracked actual cases in households – in particular, whether the first infection resulted in further infections within the same domestic unit.

This showed a clear reduction in secondary infections with a headline reduction of just under 50%. There was little evidence of age being a material factor in either the initial case, or in those subsequently infected. Additionally, the effect emerged after around 14 days post vaccination, which is a similar time period as expected for protection against primary infection.

An additional point made by the Deputy CMO in the press briefing to publicise the results is that some infections classified as secondary are likely to have been acquired directly from the same source as the primary one, meaning that it is likely that the results understate the true level of benefit.

This second study, which included nearly 1m infections in its dataset, thus provides robust evidence that the lower viral shedding loads seen in the first study do indeed translate into reduced transmission in the home environment, a point reinforced in the press briefing as part of the messaging that getting vaccinated protects those you live with, not just yourself.

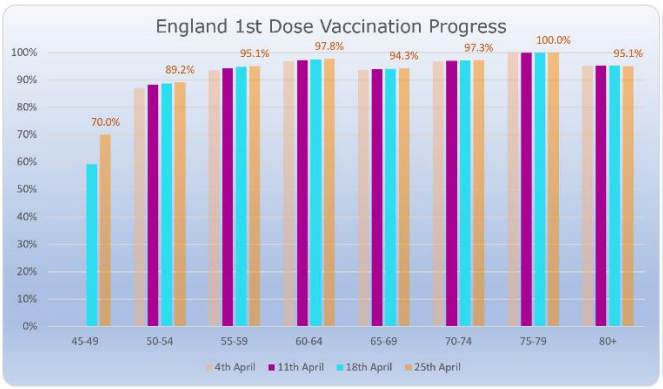


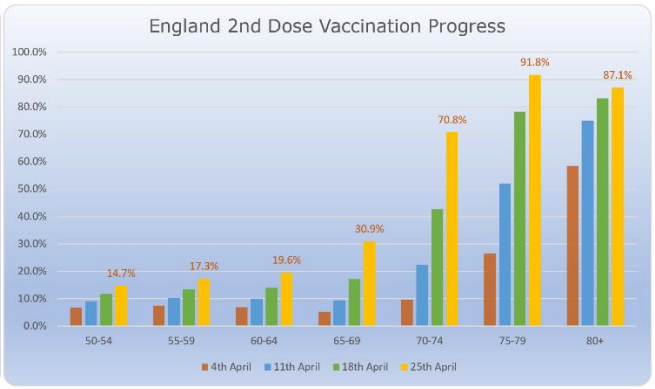
Vaccine Roll-out (link)

The weekly analysis of vaccinations in England shows that whilst in general very high take-up has been seen over age 50, there are clear signs of it dropping slightly as we progress down the age bands. In particular, the 50-54 cohort has levelled off at 89%, and there is a clear trend now we are vaccinating those below age 65. This reduction is consistent with several surveys of age-related hesitancy, although the level of fall in just one age band is a little worrying.

Meanwhile, the main focus during April has been on second doses, and we are getting second dose take-up rates in the region of 90% for those above 75 (by which we mean those presenting for a second dose as a proportion of those receiving a first jab).

With this data already being four days old, we can safely say that the vast majority of those above aged 70 (which are the age bands for Groups 1 to 4) will have had an opportunity to have their second dose by the end of April. Along with care home residents, these represented around 88% of deaths in earlier waves.





Ethnic differences in vaccine hesitancy

There has been much investigation in differences in vaccine "hesitancy" around the world, looking at differences by age, sex, ethnicity, occupation, roles and political attitudes. A further study (link) of 12,000 from the UK-REACH nationwide prospective cohort (link) has specifically examined differences in vaccine hesitancy in UK healthcare workers. This study was able to consider more granular ethnic categories and healthcare roles than many previous studies. Age, lack of influenza vaccine last year (aOR 0.96 95% CI 1.75-2.17) and being female (aOR 1.42 95% CI 1.24-1.62) were found to be the strongest predictors, but no differences were found for different occupational roles after adjustment for interactions.

