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Hospital-onset COVID-19 infection surveillance systems: a systematic review

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SUMMARY

Hospital-onset COVID-19 infections (HOCl) are associated with excess morbidity and mortality in patients and healthcare workers. The aim of this review was to explore and describe the current literature in HOCl surveillance. Medline, EMBASE, the Cochrane Database of Systematic Reviews, the Cochrane Register of Controlled Trials, and MedRxiv were searched up to 30 November 2020 using broad search criteria. Articles of HOCl surveillance systems were included. Data describing HOCl definitions, HOCl incidence, types of HOCl identification surveillance systems, and level of system implementation were extracted. A total of 292 citations were identified. Nine studies on HOCl surveillance were included. Six studies reported on the proportion of HOCl among hospitalized COVID-19 patients, which ranged from 0 to 15.2%. Six studies provided HOCl case definitions. Standardized national definitions provided by the UK and US governments were identified. Four studies included healthcare workers in the surveillance. One study articulated a multimodal strategy of infection prevention and control practices including HOCl surveillance. All identified HOCl surveillance systems were implemented at institutional level, with eight studies focusing on all hospital inpatients and one study focusing on patients in the emergency department. Multiple types of surveillance were identified. Four studies reported automated surveillance, of which one included real-time analysis, and one included genomic data. Overall, the study quality was limited by the observational nature with short follow-up periods. In conclusion, HOCl case definitions and surveillance methods were developed pragmatically. Whilst standardized case definitions and surveillance systems are ideal for integration with existing routine surveillance activities and adoption in different settings, we acknowledged the difficulties in establishing such standards in the short-term.

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Background

Nosocomially acquired coronavirus disease 2019 (COVID-19) reflects a failure in healthcare systems to prevent transmission and acquisition. Hospital-onset COVID-19 infections (HOCl) are

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fuelling the global pandemic and are associated with excess morbidity and mortality in both patients and healthcare workers (HCWs). Hospitals are facing challenges in preventing cross-transmission, particularly in settings with extensive community transmission prior to implementation of stringent social distancing measures [1]. Factors such as continuation of clinical services, surge in intensive care, uncertainty in transmission dynamics, staff-to-staff transmission, and shortages and inadequate use of personal protective equipment (PPE) increased the difficulty in managing SARS-CoV-2 transmission in healthcare facilities. Understanding nosocomial acquisition, outbreaks, and transmission chains in real time are fundamental to ensuring infection-prevention measures are effective in controlling SARS-CoV-2 in healthcare. Tackling HOCl is vital to ensure patient safety, maintain public confidence and protect the health and wellbeing of healthcare professionals [2].

Surveillance systems reduce the incidence of nosocomial infection [3]. National surveillance systems of HOCl have been developed in the UK to support understanding national trends, emerging issues and geographical areas of concern [4,5]. However, they are limited by lack of resolution to clarify the finer details of transmission and acquisition events in a real-time manner to support infection prevention and control (IPC) interventions on the ground. Accurate, real-time recognition of HOCl has the potential to improve patient outcomes, optimize IPC measures, and impact on the trajectory of the pandemic. In addition, surveillance will play a key part in healthcare recovery. To accomplish this, there is a need for standardized definitions to categorize HOCl cases, as well as surveillance systems which can be adopted globally and integrated with existing routine surveillance activities for other healthcare-associated infections (HCAIs). HCAIs are frequently defined as development of disease more than 48 h after admission. However, such a definition is not suitable for COVID-19 considering that the incubation period between infection of SARS-CoV-2 and symptoms onset is up to 14 days with a median of 5 days [6]. At present, multiple definitions of COVID-19 infections within healthcare have been developed pragmatically, along with *ad hoc* approaches to deploy systems for monitoring of HOCl. To inform and enable the development of a standardized yet translatable approach, we aimed to review the current literature in surveillance systems that are in place to identify and monitor HOCl.

Methods

Study eligibility

We conducted a systematic review of published literature to identify and compare existing surveillance frameworks for HOCl implemented in different countries in a range of clinical settings, and highlight any gaps in HOCl reporting. This review protocol was registered on the International Prospective Register of Systematic Reviews (PROSPERO) and is available in full on the PROSPERO website (CRD42021235412). In addition, we also identified the standardized HOCl definitions published by governmental health authorities (grey literature).

