

Summary of paper

1. Reason for bringing to SAGE (include links to any commissions from SAGE or elsewhere); how does this build on previous SAGE discussions?

To help inform policy for the winter, it is important to understand the contribution of nosocomial infections (i.e. those acquired in hospital) to both hospital cases as well as the epidemic as a whole over the first wave.

This paper provides an estimate of hospitalised COVID-19 cases that could have been due to nosocomial transmission; it makes some large assumptions about such cases, notably during a period when testing for COVID-19 was often limited. Assuming these limitations, the paper estimates how the first wave could have been affected by nosocomial infections.

2. What are the key conclusions of the paper (and confidence in these)?

- Estimated nosocomial infections in the first wave represent approximately just over 1% of total infection numbers at a population level [confidence level – high].
- Out of all COVID-19 infections in hospital patients, we estimate approximately 20-25% may have been nosocomial across the first wave (beginning February to end of July 2020) (Figure 1, 4), including those acquiring infection on a previous admission. This uses two alternative methods applied to different data sources (namely Secondary Usage Service (SUS) hospital episode data linked with COVID-19 test data, and CO-CIN study data). [confidence level – high].
- Nosocomial infections, and onward community cases due to them, may lead to a substantial number of subsequent COVID-19 admissions, representing ~20% of admissions in the tail of the first wave when community prevalence was considerably lower than for most of this wave (Figure 7). [confidence level – high].
- Due to age/frailty of the population the impact of nosocomial infections in terms of morbidity and mortality may be high [confidence level – medium].
- Estimates of the effective reproduction number for SARS-CoV-2 have been projected to be up to 14 in hospitals. Our work suggests that without the implemented infection prevention measures there would have been many more infections and so Wave 1 may have been longer. However, model estimates show that without any nosocomial transmission the duration of the first wave in hospitals may have been shortened, due to fewer COVID-19 admissions in the final quarter of the first wave (Figure 9) [confidence level – medium].

A. Quantifying the total number of nosocomial infections in the first wave

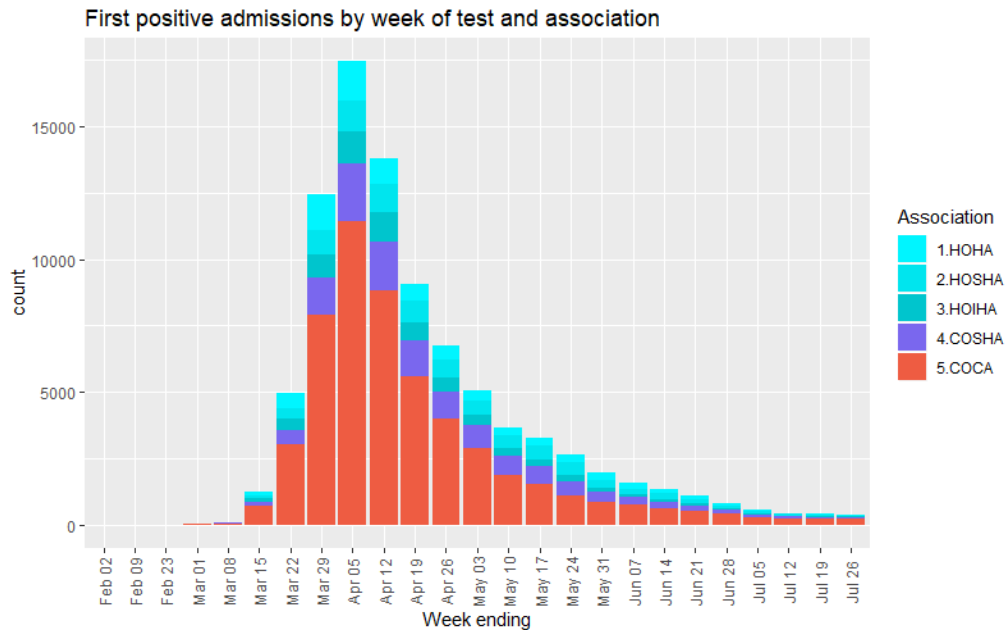
Estimate from descriptive analysis of Secondary Usage System + laboratory confirmed COVID-19 positive test data (beginning Feb to end July 2020)