Variable	OR (95% CI)	p value	aOR (95% CI)	p value
Age (for each decade increase)	0·71 (0·69 - 0·74)	<0·001	0·74 (0·70 - 0·78)	<0·001
Sex				
Male	Ref	-	Ref	-
Female	1·72 (1·54 - 1·93)	<0·001	1·42 (1·24 - 1·62)	<0·001
Ethnicity				
White - British	Ref	-	Ref	-
White - Irish	1·18 (0·85 - 1·63)	0·32	1·39 (0·96 - 2·02)	0·08
White - Other/Gypsy Irish Traveller	1·55 (1·33 - 1·81)	<0·001	1·48 (1·19 - 1·84)	0·001
Asian - Indian	0·92 (0·79 - 1·07)	0·28	0·76 (0·57 - 1·02)	0·07
Asian - Pakistani	1·62 (1·26 - 2·08)	<0·001	1·18 (0·78 - 1·79)	0·42
Asian - Bangladeshi	0·87 (0·47 - 1·59)	0·64	0·66 (0·32 - 1·39)	0·28
Asian - Chinese	1·80 (1·37 - 2·36)	<0·001	1·59 (1·15 - 2·20)	0·005
Asian - Other	1·23 (0·96 - 1·57)	0·1	1·03 (0·74 - 1·42)	0·86
Black - African	2·09 (1·66 - 2·63)	<0·001	2·05 (1·49 - 2·82)	<0·001
Black - Caribbean	3·91 (2·62 - 5·84)	<0·001	3·37 (2·11 - 5·37)	<0·001
Black - Other	2·45 (0·99 - 6·06)	0·05	1·63 (0·52 - 5·06)	0·40
Mixed - White & Black Caribbean	2·23 (1·43 - 3·48)	<0·001	1·62 (0·98 - 2·67)	0·06
Mixed - White & Black African	1·35 (0·78 - 2·33)	0·28	1·36 (0·87 - 2·11)	0·33
Mixed - White & Asian	0·95 (0·66 - 1·38)	0·79	0·89 (0·59 - 1·36)	0·60
Mixed - Other	1·29 (0·88 - 1·90)	0·19	1·35 (0·87 - 2·11)	0·18
Arab	1·43 (0·96 - 2·13)	0·08	1·65 (0·97 - 2·82)	0·07
Other	1·36 (0·91 - 2·03)	0·13	1·41 (0·88 - 2·26)	0·15
Job role				
Doctors and medical support	Ref	-	Ref	-
Nurses, NAs, Midwives	1·75 (1·54 - 2·00)	<0·001	1·17 (0·98 - 1·41)	0·08
Allied Health Professionals	1·39 (1·24 - 1·57)	<0·001	0·99 (0·85 - 1·16)	0·90
Dental	1·21 (0·99 - 1·48)	0·06	0·75 (0·58 - 0·97)	0·03
Admin / estates / other	1·25 (0·99 - 1·57)	0·06	1·03 (0·78 - 1·36)	0·86

Clinical and medical news

Prevalence of Variants in the UK

With the successful roll-out of the vaccination programme continuing apace, and much lower levels of prevalence now in the UK, much of the focus and concern is on the possibility that variants will take hold which are either more successful in evading the vaccine or in more rapid transmission (or both).

The government regularly publishes details (link) of totals of all new variants, and this week has seen a noticeable increase in variants from India, with two new ones identified. In total, B.1.617 variants have tripled within a week, with a five-fold increase in just a fortnight, and represented 3% of all cases sequenced in the most recent period.

Variants of Concern or Under Investigation

Variant	Discovered	April 14th	April 21st			April 28th		
		Total	New	Prop'n	Total	New	Prop'n	Total
B.1.1.7	UK (Kent)	209,492	8,677	97.89%	218,169	8,466	95.70%	226,635
B.1.351	South Africa	600	70	0.79%	670	67	0.76%	737
P.2	Brazil	59	-	0.00%	59	1	0.01%	60
B.1.617	**India**	**77**	**55**	**0.62%**	**132**	**61**	**0.69%**	**193**
B.1.617.2	**India**					**202**	**2.28%**	**202**
B.1.617.3	**India**					**5**	**0.06%**	**5**
P.1	Japan	40	20	0.23%	60	22	0.25%	82
B.1.1.318	TBC	113	31	0.35%	144	6	0.07%	150
B.1.525	UK	361	11	0.12%	372	16	0.18%	388
Other		129	-	0.00%	129	-	0.00%	129
Total		**210871**	**8,864**		**219,735**	**8,846**		**228,581**

Budesonide

A recent trial reported in the BMJ (link) regarding the use of Budesonide, an anti-inflammatory drug typically used to treat those with Crohn's Disease, reported a 3 day improvement in self-reported recovery from COVID-19. 32% of those taking the drug reported recovery within 14 days from the randomisation, compared with 22% for those in the control group.

Whilst there was also a modest fall in those admitted to hospital, the researchers' view was that this was not significant enough to draw any firm conclusion.

Nevertheless, as a result of this, the NHS has recently issued guidance (link) permitting its use for those over 65 or over 50 with a relevant comorbidity.