Search strategy and information sources

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [7].

A completed PRISMA checklist is included in the Supplementary data. A Patient, Intervention, Comparator, Outcome (PICO) framework was developed to determine key components and develop a search strategy to interrogate relevant electronic resources [8], including Medline, EMBASE, the Cochrane Database of Systematic Reviews, the Cochrane Register of Controlled Trials, and MedRxiv preprint repository for a comprehensive list of articles. The PICO framework comprises: *Population*: any patient of any age in any healthcare setting with any respiratory sample yielding SARS-CoV-2 ≥ 48 h from hospital admission will be included. *Intervention*: all studies of surveillance systems applied to HOCl will be evaluated. *Comparison*: as no gold standard surveillance systems are available for comparison, we compared with routine practice (spontaneous identification). *Outcome*: we will assess outcomes in four ways: (1) HOCl definitions, (2) HOCl incidence, (3) types of HOCl identification surveillance systems, and (4) level of implementation (single site, regional, national, international). The search criteria included any full-text article in English, Chinese, French, Spanish, Portuguese, Italian, German language published since 1st January 2020. A combination of Medical Subject Headings and equivalent terms were used (see Supplementary data). The literature search was performed up to 30th November 2020.

Study selection and data extraction

Abstracts were initially screened against eligibility criteria and duplicates removed. All studies involving HCW surveillance were excluded. Following this, full-text articles were assessed. Abstract screening and full-text article assessment was performed by two independent researchers (M.A., J.R.P.) using a web-based tool for systematic review (Rayyan QCRI) [9]. Data was extracted from eligible studies by two independent researchers (M.A., N.J.Z.).

Quality assessment

Study design-specific critical appraisal tools were used to evaluate the scientific rigour of all included papers. One reviewer (N.Z.) quality appraised the studies using: Effective Public Health Practice Project (EPHPP) tool for interventional or observational study designs [10]; Newcastle–Ottawa scale for cohort studies [11]; Joanna Briggs Institute checklist for case series [12]; Scale for the Assessment of Narrative Review Articles (SANRA) scale for narrative reviews [13]; AMSTAR 2 critical appraisal tool for systematic reviews [14]; and an adapted version of the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist for modelling studies (with questions 1, 6, 8–14 and 19–21 omitted, as these were not relevant to non-economic modelling studies) [15]. In the absence of an appropriate standardized tool for appraisal of descriptive case studies, we documented key factors that were likely to influence study quality [16,17].

Ethics

Not applicable.

Results

The literature search yielded a total of 292 non-duplicate citations. A flow chart of assessed studies is presented in Figure 1. We identified 208 citations from Medline and EMBASE, eight citations from the Cochrane Database of Systematic Reviews, and 76 citations from Medrxiv. 273 citations were excluded at the abstract screening stage; most were excluded because the study did not evaluate HOCl surveillance ($N = 139$). Whilst one publication provided a protocol of an international surveillance system, at the time of review no data were available and hence it was not included [18]. Of the 19 citations that were reviewed at the full-text screening stage (full-texts available for all), nine were included in this review [2,19–26]; the remaining 10 were excluded as they did not address HOCl surveillance. Of the nine studies included in this review, four were from the UK [2,23,25,26], two were from the USA [22,24], and one each were from Hong Kong [20], Korea [21] and Taiwan [19]. All of the studies were from the so-called ‘first wave’ of the pandemic. Surveillance was retrospective in four studies [22,24–26]. The quality of the included studies was appraised using assessment tools for interventional, observational, and case study designs. The quality grading of individual studies is included in the Supplementary data. Overall, the quality of studies was limited by their observational nature with short follow-up periods, and lack of prespecified protocols. Two observational studies [21,22] were deemed to have strong quality considering the aims of reporting incidence of COVID-19 infections. Two prospective surveillance studies [2,23] were deemed to have moderate quality when the comparison of efficacy of case detection was not compared against conventional approaches. One interventional study [20] was deemed to

be of low quality (described escalating infection control responses) due to the absence of definition of outcome(s) of interest and providing pre-/postintervention comparison. The quality of two cohort studies [24,25] was limited due to the lack of a comparable non-COVID cohort.

