Friday Report: Issue 37

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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.

Vaccines

Oxford AstraZeneca Single Dose Efficiency (link)

A pre-print recently published in *The Lancet* appears to validate, in several ways, the JCVI's decision to delay administering the second dose until twelve weeks. With more data now available, this paper also provides an update on the original efficacy results published in early December.

Efficacy, in terms of prevention of symptomatic infection is put at 76% after a single dose. Moreover, efficacy is considered not to wane during the 12 week period, consistent with constant levels of antibodies (although there is some evidence that it may do after this period). This alone suggests that the decision to delay second doses, in order to expand vaccine coverage more quickly, is justified.

In addition, efficacy after a second dose increases from 55% if the dose is given after less than 6 weeks to 82% if given after 12 weeks, suggesting a long-term benefit from delaying the second dose (albeit because of low numbers, the confidence intervals overlap making the results less firm). Some limitations in the analysis are noted, which may explain the lower effectiveness seen after a shorter duration second dose than for the first dose only period.

Symptomatic COVID-19 Cases > 14 days after second dose	N cases	ChAdOx1 nCoV-19	Control	Vaccine Efficacy (95% CI)
Time between first and second dose SD/SD				
< 6 weeks	111	35/3900 (0.9%)	76/3860 (2.0%)	54.9% (32.7%, 69.7%)
6-8 weeks	64	20/1103 (1.8%)	44/1004 (4.4%)	59.9% (32.1%, 76.4%)*
9-11 weeks	43	11/905 (1.2%)	32/957 (3.3%)	63.7% (28.0%, 81.7%)¥
≥12 weeks	53	8/1293 (0.6%)	45/1356 (3.3%)	82.4% (62.7%, 91.7%)†
Time between first and second dose SD/SD or LD/SD				
< 6 weeks	111	35/3915 (0.9%)	76/3875 (2.0%)	54.9% (32.7%, 69.7%)
6-8 weeks	64	20/1115 (1.8%)	44/1018 (4.3%)	59.7% (31.7%, 76.2%)*
9-11 weeks	66	14/1529 (0.9%)	52/1593 (3.3%)	72.3% (50.0%, 84.6%)¥
≥12 weeks	91	15/2038 (0.7%)	76/2093 (3.6%)	80.7% (66.5%, 88.9%)†

| Symptomatic COVID-19 Cases > 21 days after a single SD dose	N cases	ChAdOx1 nCoV-19	Control	Vaccine Efficacy (95% CI)
Time since first standard dose				
22 to 30 days	37	7/ 9257	30/ 9237	77% (47%, 90%)
31 to 60 days	28	6/ 7147	22/ 7110	73% (33%, 89%)
61 to 90 days	23	4/ 2883	19/ 2974	78% (36%, 93%)
90 to 120 days	10	4/ 1368	6/ 1404	32% (-142%, 81%)
22 to 90 days	**88**	**17**	**71**	**76% (59%, 86%)**

The study also notes a significant reduction in PCR positivity, by up to two thirds after the first dose (although only 50% after the second dose), suggesting that vaccination may also reduce community transmission as a result of fewer infected people.

Whilst these results support the decision to delay the second vaccine for the Oxford AstraZeneca vaccine, the question still remains as to whether it is appropriate to delay the Pfizer vaccine second doses, where no such research has been done. At this stage, we probably now need to await emerging evidence from infections and hospitalisations in the population which has received the Pfizer vaccine. Limited evidence emerging from Israel (link) suggests that efficacy reaches 90% by 21 days, although as Israel then administers the second dose in line with the guidelines from Pfizer, it is not possible to ascertain efficacy beyond that point.

Evidence from Israel (link)

With Israel being further ahead than other countries in terms of its vaccination programme, all eyes are on it to see whether the results from the Pfizer trials are beginning to translate into reduced cases, etc.