Launch of Antiviral Taskforce

The UK Government launched an Antiviral Taskforce on 20 April (link) with the aim of finding at least two effective antiviral treatments by autumn that could be delivered at home. The taskforce will be modelled on the vaccine and therapeutics taskforces which brought together academia, industry and government with clear budget and government approval processes. Success is dependent on the number of drugs currently undergoing clinical trials. The contrast with the vaccine pipeline is quite stark if we consider the situation 6 months before roll-out. In July 2020, there were 19 vaccines in human trials (link). 6 months prior to autumn (just), the list of antivirals in development is much shorter and less promising (link):

- Remdesivir – found to be ineffective against original targets hepatitis C, respiratory syncytial virus and Ebola, it was re-evaluated under the WHO's Solidarity trial involving 11,000 patients across 30 countries. No discernible benefit on mortality or duration in hospital. Further research now focusing on earlier administration.
- Favipiravir – Available in Japan since 2014 for treating influenza viruses. Added to the UK Principle trial that is investigating treatments that prevent hospital admissions and reduce recovery time.
- Molnupiravir – Currently in phase 3 trials by Merck to determine whether it prevents admissions and support recovery at home.
- PF-07321332 – Started phase 1 trials in March 2021 by Pfizer

Shift work and severe COVID-19

Studies from the ONS have investigated the likelihood of COVID infection and death in different occupational groups (link). A further study has focused on shift workers inside and outside of healthcare, and whether irregular work patterns have a detrimental effect. The study, with 235,685 participants, found that shift workers in healthcare had a 7.56x increased risk of severe COVID, whereas being a shift worker or working in healthcare was associated individually with a doubling of the risk. Possible contributory factors included greater patient-facing roles for shift workers, and greater representation in healthcare shift workers from men and ethnic minorities. However, the researchers did not control for ethnic group, place of residence or deprivation.

Comparisons between those under and over retirement age suggest the key factor is likely to be increased exposure to the virus. However, shift work is also associated with disruption to behaviours and biochemical rhythms that have been associated with chronic inflammation and higher risk of cardiovascular disease.

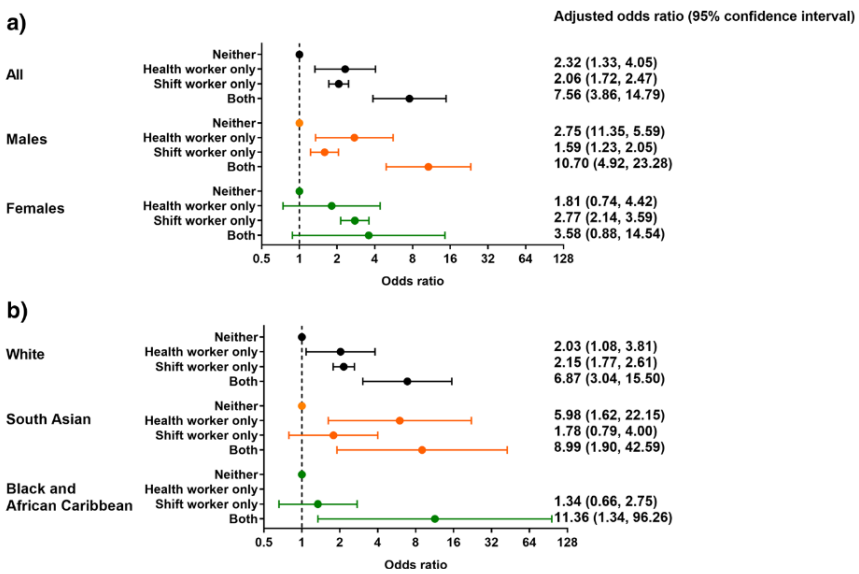


Fig. 1 Employment status and odds of severe COVID-19 stratified by **a**) sex, **b**) ethnicity. Model (**a**) adjusted for: age, sex (for all participants), Townsend score, BMI, cancer (self-reported, past or current at time of data collection), co-morbidities (yes/no), smoking status (never, previous current) and ethnicity. Model (**b**) same as model (**a**) except without ethnicity

Data

ONS Antibody data

The last ONS update on antibodies showed a levelling off across the population, and a reduction for higher ages, presumably due to a waning awaiting the second vaccination. With those second doses now proceeding apace, the latest data (link) shows a resumption in the overall level, and more specifically in those older ages.