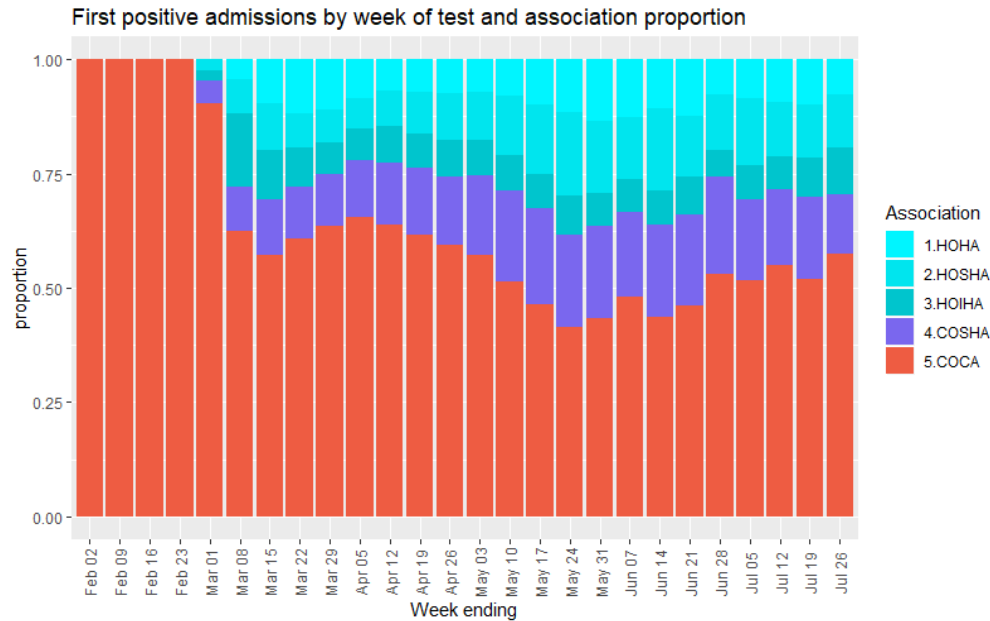
The percentage of hospital cases deemed 'nosocomial' will depend on how expansive the definition (Figure 1).

Figure 1: First positive spells by category for COVID positives by week of first positive test from beginning February 2020 to end of July 2020: counts (upper panel), proportions (lower panel)
Definitions of onset and association given below:

1. **Hospital-Onset Healthcare-Associated (HOHA):** Positive specimen date 15 or more days after hospital admission.
2. **Hospital-Onset Suspected Healthcare-Associated (HOSHA):** Positive specimen date 8-14 days after hospital admission; or specimen date 3-14 days after admission, with discharge from hospital in 14 days before specimen date.
3. **Hospital-Onset Intermediate Healthcare-Associated (HOIHA):** Positive specimen date 3-7 days after hospital admission, with no discharge from hospital in 14 days before specimen date.
4. **Community-Onset Suspected Healthcare-Associated (COSHA):** Positive specimen date up to 14 days before, or within 2 days after, hospital admission, with discharge from hospital in 14 days before specimen date.
5. **Community-Onset Community-Associated (COCA):** Positive specimen date up to 14 days before, or within 2 days after, hospital admission, with no discharge from hospital in 14 days before specimen date.

Note that none of the definitions consider whether the patient was admitted from a care home. Note that definition 4(COSHA) also includes cases where there is a discharge in the 14 days before the specimen date, with no subsequent hospital admission.





Using the most conservative definition (only those cases with a positive specimen date 15 or more days after hospital admission, HOHA) we estimate 8.8% of hospital cases over the first wave were nosocomial (total number = 7906, Table 1). Expanding this definition to all those with a positive specimen 8 or more days after admission increases this to 16.4% (total number 14635). The least conservative estimate, including all positives with a previous hospital discharge within 14 days of the positive specimen, dramatically increases the estimate to 40.5% of hospital infections in the first wave being nosocomial (total number 36152, all but COCA).

Note that estimates are dependent on testing regimen. For example, inadequate testing capacity may lead to overestimation of hospital acquired cases if patients who would test positive earlier in their stay are not tested until after the definition threshold.

Table 1. Number and percentage of patients with hospital acquired infections in the first wave, according to definition

Definition	Number of cases	Percentage of all hospital cases
HOHA (= +ve specimen ≥ 15 d after admission)	7906	8.8
HOHA + positive specimen 8+d after admission	14635	16.4
HOHA + HOSHA	16349	18.3