HOCl definitions

HOCl definitions were provided in six [2,22–26] of the nine included studies. Figure 2 is a schematic of the different definitions used in the studies (full description of the proposed definitions is included in the Supplementary data). One UK study [23] developed HOCl definitions before standardized national government definitions were published, while the other three UK studies [2,25,26] used the national definitions [27]. In addition, we identified national standardized definitions from National Health Service England and National Health Service Improvement (NHSE/I) and Public Health England (PHE) (UK) [28], National Health Service National Service Scotland (NHS NSS) and Public Health Scotland (PHS) (UK) [29], and Centers for Disease Control and Prevention (USA) [30] (Figure 2; Supplementary data).

Table I summarizes the current evidence of surveillance of hospital-onset COVID-19 infection.

HOCl incidence

Seven studies [2,20,22–26] reported a proportion of HOCl cases among all hospitalized confirmed COVID-19 patients which ranged from 0 to 15.2%.

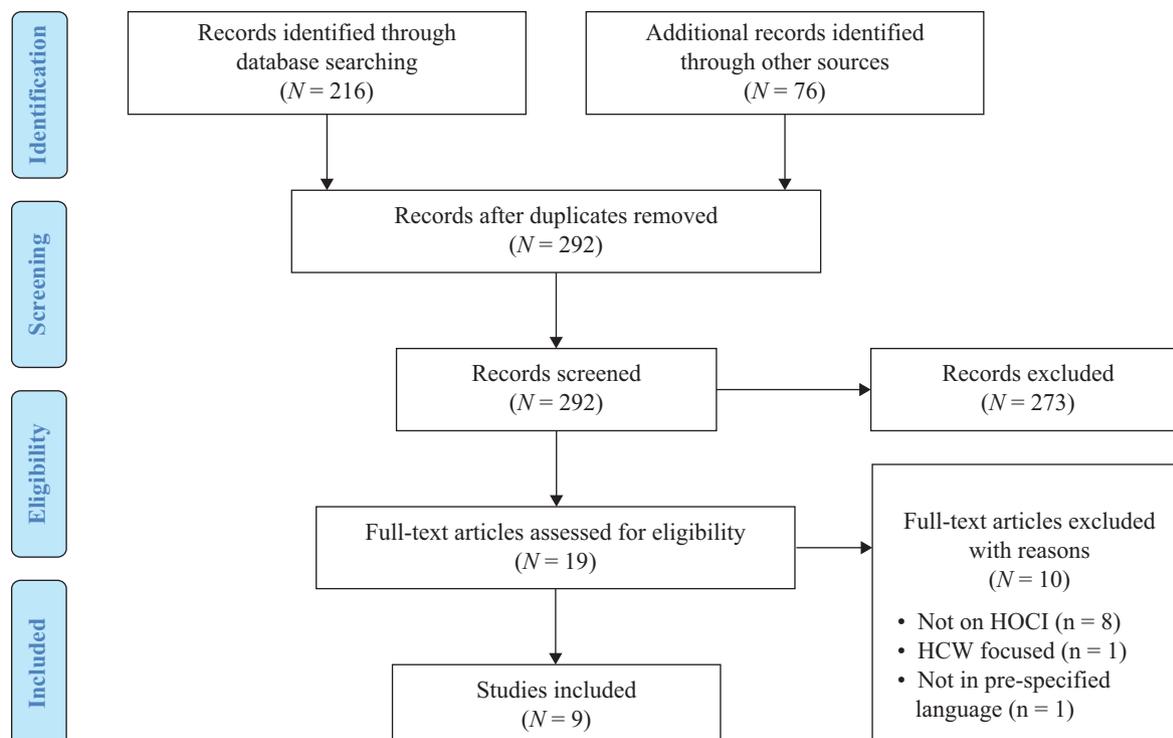


Figure 1. Study flow chart describing the identification, screening, eligibility and inclusion of literature at falls under the scope of this systematic review. HCW, healthcare worker; HOCl, hospital-onset COVID-19 infection.

