THE LANCET

Supplementary appendix

This appendix formed part of the original submission. We post it as supplied by the authors.

Supplement to: Read JM, Green CA, Harrison EM, et al. Hospital-acquired SARS-CoV-2 infection in the UK's first COVID-19 pandemic wave. *Lancet* 2021; published online Aug 12. http://dx.doi.org/10.1016/S0140-6736(21)01786-4.

Appendix

Estimating hospital acquired infections among ISARIC WHO CCP-UK study patients

The ISARIC WHO CCP-UK study enrolled patients admitted to UK hospitals diagnosed with COVID-19; it continues to run as a live cohort study. The analysis presented here uses data extracted from the study Redcap database on 02 June 2021. 78,279 patients were enrolled prior to 1 Aug 2020; an additional 1,946 patients were enrolled on or after 1 Aug 2020, but who had symptom onset date before 1 Aug 2020. In the analysis, we included all patients enrolled with valid admission and symptom onset dates recorded, and symptom onset date before 1 Aug 2020: this yielded 72,157 patients.

To impute infection date for each individual, we imputed an incubation period (integer days) for each individual, drawing randomly from a log-normal distribution with a natural logarithmic distribution mean of 1.621 days and standard deviation of 0.418, values previously estimated (Appendix Table 2 of Lauer *et al*. 2020) [1]. Infection date is, therefore, the imputed symptom onset number of days prior to symptom onset date. Hospital acquired infections (HAIs) were defined as individuals for whom their date of admission was prior to their imputed infection date. We generated 500 realisations of the infection date for each patient, determining in each realisation whether the patient acquired infection in hospital.

Weekly proportion of HAIs were calculated stratifying by the week of symptom onset date, and pooled Wilson binomial confidence intervals calculated using imputed HAIs, following the method described by Lott *et al*. 2000 [2].

Where incubation period was assumed to be a constant interval for all individuals (for the conservative 14-day estimate), we calculated exact binomial confidence intervals as no data imputation was necessary.

Estimating England-wide HAI numbers

We compared the ISARIC WHO CCP-UK study enrolments per trust to those provided in a NHS Digital Secondary Uses Service (SUS) data extract (dated 24 Aug 2020, limited to patients admitted prior to 1 Aug 2020). SUS data only contains information from discharged patients, so the comparison used COCIN patients for whom an outcome was recorded, stratified by trust. The total number of COVID-19 patients admitted prior to 1 Aug 2020 for each trust was assumed to be the number recorded in the SUS data; in a few instances where the ISARIC WHO CCP-UK study recorded a greater number of patients than the SUS data, the ISARIC WHO CCP-UK study value was taken as the number of patients. Trust-level HAI pooled Wilson binomial CIs of proportions estimated from the ISARIC WHO CCP-UK study were applied to the total number of admissions within each trust to generate lower and upper estimates of total HAIs.

Estimating proportion of HAIs by care type

We fitted a Poisson regression model to the number of HAI patients for each site, with an offset of the (logged) number of COVID-19 patients for each site and site care type as a fixed effect. This model was fitted to 500 instances of the imputed data (incorporating uncertainty in infection dates). Multiple regression model coefficients and standard errors were pooled according to Rubin's rules [3] for combining multiple model estimates from imputed data, from which we calculated the overall proportion and 95%CIs for each care type.

Sensitivity to incubation period distribution parameters

As parameters describing the incubation period distribution are themselves estimates, we also explored the sensitivity of our findings to the combinations of upper and lower 95% confidence interval estimates of these parameters as reported in Lauer *et al*. 2020 [1]; Table A1. We also estimated weekly estimated proportions using the lower and upper estimates for both parameters; Figure A1.

Table A1. Sensitivity of estimated overall proportion of hospital acquired infections to incubation period log-normal distribution parameters. Pooled Wilson 95% binomial confidence intervals are shown in parentheses. Parameter 1 and 2 are the mean and standard deviation of the natural logarithm of the distribution, respectively.