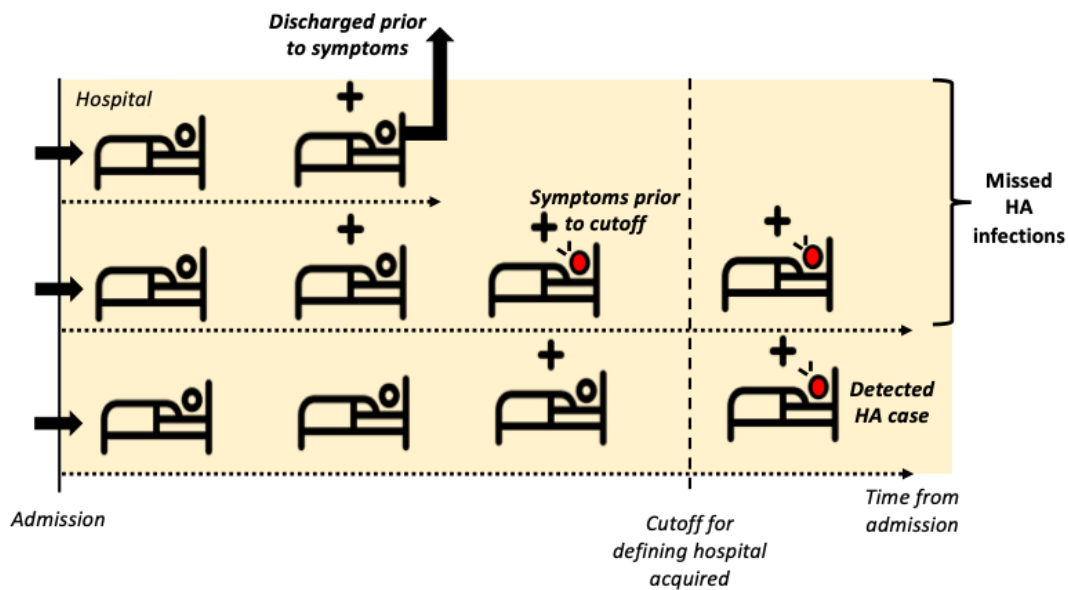
HOHA +HOSHA + HOIHA	23104	25.9
HOHA + HOSHA + HOIHA + COSHA	36152	40.5

Estimate from modelling of CO-CIN study data (to end July 2020)

CO-CIN is an enrolment-based study capturing symptom onset data, thus allowing case ascertainment according to symptom onset rather than being reliant on testing data. Using CO-CIN study data, the number of nosocomial cases in acute English Trusts for the first wave (using >8 days from admission to symptom onset as the definition of nosocomial) is approximately 4,150 (Figure 3, step 2, up to 31st July 2020). However, the CO-CIN study enrolled only approximately two thirds of known hospitalised COVID-19 cases in acute English Trusts. Adjusting for enrolment (by comparison with SUS) leads to 6,610 cases in acute English Trusts (Figure 3, step 3).

However, many true nosocomial infections will not be included in this number because either i) symptom onset in hospital occurred prior to the day 8 cut-off (but acquisition actually occurred in hospital) or ii) patients with nosocomial acquisition were discharged prior to symptom onset (Figure 2). Accounting for these two effects leads to a modelled estimate of the total number of ‘missed’ symptomatic nosocomial infections of 19,910 (Figure 3 step, 4).