A paper published this week provides clear evidence that groups vaccinated first exhibit greater falls in cases and hospitalisations than other groups. As in the UK a new lockdown was introduced in early January, but in contrast to experience here, the falls seen in Israel are broadly in those groups receiving early vaccinations, and so the causal linkage to vaccination is clearer.
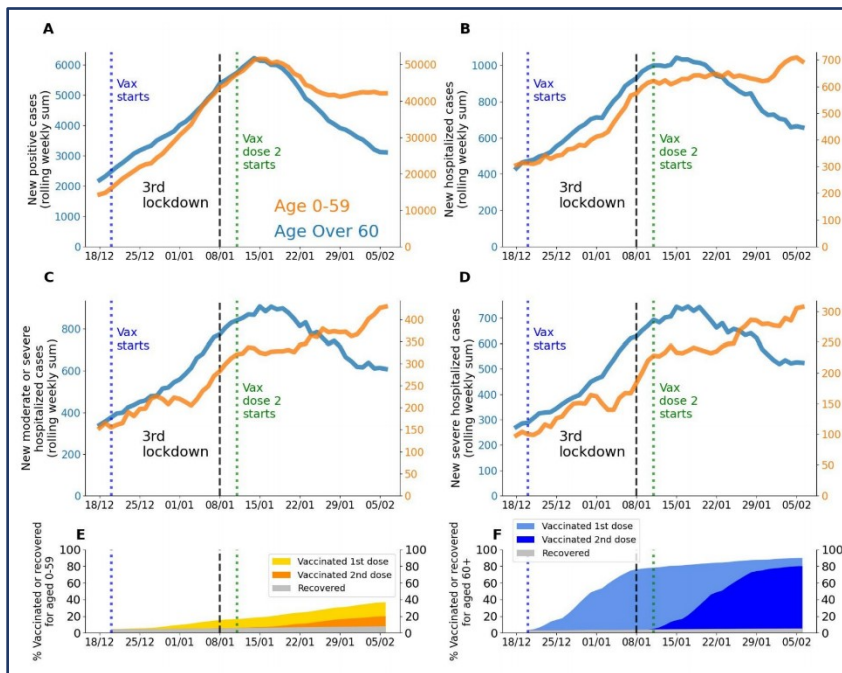
Clinical and Medical News

Revised NHS guidance on shielding based on application of QCovid risk algorithm

On Tuesday the NHS issued revised guidance on shielding, with 3.9 million people advised to stay at home "at all costs" because of the risk of becoming severely ill. This advice was based on the the risk algorithm, QCovid, first published in October 2020.

QCovid is the latest algorithm to be developed from the QResearch database of electronic medical records. The QResearch database contains 45 million patient medical records from 1,800 general practices across the UK. The first algorithm from QResearch, QRISK, was developed to estimate the risk of cardiovascular disease under the leadership of Professor Julia Hippisley-Cox at University of Nottingham. COVID has made all of us acutely aware of the need and importance of incorporating rapidly emerging evidence. Static algorithms are now being replaced by living risk algorithms, expected to be updated regularly.

QCovid was developed under the same leadership, but now at the Nuffield Department of Primary Care Health Sciences, part of the University of Oxford. QCovid links together COVID-19 test results, data from the Hospital Episode Statistics and death registry data, using a cohort approach to consider deaths in different time periods. The underlying research identified the relative importance of different factors such as age, sex, ethnicity and prior medical conditions to the risk of death or hospitalisation from COVID-19.

The table from the underlying research predicted that almost 80% of all COVID-19 related deaths would come from the 6% of the population most at risk.

Table 4 | Sensitivity for covid-19 related death over 97 days in validation cohort (24 January to 30 April 2020) comprising 2 173 056 patients with 1722 covid-19 related deaths at different absolute risk thresholds*				
Top centile	Total patients in each centile	Absolute risk centile cut-off (%)	Total deaths in each absolute risk centile	Cumulative % deaths based on absolute risk (sensitivity†)
1	21730	0.9093	708	41.11
2	21731	0.5182	263	56.39
3	21730	0.3703	136	64.29
4	21731	0.2892	105	70.38
5	21730	0.2369	92	75.73
6	21731	0.1990	58	79.09

Care homes at risk of COVID

In Bulletin 43 (June 2020) we highlighted the crisis that had unfolded in care homes across the UK during the first wave, drawing on high-quality international evidence gathered and published by the International Long-Term Care Policy Network and highlighting the extent of variation in experience across the sector.