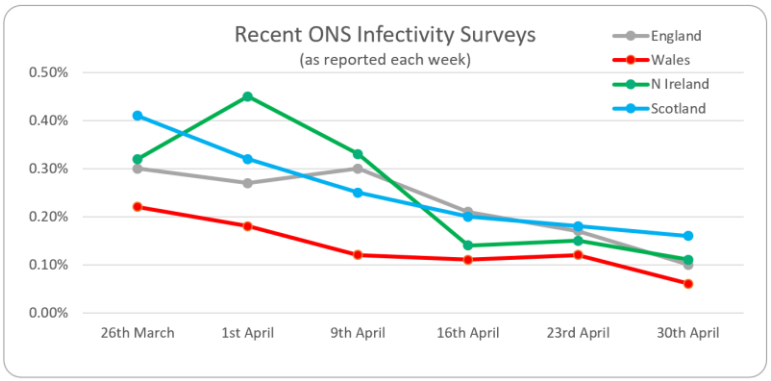
In England the overall level has increased from 55% to 68%, with slightly lower levels elsewhere. It should also be noted that this data is for the week ending April 11th. The effect of vaccinations since then (and indeed the time taken for immunity to develop) means that the current position will be even better than shown here.

The "wobble" seen in the older age groups is clear in the graphs below, along with the subsequent increases referred to above.

ONS Infection Survey (link)

This week has seen big reductions in the ONS estimates of infectivity levels, with England down by over 40% and Wales even more at a 50% reduction, to remain the lowest in the UK.

We're also seeing some individual regions and age groups round to 0.0% in the report, with the South West now at 0.03% and Over 70s at 0.04%. These are very encouraging results given the easing of restrictions to date.



	Report Issued					
	26th March	1st April	9th April	16th April	23rd April	30th April
England	0.30%	0.27%	0.30%	0.21%	0.17%	0.10%
Wales	0.22%	0.18%	0.12%	0.11%	0.12%	0.06%
N Ireland	0.32%	0.45%	0.33%	0.14%	0.15%	0.11%
Scotland	0.41%	0.32%	0.25%	0.20%	0.18%	0.16%

"R" Estimate (link)

Over the last two weeks SAGE's estimate of R for England has risen from (0.7 to 1.0), firstly to (0.8 to 1.0), and today to (0.8 to 1.1). The regional estimates are shown below.

These estimates would appear to be at odds with the ONS data on infections reported above, and show the difficulty that there is in coming up with a reliable R when prevalence is at much lower levels in the community.

Latest by NHS England regions

These are the latest R and growth rate estimates by NHS England regions.

Region	R	Growth rate % per day
England	0.8 to 1.1	-4 to -1
East of England	0.8 to 1.1	-4 to 1
London	0.8 to 1.1	-5 to 0
Midlands	0.7 to 1.0	-4 to -1
North East and Yorkshire	0.8 to 1.0	-7 to -2
North West	0.7 to 0.9	-6 to -2
South East	0.8 to 1.0	-4 to 0
South West	0.8 to 1.2	-4 to 1

Other

Elimination or Mitigation

Commentary published in The Lancet (link) compares the success of the two strategies in terms of both mortality and economic impact. Countries following an elimination strategy are Australia, New Zealand, Japan, Iceland and South Korea, whereas no less than 32 countries are considered for the mitigation approach.

The conclusion drawn is that those countries which adopted an elimination strategy fared better both in terms of mortality and in term of minimising GDP impact. Whilst it hard to argue with this conclusion in respect of mortality, relevant factors that may have affected the ability of a country to adopt a successful elimination strategy are not discussed, which may be regarded as a weakness of the conclusion. It's of note that all five countries are (or in South Korea's case is effectively) islands, with more ability to reduce border transits effectively than, say, mainland Europe.