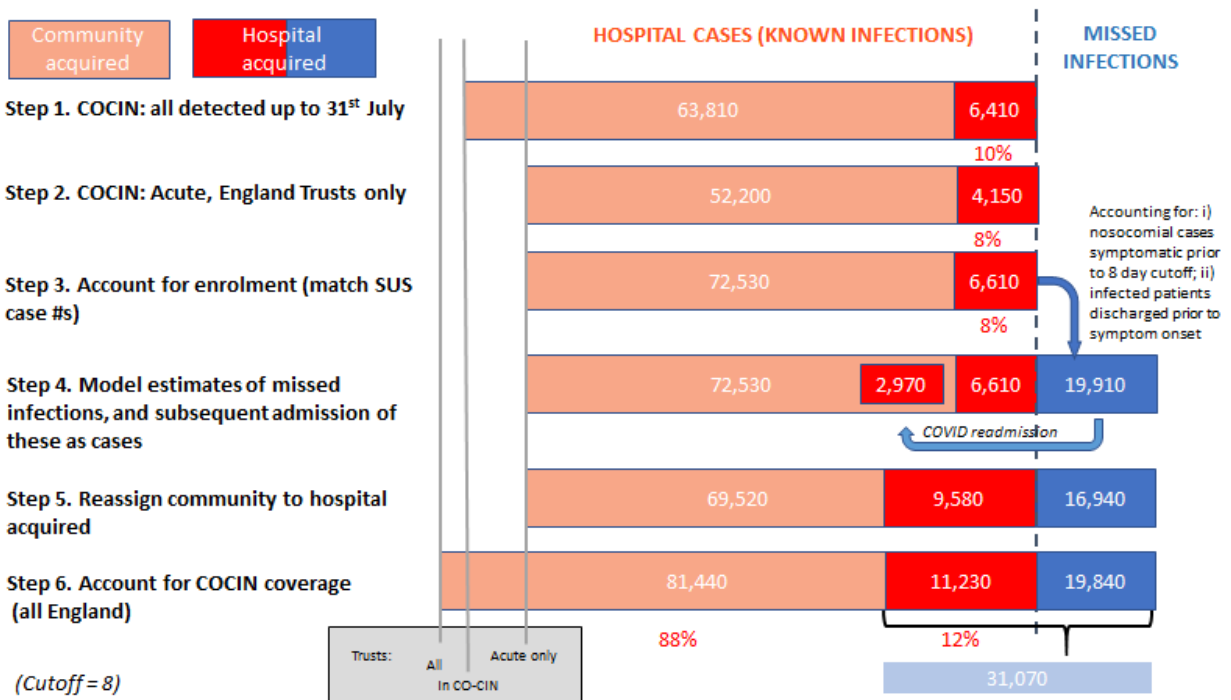
Figure 2: How might hospital acquired (HA) infections be missed? With little routine screening in hospitals, detection of a hospital acquired case in CO-CIN relies on symptom onset. In the schematic a “+” above the bed denotes a hospital acquired infection, and a red patient denotes one with symptoms. A detected case is one with symptom onset after a defined cutoff (e.g. 8 days from admission, bottom row patient). Missed hospital acquired infections are those with a symptom onset after discharge (top row patient) or those with symptom onset prior to the defined cutoff (middle row patient).



Assuming 15% of these missed infections would progress to serious disease, requiring hospitalisation, we estimate 2,970 cases (Figure 3, step 4) would return and should be classified as hospital acquired, not community acquired. This leads to an estimated total of 9,580 hospital acquired cases (Figure 3, step 5).

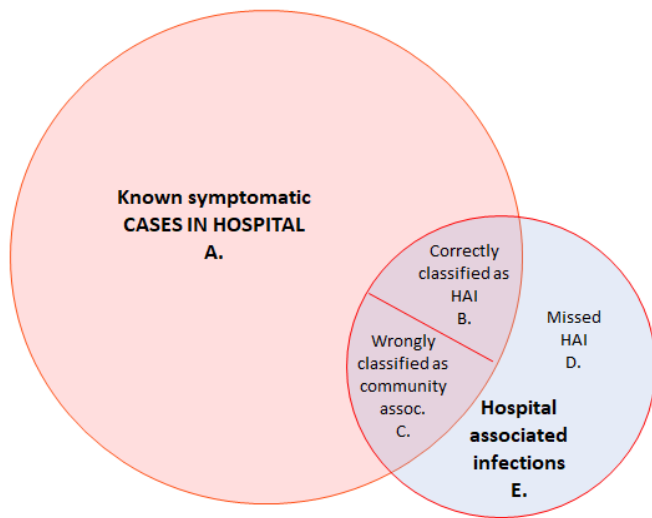
If we then inflate from Acute Trusts to the total burden in England to account for those Trusts not included in CO-CIN (assuming all Trusts reflect the distribution in Acute Trusts), we estimate 11,230 hospital cases were hospital acquired (Figure 3, step 6). Including both identified cases and missed infections gives a total of 31,070 nosocomial infections in England over the first wave.

Figure 3. Stepwise modelling process estimating total nosocomial infections in English Trusts



The proportion of COVID-19 infections that are classified as nosocomial depends on the denominator (i.e. whether the question is ‘how many known cases are nosocomial?’ or ‘how many of all infections in hospital are nosocomial?’), Figure 4.

Figure 4. Representation of estimates of COVID-19 cases and infections in hospitals using CO-CIN data