	Proportion HAI (95% confidence interval)		
	Parameter 1		
	1.504 (lower)	1.621 (central)	1.755 (upper)
Parameter 2			
0.271 (lower)	11.8% (11.6 to 12.1)	11.5% (11.3 to 11.7)	11.0% (10.8 to 11.3)
0.418 (central)	11.6% (11.4 to 11.9)	11.3% (11.1 to 11.6)	10.9% (10.7 to 11.1)
0.542 (upper)	11.5% (11.3 to 11.8)	11.2% (11.0 to 11.4)	10.8% (10.5 to 11.0)

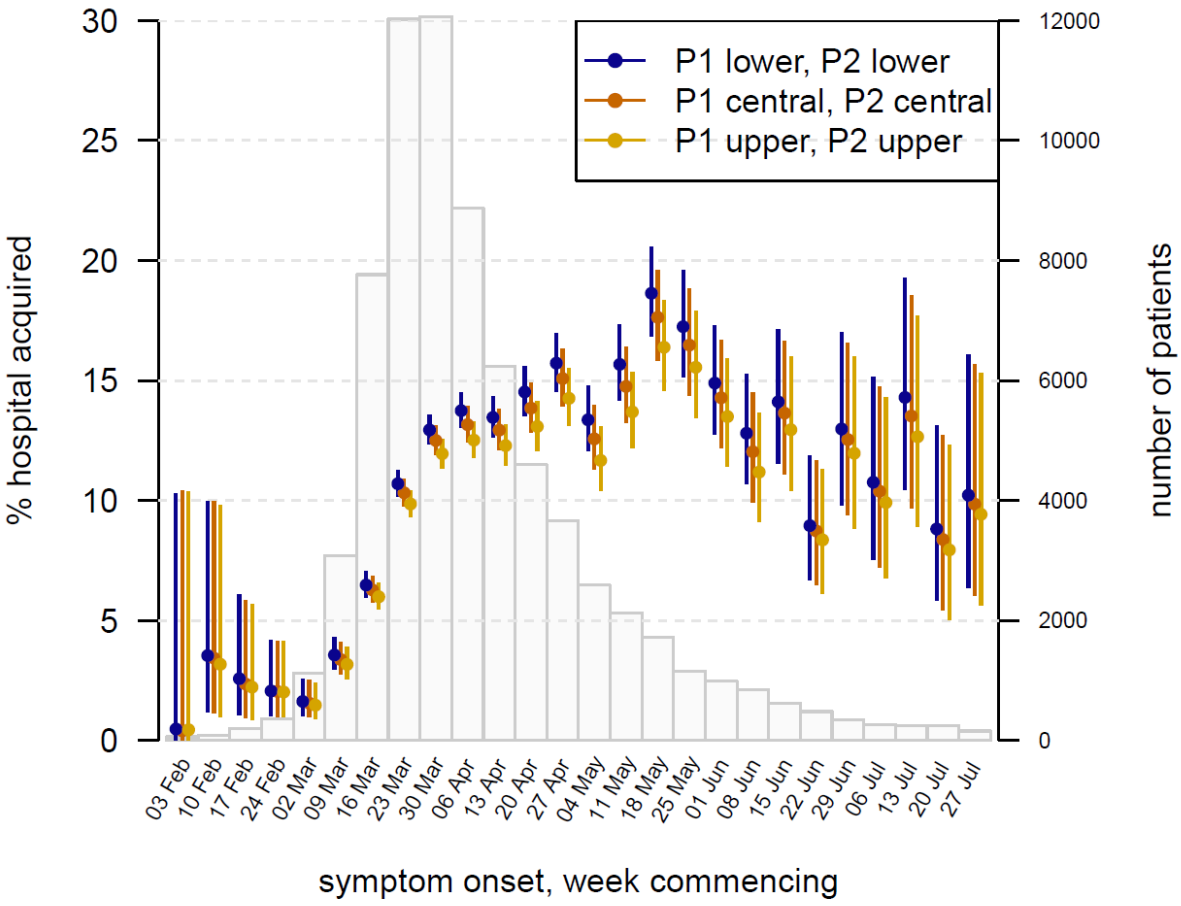

Figure A1. Weekly estimated proportions of HAIs, and their sensitivity to the incubation period distribution parameter estimated. P1 = parameter 1; P2 = parameter 2.

References

1. Lauer SA, Grantz KH, Bi Q, *et al*. The incubation period of coronavirus disease 2019 (COVID-19) from publicly reported confirmed cases: estimation and application. *Annals of Internal Medicine* 2020; M20-0504. doi: 10.7326/M20-0504.
2. Lott A, Reiter JP. Wilson confidence intervals for binomial proportions with multiple imputation for missing data. *The American Statistician* 2020; **74**(2): 109-15.
3. Rubin DB. Multiple imputation for nonresponse in surveys. John Wiley & Sons; 2004.

Supporting statements

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