A national cross-sectional survey based on data from just over half of all long-term care facilities (LTCF) was published last week in the Lancet with the following main findings:

- 47% of LTCF had no COVID outbreaks during the first wave last year;
- Likelihood of infection in both residents and staff was 19% higher in for-profit LTCF as compared to not-for-profit LTCF;
- Those LTCF that frequently used agency nurses/carers had a higher odds ratio of outbreaks (2.3, 95% CI 1.7-3.2) given the increased likelihood of spreading between LTCF;
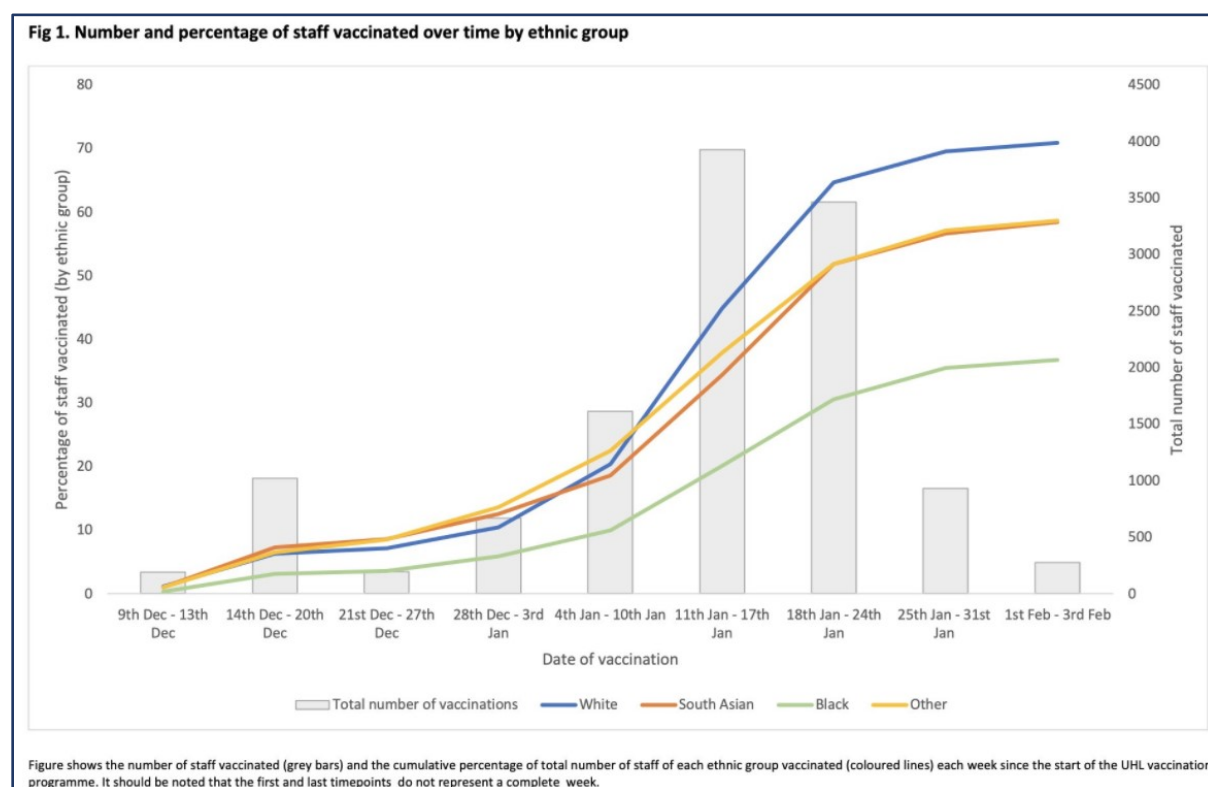
- Risk of infection in LTCF where staff were paid statutory sick pay was 20% lower for residents and 30% lower for staff;
- Lack of zoning in LTCF meant that risk of infection for residents was 30% higher when staff looked after both infected and uninfected residents;
- Lower staff-to-bed ratios were associated with higher rates of infection, with each unit increase in the ratio being associated with an 18% reduction in the risk of infection.

The survey was based on data up to June 2020. Care homes across the sector will have implemented revised operating guidelines since then, with changes summarised by the Care Quality Commission. Further analysis should be forthcoming on the extent to which those changes have affected deaths during the second wave and the heterogeneity between care homes.

Vaccine hesitancy in the UK

By today, 17 million in the UK will have received their first dose of the vaccine as the programme shifts focus to ages 65-69 (priority group 5) and adults with at-risk health conditions (priority group 6). This is an amazing collective achievement. However, there is growing concern over different groups that are apparently hesitating over whether to take the offered vaccines, with some surprising results in the healthcare sector.

A study of almost 20,000 (as at 3 February 2021) healthcare staff identified that doctors had the lowest vaccination rates of all healthcare occupations, 57% vs 65% all occupations. Furthermore, 59% of South Asian and 37% of black healthcare staff had had the vaccine compared with 71% of white staff.