Total nosocomial COVID-19 infections
= 31,070 = E

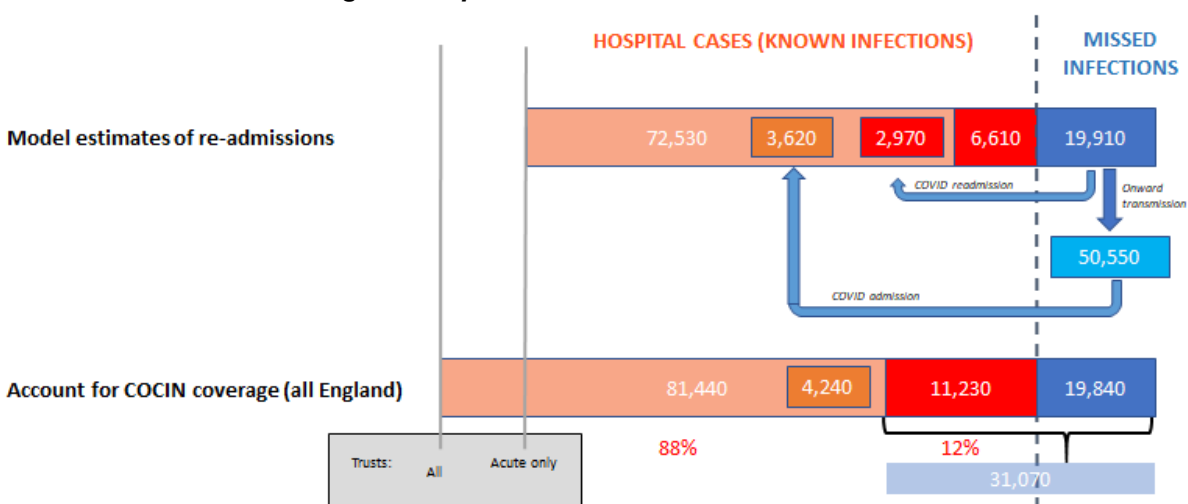
Percentage of known COVID-19 cases in hospital
that are nosocomial = 12.1% = (B + C)/ A

Percentage of all infections in hospital patients
(known and 'missed') where acquisition
occurred in hospital = 27.6% = E / (A + D)

Modelling onward transmission in the community

A number of the nosocomially infected patients will be discharged and lead to onward community transmission. Modelling this onward transmission crudely, with a time-varying r_t , up to the 4th generation of transmission, gives 50,550 onward infections (Figure 5). A proportion of these infections will progress to disease and subsequently be hospitalised (Figure 5). Note that onward transmission in the community from infectious staff is not included.

Figure 5. Schematic of modelling including onward community transmission in estimation of total nosocomial infections in English Hospital Trusts



Adding only those hospital-linked community cases who end up being hospitalised into the estimation of the contribution of nosocomial infections to the first wave gives an estimate of 31.4% of infections in hospital that are nosocomial or due to transmission from a nosocomial case (Figure 6).

Figure 6. Representation of COVID-19 infections in hospitals and onward community transmission