			Days from admission																					
			1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	
Long	US	2020			Possible healthcare-associated				Likely healthcare-associated															
Rhee	US	2020																						
Meredith	UK	2020																						
Price	UK	2020																						
Taylor	UK	2020																						
Wake	UK	2020																						
CDC	US	2000																						
NHSE/I PHE	UK	2000																						
NHS NSS PHS	UK	2000	Non-hospital-onset																					

Figure 2. Visual representation of definitions of hospital-onset COVID-19 infection. CDC, Centers for Disease Control and Prevention; NHSE/I, National Health Service England and National Health Service Improvement; NHS NSS, National Health Service National Service Scotland; PHE, Public Health England; PHS, Public Health Scotland.

Types of surveillance systems

The majority of studies ($N = 6$) [2,21,22,24–26] did not undertake surveillance as part of a multimodal approach. Of the three studies [19,20,23] that reported adoption of a multimodal strategy, only one study [19] articulated how such strategy had been applied to IPC activities, including screening, hospital zone partition, patient flow re-arrangement, education targeting both staff and patients, and evaluation and feedback.

Only one study [21] focused on a particular patient population (emergency room patient exposure). Four studies [2,20,21,25] included HCWs in the surveillance, and in one study the inclusion of HCWs was unclear [19].

Automated surveillance systems were reported in four studies [2,19,20,23]; two studies [2,23] reported automated utilization of administrative data (e.g., admission dates, ward location, etc.) as well as clinical and laboratory data to support

their surveillance system; in two studies [19,20] it is unclear which data were automatically extracted. One study [2] involved genomic surveillance to investigate HOI, incorporating large-scale sequencing of SARS-CoV-2 isolates from patients and HCWs. Of the four studies with automated surveillance, three [19,20,23] reported real-time analysis of incidence data. One study [2] performed epidemiological and cluster analysis, and another [23] performed network analysis. The recipients of the reports were hospital management, and IPC professionals in two studies [2,23] with front-line clinicians being additional recipients in one of these [2].

Interventions reported to have been implemented to prevent SARS-CoV-2 transmission within the healthcare institutions of each study site were examined, including environmental and hand hygiene practices, use of PPE, and antimicrobial stewardship activities. All sites segregated COVID-19 patients, and four sites [21,22,24,26] screened all admitted patients for SARS-CoV-2 (by reverse transcription

Table 1
Summary of studies in surveillance of hospital-onset COVID-19 infection

Study	Country	Proportion of HOCl cases	Type of surveillance	Automated surveillance	Population	Inclusion of HCWs
[19]	Taiwan	Not reported	Real-time	Yes	General hospital inpatients	Unclear
[20]	China (HK)	0.0% (0/42) nosocomial	Real-time	Yes	General hospital inpatients	Yes
[21]	Korea	Not reported	Retrospective	No	Emergency department inpatients	Yes
[22]	US	12.5% (1/8) possibly healthcare-associated; 0.0% (0/8) definitely healthcare-associated	Retrospective	No	General hospital inpatients	No
[2]	UK	15.2% (57/374) suspected or highly likely to be hospital-acquired	Prospective genomic	Yes	General hospital inpatients	Yes
[23]	UK	9.9% (90/907) hospital-onset; 3.1% (28/907) possible hospital-onset	Real-time	Yes	General hospital inpatients	No
[24]	US	0.3% (2/697) hospital-acquired	Retrospective	No	General hospital inpatients	No
[25]	UK	8.3% (42/505) highly probable nosocomial; 3.0% (15/505) probable nosocomial	Retrospective	No	General hospital inpatients	Yes
[26]	UK	1.2% (8/662) likely hospital-acquired; 5.9% (39/662) highly likely hospital-acquired	Retrospective	No	General hospital population inpatients	No

HCW, healthcare worker; HOCl, hospital-onset COVID-19 infection.

polymerase chain reaction (RT-PCR) or other). It was unclear whether inpatient admission screening was performed in four sites [2,19,23,25].

Two studies [2,23] detected and reported nosocomial clusters, while this was unclear in three studies [19,25,26]. Eight studies [2,19–25] had developed the surveillance system for nosocomial outbreak detection; this was unclear in one study [26]. One study [25] captured the symptoms of the confirmed COVID-19 cases [26].

Level of implementation

All nine included studies reported single-centre, institution-wide implementation of HOCl surveillance [2,19–26].