Fig 1. Number and percentage of staff vaccinated over time by ethnic group

Figure shows the number of staff vaccinated (grey bars) and the cumulative percentage of total number of staff of each ethnic group vaccinated (coloured lines) each week since the start of the UHL vaccination programme. It should be noted that the first and last timepoints do not represent a complete week.

Hesitancy is not confined only to the healthcare sector, with the latest data from OpenSAFELY (link) showing a much lower take-up in minority groups. As an example, 93% of whites have been vaccinated in the Over 80 group, whereas the equivalent figure in the black community is just 61%.

RECOVERY Trial Preliminary Results for Tocilizumab (link)

A recent press release by the Recovery Trial suggests that Tocilizumab, an anti-inflammatory treatment currently used to treat rheumatoid arthritis, appears to reduce the risk of death by 14% (95% CI 4% - 23%). The absolute figures are a reduction in mortality from 33% to 29%, suggesting that 4 in every 100 patients offered the treatment would be saved.

The drug appears to be effective at avoiding the need for invasive mechanical ventilation, but did not offer any benefits to those already undergoing ventilation.
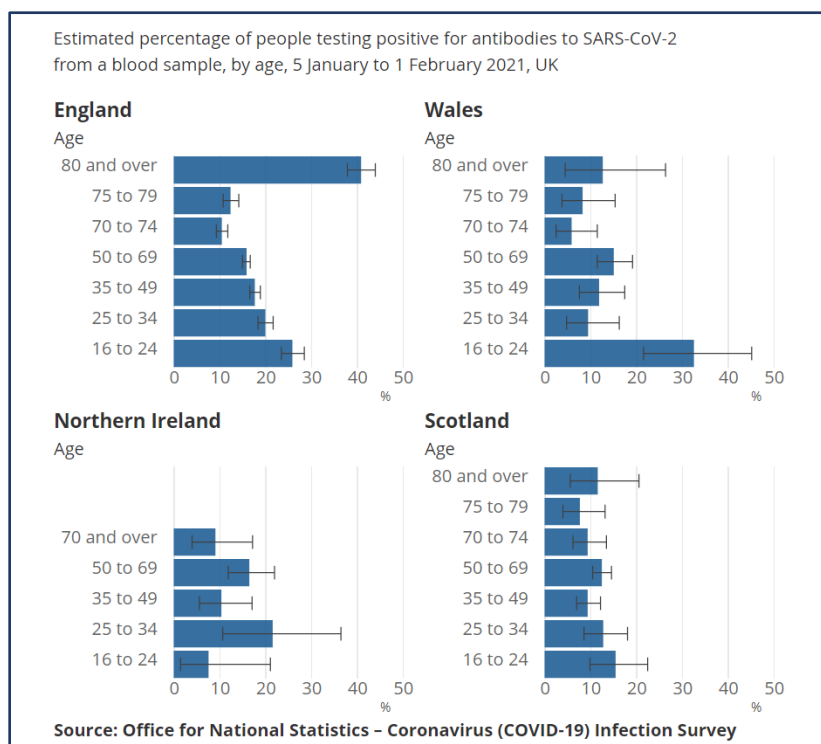
The results have yet to be presented in a paper, but that did not prevent it being mentioned at Monday's No 10 briefing, resulting in a rather amusing moment when the Prime Minister attempted unsuccessfully to pronounce it several times, despite the CMO's coaching (link).

Data

ONS Antibody Study (link)

Now coming out every two weeks, the latest antibody study from ONS shows levels increasing steadily, up from 15% to 19% in England since the last report. Most notable is a very marked jump in the Over 80 year old cohort, where it has increased from 26% to 41%. The overall increase results from a combination of the very high infection levels seen in the last two months, together with vaccinations, particularly in the older age groups (as evidenced by the Over 80 results).

However, we are not yet seeing similar effects in the Over 80s for the other three nations. Note though that this data relates to the period 5th Jan to 1st Feb, so when the immunity period is allowed for, any differences in the early stages of the roll out may materially affect results. As an example, Scotland prioritised care home residents, who are excluded from this community survey.

Estimated percentage of people testing positive for antibodies to SARS-CoV-2 from a blood sample, by age, 5 January to 1 February 2021, UK

Source: Office for National Statistics – Coronavirus (COVID-19) Infection Survey

REACT Infectivity Survey (link)

The latest REACT survey from Imperial College shows a dramatic fall in infection levels since the previous one. Infection levels have fallen by two thirds in under a month, and the halving time is put at around 15 days, with Rt at 0.72.