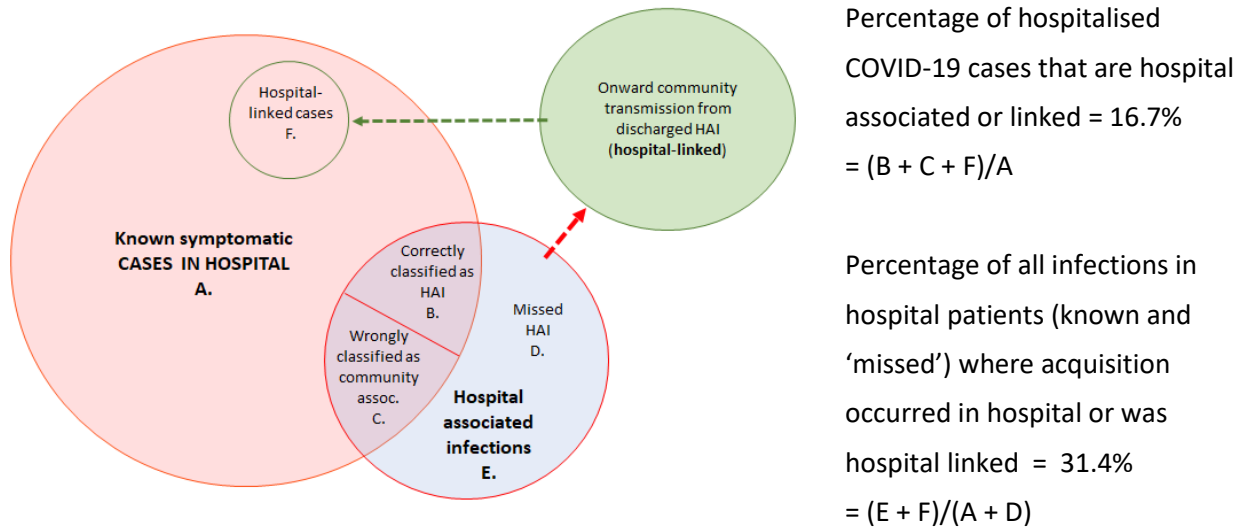
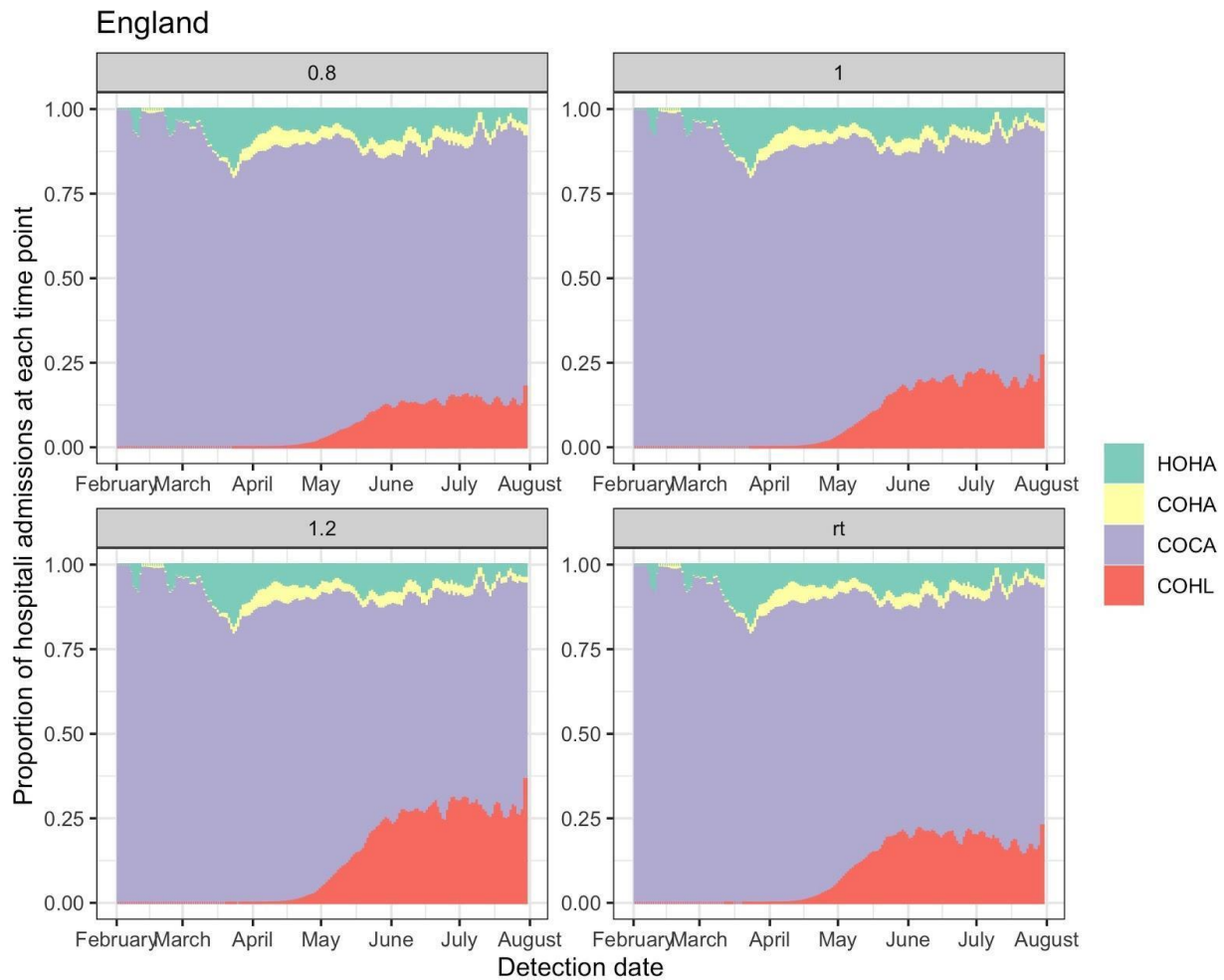