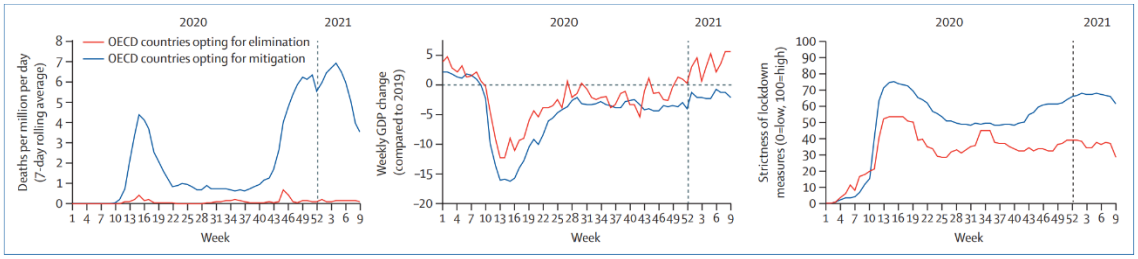
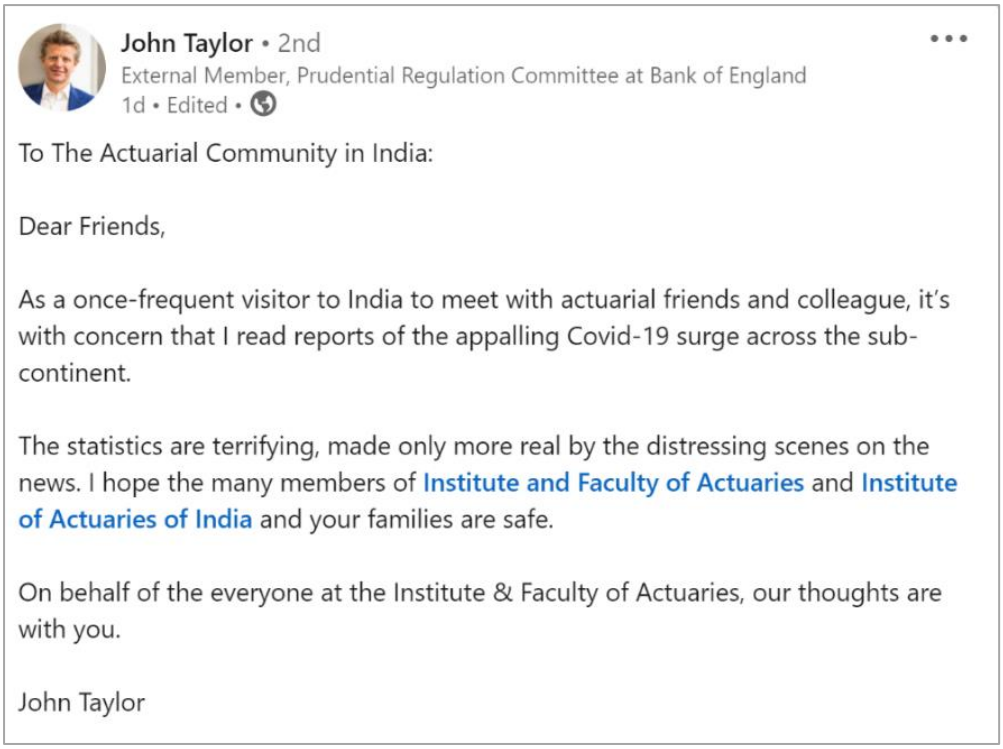


Figure: **COVID-19 deaths, GDP growth, and strictness of lockdown measures for OECD countries choosing SARS-CoV-2 elimination versus mitigation**
OECD countries opting for elimination are Australia, Iceland, Japan, New Zealand, and South Korea. OECD countries opting for mitigation are Austria, Belgium, Canada, Chile, Colombia, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Israel, Italy, Latvia, Lithuania, Luxembourg, Mexico, the Netherlands, Norway, Poland, Portugal, Slovakia, Slovenia, Spain, Sweden, Switzerland, Turkey, the UK, and the USA. Data on strictness of lockdown measures are from Oxford COVID-19 government response tracker.[2] Data on COVID-19 deaths are from Our World in Data.[3] Data on GDP growth are from OECD Weekly Tracker of economic activity.[4] GDP=gross domestic product. OECD=Organisation for Economic Co-operation and Development.

And Finally…

It would be remiss of us not to acknowledge the current situation in India, and the desperate plight that the population is suffering as a consequence of the high prevalence of the virus and overloaded health care systems. As actuaries, we rely very heavily on data to inform and advise, but the one thing that appears very clear is that the figures coming out from the country, distressing as they are, are likely to be just a fraction of the true situation.

Our profession is well represented in India, and Indian actuaries, both historically and today, enjoy a close relationship with the IFoA. Our Immediate Past-President John Taylor recently sent a message to the actuarial community there, reproduced below, and we can do no better than echo his words and thoughts at this concerning time for all in the Indian subcontinent.



John Taylor • 2nd
External Member, Prudential Regulation Committee at Bank of England
1d • Edited •

To The Actuarial Community in India:

Dear Friends,

As a once-frequent visitor to India to meet with actuarial friends and colleague, it's with concern that I read reports of the appalling Covid-19 surge across the sub-continent.

The statistics are terrifying, made only more real by the distressing scenes on the news. I hope the many members of **Institute and Faculty of Actuaries** and **Institute of Actuaries of India** and your families are safe.

On behalf of the everyone at the Institute & Faculty of Actuaries, our thoughts are with you.

John Taylor

30 April 2021