Table 1. Unweighted and weighted prevalence of swab-positivity across nine rounds of REACT-1.

Round		Tested swabs	Positive swabs	Unweighted prevalence (95% CI)	Weighted prevalence (95% CI)	First sample	Last sample
1		120,620	159	0.13% (0.11%, 0.15%)	0.16% (0.13%, 0.19%)	1/5/2020	1/6/2020
2		159,199	123	0.077% (0.065%, 0.092%)	0.088% (0.068%, 0.11%)	19/6/2020	7/7/2020
3		162,821	54	0.033% (0.025%, 0.043%)	0.040% (0.027%, 0.053%)	24/7/2020	11/8/2020
4		154,325	137	0.089% (0.075%, 0.11%)	0.13% (0.096%, 0.15%)	20/8/2020	8/9/2020
5		174,949	824	0.47% (0.44%, 0.50%)	0.60% (0.55%, 0.71%)	18/9/2020	5/10/2020
6		160,175	1,732	1.08% (1.03%, 1.13%)	1.30% (1.21%, 1.39%)	16/10/2020	2/11/2020
	6a	85,965	863	1.00% (0.04%, 1.07%)	1.28% (1.16%, 1.42%)	16/10/2020	25/10/2020
	6b	74,210	869	1.17% (1.10%, 1.25%)	1.32% (1.20%, 1.45%)	26/10/2020*	2/11/2020
7		168,181	1,299	0.77% (0.73%, 0.82%)	0.94% (0.87%, 1.01%)	13/11/2020	3/12/2020
	7a	105,122	821	0.78% (0.73%, 0.84%)	0.96% (0.87%, 1.05%)	13/11/2020	24/11/2020
	7b	63,059	478	0.76% (0.69%, 0.83%)	0.91% (0.81%, 1.03%)	25/11/2020*	3/12/2020
8		167,642	2,282	1.36% (1.31%, 1.42%)	1.57% (1.49%, 1.66%)	06/01/2021*	22/01/2021
	9a	85,473	378	0.44% (0.40%, 0.49%)	0.51% (0.45%, 0.59%)	04/02/2021	13/02/2021

* Includes small number of samples from previous days

The fall has been most marked in the London region, which is now back "in the pack" with other regions. There have been significant falls in all age groups, particularly older children and young adults, although these remain the ages of highest prevalence.
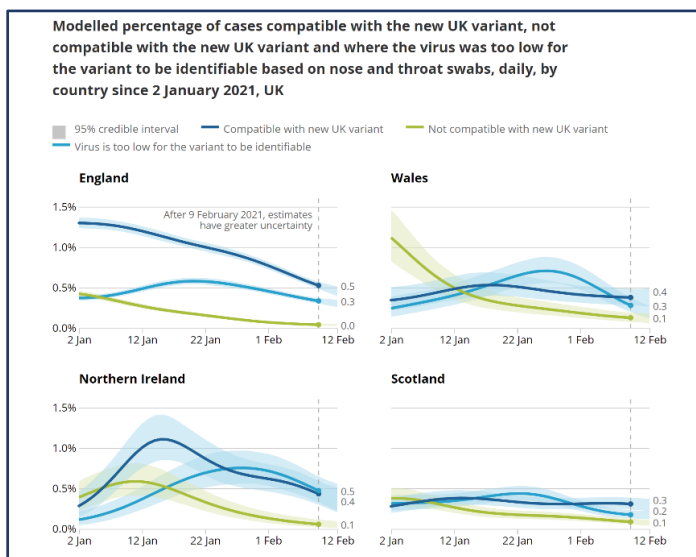
One result of much lower prevalence is that any subdivision of data quickly results in low numbers of positive results, and much wider confidence intervals for any analysis. Nevertheless, there's a concerning, and possibly surprising, feature that the prevalence in health and care workers has increased since January, despite this group being prioritised for vaccination. The findings above regarding ethnicity variances in health and care workers may partly explain this.

ONS Infectivity Survey (link)

The weekly ONS study paints a very similar picture to REACT, with reductions across the UK in the last week of between 18% and 31%.

Of particular interest is the decline of the original variant, having been almost completely usurped by the "Kent variant". Whilst low levels of virus detected in positive samples make it impossible to ascertain which variant is present, in those where it is possible to identify the variant, the number of original versions has dwindled to a very low number.