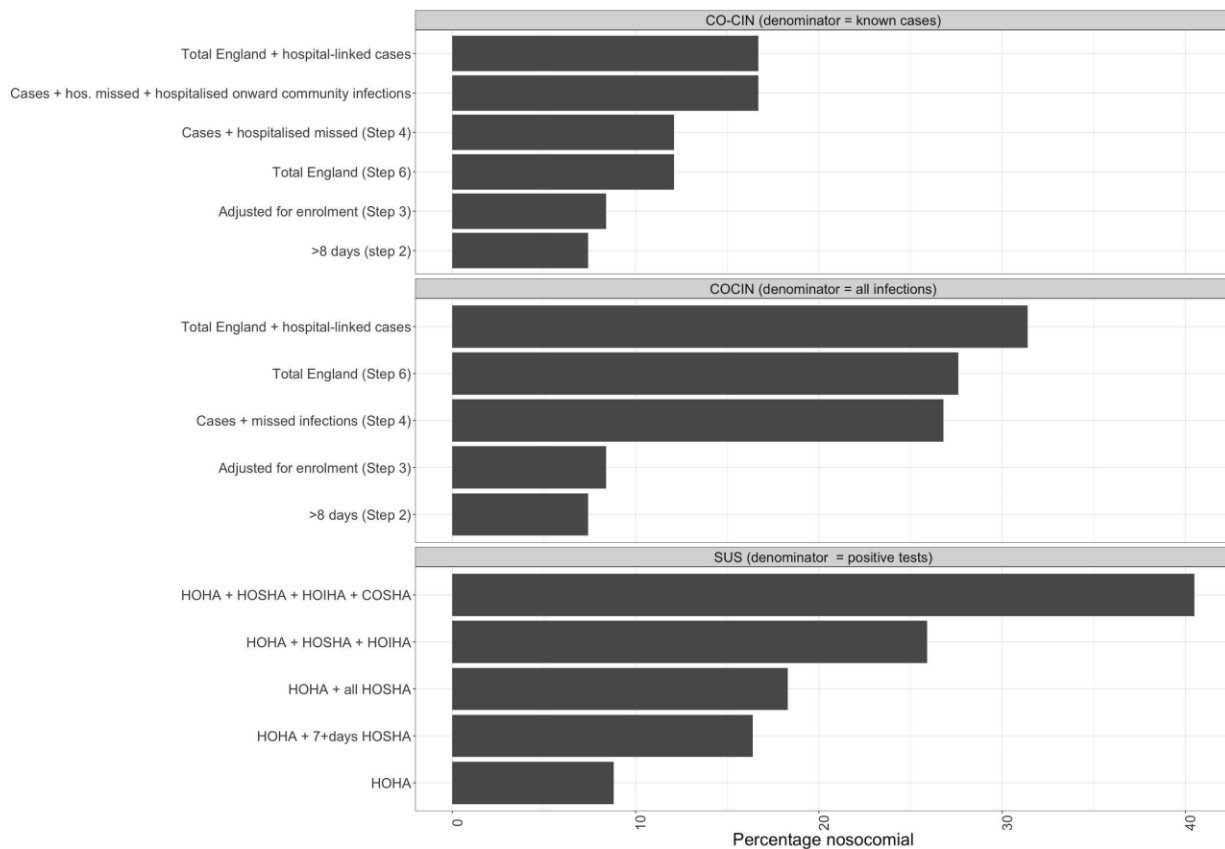
Figure 7 depicts the classification of all hospital COVID-19 cases in English Acute Trusts over the first wave.

Figure 7: Proportion of all hospital admissions in England that are estimated to be hospital onset, hospital acquired (HOHA, green), hospital acquired, community onset, hospital acquired (COHA, yellow), community onset, community acquired (COCA, purple), and community onset hospital linked (onward transmission from discharged patients (red, COHL) at four example R values (constant: 0.8, 1, 1.2 and time varying “rt” (from EpiForecasts) with a mean over this period of 1.3) and a threshold cutoff value of 8 days from admission.



Summarising all estimates from SUS and CO-CIN, Figure 8, exhibits the range of plausible values of percentage of cases or infections in the first wave that were nosocomial.

Figure 8: Percentage of cases or infections that are nosocomial according to the different datasets and definitions



Despite this modelling (which accounts for ‘missed infections’) estimating a slightly greater proportion of hospital acquired infections than previous estimates, we propose this is still indicative of the vast majority of potential hospital infection being averted.

Simple models suggest that, at the peak of the first wave, if transmission in hospitals were to be similar to that in the community (equating to a within-hospital R_0 of approximately 1), approximately 25% of the non-COVID patients in hospital could be transmitted to while in hospital. A crude calculation using NHS data¹ gives approximately 60,000 non-COVID patients in NHS England hospitals at the peak (April 2020). If 25% of these non-COVID patients were transmitted to, this would give a further 15,000 nosocomial SARS-CoV-2 infections at the peak of the first wave (of which we would detect approximately 5,000, which is more than double

¹ Using NHS data (<https://www.england.nhs.uk/statistics/statistical-work-areas/bed-availability-and-occupancy/bed-data-overnight/>) there were an estimated 75,000 patients in NHS England hospitals in April 2020 (taking 120,000 beds and 64% overnight occupancy). At the peak (in April), there were roughly 15,000 beds occupied by COVID-19 patients (<https://coronavirus.data.gov.uk/>) per day, therefore leaving approximately 60,000 non-COVID patients.