Discussion

Surveillance of healthcare-associated infections is key to effective infection prevention and control programmes and will form a core element in the recovery from the COVID-19 pandemic. Following an exhaustive systematic review of all available literature, at the time of writing there are only nine published studies that describe surveillance systems for HOCl. We interrogated these studies and identified heterogeneity in (1) definitions of HOCl; (2) reported incidence of HOCl; (3) surveillance methods. The level of HOCl surveillance implementation remained at institutional level.

Definitions

There was wide heterogeneity in HOCl definitions employed by the studies, with most using custom in-house definitions. Although this highlights the difficulties in ascertaining whether hospital-onset COVID-19 cases are truly healthcare-associated,

it does complicate comparisons between institutions or surveillance systems in terms of disease burden.

Of the four UK studies, three utilized national definitions [2,25,26]. Although in line with the eventual definitions provided by the UK government, an additional UK study developed their own definition as their study was undertaken prior to the governmental publication [23].

Incidence

There are many examples of nosocomial COVID-19 outbreaks with variable but often high attack rates up to 60% with high mortality [31]. Unfortunately, as in community-acquired COVID-19, it is the elderly and frail population and those with underlying conditions that bear the highest burden of disease.

Surveillance methods

It is essential to share and disseminate knowledge on surveillance systems to guide hospitals or other healthcare institutions who have not yet developed a surveillance system or who seek to improve an existing one.

Level of implementation

Surveillance should ideally be accompanied with other preventive measures and hospitals should be prepared not only for the large influx of community-acquired COVID-19 cases, but also to protect those patients requiring urgent or semi-urgent care, as well as HCWs [32,33]. At the time when the review was conducted, none of the identified HOCl surveillance systems matched the surveillance definition developed by the Centers for Disease Control and Prevention (CDC) in that the results of the surveillance were not provided by a central network [34]. The UK later introduced a centralized system,

through a research consortium, to investigate HOICs across providers [5].

HCWs are at the interface between the community and the healthcare environment and can thus play an important role in initiating or amplifying nosocomial outbreaks of viral respiratory diseases, including COVID-19. Whole genome sequencing data has been used to demonstrate cross-transmission of SARS-CoV-2 between patients and HCWs [35,36]. Therefore, it is important to consider assessing HCW infection that is epidemiologically associated with patients who develop HOICs. In turn this will rely on robust systems, especially genomics-based surveillance in place for testing symptomatic and asymptomatic staff and collaborating with occupational health will be essential. As COVID-19 vaccination programmes expand globally, these surveillance systems may provide a robust method to assess the impact of HCW vaccination. In turn, vaccine uptake may form part of these surveillance systems.

This study has several limitations. First, local HOIC surveillance has been likely to rely on already established systems. Therefore, some characteristics of surveillance systems may not have been adequately captured by this systematic review of published literature. We acknowledge that many institutes without established surveillance systems are likely to be under-resourced during the pandemic to develop new systems. Second, our search strategy was not designed to focus on outbreak reports, which are likely to have been detected by some form of surveillance system. However, we believe that it is justified to exclude these reports as, presumably, their focus would be more on outbreak management strategies than on the surveillance system *per se*.

In conclusion, HOIC surveillance is going to be an essential component in the pandemic recovery. Proactive, real-time surveillance will provide accurate and rapid data to support healthcare recovery. Establishing robust HOIC surveillance will enable assessment and effective IPC interventions. We acknowledge that this will not be easily applicable to all healthcare settings and in turn baseline standards need to be determined. Whilst the development of evidence-based standards is ideal, the variability of settings and resources coupled with need for urgent action, suggests that in the short term these will rely on expert consensus.

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Author contributions

M.A., A.H., J.R.P. developed the study conception and design. NZ, M.A., J.R.P. undertook data curation. M.A., NZ, J.R.P. performed data analysis and interpretation. M.A., N.Z., A.H., J.R.P. drafted manuscript. N.Z., M.A., S.M., F.B., J.A.O., A.H., J.R.P. conducted critical revision of the manuscript for important intellectual content. N.Z., M.A., J.R.P. provided administrative, technical or material support. A.H. supported funding acquisition. J.R.P. is the guarantor of the study. The corresponding author attests that all listed authors meet the ICMJE criteria for authorship and that no others meeting the criteria have been omitted.

Conflict of interest statement

All other authors report no potential conflicts.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jhin.2021.05.016>.

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