With some doubt over the effectiveness of the vaccine against the South African variant, which is present (albeit in small numbers) in this country, the speed at which the Kent variant took over here should be a warning that there is still much to be concerned about both regarding the current South African variant and any others that might be vaccine resistant.

Modelled percentage of cases compatible with the new UK variant, not compatible with the new UK variant and where the virus was too low for the variant to be identifiable based on nose and throat swabs, daily, by country since 2 January 2021, UK

NHS England Vaccination Data (link)

At the start of the vaccination process, NHS England noted that the granularity of their data (initially only split by age below / above 80 and by first and second doses) would increase over time. This has proven to be the case, with the latest weekly data including numbers of vaccinations split by dimensions including:

- First or second dose
- 5-year age bands, starting with under-70s and finishing with over-80s
- Region of residence
- Ethnicity
- Care homes
- Health Care Workers
- Clinically Extremely Vulnerable cohort

Population estimates for each of the splits are also provided.

Whilst more information would be useful (for example, numbers on those declining, and splits between the types of vaccines given), it is heartening that more data is becoming available on vaccinations over time.

"R" Estimate

The latest government estimate of R is 0.6 to 0.9 for the UK, slightly down from 0.7 to 0.9 last week. England remains unchanged at 0.7 to 0.9. Regionally, all areas are clearly below 1, with the exception of the North East, where the upper bound is set at 1.0, consistent with the REACT study's uncertainty as to future direction.

In contrast, our own estimate currently puts R for England at around 0.8 and has crept up a little, with signs of a levelling off of admissions. We continue to monitor this closely for signs that a fall in upper age admissions due to vaccination means that our estimate is no longer representative of overall community infection levels.

As such, any sign that it might be rising is of concern, as it might suggest that the increase is greater at those ages yet to be vaccinated.
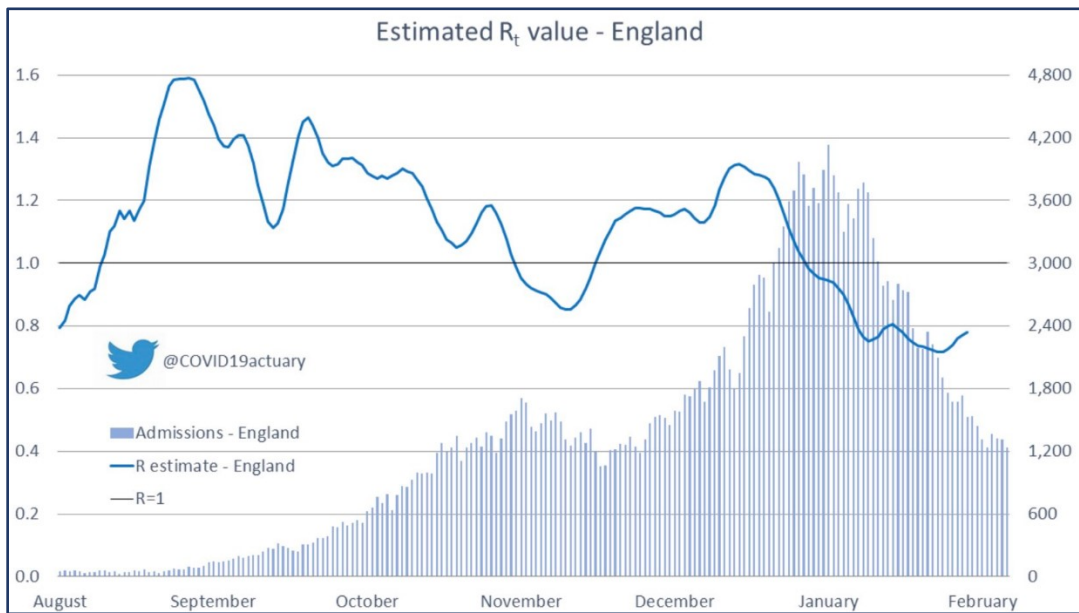
And finally ...

Pancake day?

Spare a thought for Liam Thorp – aged 32 and in good health, he was contacted by his GP to arrange an appointment for a vaccination. He phoned back to query why he'd been assumed to be at high risk, whereupon it turned out that the GP had recorded his height as 6.2cm instead of the correct 6ft 2in – making his BMI an astronomical 28,000! A good case for sense-checking your data! (link)