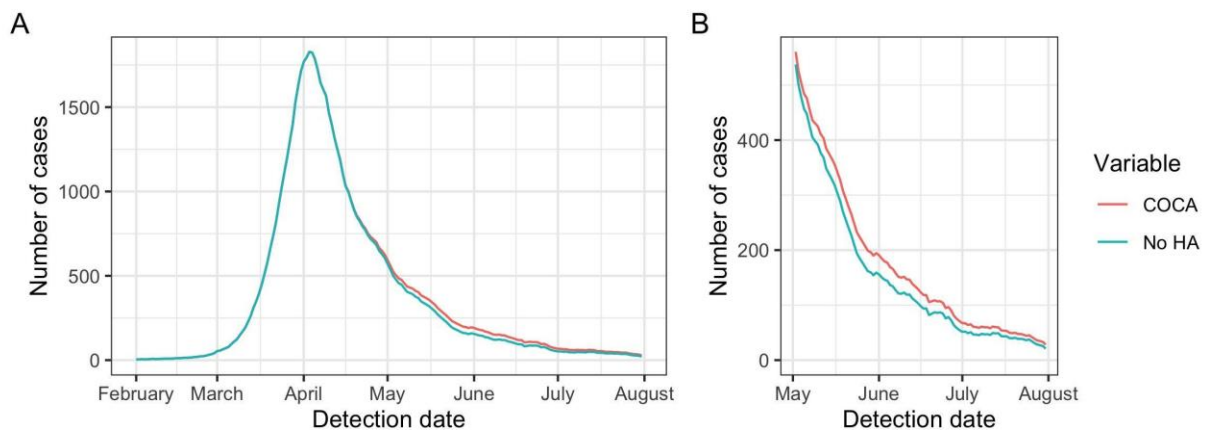
estimates of detected nosocomial cases at the peak). However, this is likely to be a conservative calculation, as the effective reproduction number for SARS-CoV-2 has been estimated to be up to 14 in hospitals (Temime et al, 2020).

B. Impact of nosocomial infection on total infections in England

Whilst the proportion of hospitalised COVID-19 cases that are linked to hospital transmission is considerable, at the population level, the proportion is relatively small. A simple calculation assuming 5% of infections are hospitalised and of these hospital cases, if 25% are due to nosocomial infection, the complete prevention of nosocomial transmission would have led to approximately 1% impact on the number of infections in the English epidemic overall. However, since hospitalised patients tend to be old and/or frail, the impact in terms of morbidity and mortality would nonetheless be expected to be substantial.

An exploration of the counterfactual (i.e. numbers of hospital admissions of COVID-19 cases in the absence of nosocomial transmission) shows little impact of nosocomial transmission initially, but in the last quarter of the first wave the impact of nosocomial transmission may have been to prolong the epidemic (potentially by several weeks, with an r_t with mean >1), Figure 9.

Figure 9: Total COVID-19 admissions and how they change if hospital admissions due to onward transmission from missed, discharged nosocomial infections (according to an estimated time varying R) are removed from COCA to give the counterfactual (blue, “no HA”). Panel A depicts curves over the study period, while B focuses on the end of the period.



3. What are the key questions to be considered at SAGE?

- What are the implications for the second wave?

Nosocomial transmission may not necessarily play the same role in a second wave. There are a number of ways in which a second wave may be different e.g. potentially greater transmission due to business as usual in hospitals and higher occupancy, and conversely potentially less transmission due to better IPC or residual immunity in staff. In addition, more extensive testing at admission and day 5-7 may impact both assignment and impact of nosocomial cases.

- How can nosocomial transmission and infectious discharges be prevented?

We currently have little evidence to determine the impact of IPC on preventing nosocomial transmission, or on implementation of IPC measures (and how this differs across Trusts).

Onward transmission in the community may lead to a considerable number of future hospitalisations. How can this feedback loop between the hospital and community be broken?

4. Are there any proposed next steps?

- Refinement of presented work, including consideration of asymptomatics.
- There is considerable heterogeneity between Trusts. Analytical work to be undertaken to understand these between-Trust differences, including for example the number of single rooms, measures of success with other HCAI, nurse:bed ratios.
- Model-based evaluation of interventions and testing strategies.
- Consider more realistic modelling of onward cases in the community from discharged patients as well as from infectious HCW (which are not considered here).
- More work is required to estimate to what extent the epidemic in hospitals was, and continues to be, driven by the community and *vice versa*.